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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: April 1, 2009

SUBJECT: Permethrin: Sixth Revision of the HED Chapter of the Reregistration Eligibility Decision Document (RED).

PC Code: 109701
Decision No.: NA
Petition No.: NA

Risk Assessment Type: Single Chemical/Aggregate
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DP Barcode: D357566
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Regulatory Action: Reregistration Eligibility Decision
Case No.: 2510

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This document is the Health Effects Division's (HED) Revised Chapter of the Reregistration Eligibility Decision (RED) Document for the chemical permethrin (109701). The document is generated as part of the post final phase of the public participation process. The HED chapter reflects the Office of Pesticide Programs (OPP) current policies and guidelines concerning risk assessment. This assessment includes three major updates:

- Revised occupational and residential cancer risks based on the recent submission of a study (MRID 47514801) by the permethrin registrants to estimate dermal penetration of permethrin in humans based on *in vitro* dermal penetration studies with rat and human skin and an *in vivo* dermal absorption study in rats. This submission was reviewed by HED and a dermal absorption factor of 5.7% was selected for permethrin compared to the 15% dermal absorption factor used in the April 2006 permethrin risk assessment.
- The addition of deposition data to assess broadcast, baseboard, and crack and crevice

- Revised short-term and cancer aggregate risk assessments.

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1.0 Executive Summary

This assessment provides information to support the issuance of a risk management decision document known as a Reregistration Eligibility Decision (RED) Document for permethrin. EPA's pesticide reregistration process provides for the review of older pesticides (those initially registered prior to November 1984) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to ensure that they meet current scientific and regulatory standards. The process considers the human health and ecological effects of pesticides and incorporates a reassessment of tolerances (pesticide residue limits in food) to ensure that they meet the safety standard established by the Food Quality Protection Act (FQPA) of 1996.

Permethrin [(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate] is a broad spectrum, non-systemic, synthetic pyrethroid insecticide registered for use on numerous food/feed crops, livestock and livestock housing, modes of transportation, structures, buildings (including food handling establishments), and for residential uses. Permethrin is formulated as an emulsifiable concentrate, a wettable powder (including water soluble bags), a granular, a dust, as well as a number of ready to use formulations, such as aerosol cans, foggers, trigger pump sprayers, ear tags, etc. When end-use product DCIs are developed, RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer's labels.

In addition to the pesticidal uses, there is also a non-FIFRA pharmaceutical use of permethrin as a pediculicide for the treatment of head lice and scabies. The Food and Drug Administration (FDA) approves uses of the pesticidal-containing pharmaceutical products under FFDCA. This analysis is not included in this document but will be incorporated into the Agency's RED as a supplementary assessment.

Permethrin is classified as category III for acute oral and acute dermal toxicity. No acceptable data on acute inhalation toxicity for permethrin technical is available. Permethrin is classified as category III for eye irritation potential and category IV for dermal irritation potential. Permethrin technical is not considered a skin sensitizer based on a weight-of-evidence evaluation of available data.

Permethrin is a type I pyrethroid with the primary target organ being the nervous system. The neurotoxic effects are consistently characterized by tremors, hyperactivity, and altered FOB observations. Following oral administration, permethrin is rapidly absorbed, metabolized, and excreted in urine and feces. Developmental and reproductive toxicity studies demonstrated that there is no evidence (qualitative or quantitative) for increased susceptibility of infants and children, and there is no evidence that permethrin induces any endocrine disruption. There is, however, a concern for developmental neurotoxicity based on evidence of neurotoxicity and increased incidence of microscopic lesions associated with neurotoxic effects at high doses in a subchronic neurotoxicity study. A developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects. Although a DNT has been required, a dose-analysis with the existing reliable toxicity data for permethrin

provided the HED with the confidence that the risk assessment conducted with no additional factor will provide reasonable certainty of no harm to the safety of infants and children. A database uncertainty factor (UF_{DB}) is not required for acute and chronic dietary risk assessments or for residential (non-dietary) exposure scenarios. In addition, the permethrin risk assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA SF be reduced to 1x.

An acute dietary endpoint for the general U.S. population including infants and children was selected from an acute neurotoxicity study in rats, based on observations of clinical signs (i.e., aggression, abnormal and or decreased movement) and increased body temperature. No appropriate endpoint attributable to a single dose was identified for the females 13-50 years of age. Chronic dietary, short-term incidental oral, intermediate-term incidental oral endpoints were also selected from the acute neurotoxicity study in rats and are based on observations of clinical signs (i.e., aggression, abnormal and or decreased movement) and increased body temperature. Short-, intermediate-, and long-term dermal endpoints were selected from a 21-day dermal toxicity study in rats, and short-, intermediate-, and long-term inhalation endpoints were selected from a 15-day inhalation study in rats based on body tremors and hypersensitivity to noise.

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), the CARC classified permethrin as **"Likely to be Carcinogenic to Humans"** by the oral route. This classification was based on evidence of two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in Long-Evans rats, and supportive SAR information. The Committee recommended using a linear low-dose extrapolation approach for the quantification of human cancer risk based on female mouse lung adenoma and/or carcinoma combined tumor rates. The unit risk for permethrin is based on female mouse lung adenoma and/or carcinoma combined tumor rates.

Highly refined acute, chronic, and cancer dietary exposure analyses (food + water) were performed in order to determine the exposure and risks resulting from the registered uses of permethrin. Acute, chronic, and cancer dietary (food and water) risk assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. Permethrin residue estimates used in this assessment include cis- and trans-permethrin calculated as total permethrin along with the percent crop treated (%CT) estimates reported by the Biological and Economic Analysis Division (BEAD). The anticipated residue (AR) estimates are based primarily on the USDA PDP food sampling data. Processing data were also used on a number of crops if available. Acute dietary risk estimates are provided for the general U.S. population and various population subgroups and concludes that for all supported commodities, the acute dietary risk estimates do not exceed HED's level of concern (100% aPAD) at the 99.9^{th} exposure percentile. The most highly exposed population subgroup in the acute dietary exposure analysis is all infants less than 1 year of age (16% aPAD). Chronic dietary risk estimates were also calculated for the U.S. population (total) and various population subgroups. The chronic assessment concludes that for all supported commodities, the chronic

dietary risk estimates do not exceed HED's level of concern for the U.S. population and all population subgroups (all populataions <1% cPAD). The cancer dietary risk estimated for the general U.S. population to permethrin is 1.1×10^{-6} and does not exceed the level of concern. The significant contributors were identified as water (direct and indirect, all sources), spinach, and egg (whole).

HED has also considered a number of exposure scenarios for products that can be used in the residential environment representing different segments of the population including toddlers, youth-aged children, and adults. Short-term noncancer MOEs were calculated for all scenarios. Risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) for all postapplication noncancer exposures (adults, youths, and toddlers).

Cancer risks do not exceed HED's level of concern (1×10^{-6}) on the day of application most scenarios. All postapplication cancer risks were estimated based on an annual frequency of 1 exposure-day per year (assuming exposure on the day of application (i.e., the day of application). It is likely that additional events could occur, but data linking postapplication activities and permethrin use patterns are not available. To address this issue, HED calculated the number of daily exposures that can occur and still do not exceed HED's risk level of concern of 1×10^{-6} and determined that from 2 exposure-days per year to 365 exposure-days per year could occur depending upon the scenario.

HED combines risks resulting from different routes of exposures to individuals when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. For permethrin, HED has combined risk values (i.e., MOEs) for different routes of exposures associated with the turf (dermal, hand-to-mouth, object-to-mouth, and soil ingestion), pet scenarios (dermal and hand-to-mouth), and impregnated clothing scenarios (dermal and object-to-mouth). These are typically added together when pesticides are used on turf or on pets because it is logical they can co-occur. All of these combined risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100). Risks were not combined when one or more of the individual risks in a scenario exceeded the level of concern (indoor surfaces - directed spray).

The acute and long-term (noncancer) aggregate risk estimates include the contribution of risk from dietary (food + drinking water) sources only. Acute and chronic risk estimates from exposures to food and water, associated with the use of permethrin do not exceed the HED's level of concern.

For short-term aggregate assessment, preliminary results from the *Residential Exposure Joint Venture (REJV)* survey were used to further refine HED's aggregate assessment. This information is critical because it can be used for comparison to the deterministic inputs used for the HED's aggregate risk assessment and it can be used to characterize the results of the companion probabilistic risk assessment that has recently been submitted for permethrin. Aggregate short-term risk estimates include the contribution of risk from chronic dietary sources (food + water) and short-term residential sources. There are a number of exposure scenarios that could be aggregated. According to the preliminary results of the *REJV* survey, uses on lawns

and on indoor crack and crevice sites account for the most use in the residential marketplace. For this assessment, HED used the *REJV* survey to look at the likelihood of a co-occurrent application scenario. This was examined using a conditional probability approach.

For short-term adult aggregate risk estimates, chronic food and water exposures for the U.S. general population and for females 13-49 years of age were combined with residential handler and postapplication exposures. Short-term aggregate risk estimates do not exceed HED's level of concern (i.e., the MOEs are greater than 100) for the scenarios considered. For short-term toddler aggregate risk estimates, combined residues of permethrin from food, drinking water, and residential exposures do not result in short-term aggregate risks of concern.

For cancer adult aggregate risk estimates, cancer food and water exposures for the U.S. general population were combined with residential handler and postapplication exposures. HED can conclude that combined residues of permethrin from food, drinking water, and other potential residential exposures do not result in cancer risks of concern to population subgroups.

Risk assessments have also been completed for occupational handler scenarios as well as occupational postapplication scenarios since there is potential for exposure to permethrin in occupational scenarios from handling permethrin products during the application process (i.e., mixer/loaders, applicators, flaggers, and mixer/loader/applicators) and a potential for postapplication worker exposure from entering into areas previously treated with permethrin. Short-term noncancer MOEs as well as postapplication cancer risks were calculated for all scenarios.

For most occupational handler scenarios, risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) at some level of risk mitigation. For the most part, cancer risk estimates for occupational handler scenarios do not exceed HED's level of concern for cancer risks with the single layer clothing, gloves, and no respirator level of personal protection.

For all agricultural postapplication exposure scenarios, postapplication occupational risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application – approximately 12 hours following application. Also, all postapplication exposure scenarios for permethrin-impregnated clothing do not exceed HED's level of concern (i.e., the MOEs are greater than 100).

Postapplication occupational cancer risks were estimated for hired hands (i.e., 10 exposures/year) and commercial/migratory farmworkers (i.e., 30 exposures/year) with the only difference being the annual frequency of exposure days. All of the postapplication cancer risk estimates for both "hired hands" and commercial/migratory farmworkers are less than 1×10^{-5} and most are in the 10^{-6} to 10^{-7} range. Postapplication occupational cancer risks for military personnel and garment workers were also estimated for exposure to permethrin impregnated clothing. All of the postapplication cancer risks for both populations are in the 1×10^{-6} range.

2.0 Ingredient Profile

Permethrin [(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate] is a broad spectrum, non-systemic, synthetic pyrethroid insecticide registered for use on numerous food/feed crops, livestock and livestock housing, modes of transportation, structures, and buildings (including food handling establishments). Producers supporting the use of permethrin on crops and livestock include FMC Corporation, Syngenta Crop Protection, Inc., and Amvac Chemical Corporation under the trade names Astro®, Pounce® and Ambush®. Permethrin formulations registered by these companies for use on food/feed crops and livestock include emulsifiable concentrates (ECs), wettable powders (WPs), dusts (D), and a granular (G) formulation. These products may be applied to crops as broadcast or banded applications, pre- or post-emergence using ground or aerial equipment. Several of these formulations can also be applied directly to livestock and as surface sprays to livestock housing and premises.

Plant Uses: Permethrin formulations registered by the basic producers for use on food/feed crops include emulsifiable concentrates (ECs), wettable powders (WPs), and a granular (G) formulation. These products may be applied to crop plants as broadcast and banded preemergence applications or foliar applications using ground or aerial equipment.

Livestock Uses: For direct application of permethrin to ruminants and their housing, the available residue data support repeated applications to livestock premises at a rate of 0.21 oz ai/1,000 ft^2 with a 14-day retreatment interval (RTI). The data also support direct applications to ruminants at 950 mg ai/animal (2 mg ai/kg body weight) with a 14-day RTI along with the use of self-oilers containing permethrin at 0.17 oz ai/gal. A 1-day preslaughter interval (PSI) should be specified for ruminants.

For direct application of permethrin to swine and their housing, the available residue data support repeated applications to swine housing at a rate of 0.18 oz ai/1,000 ft^2 with a 14-day RTI. The data also support direct applications to swine at 240 mg ai/animal with a 14-day RTI along with the use of self-oilers containing permethrin at 0.17 oz ai/gal. A 5-day PSI may be specified for swine.

For direct application of permethrin to poultry and their housing, the available residue data support repeated applications to poultry houses at a rate of 0.18 oz ai/1,000 ft^2 with a 14-day RTI. The data also support direct applications to hens at ~20 mg/bird with a 14-day RTI. A 1-day PSI should be specified for poultry.

Non-Agricultural Uses: In addition to agricultural uses, permethrin can be used for non-crop sites such as non-cultivated crop areas, certain recreational, commercial and industrial areas, greenhouses, ornamental areas, animal premises, pet treatment, and wood treatment. Permethrin is used to control many pests including but not limited to mosquitoes, ants, and termites.

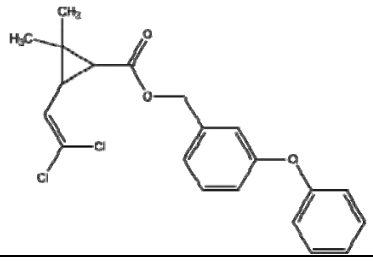
Permethrin can also be used by Public Health Officials and trained personnel in certain districts for mosquito abatement and other mosquito control programs. It can be formulated with piperonyl butoxide and applied by nonthermal ULV by ground or aerial methods.

2.1 Summary of Registered and Proposed Uses

Permethrin is a widely used insecticide in the United States. Permethrin is used in agricultural, commercial, and residential settings. Permethrin is formulated as an emulsifiable concentrate, a wettable powder (including water soluble bags), a granular, a dust, as well as a number of ready to use formulations, such as aerosol cans, foggers, trigger pump sprayers, ear tags, etc. A comprehensive summary of the registered use patterns of permethrin is presented in Appendix A. Conclusions regarding the reregistration eligibility of permethrin uses are based on the use patterns being supported by FMC, Syngenta, and Amvac. When end-use product DCIs are developed, RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer's labels.

2.2 Structure and Nomenclature

Table 2.2. Chemical Structure and Nomenclature of Permethrin

Chemical structure	
Common name	Permethrin
Molecular Formula	$C_{21}H_{20}Cl_2O_3$
Molecular Weight	391.3
IUPAC name	3-phenoxybenzyl (1RS)-*cis-trans*-3-(2,2-dichlorovinyl)-2,2- dimethylcyclopropanecarboxylate
CAS name	(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate
CAS #	52645-53-1
PC Code	109701
Current Food/Feed Site Registration	Numerous food/feed crops, livestock, livestock housing and premises, and food-handling establishments

Permethrin, a racemic mixture of the cis- and trans-isomers, is a synthetic pyrethroid insecticide. The current registered technical active product has a content of cis isomer ranging from 35% to 55%.

2.3 Physical and Chemical Properties

Table 2.3. Physicochemical Properties of Permethrin		
Parameter	Value	Reference
Boiling point	220 °C (0.05 mm Hg; decomposes)	2001 Farm Chemicals Handbook
Melting point	31 °C 35 °C	RD D274107, 7/12/01, S. Mathur 2001 Farm Chemicals Handbook
pH	4.44 at 20 °C	RD D274107, 7/12/01, S. Mathur
Density, bulk density, or specific gravity	1.229 g/cc 1.190-1.272 specific gravity at 20 °C	RD D274107, 7/12/01, S. Mathur 2001 Farm Chemicals Handbook
Water solubility	0.21 mg/L at 20 °C <1 ppm	RD D274107, 7/12/01, S. Mathur 2001 Farm Chemicals Handbook
Solvent solubility	258 mg/kg in methanol at 25 °C >1000 g/kg in hexane at 25 °C Miscible in most organic solvents except ethylene glycol; soluble in acetone, ethanol, ether, and xylene	RD D274107, 7/12/01, S. Mathur 2001 Farm Chemicals Handbook
Vapor pressure	0.07 mPa at 20 °C <10 Torr at 50 °C	RD D274107, 7/12/01, S. Mathur 2001 Farm Chemicals Handbook
Dissociation constant, pK_a	Not applicable because permethrin is neither an acid nor a base.	
Octanol/water partition coefficient	log P_{OW} = 4.19 at 20 °C	RD D274107, 7/12/01, S. Mathur
UV/visible absorption spectrum	At pH 7 λmax 1 = 273 nm, 3.22 log ε λmax 2 = 207 nm, 4.55 log ε At pH <2 λmax 1 = 276 nm, 3.24 log ε λmax 2 = 209 nm, 4.43 log ε At pH >10 λmax 1 = 272 nm, 3.19 log ε λmax 2 = 212 nm, 4.99 log ε	RD D274107, 7/12/01, S. Mathur

Permethrin [(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate] is a synthetic pyrethroid insecticide. Permethrin is a racemic mixture of the cis- and trans- isomers. Permethrin is a colorless crystal to a pale yellow viscous liquid with a melting point of 35°C and a boiling point of 220°C (0.05 mm Hg). Permethrin is soluble in water at less than 1 ppm, and is miscible in most organic solvents except ethylene glycol. Permethrin is soluble in acetone, ethanol, ether, and xylene.

3.0 Metabolism Assessment

3.1 Comparative Metabolic Profile

The qualitative nature of the residue in plants, livestock, and rotational crops is adequately understood based on soybean, cabbage, sweet corn, livestock (oral and dermal), and rotated crop metabolism data. DCVA, MPBA, and 3-PBA are the major residues (>10% TRR). All submitted rat metabolism studies on permethrin have been classified as unacceptable/guideline

based on deficiencies in the level of detail provided which prevent verification/validation of findings (e.g., insufficient data regarding characterization of recovered radioactivity, no dose confirmation, no lot/batch numbers for the test article). However, when considering all rat metabolism studies together, it provides information on absorption, distribution, and excretion which indicated that permethrin is rapidly absorbed, metabolized, and excreted in urine and feces. Most of the urinary metabolites and some fecal metabolites appeared to be hydroxylation products, glucuronide, and sulfate conjugates.

3.2 Nature of the Residue in Foods

MARC had previously concluded that tolerances will be expressed in terms of the parent, *cis*- and *trans*-permethrin only, but that the risk assessment will consider residues of *cis*- and *trans*-DCVA in addition to the parent compound (C. Olinger, 2/1/96). However, based on the weight of all the available evidence, the MARC concluded in a meeting on January 15, 2004 that there are not sufficient grounds to include DCVA in the cancer risk assessment at this time, and that for tolerance expression and risk assessment purposes; parent only is the residue of concern.

3.2.1. Description of Primary Crop Metabolism

The qualitative nature of the residue in plants is adequately understood based on three adequate plant metabolism studies. Plant metabolism studies on cabbage, sweet corn, and soybean indicated that parent, DCVA, and MPBA are major residues (>10% TRR). Multiple applications were made to the sweet corn at a 5X rate. Forage was sampled one day after the third application while the grain was sampled one day after the fifth application. Product labels specify a one-day PHI.

A translocation study was also conducted with soybean plants where foliar and pod applications were made and samples of the plant parts were taken 15 and 45 days post-treatment. Permethrin, *cis*- and *trans*-DCVA, and MPBA were the major metabolites in corn forage and fodder, cabbage, and soybean leaves. Hydroxylated MPBA and MPBAcid were also found in minor amounts.

All three studies demonstrate that the major residue is permethrin when the RAC is harvested soon after treatment (within one day). As the time between treatment and harvest increases, hydrolysis of the ester bond occurs, yielding DCVA and MPBA. Hydroxylation of the alcohol or conversion to the corresponding acid may then occur.

3.2.2 Description of Livestock Metabolism

The qualitative nature of the residue in animals is adequately understood based upon acceptable poultry and ruminant metabolism studies using both oral and dermal dosing of [^{14}C]permethrin.

Oral and dermal metabolism studies have been conducted in ruminants and poultry. All studies were conducted with cyclopropyl- and phenyl-labeled permethrin in separate tests. The ruminant oral study was conducted at an approximately 1x rate, while the poultry oral study was

conducted at a 116x rate. Dermal studies were conducted at a 1x rate per application, but with a much shorter retreatment interval. The poultry studies are considered adequate, but additional characterization of two organosoluble unknowns have been requested for the ruminant studies.

Permethrin was the major residue found in fat, muscle, milk, and eggs for orally and dermally dosed animals. Hydrolysis to DCVA and 3-PBA occurred in liver and kidney in the oral and dermal studies; minimal permethrin was found. MPBA was also found in the muscle of hens treated dermally.

3.2.3 Description of Rotational Crop Metabolism, including identification of major metabolites and specific routes of biotransformation

An adequate confined rotational crop study is available. These data indicate that residues of permethrin in rotational crops are qualitatively similar to the residues resulting from the direct application of permethrin to the primary crops. Based on this study and the label-specified 60-day plant-back interval, limited field rotational crop studies are required.

Residues of *cis* and *trans* permethrin and DCVA were each <0.01 ppm (<LOD) in/on all crop samples tested; therefore, tolerances for residues of permethrin in/on rotated crops are not required, provided all labels specify a 60-day plant-back interval.

3.3 Rat Metabolism

All submitted rat metabolism studies on permethrin were classified unacceptable/guideline based on deficiencies in level of detail provided which prevent verification/validation of findings (e.g., insufficient data regarding characterization of recovered radioactivity, no dose confirmation, no lot/batch numbers for the test article). No data on quantification of metabolites are available. Studies indicate that permethrin is rapidly absorbed, metabolized, and excreted in urine and feces. Most of the urinary metabolites and some fecal metabolites appeared to be hydroxylation products, glucuronide, and sulfate conjugates.

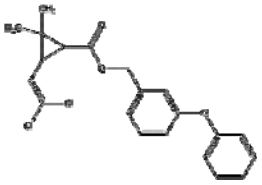
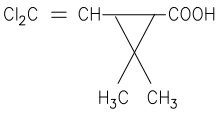
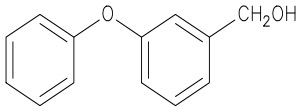
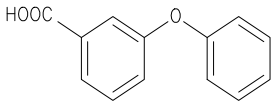
3.4 Environmental Degradation

Permethrin appears to dissipate primarily through binding to the soil, and by soil microbial degradation. It does not degrade through abiotic means (hydrolysis or photolysis).

The moderately high reported half-life for permethrin by aerobic soil metabolism was 37 days. The major degradates reported were $^{14}CO_2$ (34-40% after 6 months), trans-DCVA and 3-(2,2-dichlorovinyl)-2-methylcyclopropane-1,2-dicarboxylic acid, and 3-PBA. In an acceptable aerobic aquatic metabolism study the reported half-life ranged from 38 to 42 days. The half-life in an anaerobic soil metabolism study was 204 days when applied at a rate of 3.2 lb ai/A. The major degradates were trans-DCVA and 3-PBA. The half-life reported for permethrin in an anaerobic aquatic study ranged from 113 days to 175 days which indicates that the degradation is slower as the oxygen levels are reduced.

3.5 Tabular Summary of Metabolites and Degradates

Table 3.5. Tabular Summary of Metabolites and Degradates

Chemical Name	Commodity	Percent TRR		Structure
		Major Residue (>10%TRR)	Minor Residue (<10%TRR)	
Permethrin	Cabbage	permethrin, DCVA, MPBA	3-PBA, 4'OH MPBA, 2'OH MPBA	
	Corn, sweet	permethrin, *trans*-DCVA, MPBA	*cis*-DCVA, 4-OH PBA, 3-PBA	
DCVA	Soybean	permethrin, DCVA, MPBA	3-PBA, 4'OH MPBA, 2'OH MPBA	
	Rotational Crops	none	permethrin, DCVA	
MPBA	Ruminant and Poultry	permethrin, DCVA, OH-DCVA, DCVA-Glucuronide, 3PBA, 4'OH-3-PBA	OH-permethrin, DCVA-lactone	
3-PBA	Water	permethrin, DCVA, 3PBA, 3PBalcohol	----	

Cabbage; 00025919 and 92142094; 1X rate; 0, 30, and 60 days.
Corn, sweet; 43307801 ; 5X rate; 1 day.
Soybean; 00094393 and 92142095; 1X rate; 30, 50, and 78 days and 15 and 45 days.

Goat (oral); 42410001, 43505201, 43962801, and 44417803; 1X MTDB; days of dosing..
Hen (oral); MRID No. 42503201; 116X MTDB; 7 days.
Cows (dermal); 43713303, 43713304, and 44196102; 2 mg/kg body wt./day; 1X rate; 3 days.
Hen (dermal); 43458802; 10.3 mg/kg body wt./day; 1X rate; 3 days.

Rotational Crops; 43174401, 44428201, 44428202, 44428203; Lettuce, Radish, and Spring Wheat, 1X rate; 60 day PBI.

Rat; No guideline studies available.

3.6 Toxicity Profile of Major Metabolites and Degradates

The HED Metabolism Committee has previously determined tolerances will be expressed in terms of the parent, *cis*- and *trans*-permethrin only, but the risk assessment will consider residues of *cis*- and *trans*-DCVA in addition to the parent compound (CBRS No. 16744, DP Barcode 222362, C. Olinger, 2/1/96); however, in a meeting on January 15, 2004, MARC decided that DCVA will not likely cause the same neurotoxic effects as the parent pyrethriods and, based on the weight of all the available evidence, the MARC concluded there are not sufficient grounds to include DCVA in the cancer risk assessment at this time. The following points were considered in drawing this conclusion.

- Based on the amount and nature of the radioactivity appearing in the urine of rats it is likely that the three pyrethroids permethrin, cypermethrin/zeta-cypermethrin, and cyfluthrin are metabolized to a significant extent by cleavage of the ester linkages with the resulting formation of DCVA. In the case of cypermethrin, similar metabolism and pharmacokinetics are observed in mice and dogs. The results of cancer studies in mice for the three pyrethroids were significantly different. Permethrin is classified as a likely human carcinogen with a q* based on lung adenomas and carcinomas plus liver adenomas in mice. Cypermethrin is a possible human carcinogen without a q* based on lung adenomas plus carcinomas also in mice. Cyfluthrin is classified as not likely to be carcinogenic to humans based on no evidence of carcinogenicity rat or mouse studies. Considering that cyfluthrin and permethrin are both metabolized to a significant extent in mammalian systems to DCVA and the different cancer classifications for the two insecticides, the weight of evidence suggests that DCVA per se does not contribute significantly to the carcinogenic effect.

- Looking at the total human exposure to permethrin related residues from all possible sources, DCVA is expected to be a minor contributor compared to the parent. This conclusion is based on the wide array of residential uses of permethrin, the relative levels of parent and DCVA observed in crops and livestock, and the low absolute levels (ppb) of DCVA anticipated in drinking water.

- It is noted that the above decision is consistent with those made for DCVA as a metabolite of the pyrethroid cyfluthrin (see 6/13/02 memo, D283553, PC code 128831) and for the November 1997 assessment to address expiring tolerances for most of the pyrethroids.

- The salmonella reverse mutation assay (Ames assay) conducted with DCVA indicated that the compound was negative in the presence and absence of metabolic activation in all five tester strains.

3.7 Summary of Residues for Tolerance Expression and Risk Assessment

3.7.1 Tabular Summary

Table 3.7.1 Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Parent only (both *cis*- and *trans*-)	Parent only (both *cis*- and *trans*-)
	Rotational Crop	Not Applicable	Not Applicable
Livestock	Ruminant	Parent only (both *cis*- and *trans*-)	Parent only (both *cis*- and *trans*-)
	Poultry	Parent only (both *cis*- and *trans*-)	Parent only (both *cis*- and *trans*-)
Drinking Water		Parent only (both *cis*- and *trans*-)	Not Applicable

3.7.2 Rationale for Inclusion of Metabolites and Degradates

MARC has concluded that for tolerance expression and risk assessment, parent only is the residue of concern; therefore, there is no need for the rationale for inclusion of metabolites and degradates. For the rationale on not including DCVA in the risk assessment, please refer to section 3.6 Toxicity Profile of Major Metabolites and Degradates.

4.0 Hazard Characterization and Assessment

4.1 Hazard and Dose-Response Characterization

4.1.1 Database Summary

4.1.1.1 Studies available and considered

- Acute - Oral rat neurotoxicity
- Subchronic - Oral rat neurotoxicity, 21-day rat dermal toxicity
- Chronic - Oral rat neurotoxicity; 2-year rat and mouse cancer studies; 1-year dog
- Repro/developmental - Rat and rabbit developmental; 3-generation reproductive rat
- Other - mutagenicity screens

4.1.1.2 Mode of action, metabolism, and toxicokinetic data

Permethrin is a Type I pyrethroid (i.e., it lacks a cyano group at the α carbon position of the alcohol moiety). This structural group targets sodium channels and affects neuromuscular signal conduction. Permethrin is absorbed by all routes with an estimated factor of 15%. Following oral administration, permethrin is rapidly absorbed, metabolized, and excreted via urine and feces.

4.1.1.3 Sufficiency of studies and data

Data are sufficient for each exposure scenario, FQPA evaluation, and for important endpoints and dose-response evaluation. A developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects.

4.1.2 Toxicological Effects

Permethrin has a low acute toxicity via the oral, dermal, or inhalation route of exposure. Permethrin is not an eye or skin irritant and not a skin sensitizer. Permethrin is a type I pyrethroid with the primary target organ being the nervous system. The neurotoxic effects are consistently characterized by tremors, hyperactivity, and altered FOB observations. In studies where the liver is affected, it appears to be an adaptive response and is not considered an adverse effect. Following oral administration, permethrin is rapidly absorbed, metabolized, and excreted in urine and feces. Developmental and reproductive toxicity studies demonstrated that there is no evidence (qualitative or quantitative) for increased susceptibility to infants and children following *in utero* and/or pre-/post-natal exposure of permethrin. There is no evidence that permethrin induces any endocrine disruption. However, there is a concern for developmental neurotoxicity based on evidence of neurotoxicity and increased incidence of microscopic lesions associated with neurotoxic effects at high doses in a subchronic neurotoxicity study. A developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects. Although a DNT is required, a dose-analysis with the existing reliable toxicity data for permethrin provided the HED with the confidence that the risk assessment conducted with no additional factor will provide reasonable certainty of no harm to the safety of infants and children. Permethrin is classified as **"Likely to be Carcinogenic to Humans"** by the oral route based on evidence of two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in Long-Evans rats, and supportive SAR information. Mutagenicity studies did not demonstrate any evidence of mutagenic potential for permethrin.

4.1.3 Dose-response

The critical effect (neurotoxicity) for the overall risk assessment is based on the most sensitive species, rats. The oral exposure limits for all durations were based on an acute neurotoxicity study in rats. The effects of permethrin in several species are early in onset and short-term, without indications that incidence or severity of effects would increase based on metabolism studies that permethrin is rapidly absorbed, metabolized, and almost completely eliminated from the body within a short period of time. This finding that permethrin does not bioaccumulate is supported by a close range of NOAEL and LOAEL among acute, subchronic, and chronic toxicity studies associate with clinical signs of neurotoxicity.

The dermal exposure limits for all durations were based on a 21-day rat dermal toxicity study. The selected dose/endpoint is appropriate for the route of exposure. The dermal absorption factor is estimated to be 15%.

The inhalation exposure limits for all durations were based on a rat 15-day inhalation study. The selected dose/endpoint is appropriate for the route of exposure.

Quantification of cancer risk will use a Q_1^*(mg/kg/day)$^{-1}$ of 9.567 x 10^{-3} in human equivalents based on female mouse lung adenoma and/or carcinoma combined tumor rates

The uncertainty factors used in determining RfD exposure limits were 100 (10x for intraspecies variation and 10x for interspecies extrapolation).

4.1.4 FQPA

The database is adequate in terms of endpoint studies and dose response information to characterize any potential for prenatal or postnatal risk for infants and children. There is no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure in the developmental toxicity studies in rats and rabbits and multi-generation reproduction studies in rats. Since there is no developmental or reproductive toxicity observed in the developmental studies in rats and rabbits or reproduction study in rats, the HIARC concluded that there are no concerns or residual uncertainties for pre- and post-natal toxicity.

The HIARC also concluded that there is a concern for developmental neurotoxicity resulting from exposure to permethrin based on the weight of evidence. However, a dose analysis of database that included an evaluation of the acute and subchronic neurotoxicity studies in addition to the 3-generation reproduction study indicated that a database uncertainty factor (UF_{DB}) is not required for acute and chronic dietary risk assessments or for residential (non-dietary) exposure scenarios.

Table 4.1.4.a. Acute Toxicity Profile on Permethrin*

OPPTS Guideline	Study Type	MRID No.	Results	Toxicity Category
870.1100	Acute oral toxicity in Rats	242899	LD_{50} = 3580 mg/kg (M) 2280 mg/kg (F)	III
870.1200	Acute dermal toxicity in Rabbits	242899	LD_{50} >2000 mg/kg	III
870.1300	Acute inhalation toxicity in Rats	Data Gap		ND*
870.2400	Acute eye irritation in Rabbits	242899	Irritation 24-48 hrs. All cleared by 72 hrs.	III
870.2500	Acute dermal irritation in Rabbits	242899	All irritation cleared by 48 hrs	IV
870.2600	Skin sensitization in Guinea Pigs	EPA Memo **	Non-sensitizer***	Not Applicable

* ND = No Data

** EPA Memorandum (June 13, 1995) "Permethrin: Review of a series 81-6 dermal sensitization study (guinea pig maximization test) and a series 85-2 dermal penetration study."

*** Based on a weight of evidence evaluation of other sensitization study data do not indicate that permethrin should

be regulated as a potential sensitizer.

Table 4.1.4.b. Subchronic, Chronic and Other Toxicity Profile on Permethrin		
Guideline No./ StudyType	**MRID Nos. Doses/Classification**	**Results**
870.3200 21-Day dermal toxicity - Rat	41143801,42653301 Ph III Summ: 92142030 0, 50, 150, 500 mg/kg/day Acceptable/guideline	The systemic NOAEL was 500 mg/kg/day (the highest dose tested), the systemic LOAEL was not established. The dermal LOAEL was 50 mg/kg/day based on skin irritation. A dermal NOAEL was not identified.
870.3465, 82-4 15-Day inhalation toxicity - Rat	00096713 0, 0.0061, 0.042, 0.583 mg/L Acceptable/non-guideline	The LOAEL is 0.583 mg/L in male and female rats based on body tremors and hypersensitivity to noise. The NOAEL is 0.042 mg/L.
870.3700a Prenatal developmental - Rat	40943603 0, 15, 50, 150 mg/kg/day Acceptable/Guideline	The maternal toxicity LOAEL is 150 mg/kg/day based on clinical signs of toxicity and decreased body weight gain and food consumption. The maternal toxicity NOAEL is 50 mg/kg/day.the developmental toxicity LOAEL is 150 mg/kg/day based on decrease in fetal body weights and an increase in the incidence rate of short length extra ribs. The developmental toxicity NOAEL is 50 mg/kg/day.
870.3700b Prenatal developmental - Rabbit	92142091,40943602, 92142036 0, 600, 1200, 1800 mg/kg/day Acceptable/guideline	The maternal toxicity LOAEL is estimated to be <600 mg/kg/day based on decreased body weight gain. The maternal toxicity NOAEL is not identified. The developmental toxicity LOAEL is 1200 mg/kg/day based on increased post-implantation loss, greater numbers of early and late resorptions and an equivocal decrease in ossification of the fore- and hind-limbs. The developmental toxicity NOAEL is 600 mg/kg/day.
870.3800 Reproduction and fertility effects - Rat	00102108 00120271 92142092 92142037 0, 500,1000,2500 ppm (0, 25,50,125 mg/kg/day) Acceptable/guideline	The LOAEL for systemic toxicity is 2500 ppm (125 mg/kg/day) based on tremors observed in the F_0 females, and the F_1 and F_2 males and females. The systemic toxicity NOAEL is 1000 ppm (50 mg/kg/day). The reproductive toxicity NOAEL is ≥2500 ppm (125 mg/kg/day) and the reproductive toxicity LOAEL is not identified. The NOAEL for offspring growth and development is ≥2500 ppm (125 mg/kg/day) and the offspring LOAEL is not identified.
870.4300 Chronic toxicity -Rat	92142123 0, 500, 1000, or 2500 ppm 0, 19.4, 36.9, 91.5 mg/kg/day (M) 0, 19.1, 40.2, 104 mg/kg/day (F) Acceptable/guideline	The chronic toxicity LOAEL is 2500 ppm (91.5 mg/kg/day for males and 104 mg/kg/day for females), based on tremors and hypersensitivity. The NOAEL is 500 ppm (36.9 mg/kg/day for males and 19.4 mg/kg/day for females). No tumor
870.4100b Chronic toxicity - dog	00129600 0,5,100,1000 mg/kg/day (capsule) Acceptable/Guideline	The systemic toxicity LOAEL is 1000 mg/kg/day based on clinical neurotoxic signs and decreased body weight gain and food consumption. The NOAEL is 100 mg/kg/day.
870.4200b Carcinogenicity - mouse	00062806, 92142033 0, 3, 71, 286 mg/kg/day (M) 0, 3, 357, 714 mg/kg/day (F) Acceptable/guideline	There were statistically significant increases in liver adenoma at all doses for males and at mid- and high-doses for females with a significant dose-related trend in both sexes.
870.4200b	00102110, 92142032	There was no evidence of significant increase in unusual tumor

Table 4.1.4.b. Subchronic, Chronic and Other Toxicity Profile on Permethrin		
Guideline No./ StudyType	**MRID Nos. Doses/Classification**	**Results**
Carcinogenicity - mouse	0, 26.9, 110.5, 287.2 mg/kg/day (M). 0, 29.8, 124.2, 316.1 mg/kg/day (F) Acceptable/guideline	types. A non-significant increase in lung adenomas in males and in lung adenomas plus carcinomas in females was seen at the highest dose.
870.4200b Carcinogenicity - mouse	45597105 0, 5000 ppm (Females only) (0, 780-807 mg/kg/day) Acceptable/non-guideline	There were significant increases in the incidences of lung bronchioloalveolar adenomas in mice. The increased incidences of basophilic hepatocellular adenoma did not show a relationship to the treatment duration. No progression to carcinoma was observed in the lung or liver.
870.5100 Gene mutation Salmonella typhimurium	41031107 Acceptable/guideline	There were no evidence of increased revertant colonies above control in 5 Salmonella strains up to 5000 µg/plate (solubility limit).
870.5550 Unscheduled DNA	40943604 Acceptable/guideline	There was no evidence of unscheduled DNA synthesis above control up to 10^{-4} M and possibly 10^{-2} M Limits of cytotoxicity).
870.5395 Mouse Bone Marrow Micronucleus	42723302 Acceptable/guideline	There was no evidence that permethrin is clastogenic in the bone marrow cells of mice.
870.6200 Acute Neurotoxicity - Rat	43046301 45657401 Acceptable when considered together	NOAEL = 25 mg/kg/day LOAEL = 75 mg/kg/day based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature.
870.6200 Subchronic neurotoxicity - Rat	00071952 2500,3000,3750,4500, 5000, 7500 ppm Acceptable/nonguideline	The systemic and neuro- toxicity LOAEL is 2500 ppm (125 mg/kg) based on clinical signs of toxicity and decreases in body weight gain and food consumption. The systemic and neuro- toxicity NOAEL was not identified for this preliminary study.
870.6200b Subchronic neurotoxicity -Rat	40766807 0, 100, 200, 400 mg/kg/day Acceptable/nonguideline	The systemic LOAEL is 200 mg/kg/day based on tremors and irritability. The systemic NOAEL is 100 mg/kg/day. The NOAEL is > 400 mg/kg/day with respect to morphological and histological changes.
870.6100b Delayed Neurotox - Hen	00112933 approx. 9000 mg/kg (94.9% a.i.) cis:trans 36:58.9 Acceptable/guideline	Oral administration of permethrin does not produce delayed neuropathy in the hen.
870.6100b Delayed Neurotox - Hen	00097426 0, 2000,4000 mg/kg cis:trans 25:75 Acceptable/guideline	Oral administration of permethrin up to 4000 mg/kg does not produce delayed neuropathy in the hen.

4.2 FQPA Hazard Considerations

4.2.1 Adequacy of the Toxicity Data Base

The HIARC concluded that the toxicology database for permethrin is adequate for FQPA considerations. However, a developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects.

- Acute neurotoxicity study in hens (acceptable).
- Acute and subchronic neurotoxicity studies in rats (acceptable).
- Developmental toxicity studies in rats and rabbits (acceptable).
- Three generation reproduction study in rats (acceptable).
- Developmental neurotoxicity study in rats (data gap)

4.2.2 Evidence of Neurotoxicity

The HIARC concluded that there is a concern for neurotoxicity resulting from exposure to permethrin based on neurotoxic effects characterized by tremors, hyperactivity, and altered FOB observations.

4.2.2.1 Acute Neurotoxicity

Executive Summary: In an acute neurotoxicity study (MRID 43046301), permethrin (95.3% a.i., Lot # PL90-269, cis:trans 50:50) was administered by gavage to Sprague-Dawley rats (4/sex/group) at dose levels of 0, 10, 150, or 300 mg/kg in corn oil. Following administration, the rats were assessed for clinical signs daily. FOB and motor activity assessments were made pre-test and at day 0, (at estimated time of peak effect) and days 7 and 14. After day 14, the rats were sacrificed and the nervous system assessed histopathologically.

Reactions to treatment were noted in the 300 mg/kg treated males and females only. The reactions attributed to treatment included one death (a female), tremors (all animals), staggered gait and gait impairment (8/sex), splayed hindlimbs (2 males, 6 females),decreased forelimb grip strength (21% decrease in males, 13.5% decrease in females) as well as other symptoms occurring in 2 or fewer animals but not in the controls (convulsion, ataxia, exaggerated hindlimb flexion, increased auditory response, uncoordinated landing). No evidence of compound related neurohistopathology was noted in tissues from animals perfused in vivo. **The LOAEL was 300 mg/kg based on tremors and gait impairment. The NOAEL was 150 mg/kg.**

This acute neurotoxicity study was classified unacceptable/guideline because the study was determined to have used inappropriate dose levels and dosing volume of corn oil. A pilot study was reported to indicate clinical signs due to treatment with 50 mg/kg of permethrin when administered as a 10% corn oil solution. The main study was assessed using a 1% corn oil solution and the LOAEL was determined to be 300 mg/kg or 4 times greater. The 1% corn oil solution required dosing the rats with 30 ml/kg for the control and high dose groups and 15 ml/kg for the mid-dose group and 1 ml/kg for the low-dose group. It is considered that dosing

with volumes greater than 10 ml/kg results in confounding the interpretation of the study data because of potential effects on compound absorption.

However, the Toxicology Branch has determined that the requirement for an acute neurotoxicity screen study has been satisfied when taken together with another acute oral neurotoxicity study (MRID 45657401, McDaniel and Moser, Neurotoxicology and Teratology 15:71-83, 1993). An executive summary of this study is as follows.

Executive Summary: In a published literature study (MRID 45657401), permethrin (95%, a.i., cis:trans 50:50) was administered by gavage to Long-Evans rats (8/sex/group) at dose levels of 0, 25, 75, or 150 mg/kg in corn oil. FOB and motor activity were assessed prior to dosing and at 2, 4, 24 and 48 hours after dosing.

At 75 mg/kg, the rats displayed a general pattern of increased excitability and aggressive behavior. Some of the more pronounced responses included abnormal motor movement (3/8, both sexes) decreased grip strength for forelimb (males) and hindlimb (males and females), motor activity (males), and increased body temperature (males). At 150 mg/kg, arousal score (males), righting reflex (males) and approach response score (females) were affected and 7/8 of both sexes had abnormal motor movement and motor activity was further decreased and body temperature was increased >2°C. Slight decreases in body weight (3-4%) were evident. Recovery from the symptoms was within 24 hours. **The LOAEL is 75 mg/kg based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature. The NOAEL is 25 mg/kg.**

The study is classified as **acceptable/nonguideline.** Study is in the form of a literature reprint and was not designed to meet a specific guideline protocol.

4.2.2.2 Acute Delayed Neurotoxicity

Executive Summary: In a delayed neurotoxicity study (MRID 00097426), a group of 10 domestic hens were administered 0, 2000, or 4000 mg/kg of permethrin (Lot No.: ZJ; isomer ratio 25 cis:75 trans) in corn oil by oral gavage. An additional group of 10 birds was given 500 mg tri-*ortho*-cresyl-phosphate (TOCP)/kg as the positive control. All birds were given a single oral dose on study day 0 and observed for 21 days. Birds in the permethrin and negative control groups were redosed on study day 21 and observed for an additional 21 days. Toxicity assessments were limited to clinical observations, assessment of ataxia, body weight measurements, and microscopic evaluation of the spinal cord and sciatic nerve. Acetylcholinesterase and neurotoxic esterase activities were not measured.

No treatment-related clinical signs of toxicity and no effects on body weights or food consumption were observed in birds administered permethrin. Ataxia was not seen in birds treated with the test article and no treatment-related lesions were observed on microscopic examination of the nervous tissues.

Following treatment with TOCP, clinical signs and neurohistopathological lesions indicative of

delayed neuropathy were observed in these birds.

Therefore, under the conditions of this study, oral administration of permethrin up to 4000 mg/kg does not produce delayed neuropathy in the hen.

This study is classified **acceptable/guideline** and does satisfy the requirements for a delayed neurotoxicity study [OPPTS 870.6100 (81-7)] in hens. Although a deficiency was that AChE and NTE activities were not measured, the study is considered sufficient for determining the potential of permethrin to produce delayed neurotoxicity in the hen. This study was conducted prior to initiation of current guidelines.

Executive Summary: In a delayed neurotoxicity study (MRID 00112933), a group of 15 domestic hens were administered 15 mL of permethrin (Lot No.: not given; isomer ratio 36 cis:58.9 trans, 94.9% a.i.) by oral gavage. Based on a specific gravity of 1.2, mean body weight on study day 0, and not correcting for purity of the test article, the dose to the hens was approximately 9000 mg/kg. Additional groups were given water as the negative control (n = 10) or 500 mg TOCP/kg as the positive control. All birds were given a single oral dose on study day 0 and observed for 21 days. Birds in the permethrin and negative control groups were redosed on study day 21 and observed for an additional 21 days. Prior to redose, birds in the permethrin group were protected with 10 mg atropine/kg and 50 mg 2-PAM/kg given by intramuscular injection.

Toxicity assessments were limited to clinical observations, assessment of ataxia, measurements of body weights and food consumption, and microscopic evaluation of the brain, spinal cord, and sciatic nerve. Acetylcholinesterase and neurotoxic esterase activities were not measured.

No treatment-related clinical signs of toxicity and no effects on body weights or food consumption were observed in birds administered permethrin. Ataxia was not seen in birds treated with the test article and no treatment-related lesions were observed on microscopic examination of the nervous tissues.

Following treatment with TOCP, clinical signs and neurohistopathological lesions indicative of delayed neuropathy were observed in these birds.

Therefore, under the conditions of this study, oral administration of permethrin does not produce delayed neuropathy in the hen.

This study is classified **acceptable/guideline** and does satisfy the requirements for a delayed neurotoxicity study [OPPTS 870.6100 (§81-7)] in hens. Although a major deficiency was that AChE and NTE activities were not measured, the study is considered sufficient for determining the potential of permethrin to produce delayed neurotoxicity in the hen. This study was conducted prior to implementation of current guidelines.

4.2.2.3 Subchronic Neurotoxicity

Executive Summary: In a subchronic neurotoxicity study (MRID 42933701), permethrin (95.3% a.i., Lot# PL90-269, cis:trans 50:50) was administered via diet to Sprague-Dawley rats (10/sex/group) at dose levels of 0, 250, 1500, or 2500 ppm (0, 15.49, 91.51, or 150.35 mg/kg/day for males and 0, 18.66, 111.37, or 189.63 mg/kg/day for females, respectively) for 13 weeks. Assessments for clinical signs were made daily and FOB and motor activity assessments were made at pretest, and 4, 8, and 13 weeks of the study. Following sacrifice, the control and high dose group rats were perfused and subjected to histopathological assessment.

Reactions to treatment noted in the 1500 ppm dose group included tremors (in 3 males and 5 females), staggered and/or impaired gait, splayed hindlimbs, increased landing feet splay and abnormal posture and decreased grip strength. Only splayed hindlimb and staggered gait were noted in the FOB battery at 1500 ppm. At 2500 ppm, all of the rats had tremors, staggered gait and splayed hindlimbs. Staggered gait and splayed hindlimbs started later. No effects on motor activity or neurohistopathological lesions were noted. Body weight in the high dose group males was 5% decreased and a corresponding slight decrease in food consumption was also noted for this group. **The LOAEL for neurotoxicity is 1500 ppm (91.51 mg/kg/day in males) based on clinical signs (tremors and staggered gait). The NOAEL is 250 ppm (15.49 mg/kg/day).**

This subchronic neurotoxicity study is classified **acceptable/guideline** and satisfied guideline requirement for a subchronic neurotoxicity study.

Executive Summary: In a preliminary subchronic oral neurotoxicity study (MRID 00071952), groups of 10 male Wistar rats were administered 2500, 3000, 3750, 4500, 5000, or 7500 ppm of permethrin (PP 557) in the diet for 14 days. The isomeric ratio of the test article (Batch No. P48; 90.4% a.i.) was 39.9% cis and 60.1% trans. Based on a food factor of 0.05 for the rat, doses for the treated groups were 125, 150, 187.5, 225, 250, and 375 mg/kg, respectively. Each treated group had a paired control group consisting of litter mates with similar body weights. Toxicity assessments were limited to clinical observations, measurements of body weights and food consumption, and light and electron microscopic evaluation of the sciatic nerve.

At 7500 ppm six rats were found dead on day 1 and the remainder were sacrificed *in extremis* on day 1 or 2. Prior to sacrifice the animals were observed with convulsive tremors and excessive salivation and those animals for which data were available showed marked weight loss and decreased food consumption. In the 5000-ppm group, two rats were found dead on day 1 and six were sacrificed on day 2; convulsive tremors were observed in one animal prior to death.

Slight to moderate whole body tremors were observed initially in all animals in the 2500 and 3000 ppm groups but almost complete remission occurred by day 5. Moderate tremors were seen in most animals of the 3750 and 4500 ppm groups which lessened during the study but were still evident on day 14. Also at 3750 and 4500 ppm hyperactivity and hypersensitivity to noise were observed mainly during the first 7 days. In the two surviving 5000-ppm animals, slight to moderate tremors were observed until day 10.

Mean absolute body weights of the 3000-, 3750-, and 4500-ppm groups were significantly ($p \leq 0.05$ or 0.01) less than their paired control group weights beginning on day 1 and continuing until termination. Body weights of the surviving 5000-ppm animals were also clearly less than the control. Body weight gains by the 2500-, 3000-, 3750-, 4500-, and 5000-ppm groups were 81%, 60%, 61%, 28%, and 22%, respectively, of their control group level during the first week. However, during the second week body weight gains by all treated groups were 98-104% of the control levels with the exception of the 5000-ppm group which was 83% of the controls.

Food consumption for the first week was significantly ($p \leq 0.01$) reduced in all treated groups to 67-84% of their paired control group levels. Consequently, food utilization was increased in a dose-related manner for all treated groups as compared with the control groups.

The number of rats with degenerating nerve fragments in the treated and paired control groups was 5/10 each at 2500 ppm, 8/10 and 2/9, respectively, at 4500 ppm, and 6/10 and 2/10, respectively, at 5000 ppm. The number of fragments per nerve ranged from 1-5 for animals in the control, 2500-, and 4500-ppm groups and for animals in the 5000 ppm group that died or were killed intercurrently. In contrast, the two surviving rats in the 5000 ppm group had 19 and 44 fragments respectively.

Nerves from rats in the 2500- and 5000-ppm groups were also examined by electron microscopy. No treatment-related abnormalities were observed in the 2500-ppm group. At 5000 ppm, the ultrastructural changes observed were similar in animals that died and in the two rats that survived to scheduled termination. In the unmyelinated nerves, 7/7 rats given 5000 ppm had degenerative changes including axonal swelling, disorganization of the neurofilaments, an increase in multivesicular-type and vesicular structures, and vacuolation. Only a minimal increase in vesicular structures was observed in 3/7 paired controls. Mild to marked vacuolation of the Schwann cell cytoplasm was seen in 5/7 rats treated with 5000 ppm and mild vacuolation was seen in 2/7 controls. Also in the Schwann cells, dense bodies occurred in the cytoplasm of 6/7 treated rats vs. 0/7 controls and hypertrophy and increased nuclear chromatin with multiple nucleoli were seen in 5/7 treated and 1/7 control rats. Intercellular vacuolation was observed in 4/7 treated and 1/7 control rats.

Therefore, the systemic and neurotoxicity LOAEL is 2500 ppm (125 mg/kg) based on clinical signs of toxicity and decreases in body weight gain and food consumption. The systemic and neurotoxicity NOAEL was not identified for this preliminary study.

This study is classified **acceptable/nonguideline** and does not satisfy the requirements for a subchronic oral neurotoxicity study [OPPTS 870.6200 (§82-7)] in rats. The study is sufficient for the purposes for which it was intended, as an evaluation of the effects of feeding high concentrations of PP 557 to male rats on body weights, food consumption, clinical signs, and microscopic lesions in the sciatic nerve.

Executive Summary: In a subchronic oral neurotoxicity study (MRID 40766807), Sprague-Dawley rats (10/sex/group) were administered Permethrin (98%, 40:60 cis/trans, Lot No. PL85-216) in acetone at concentrations of 0, 100, 200, or 400 mg/kg/day in the diet for 90 days (main study). Two control groups were included, one was an untreated control group and the other was a vehicle (acetone treated diet) control group. After the 90 days, the rats in the main study were sacrificed by a special procedure designed to allow for fixation of the nervous system *in situ*. The experiment also included a special recovery component that consisted of 10 male and 10 female rats in the 400 mg/kg/day and untreated control groups; these animals were sacrificed 6 weeks after the completion of dosing after being maintained on untreated control diet. Neurological tissues from control and high-dose animals were examined microscopically. Functional observational battery (FOB) and motor activity testing were not performed.

There were no treatment-related deaths. Clinical signs included hyperexcitability, intermittent tremors, and irritability in mid-dose males during the first 3 weeks of treatment and intermittent tremors in mid-dose females during the first week of treatment. High-dose rats exhibited hyperexcitability, intermittent and continuous tremors, twitching, nystagmus (males only) and combativeness (males only) throughout the treatment period. Body weight gain was decreased 6 to 13% in high-dose males from treatment week 11 to post-dosing week 2; and 5 to 9% in high-dose females compared to controls from weeks 3 to 13. No treatment-related food consumption effects were noted. There were no gross lesions associated with treatment and there were no microscopic observations indicative of a neurotoxic effect.

The systemic LOAEL is 200 mg/kg/day based on tremors and irritability. The systemic NOAEL is 100 mg/kg/day. The NOAEL is > 400 mg/kg/day with respect to morphological and histological changes.

This study is classified **acceptable/nonguideline**. The data provide useful information suggesting no morphological or histological effects in rats fed 400 mg/kg/day in the diet for 90 days.

Executive Summary: In a nonguideline repeated dose oral neurotoxicity study (MRIDs 00059066 and 00070627), groups of 10-16 Sprague-Dawley rats/sex/dose were administered 700, 2000 or 6000 ppm of NRDC 143 (Lot No.: 60307, 93.3% a.i.; 45 *cis*:55 *trans*) in the diet for 8 days. Additional groups of 8-10 animals/sex served as controls. Doses for the treated groups were 57, 160 or 454 mg/kg/day, respectively, males and 58, 198 or 453 mg/kg/day, respectively, females. Toxicity assessments were limited to clinical observations, body weights, food consumption and microscopic evaluation of the brain, spinal cord and sciatic nerve. In addition, groups of 16 Sprague-Dawley rats/sex/dose group were treated with three other synthetic pyrethroids: NRDC 149 at 500, 1500 or 3000 ppm (average daily dose levels 42, 72 or 126 mg/kg/day, males and 37, 80 or 115 mg/kg/day, females); S3206 at 1000 ppm (77 mg/kg/day, males or 58 mg/kg/day, females) and S5602 at 3000 ppm (146 mg/kg/day, males or 142 mg/kg/day, females) and were similarly evaluated.

At 6000 ppm permethrin, a total of 3 males and 2 females died during the study; one each on day 5 and the remainder on day 6. In addition, 4 moribund high-dose rats of each sex were sacrificed on day 7 and again on day 8. Clinical signs of toxicity, including severe tremor and muscle twitch, were reported in high-dose males and females beginning on day 1, but the frequency of these signs was not given. Body weight gains by the high-dose males and females (taken on day 7) were -74% and -58% lower than their respective control group levels (mean body weights were about -8.4% below controls, both sexes).

Food consumption was not affected at any dietary concentration. No clinical signs of toxicity or mortalities and no effects on body weight gains occurred in the low- and mid-dose groups. Very slight or slight swelling of the sciatic nerve fibers was seen in 5/5 high-dose males and females, but only very slight swelling was observed in 6/15 control males, 5/13 control females, 1/8 low-dose males and 1/9 mid-dose females. No abnormalities were noted in the brains or spinal cords from any high-dose or control animal. Findings in the brains and spinal cords from the low- and mid-dose groups were not reported. **The LOAEL is 6000 ppm (453 mg/kg/day, females; 454 mg/kg/day, males) based on mortality, clinical signs of toxicity, decreased body weight gain and microscopic lesions in the sciatic nerve. The NOAEL is 2000 ppm (160 mg/kg/day, males; 198 mg/kg/day, females).**

Similar clinical findings (mortality, clinical signs in addition to tremor including hindlimb ataxia, erratic jumping and hypersensitivity) and neuropathology (sciatic nerve swelling, fiber disintegration and/or occasional nodal demyelination) were observed at variable incidence with NRDC 149 (3000 ppm), S3206 (1000 ppm)and S5602 (3000 ppm). Body weight/weight gain decreases were observed in all groups. Effects at 1500 ppm NRDC 149 included slight hypersensitivity, decreased body weight/weight gain and in females, very slight sciatic nerve fiber swelling and disintegration. No findings were reported at 500 ppm NRDC 149. NOAELs were not established for S3206 or S5602 in these studies.

This study is classified **unacceptable/nonguideline (upgradable)** and does not satisfy the requirements for a subchronic oral neurotoxicity study [OPPTS 870.6200 (§82-7)] in rats. These studies were performed as a comparative evaluation of neurobehavioral observations and neuropathology. The study was not conducted to fulfill a guideline requirement and a new study is not required. However, this study may be upgraded to acceptable if the deficiencies listed in the Discussion section of this review can be satisfactorily addressed.

4.2.3 Developmental Toxicity Studies

4.2.3.1 Developmental Toxicity Study in Rats

Executive Summary: In a developmental toxicity study (MRID 40943603), 24 presumed pregnant Wistar rats per group were administered 0, 15, 50, or 150 mg/kg/day of permethrin (93.9% a.i.; 38 cis:62 trans isomers; Reference No. RS 78/E) by gavage on gestation days (GD) 7-16, inclusive. The vehicle was corn oil. On GD 22, all surviving dams were sacrificed and all fetuses were weighed, sexed, and examined for external malformations/variations. All fetuses

were examined for visceral anomalies and the heads cut along the fronto-parietal suture line. All carcasses were processed for skeletal examination.

All animals survived to scheduled termination and no treatment-related abnormalities were noted at gross necropsy. No maternal effects on clinical signs of toxicity, body weight gains, or food consumption were observed in the low- or mid-dose groups. In the high-dose group, clinical signs of toxicity seen between GD 8-19 included tremors in 21/24 rats and head flicking in 6/24 rats. Body weight gains by the high-dose dams were significantly ($p \leq 0.05$ or 0.01) less than that of the controls throughout the dosing interval. For GD 7-10, 10-13, and 13-16, body weight gains were decreased by 88%, 32%, and 18%, respectively, as compared with the controls. Food consumption by the high-dose group was significantly ($p \leq 0.05$ or 0.01) less than that of the controls during the dosing interval.

Therefore, the maternal toxicity LOAEL is 150 mg/kg/day based on clinical signs of toxicity and decreased body weight gain and food consumption. The maternal toxicity NOAEL is 50 mg/kg/day.

No dose- or treatment-related effects were observed on gravid uterine weights, fetal sex ratios, pre- or post-implantation losses, or numbers of corpora lutea/dam or live fetuses/dam. Mean fetal body weight of the high-dose group was 3.2% ($p \leq 0.05$) less than that of the controls. However, mean litter weight of the high-dose group was 3% (n.s.) greater than that of the controls. Therefore, the reduced fetal body weights were considered a questionable toxic response.

No treatment-related external or visceral fetal malformations/variations were noted. The fetal and litter incidence rates of short length extra ribs were significantly ($p \leq 0.05$ or 0.01) increased in the high-dose group as compared with the controls. Short length extra ribs were observed in 31% of the high-dose fetuses vs. 11% of the control fetuses and in 87% of high-dose litters vs. 57% of control litters.

Therefore, the developmental toxicity LOAEL is 150 mg/kg/day based on decrease in fetal body weights and an increase in the incidence rate of short length extra ribs. The developmental toxicity NOAEL is 50 mg/kg/day.

This study is classified as **acceptable/guideline** and does satisfy the requirements for a developmental toxicity study [OPPTS 870.3700 (83-3a)] in rats.

4.2.3.2 Developmental Toxicity Study in Rabbits

Executive Summary: In a developmental toxicity study (MRID 92142091), presumed pregnant Dutch rabbits were administered 0, 600, 1200, or 1800 mg/kg/day of permethrin (92.5% a.i.; 32.3 cis:60.2 trans isomers; Batch No. D108136E) by gavage on gestation days (GD) 6-18, inclusive. The number of does mated for each group was 19, 21, 20, and 23, respectively. The vehicle was 0.5% aqueous Tween 80. On GD 29, all surviving does were sacrificed and all fetuses were weighed and examined for external malformations/variations. Approximately one-

half of the fetuses was processed for skeletal examination and the remaining one-half was fixed and examined for visceral anomalies. Maternal food consumption was not measured.

A total of 0, 5, 5, or 4 does died or were sacrificed moribund in the control, low-, mid-, or high-dose groups, respectively. Due to the lack of a dose-response, the deaths could not be definitively attributed to test article administration. Clinical signs of toxicity included body tremors observed in 5 of the high-dose animals only. Little or no feces or urine was noted on at least one occasion for 2/19 (11%), 4/21 (19%), 6/20 (30%), and 8/23 (35%) animals in the control, low-, mid-, and high-dose groups, respectively.

Absolute body weights were similar between the treated and control groups throughout the study. However, after examining the replotted body weight data, there was a sharp drop in weight for the low, mid, and high dose groups after day 6 and only a slight drop for the control that was noticeable after day 12. Body weight gain by the low-, mid-, and high-dose groups was 21%, 50%, and 9%, respectively, of the control level during GD 0-18 with statistical significance ($p \leq 0.05$) attained for the low- and high-dose groups. During the post-dosing interval, recovery of body weights was noted for the low- and mid-dose groups, but not for the high-dose group.

The maternal toxicity LOAEL is estimated to be <600 mg/kg/day based on decreased body weight gain. The maternal toxicity NOAEL is not identified.

The number of live fetuses and mean litter size was decreased for all dose groups compared to the control group (110(15), 80(13), 69(14), and 72(13) for control, low-, mid-, and high-dose groups, respectively). However, no dose-response was evident or statistical significance noted.

Post-implantation loss was significantly ($p \leq 0.05$) increased in the mid- and high-dose groups to 155% and 248% of the control level. Correspondingly, the number of early and late resorptions were higher in these groups as compared to the control group values (statistical significance was not reported). Mean fetal body weights in the high-dose group were slightly (-9%; n.s.) less than that of the controls and attributed to maternal body weight decreases. No dose-related or statistical differences were observed between the treated and control groups for number of fetuses/litter or mean gravid uterine weights.

No treatment-related external or visceral fetal malformations/variations were noted. In the mid- and high-dose groups, reduced ossification of the fore- and hind-limbs was indicated by slightly (n.s.) greater ossification scores as compared with the controls. Mean scores for the control, low-, mid-, and high-dose groups were 1.92, 1.99, 2.00, and2.25, respectively, for the forelimb and 1.65, 1.56, 1.89, and 1.90, respectively, for the hindlimb.

Therefore, the developmental toxicity LOAEL is 1200 mg/kg/day based on increased post-implantation loss, greater numbers of early and late resorptions and an equivocal decrease in ossification of the fore- and hind-limbs. The developmental toxicity NOAEL is 600 mg/kg/day.

This study is classified as **acceptable/guideline** and does satisfy the guidelines for a developmental toxicity study [OPPTS 870.3700 (83-3b)] in rabbits. It should be noted that this study was conducted prior to implementation of the current guidelines. Because the mid- and high-doses exceeded the limit dose of 1000 mg/kg/day, the study is considered sufficient for determining the developmental toxicity potential of permethrin in the rabbit even though a maternal toxicity NOAEL was not identified.

4.2.4 Reproductive Toxicity Study

Executive Summary: In a three generation reproduction study (MRID 92142092, 120271, 92142037), permethrin, PP557, (purity, 94.0-98.8%; cis:trans 40:60) was administered to groups of 12 male and 24 female Wistar rats in the diet at concentrations of 0, 500, 1000, or 2500 ppm (0, 25, 50, and 125 mg/kg/day, respectively, using a standard conversion factor of 0.05). Two litters were produced by each generation. F_0, F_1, and F_2 parental animals received test or control diet for 12 weeks post weaning and were then paired for mating to produce the A litters. After various rest periods, the F_0, F_1, and F_2 parental animals were remated to produce the B litters. Test diets were administered during mating, gestation and lactation for three successive generations throughout the study. The F_2 parents were mated for a third time, using the same breeding pairs as for the B litters, producing the C litters for a developmental toxicity evaluation. Ten males of the F_1 generation were maintained on experimental diets until they were 54-55 weeks old and were submitted for microscopic examination of selected neurological tissues.

No animals of the parental generations died during the study, although a few were killed because of conditions not related to administration of PP557. There were no dose- or treatment-related effects on body weights, body weight gains, food consumption, or food efficiency.

Treatment-related clinical signs in high-dose parental animals were limited to whole body tremors, occurring in all parental generations (exception: tremors were not observed in the F_0 males) during the first few days of the premating period. In the 2500-ppm groups, the incidence rates for the tremors were 20/24 (F_0 females), 11/12 and 24/24 (F_1 males and females, respectively), and 12/12 and 24/24 (F_2 males and females, respectively). Tremors were also observed in pregnant and lactating females exposed to 2500 ppm PP557. There were no tremors at 0 ppm in any generation. The tremors were intermittent and transient. Neuropathy was not observed in a special microscopic examination of selected neurological tissues from F_1 males continued on test for one year. Gross examination at necropsy did not reveal any dose- or treatment-related findings, nor did microscopic examination of grossly abnormal tissues from all parents surviving to scheduled termination and of reproductive tissues from animals suspected of infertility.

Therefore, the LOAEL for systemic toxicity is 2500 ppm (125 mg/kg/day) based on tremors observed in the F_0 females, and the F_1 and F_2 males and females. The systemic toxicity NOAEL is 1000 ppm (50 mg/kg/day).

Mating performance, fertility, and pup growth and survival were not affected by PP557 treatment in the F_1, F_2, and F_3 generations.

In the F_3C litters, there were no developmental effects associated with the administration of PP557 over three generations. The percentages of male fetuses of the 1000- and 2500-ppm groups (39.0 and 44.7%, respectively) were lower than the control value (53.2%), but the effect was not associated with increased resorptions and was not dose-related. Also, no consistent effect on sex ratios was observed in other litters or generations of the study and the effect is not considered to be treatment-related.

Therefore, the reproductive toxicity NOAEL is >2500 ppm (125 mg/kg/day) and the reproductive toxicity LOAEL is not established.

Microscopic examination of F_3B weanlings revealed dose-related increases in centrilobular hypertrophy of the liver. The incidences of slight and moderate centrilobular hypertrophy were dose-related, ranging from 0 to 80% for the males and from 10 to 100% for the females. The HIARC determined that the hypertrophy of the liver is an adaptive and reversible effect and is not considered as an adverse effect. This conclusion is supported by a 90-day rat feeding study (MRID 00054737) where the hepatocellular hypertrophy was observed at 185 mg/kg/day with a NOAEL of 92.9 mg/kg/day. In addition, similar findings might have been observed if histopathological examinations were conducted during the parental evaluation.

The NOAEL for offspring toxicity is >2500 ppm (125 mg/kg/day). The offspring LOAEL is not established.

The study is classified as **acceptable/guideline** and satisfies the requirements for a reproduction study (OPPTS 870.3800 [§83-4a]) in rats.

4.2.5 Additional Information from Literature Sources

A literature search was conducted and found a few studies on the neurotoxicity of permethrin. The information is summarized as follows.

(1) The effects of permethrin on schedule-controlled behavior were investigated in rats following oral doses of 100-400 mg/kg (Peele and Crofton, 1987). Animals had been trained to respond for food according to a multiple schedule consisting of four different variable-interval schedules. A monotonic dose-dependent decrease in response rate was observed with a calculated ED_{50} of 350 mg/kg. Statistically significant decreases in response occurred at doses of 300 and 400 mg/kg as compared to vehicle controls. In a similar study, rats injected i.p. with 15-60 mg permethrin/kg showed a dose-related decrease in operant response rate and significantly decreased total food intake at the highest dose (Bloom et al., 1983).

(2) Male and female rats were dosed by gavage with 400, 800, or 1200 mg/kg/day for 7 days. Clinical signs in all groups included hyperexcitability, ataxia, and tremor and 30% of high-dose males died. All groups showed a significant transient functional impairment on the inclined plane test with maximal effect at the end of the dosing period. Significant increases in β-glucuronidase and β-galactosidase activities in the distal section of the sciatic/posterior tibial

nerve were found 3-4 weeks postdosing. The study authors concluded that there was no correlation between neuromuscular dysfunction and neurobiochemical changes (Rose and Dewar, 1983).

(3) Tremors and hypersensitivity to noise were observed during the first 2 weeks of a 2-year study in rats fed 2500 ppm (Ishmael and Litchfield, 1988). Male Wistar rats treated by gavage with 300 mg permethrin/kg/day for 5 days had tremors and convulsions (incidence and severity not stated); microscopic examination revealed segmental demyelination in a cervical nerve and inflammatory and degenerative changes in the diaphragm muscle (Cavaliere et al., 1990).

4.2.6 Pre- and/or Postnatal Toxicity

4.2.6.1 Determination of Susceptibility

The HIARC determined that there is no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure in the developmental toxicity studies in rats and rabbits and multi-generation reproduction studies in rats.

4.2.6.2 Degree of Concern Analysis and Residual Uncertainties for Pre and/or Post-natal Susceptibility

The HIARC concluded that there are no residual uncertainties for pre- and post-natal toxicity since there is no developmental or reproductive toxicity observed in the developmental studies in rats and rabbits or reproduction study in rats.

4.3 Recommendation for a Developmental Neurotoxicity Study

The HIARC has concluded that there is a concern for developmental neurotoxicity resulting from exposure to permethrin. A developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects.

4.3.1 Evidence that supports requiring a Developmental Neurotoxicity Study

Evidence of neurotoxicity was shown in the acute and subchronic neurotoxicity studies and other subchronic and chronic toxicity studies in dogs and rats. The subchronic neurotoxicity studies showed increased incidence of microscopic lesions associated with neurotoxic effects at high doses.

4.3.2 Evidence that supports not requiring for a Developmental Neurotoxicity Study

There was no evidence of increased susceptibility in the fetuses of rats or rabbits following *in*

utero exposure or in the offspring following postnatal exposure to permethrin.

4.3.3 Rationale for the UF_{DB} (when a DNT is recommended)

On September 9, 2003, the Hazard Identification Assessment Review Committee (HIARC) recommended a 10X Database Uncertainty Factor (UF_{DB}) to account for the lack of a developmental neurotoxicity study (DNT) in rats. The 10X UF_{DB} was determined based on a dose analyses as described in the HIARC report dated May 12, 2004 (TXR No. 0052543).

The Health Effects Division, since then, has revised the dose analyses procedure to determine the need for and size of the UF_{DB} to account for the lack of a DNT. This revised procedure was based on an analysis of the DNT data submitted and reviewed to date.

The Reregistration Branch, using the above procedure, re-analyzed the size of the UF_{DB} for the lack of the DNT for permethrin. The re-analysis indicates that a UF_{DB} is not required for the DNT data gap. This decision is based on the following considerations:

- The dose levels tested in the subchronic neurotoxicity study (0, 15, 92 or 150 mg/kg/day) is lower than the doses tested in the three generation reproduction study (25, 50 or 125 mg/kg/day). Therefore, it is assumed that the doses used in a DNT study may be similar to those used in the subchronic neurotoxicity study in rats. The NOAEL in the subchronic study was 15 mg/kg/day and the LOAEL was 92 mg/kg/day.

- It is presumed that the offspring NOAEL in the DNT would be the lowest dose tested (i.e, 15 mg/kg/day).

- The results of the DNT would have no impact on the risk assessment because: 1) the endpoint of concern (neurotoxicity) is used for overall risk assessments; 2) the DNT is not likely to identify new hazard at a lower dose since the potential NOAEL (i.e, 15 mg/kg/day) from that study is comparable to the current dose (25 mg/kg/day) used for dietary (acute and chronic), non-dietary (incidental oral and dermal), and inhalation (11 mg/kg/day) exposure risk assessments; 3) because of the wide gap in the candidate study (i.e, subchronic neurotoxicity), the true NOAEL could have been higher than the one that was established (i.e, higher than the 15 mg/kg/day; 4) the DNT is being requested as a "confirmatory" data due to clinical signs seen at high doses (125-450 mg/kg/day) in adult animals and there is a large margin of safety between these doses and the doses used for risk assessment; and 4) it is also worth reiterating that there is no evidence (quantitative or qualitative) of increased susceptibility in the pre-natal developmental or the two generation reproduction study.

Therefore, HED is confident that the existing toxicity data for permethrin provided the Agency with the confidence that the risk assessment conducted with no additional factor will provide reasonable certainty of no harm to the safety of infants and children.

4.4 Hazard Identification and Toxicity Endpoint Selection

4.4.1 Acute Reference Dose (aRfD) - Females age 13-49

Since there is no developmental or reproductive toxicity of concern for permethrin, no appropriate endpoint or study is selected for the female (13-49) group. The selected dose/endpoint for general population would provide adequate protection for females 13-49 years old.

4.4.2 Acute Reference Dose (aRfD) - General Population

Study Selected: Acute Neurotoxicity Study in Rats § 870.6200a

MRID No.: 45657401

Executive Summary: In a published literature study (MRID 45657401), permethrin (95%, a.i., cis:trans 50:50) was administered by gavage to Long-Evans rats (8/sex/group) at dose levels of 0, 25, 75, or 150 mg/kg in corn oil. FOB and motor activity were assessed prior to dosing and at 2, 4, 24 and 48 hours after dosing.

At 75 mg/kg, the rats displayed a general pattern of increased excitability and aggressive behavior. Some of the more pronounced responses included abnormal motor movement (3/8, both sexes) decreased grip strength for forelimb (males) and hindlimb (males and females), motor activity (males), and increased body temperature (males). At 150 mg/kg, arousal score (males), righting reflex (males) and approach response score (females) were affected and 7/8 of both sexes had abnormal motor movement and motor activity was further decreased and body temperature was increased >2°C. Slight decreases in body weight (3-4%) were evident. Recovery from the symptoms was within 24 hours. **The LOAEL is 75 mg/kg based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature. The NOAEL is 25 mg/kg.**

The study is classified as **acceptable/nonguideline.**

Dose and Endpoint for Establishing aRfD: 25 mg/kg (NOAEL) based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature at 75 mg/kg (LOAEL).

Uncertainty Factor (UF): 100 (10x for interspecies extrapolation, 10x for intraspecies variations).

Comments about Study/Endpoint/Uncertainty Factor: The study is appropriate for a single dose exposure with the effects of concern via the oral route and length of exposure for an acute dietary endpoint. The endpoints for risk assessment are based on clinical signs of neurotoxicity.

Acute RfD (General Population) = $\frac{25 \text{ mg/kg/day}}{100}$ = **0.25 mg/kg/day**

4.4.3 Chronic Reference Dose (cRfD)

Study Selected: Acute Neurotoxicity Study in Rats §870.6200a

MRID No.: 45657401

Executive Summary: See acute RfD.

Dose and Endpoint for Establishing cRfD: 25 mg/kg (NOAEL) based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature at 75 mg/kg (LOAEL).

Uncertainty Factor(s): 100 (10x for interspecies extrapolation, 10x for intraspecies variations).

Comments about Study/Endpoint/Uncertainty Factor: Previously, the HED TES Committee has established a RfD for permethrin at 0.05 mg/kg/day based on increased liver weight in several chronic rat and mouse studies (HED Doc. 013494). This HIARC determined that the increased liver weight and hypertrophy observed in the liver are adaptive and reversible effects and are not considered adverse effects. Therefore, liver weight increase is not an appropriate endpoint to be selected for a chronic RfD of permethrin. The HIARC concluded that a dose and endpoints based on clinical signs of neurotoxicity are more appropriate for risk assessment on permethrin.

A metabolism study indicated that permethrin is rapidly absorbed and excreted (HED Doc. No. 001660). The World Health Organization report (1990) also suggested that permethrin administration to mammals was rapidly metabolized and almost completely eliminated from the body within a short period of time. This finding that permethrin does not bioaccumulate is supported by a close range of NOAEL and LOAEL among acute, subchronic , and chronic toxicity studies associate with clinical signs of neurotoxicity. Ranges of NOAEL/LOAEL (mg/kg/day) are: 25/75 in an acute neurotoxicity in rats (MRID 45657401), 15.5/91.5 in a subchronic neurotoxicity study in rats (MRID 42933701), 92.9/185 in a subchronic oral toxicity in rats (MRID 00054737), 50/150 in a developmental toxicity study in rats (MRID 40943603), 50/125 in a 3-generation reproduction study in rats (MRID 92142037), and 40.2/104 in a 2-year chronic feeding study in rats (MRID 92142123), respectively. Base on the dose spacing of these studies, the HIARC determined that a NOAEL/LOAEL of 25/75 based on clinical signs of neurotoxicity from the acute neurotoxicity study in rats is appropriate for the dose/endpoint selection of the chronic RfD. In addition, since long-term studies do not indicate that neurotoxic effects are cumulative, an additional uncertainty factor for using a short-term study for a long-term risk assessment is not required.

Chronic RfD = $\frac{25 \text{ mg/kg/day}}{100}$ = **0.25 mg/kg/day**

4.4.4 Incidental Oral Exposure: Short-Term (1-30 days)

Study Selected: Acute Neurotoxicity Study in Rats § 870.6200a

MRID No.: 45657401

Executive Summary: See acute RfD.

Dose and Endpoint for Risk Assessment: 25 mg/kg (NOAEL) based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature at 75 mg/kg (LOAEL).

Comments about Study/Endpoint: This dose/endpoint is appropriate for the population of concern (infants and children). Also see comment under chronic RfD.

4.4.5 Incidental Oral Exposure: Intermediate-Term (1 - 6 Months)

Study Selected: Acute Neurotoxicity Study in Rats § 870.6200a

MRID No.: 45657401

Executive Summary: See acute RfD.

Dose and Endpoint for Risk Assessment: 25 mg/kg (NOAEL) based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature at 75 mg/kg (LOAEL).

Comments about Study/Endpoint: This dose/endpoint is appropriate for the population (infants and children) and duration of concern.

4.4.6 Dermal Absorption

Dermal Absorption Factor: 5.7%

Since the completion of HED's final human health risk assessment for permethrin (dated April 4, 2006), the permethrin registrants have submitted a study (MRID 47514801) that attempts to estimate permethrin human dermal absorption via a method referred to as the parallelogram approach (triple pack approach). The basic concept behind the parallelogram approach is that if the *in vivo* human and rat dermal absorption data is generated under the same conditions as the *in vitro* human and rat skin data, the ratio of dermal absorption factors (human skin/rat skin) measured *in vitro* will be the same as the ratio of dermal absorption factors (human/rat) measured *in vivo*. This estimation is based on a study design that consists of at least three studies conducted using the same dose/duration regimen: (1) an *in vitro* study using human skin, (2) an *in vitro* study using rat skin, and (3) an *in vivo* rat dermal absorption study.

This study was reviewed by the Toxicology and Epidemiology Branch of HED (TXR 0054971) and the resulting memo (D356089) discussed the most appropriate dermal absorption factor for use in permethrin exposure and risk assessments. Table 4.4.6 lists the measured dermal absorption in the human and rat in vitro studies and the rat in vivo study. Using the rat and human *in vitro* dermal absorption data with the rat *in vivo* dermal absorption data, an estimated human in vivo dermal absorption factor can be calculated with an equation: (human *in vitro*/rat *in vitro*) x rat in vivo = human *in vivo*.

Using this methodology, the estimated *in vivo* human dermal absorption factors ranged from 1.4% to 5.7%. Based on the rat *in vivo* study, the increase in absorption at 120 hours indicated that radiolabel (permethrin) remaining in the skin after washing at 24 hours was bioavailable. Also, the *in vivo* or *in vitro* absorption of permethrin was relatively consistent at all three doses. Therefore, 5.7% is the selected dermal absorption factor for use in permethrin exposure and risk assessments. It should be noted that 5.7% was the highest estimated human *in vivo* dermal absorption using the parallelogram approach for permethrin and thus, the revised cancer risk

assessments using this dermal absorption factor should be considered conservative in nature.

Table 4.4.6: Permethrin Dermal Absorption Using the Parallelogram Approach			
	Dermal absorption (% of application)		
	Permethrin ($\mu g/cm^2$)		
	2.25	20	200
Human/ *in vitro*	1.3	2.7	2.1
Rat/ *in vitro*	20	18	24
Rat/ *in vivo* (1 day)	22	22	28
Rat/ *in vivo* (5 day)	38	38	30
Estimated Human/ *in vivo* (1 day)	**1.4**	**3.3**	**2.5**
Estimated Human/ *in vivo* (5 day)	**2.5**	**5.7**	**2.7**

4.4.7 Dermal Exposure: (All Durations)

Study Selected: 21-Day Dermal Toxicity Study in Rats

MRID No.: 41143801 & 42653301

Executive Summary: In a 21-day repeated dose dermal toxicity study (MRIDs 41143801 & 42653301), groups of 5 male and 5 female Wistar Alpk:Apfsd SPF rats were treated with undiluted Permethrin (95.6%, Batch No. Y00040/85, RS/38F). Animals were treated by dermal occlusion for 6 hours/day for 21 days at doses of 0, 50, 150, or 500 mg/kg/day.

There were no treatment-related deaths and no effects on body weight, food consumption, hematology, clinical chemistry, or gross or microscopic lesions. Increases in absolute ($p<0.05$; 10.3% increase) and relative ($p<0.05$; 10.6% increase) liver weight were noted in high-dose females only. No histopathological evidence of adaptive liver change was seen in any treatment group. Therefore, the increase of liver weight in females was not considered biologically significant. Skin irritation was observed at the application site of all treatment groups.

The systemic NOAEL was 500 mg/kg/day (the highest dose tested), the systemic LOAEL was not established. The dermal LOAEL was 50 mg/kg/day based on skin irritation. A dermal NOAEL was not identified.

Dose and Endpoint for Risk Assessment: 500 mg/kg/day (the highest dose tested), the systemic LOAEL was not established.

Comments about Study/Endpoint: Previously, the HIARC stated that the 21-day dermal toxicity study in rats was not used for dermal risk assessment for permethrin because the endpoint of concern (parameters indicative of neurotoxicity) was not measured. However, the neurotoxic signs (i.e., aggression, abnormal and/or decreased movement) observed in the oral studies are conspicuous and would have been observed in the 21-day dermal toxicity had they occurred. No signs of neurotoxicity were observed in the 21-day dermal study at 500 mg/kg/day (HDT) which

clearly shows that the compound was negative for neurotoxicity at the doses and conditions of the test. Thus, the reported NOAEL is an acceptable NOAEL for systemic effects. Therefore, the 21-day dermal toxicity should be used for dermal route of exposure and a dermal absorption factor is not needed at this time. Although no neurotoxic signs were seen in the 21-day dermal toxicity study, there is evidence that there was some degree of dermal penetration in this study. An observed increase of liver weight (↑10.3%) in females at 500 mg/kg/day in the 21-day dermal study indicated that absorption through skin did occur as liver weight gain is a typical response to permethrin based on the oral feeding studies. See chronic RfD section for rationale of using a short-term study for all exposure durations.

4.4.8 Inhalation Exposure: (All Durations)

Study Selected: 15-Day Inhalation Study in Rats §870.3465

MRID No.: 00096713

Executive Summary: In a 15-day inhalation toxicity study (MRID 00096713), permethrin (94.7% a.i., Lot # ZJ, cis:trans 25.2:69.5) was administered to groups of 5 male and 5 female Charles River rats/concentration by dynamic whole-body inhalation exposure at concentrations of 0, 6.1, 42.2, or 583 mg/m^3 (0.0061, 0.042, or 0.583 mg/L) for 15 exposures (6 hours/day for 2 days during week 1, 5 days during weeks 2 and 3, and 3 days during week 4).

There was no test material-related effect on mortality, body weight or weight gain, food consumption, hematology, organ weights, or gross pathology. Weight gain was actually greater in all treated groups than in the respective control groups. Clinical signs were observed in the treated groups. Two female rats in the 0.0061 mg/l group were observed to have slightly labored breathing 30 minutes into the first exposure but not subsequently. In the 0.042 mg/l (MCT) group, licking of the inside of the mouths became more extensive then in the low-treatment group and involved most of the rats. All 5 females were observed to have slightly labored breathing during the first exposure but not subsequently. Labored breathing was not observed in male rats in either the 0.0061 or 0.042 mg/L groups. All rats in the 0.042 mg/L group appeared more alert than in the control and low-dose groups and adopted a hunched posture with open eyes during the early part of some exposures. The 0.583 mg/L group (HCT) demonstrated less activity, greater response to auditory or touch stimuli, and more extensive licking behavior than the other groups. Body tremors were observed in this group beginning with 3 females during the last hour of the first exposure and in 3 males during the second exposure. In both instances, tremors continued post exposure. The tremors reached a peak incidence, 5 males and 4 females, during the 5^{th} exposure (3^{rd} day of the second week) and declined thereafter, with only 1 male and 1 female showing tremors on exposure day 15 (2^{nd} exposure of week 4). Slightly labored breathing was recorded in 1 male and 1 female in this group.

The hypersensitivity to noise or touch became evident in the 0.583 mg/L (HCT) group following the second exposure and involved 5 males and 5 females. This sign tapered off with continued exposures, but was still displayed by 3 females following the 7^{th} exposure. Rales, poor grooming, and crusty brown staining around the nose were observed occasionally in the 0.583

mg/L group, with incidences higher in females than in males. **The LOAEL is 0.583 mg/L in male and female rats based on body tremors and hypersensitivity to noise. The NOAEL is 0.042 mg/L.** Microscopic pathology on the lungs showed focal to diffuse pneumonitis and perivascular inflammation - although to some degree more severe in the treated groups, could not be clearly distinguished from the respiratory infection present in all animals.

The HIARC determined that the dose/endpoint can be used for risk assessment purpose because the clinical signs of neurotoxicity were observed in the first day of exposure. This 15-day inhalation toxicity study in the rat is classified **acceptable/non-guideline** and does not satisfy the guideline requirement for a subchronic inhalation study OPPTS 870.3465.

Dose/Endpoint for Risk Assessment: NOAEL of 11 mg/kg/day (0.042 mg/L) based on body tremors and hypersensitivity to noise in male and female rats at a LOAEL of 154 mg/kg/day (0.583 mg/L).

Comments about Study/Endpoint: The selected dose/endpoint is appropriate for the route of exposure. See the chronic RfD section for rationale of using a short-term study for all exposure durations.

4.4.9 Margins of Exposure

Table. 4.4.9. Levels of Concern (LOC) Summary (MOEs) for Risk Assessment

Route Duration	Short-Term (1-30 Days)	Intermediate-Term (1 - 6 Months)	Long-Term (> 6 Months)
Occupational (Worker) Exposure			
Dermal	100	100	100
Inhalation	100	100	100
Residential (Non-Dietary) Exposure			
Oral	100	100	N/A
Dermal	100	100	100
Inhalation	100	100	100

The MOEs for dermal and inhalation exposures may be combined for occupational exposure risk assessment because the toxicity endpoints for these routes of exposure are the same.

4.4.10 Recommendation for Aggregate Exposure Risk Assessments

As per FQPA, 1996, when there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. The toxicity endpoints selected for these routes of exposure may be aggregated as follows: for short-, intermediate- and long-term aggregate exposure risk assessments, the oral,

dermal (oral equivalent) and inhalation routes can be combined because of the common toxicity endpoints (clinical signs of neurotoxicity) via these routes.

4.4.11 Classification of Carcinogenic Potential

4.4.11.1 Combined Chronic Toxicity/Carcinogenicity Study in Rats

Executive Summary: In a chronic oral toxicity/oncogenicity study (MRID 92142123), Permethrin was administered to Wistar rats (60/sex/group) in the feed at doses of 0, 500, 1000, or 2500 ppm. The mean estimated compound intake for males was 0, 19.4, 36.9, or 91.5 mg/kg/day, respectively, and for females was 0, 19.1, 40.2, or 104 mg/kg/day. Of these animals, 12/sex/group were sacrificed at 52 weeks and the surviving rats were sacrificed at 104 weeks' exposure.

No treatment-related effect on mortality was observed during the study. No treatment-related effects were seen on tumor induction. During the first two weeks of the study, treatment-related tremors and hypersensitivity were observed in both the high-dose male and female groups. No other treatment-related clinical effects were observed. There were no toxicologically significant effects on body weight, body weight gain, food consumption, or food efficiency. There were no treatment-related effects on ophthalmologic endpoints, hematologic endpoints, clinical chemistry or urinalysis parameters.

Liver changes suggestive of adaptive hypertrophy included increased aminopyrine-N-demethylase activity in all male treatment groups, in the mid- and high-dose female at 52 weeks, and in the high-dose male and female groups at 104 weeks. This was coupled with modestly increased absolute and relative liver weights in the high-dose males and high and low-dose females at 52 weeks and in all male treatment groups and mid-dose females at 104 weeks. Further evidence for adaptive changes included hypertrophy of centrilobular hepatocytes with increased cytoplasmic eosinophilia in the mid- and high-dose male and females at 104 weeks' exposure and increased smooth endoplasmic reticulum proliferation in all treatment groups except low-dose males at 52 weeks and high-dose groups at 104 weeks. Electron microscopy evaluation on the liver showed fatty vacuoles in the mid- and high-dose males at both 52 and 104 weeks and in the high-dose females at 104 weeks.

Under the conditions of this study, the chronic toxicity LOAEL is 2500 ppm (104 mg/kg/day) based on tremors and hypersensitivity. The NOAEL is 1000 ppm (40.2 mg/kg/day).

At the doses tested, permethrin did not affect the incidence of tumor-bearing animals or the incidence of any specific tumor type in either sex. Permethrin was not carcinogenic to the rat. Dosing was considered adequate based on tremors and hypersensitivity as well as liver effects.

This chronic toxicity/oncogenicity study in the rat is **acceptable/guideline** and satisfies the guideline requirements for a chronic toxicity/oncogenicity oral study [OPPTS 870.4300 (§83-5a)] in the rat.

Discussion of Tumor Data : There are no treatment-related changes in incidence of tumors of any type in male or female rats.

Adequacy of the Dose Levels Tested: Dosing was considered adequate based on tremors and hypersensitivity as well as liver effects in rats.

Executive Summary: In a combined chronic toxicity/carcinogenicity study (MRID 97441), permethrin (technical grade, purity not specified, Batch No. 533/17/x) was administered to groups of Wistar strain rats (specific-pathogen free) (60/sex/group) at dietary concentrations delivering doses of 0, 10, 50, or 250 mg/kg/day for up to 104 weeks. Additional groups of 15 male and female rats were included for clinical pathology studies (satellite study).

No treatment-related or biologically significant effects were observed on body weight, weight gain, food consumption, food efficiency, hematology, clinical chemistry, urinalysis parameters, eyes, organ weights (females only), or gross lesions in male and female rats fed permethrin at doses up to 250 mg/kg/day. The only noteworthy clinical sign was tremors observed in ten males and five females in the high dose group for a 2-week period after week 90. The mortality rates in male rats at study termination were 58%, 78% ($p<0.05$), 67%, and 80% ($p<0.01$) at 0, 10, 50, and 250 mg/kg/day. The lack of a clear dose-related trend and treatment-related cause of death indicate that the increased mortality may not be treatment related. No treatment-related mortality was observed in females. The absolute liver weight of high-dose male rats was elevated by 19% ($p<0.05$) compared with the controls, and the relative liver weight was also slightly increased. Mid- and high-dose male and female rats had significantly increased incidences of periacinar hepatocyte hypertrophy in the liver. The incidence of hepatocyte fatty vacuolation in the liver (all locations combined) was 9/59, 16/56 ($p=0.07$), 17/58 ($p<0.05$), and 22/52 ($p<0.01$) for the control, low-, mid-, and high-dose male rats, respectively. In addition, 9/52 ($p<0.05$) high-dose male rats had hyperplasia of the pelvic epithelium in the kidney compared with 2/59 for controls and 6/52 ($p<0.05$) high-dose male rats had erythrocytes and erythrophagocytosis in the sinus of the thymic lymph nodes compared with 1/59 control. High-dose females had no other lesions that occurred with statistically significant increased incidences compared with the control incidences. These liver effects were considered adaptive effects and were not considered adverse effects.

The LOAEL for permethrin is 250 mg/kg/day in males and females based on clinical signs of neurotoxicity (tremors); the NOAEL is 50 mg/kg/day.

There were no treatment related increases in tumor incidences at any dose of the test material compared with control incidences. Dosing was considered adequate based on clinical signs of neurotoxicity at the high dose and the increased incidence of hepatocyte fatty vacuolation and periacinar hepatocyte hypertrophy at the mid- and high-dose levels.

This chronic/carcinogenicity study in the rat is **unacceptable/guideline (upgradeable)**. The study may be upgraded upon submission of data listing on the study deficiencies section. It should be noted that this study was conducted before Subdivision F or OPPTS 870.4300 guidelines were established.

Discussion of Tumor Data: There were no treatment related increases in tumor incidences at any

dose of the test material compared with control incidences.

Adequacy of the Dose Levels Tested: Dosing was considered adequate based on clinical signs of neurotoxicity at the high dose and the increased incidence of hepatocyte fatty vacuolation and periacinar hepatocyte hypertrophy at the mid- and high-dose levels.

4.4.11.2 Carcinogenicity Study in Mice

Executive Summary: In a carcinogenicity study (MRID 00062806, 92142033) FMC 33297 (permethrin, % a.i. not specified, Lot #s MR176 and MR807) was administered to Charles River CD-1 mice (75/sex/dose) in the diet at dose levels of 0, 20, 500, or 2000 ppm for males (equivalent to 0, 3, 71, or 286 mg/kg/day, respectively) and 0, 20, 2500, or 5000 ppm for females (equivalent to 0, 3, 357, or 714 mg/kg/day, respectively) for 24 months.

Mortality was significantly increased in high-dose males after 75 weeks of treatment, but was not significantly different from the control group after 104 weeks. Clinical signs consisting of distended abdomens, ano-genital staining, and alopecia were increased in treated males compared to the control during the first year of treatment, but were not dose-related at 24 months.

Insufficient data were provided on body weights (with the exception of final body weights for females), body weight gains, organ weights (with the exception of brain weights of females at study termination), hematology parameters, and gross and microscopic changes for the reviewer to evaluate. An 8% increase in final female body weight was not considered a biologically significant effect. Although difficult to evaluate in the absence of summary data, the effects listed by the study author - transient increased body weights, decreased leucocyte counts and liver and kidney inflammatory changes - do not appear to be toxicologically significant.

A NOAEL and LOAEL for FMC 33297 (permethrin) in mice could not be determined in this study due to major study deficiencies including failure to include summaries of numbers of animals with clinical signs and data on body weights, body weight gains, organ weights, hematology parameters, and gross and microscopic necropsy findings.

A joint FDA-EPA audit of this study conducted in late 1980 at Bio/Dynamics and FMC facilities did not reveal any inadequacies in the conduct or reporting of this study serious enough to compromise the usefulness of these study results for oncogenic evaluation. However, the audit concluded that this study was not useful for assessment of chronic toxicity (HED Doc. #004204).

On December 12, 1988 the HED Cancer Peer Review Committee reviewed the study and concluded that there were statistically significant increases in liver adenoma at all doses for males and at mid- and high-doses for females with a significant dose-related trend in both sexes. Combined liver adenoma/carcinoma also showed statistically significant increases at mid- and high-doses for male and female mice. Statistically significant increases in lung adenomas and combined adenoma/carcinoma at all doses were observed in females only. Carcinoma were increased at all doses but only at HDT that the increase was statistically significant. The

incidences of adenoma and carcinoma at mid- and high-doses were outside historical control ranges. There were also significant dose-related trends for lung adenomas, carcinomas and combined adenoma/carcinomas in females. The incidences of lung tumors in male mice (adenoma or carcinoma, or combined) were not statistically significant at any dose, nor was there a dose-related trend for any of them.

This carcinogenicity study in mice is classified as **acceptable/guideline (OPPT 870.4200b; §832b)** for evaluation of carcinogenicity. However, this study may not be used for regulatory purpose on assessment of chronic toxicity.

Discussion of Tumor Data: There were statistically significant increases in liver adenoma at all doses for males and at mid- and high-doses for females with a significant dose-related trend in both sexes.

Adequacy of the Dose Levels Tested : Adequate

Executive Summary: In a carcinogenicity study (MRID 00102110, 92142032) PP557 (94.0-98.9 % a.i., batch/lot #'s P24, P34, P35, P36, P44, P52, BX4, and BX6; cis:trans 40:60) was administered to pathogen free Alderley Park mice (70/sex/dose) in the diet at dose levels of 0, 250, 1000, or 2500 ppm (equivalent to 0, 26.9, 110.5, or 287.2 mg/kg/day for males and 0, 29.8, 124.2, or 316.1 mg/kg bw/day for females) for up to 98 weeks. Ten males and females per group were set aside for each of 26- and 52-week interim studies during which necropsies were done and hematology and clinical chemistry parameters were measured.

No significant compound-related effects on mortality or clinical signs were noted. Transient decreases occurred in body weight gain in high-dose males and high-dose females, but at study termination (98 weeks), the final body weight and body weight gain for male mice in the high-dose group were reduced by only 5 and 12%, respectively and the final body weight and body weight gain in females in the high-dose group were unaffected. Food consumption was decreased in the high-dose groups relative to controls during the first week of the study, but was increased at most time points thereafter. No treatment-related changes were seen in hematology or clinical chemistry parameters. Increases of 31 to 48% were seen in liver weights and liver weights corrected for body weight in high-dose males and females compared to the controls. Centrilobular hepatocellular eosinophilia was increased in high-dose males and high-dose females at 52 and 98 weeks compared to the controls. Other liver effects included smooth endoplasmic reticulum proliferation, increased nuclear microbodies, and increased aminopyrine-N-demethylase activity in high-dose animals of both sexes compared to the respective controls. Kidney weights were decreased by 21% in high-dose males, but were slightly increased in high-dose females. Proximal tubular epithelium vacuolation was decreased in number and incidence in high-dose males.

A LOAEL for Permethrin is established at 2500ppm (287.2 mg/kg/day for males and 316.1 mg/kg/day for females) based on increased liver weight, induction of microsomal enzyme activity, electron microscope evidence of increased smooth endoplasmic reticulum, and

hepatocyte eosinophilia. The NOAEL is 1000 ppm (110.5 mg/kg/day for males and 124.2 mg/kg/day for females).

At the doses tested, there was no evidence compared to controls of a significant increase in unusual tumor types or in tumor bearing animals. A non-significant increase in lung adenomas in male mice and in lung adenomas plus carcinomas in female mice at the highest dose (2500 ppm in the diet) was not considered evidence of a carcinogenic effect in light of the high incidences in the control groups of both sexes. In addition to the lungs, major organs examined included liver, kidney, testes, ovary, bladder, brain, and thyroid. The dosing based on toxic response was marginal in both males and females. However, the dosing is considered adequate because higher doses would have resulted in a significant weight deficit in male mice.

This carcinogenicity study in mice is classified **acceptable/guideline** and satisfies the guideline requirement for a carcinogenicity study [OPPTS 870.4200b; OECD 451] in mice.

Executive Summary: In a nonguideline mouse carcinogenicity study (MRID 45597105), Permethrin technical (lot no. PL95-329, 94.7% a.i.) was administered to groups of 50 to 109 Crl:CD-1®(ICR)BR female mice in the diet at 0 or 5000 ppm (equivalent to 780 - 807 mg/kg bw/day) for 39, 52, 65, or 78 weeks. Groups of mice from all treatment groups were examined immediately after treatment and at weeks 79 and 101. Matching groups of untreated control mice were examined at each interval.

There were no compound-related effects on mortality or body weight. Body weight gain was slightly less in mice treated for 65 or 78 weeks and allowed to recover to week 101 (both 86% of the control weight). The overall food consumption was slightly decreased by 2-3% in some treated groups. The overall food efficiency in the pooled 52-week treatment groups was about 5% less than that of the controls.

At the end of each treatment period, the absolute liver weights were increased by about 44-53% compared to the control groups regardless of the treatment duration. Liver centrilobular hypertrophy and karyomegaly occurred in 87-100% and Kupffer cell hypertrophy was seen in 43-61% of treated animals compared to the controls (0-5%). Centrilobular hypertrophy and Kupffer cell hypertrophy at all dose durations was reversed to or near control levels during the recovery periods. Karyomegaly incidences were reduced by about 11-70% according to the length of the respective recovery periods, but were still present in 25-75% of the treated animals at the 101-week recovery. Inflammatory liver changes were seen in 75-95% of treated animals compared to 37-63% in the controls. The inflammatory liver changes increased in the control mice as a function of age; therefore, recovery was only seen in the treated groups allowed to recover to week 79. Amyloid deposits were increased in treated animals immediately after treatment, and continued to increase during the recovery period. Incidences of eosinophilic foci were significantly increased in the livers of treated groups only after the recovery periods and appeared to be related to the length of the treatment period. The activities of cytochrome P450 (CYP) mixed function oxidases in the livers of animals treated for 52 weeks were expressed both as specific activity (nmol/mg microsomal protein) and the total enzyme activity per liver. Specific activities of total CYP, CYP1A, CYP2B, CYP2E1, and CYP3A were unaffected by treatment, whereas, the specific activity of CYP4A was increased 3-fold. The total enzyme activities per liver of total CYP, CYP1A, CYP2B, CYP2E1, and CYP3A2 were increased in treated animals by 142-283%, and the activity of CYP4A was increased by 829% compared to the control values.

The incidences of Clara cell hyperplasia were increased in the lungs of all treated animals, and the incidences were significantly decreased during the recovery periods to weeks 79 and 101. The specific activities of CYP2B, CYP2E1, and CYP4A in animals sacrificed after 52 weeks of treatment were unaffected by treatment. The total enzyme activities of CYP2E1 and CYP4A expressed as activity/g lung were increased to only 133% and 125%, respectively, of controls.

Significant increases were seen in the incidences of basophilic and eosinophilic hepatocellular

adenomas in female mice administered 5000 ppm in the diet for 39, 52, or 78 weeks followed by recovery to week 101 (7% to 10% compared to 1% in controls). The increased incidences were not treatment-duration (dose) related; treatment for 65 weeks resulted in no basophilic adenomas. Eosinophilic adenomas were increased after 78 weeks of treatment and after the recovery period (both 10% compared to 1-2% in controls). The incidences did not increase during the recovery period. No increases in hepatocellular carcinoma incidences were seen and the time to tumor onset for the adenomas was not different in treated animals compared to the controls. Lung bronchioloalveolar adenoma incidences increased immediately after treatment and continued to increase during the recovery periods compared to the controls. The incidences were 14%, 43%, 47%, 49%, and 49% for the control and 39, 52, 65, and 78 weeks exposure followed by recovery to week 101 ($p<0.01$). The lung adenomas did not occur any earlier in the treated animals than in the control groups, and there was no increase in lung carcinomas in treated animals.

This mouse carcinogenicity study is designed to test the progression and possible reversal of toxic effects including benign liver and lung tumors and is classified as **acceptable/non-guideline**.

Discussion of Tumor Data: There were significant increases in the incidences of lung bronchioloalveolar adenomas in mice. The increased incidences of basophilic hepatocellular adenoma did not show a relationship to the treatment duration. No progression to carcinoma was observed in the lung or liver.

Adequacy of the Dose Levels Tested: Only one dose was tested.

4.4.11.3 Classification of Carcinogenic Potential

The Cancer Assessment Review Committee met on August 21, 2002 to re-evaluate the carcinogenic potential of Permethrin (CARC Report, 10/23/02, TXR No. 0051220). In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), the CARC classified permethrin as **"Likely to be Carcinogenic to Humans"** by the oral route. This classification was based on evidence of two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in Long-Evans rats, and supportive SAR information. The Committee recommended using a linear low-dose extrapolation approach for the quantification of human cancer risk based on female mouse lung tumors (combined adenomas and carcinomas) using the data from the PWG assessment. The unit risk, $Q_1^*(mg/kg/day)^{-1}$ for Permethrin is 9.6×10^{-3} based on female mouse lung adenoma and/or carcinoma combined tumor rates (Memo, L. Brunsman, 9/25/02, TXR No. 0051166).

4.4.12 Mutagenicity

The HIARC concluded that there is no concern for mutagenicity resulting from exposure to permethrin.

4.4.12.1 Gene Mutation

Salmonella/mammalian reverse gene mutation assay (MRID 41031107): there were no evidence of increased revertant colonies above control in 5 Salmonella strains up to 5000 µg/plate (solubility limit).

4.4.12.2 Chromosome Aberrations

Mouse bone marrow micronucleus assay (MRID 42723302): five CD-1 mice/sex/harvest time were treated once each orally with permethrin (Batch No.: P58/D7534/30, 93.1% a.i., w/w) in corn oil at a dose of 200 mg/kg for males and 320 mg/kg for females. Bone marrow cells were harvested at 24 and 48 hours post-treatment.

The MPE/PE ratio (micronuclated polychromatic erythrocytes/1000 polychromatic erythrocytes) at 24 hours was increased for male (2.6 ± 1.1 vs 1.2 ± 1.6) and female (2.0 ± 1.6 vs 1.0 ± 2.2) mice dosed with permethrin relative to the solvent control value; however, the increases were not statistically significant. The ratio at 48 hours was less than the solvent control values in either sex. Data on the mean percentage of polychromatic erythrocytes in males and females indicated no statistical differences between the animals treated with permethrin and the solvent controls at either time interval. The solvent control and the cyclophosphamide positive control induced the appropriate responses. **Based on these data, there is no evidence that permethrin is clastogenic in the bone marrow cells of mice in this study.**

This study is classified as **acceptable/guideline**. It satisfies the requirement for FIFRA Test Guideline OPPTS 870.5395 [§84-2] for *in vivo* cytogenetic mutagenicity data.

4.4.12.3 Other Mutagenic Mechanism

Unscheduled DNA synthesis (UDS) in primary male rat hepatocytes assay (MRID 40943604): There was no evidence of unscheduled DNA synthesis above control up to 10^{-4} M and possibly 10^{-2} M Limits of cytotoxicity).

Dominant Lethal Test (MRID 40943604): No evidence of increased dominant lethal effects up to 150 mg/kg/day (oral dose administered daily for 5 days to males).

Table 4.3 Summary of Toxicological doses and endpoints for Permethrin for Use in Human Risk Assessments			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (Females 13-50 years of age)	**Acute RfD** = No applicable	An appropriate endpoint attributable to a single dose was not identified.	
Acute Dietary (General population including infants and children	Oral NOAEL = **25** mg/kg/day UF = **100** **Acute RfD** = 0.25 mg/kg/day	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 0.25 mg/kg/day	**Acute Neurotoxicity Study in Rats** LOAEL = **75** mg/kg/day based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature.
Chronic Dietary (All populations)	Oral NOAEL= **25** mg/kg/day UF = **100** **Chronic RfD** = 0.25 mg/kg/day	FQPA SF = 1X **cPAD** = chronic RfD / FQPA SF = 0.25 mg/kg/day	**Acute Neurotoxicity Study in Rats** LOAEL = **75** mg/kg/day based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature.
Short-Term Incidental Oral (1 - 30 Days)	Oral NOAEL = 25 mg/kg/day	**Residential** LOC for MOE = 100	**Acute Neurotoxicity Study in Rats** LOAEL = **75** mg/kg/day based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature.
Intermediate-Term Incidental Oral (1 - 6 Months)	Oral NOAEL = 25 mg/kg/day	**Residential** LOC for MOE = 100	**Acute Neurotoxicity Study in Rats** LOAEL = **75** mg/kg/day based on observations of clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature.
Short-Term Dermal (1 - 30 days)	Dermal NOAEL= 500 mg/kg/day	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**21-Day Dermal Toxicity Study in Rats** LOAEL was not established.
Intermediate-Term Dermal (1 - 6 Months)	Dermal NOAEL= 500 mg/kg/day	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**21-Day Dermal Toxicity Study in Rats** LOAEL was not established.
Long-Term Dermal (> 6 Months)	Dermal NOAEL= 500 mg/kg/day	**Residential** LOC for MOE = 100 **Occupational** LOC for	**21-Day Dermal Toxicity Study in Rats** LOAEL was not established.

Table 4.3 Summary of Toxicological doses and endpoints for Permethrin for Use in Human Risk Assessments			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
		MOE = 100	
Short-Term Inhalation (1 - 30 days)	Inhalation NOAEL= 0.042 mg/l (Converts to oral equivalent of 11 mg/kg/day)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**15-Day Inhalation Study in Rats** LOAEL = 0.583 mg/l (converts to oral equivalent of 154 mg/kg/day) based on body tremors and hypersensitivity to noise.
Intermediate-Term Inhalation (1 - 6 Months)	Inhalation NOAEL= 0.042 mg/l (Converts to oral equivalent of 11 mg/kg/day)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**15-Day Inhalation Study in Rats** LOAEL = 0.583 mg/l (converts to oral equivalent of 154 mg/kg/day) based on body tremors and hypersensitivity to noise.
Long-Term Inhalation (>6 Months)	Inhalation NOAEL= 0.042 mg/l (Converts to oral equivalent of 11 mg/kg/day)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**15-Day Inhalation Study in Rats** LOAEL = 0.583 mg/l (converts to oral equivalent of 154 mg/kg/day) based on body tremors and hypersensitivity to noise.
Cancer (Oral, dermal, inhalation)	Classification: "Likely to be Carcinogenic to Humans" based on female mouse lung adenoma and/or carcinoma combined tumor rates. Q_1* $(mg/kg/day)^{-1} = 9.567 \times 10^{-3}$		

4.5 Special FQPA Safety Factor

Based on the hazard data, there are no concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity. Although a DNT has been required, a dose-analysis with the existing reliable toxicity data for permethrin provided the Agency with the confidence that the risk assessment conducted with no additional factor will provide reasonable certainty of no harm to the safety of infants and children. In addition, the permethrin risk assessment team evaluated the quality of the exposure data and based on these data, recommended that the special FQPA SF be reduced to 1x. The recommendation is based on the following:

- The dietary food exposure assessment demonstrates that acute and chronic exposures do not underestimate the risk and are not of concern.
- The residential exposure assessment is based on reliable data and is unlikely to underestimate exposure and risk.

4.6 Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may

have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administration may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and FFDCA authority to require wildlife evaluations, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the available toxicity studies on permethrin, there was no toxicologically significant evidence of endocrine disruptor effects. When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, permethrin may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

5.0 Public Health Data

5.1 Human Incident Reports

It is likely that most poisonings due to permethrin resulted from misuse or inadvertent exposures. The large majority of cases resulted in minor effects to the skin (primarily rash, irritation, itching), eyes (redness, pain, burning), headache, dizziness, nausea, vomiting, and shortness of breath or difficulty breathing. Loss of consciousness appears to occur only in cases of ingestion involving 700 mg/kg body weight or more (Yang et al. 2002). Persons handling permethrin directly are the most likely to experience symptoms. Permethrin does not appear to pose significant risks from exposure to residues or drift, based upon a relatively small number of documented cases. Compared to other pesticides, permethrin is much less likely to result in serious or persistent medical outcome/condition. Even ingestion of suicidal/potentially lethal doses can be resolved within a few days with medical treatment. The only death reported was due to pneumonitis likely due to the xylene solvent rather than the permethrin. Though a relatively safe product, permethrin can readily cause problems to skin and eyes and inhalation may lead to headache, dizziness, and difficulty breathing. A number of the data sources reviewed for the permethrin human incident report suggest permethrin can aggravate asthma or lead to asthma like symptoms. Ingestion or inhalation has led to nausea and vomiting.

There are a number of different datasets from which HED compiles a human exposure incident report. The OPP Incident Data system items are anecdotal or represent allegations only. Information in this system comes from registrants, other federal and state health and environmental agencies and individual consumers. The most prevalent complaints reported by ten or more individuals included: headache (43 cases); rash (32 cases); tingling/burning skin (29 cases); nausea (22cases); difficulty breathing/shortness of breath/asthma (17 cases); eye irritation (15 cases); itching (14 cases); dizziness (13 cases); and vomiting (12 cases). Note that 20 of the 29 case of tingling or burning skin were tingling, a symptom known to be associated with exposure to the class of pesticides, pyrethroids. Other dermal symptoms including burning,

itching, and irritation to skin are known to be related to exposure to pyrethroids (Reigart and Roberts 1999 summarized by Blondell and Hawkins, 2004).

EPA also accesses Poison Control Center Data (1993-1998) to examine poisoning information noted in occupational cases, non-occupational cases involving adults and older children, and for cases involving children under the age of six. In this data set, the ratio of the percent of cases involving permethrin and the percent of cases for all other pesticides is compared using several severity metrics, *e.g.*, symptomatic cases and cases seen at an intensive care facility. The non-occupational category is probably the most representative of general population exposure to permethrin pesticides because the children were much more likely exposed to head lice control products regulated by the Food and Drug Administration (FDA). Note, that 84% of the permethrin exposure to children identified by specific products, were products for the control of head lice. Ten or more people reported eye (40 persons) or skin (26 persons) irritation and/or pain. Other dermal symptoms included edema (15 persons), erythema/flushed (21 persons), hives/welts (11 persons), pruritus (itching - 22 persons), and rash (18 persons). Tingling is not a choice coded by Poison Control Centers, but may indeed be present in the cases. Neurological symptoms reported in ten or more people included dizziness/vertigo (21 persons) and headache (18 persons). Gastrointestinal symptoms reported in ten or more people included nausea (25 persons), vomiting (23 persons), and diarrhea (15 persons). Respiratory symptoms were reported by10 persons with broncho spasm, 16 with cough/choke, and 32 person with dyspnea (difficulty breathing). The relatively high occurrence of dyspnea (second most common symptom among Poison Center cases and fifth most common among cases reported to the Incident Data System) suggests that permethrin may pose a hazard of asthma-like reactions in sensitive individuals.

Detailed descriptions of 432 cases submitted to the California Pesticide Illness Surveillance Program (1982-2001) were also reviewed to prepare the permethrin incident report. In 79 of these cases, permethrin was used alone or was judged to be responsible for the health effects reported. According to the above activity categories, routine indoor use was associated with more exposures than any other category. Outside handlers, applicators and mixer/loaders accounted for the next largest group. Together, indoor and outdoor handlers accounted for two-thirds of the illnesses reported. The most prevalent symptoms in ten or more individuals were eye irritation (including burning, pain, redness, and swelling), rash, headache, dizziness, nausea, and shortness of breath or difficulty breathing.

The National Pesticide Information Center receives calls concerning human incidents of pesticide exposure. There were 220 calls received concerning exposure to permethrin. Of this number, 36 vases were considered probable cases of permethrin exposure incidents. Nearly half of these cases had skin complaints (e.g., rash, itching, pain or burning sensation) and nearly half also report effects to the eyes (e.g., pain, irritation, tearing). Headache, dizziness, or light-headedness were reported by nearly half the cases and respiratory problems such as tight chest or difficulty breathing were reported by 22% of the probable cases. Six (17%) reported asthma or asthma-like symptoms and 6 cases reported problems with the permethrin product used for termite treatment.

The National Institute of Occupational Safety and Health manages a program called SENSOR - Sentinel Event Notification *System for Occupational Risk.* Through this program, from 1998 through 2002, seven NIOSH SENSOR states received 40 reports of exposure to permethrin in a single product, 22 of which were from states other than California. Because California pesticide poisoning incidents have already been discussed, an analysis of the other cases is presented here. Eighteen of the non-California cases were reported as having minor effects and four were classified as moderate. Three cases were classified as definite, three probable, 13 as possible, and 3 as suspicious. Dermal symptoms were most common reported in 10 of 22 cases. Ocular symptoms were reported in six cases, respiratory and gastrointestinal symptoms in 9 cases each, and neurological symptoms in 7 cases.

A review of the scientific literature indicates symptoms similar to those already reported are common in study groups. Reported symptoms included eye irritation, itching, nasal secretions, headache (Kolomodin-Hedman et al., (1982) as reported by Blondell and Hawkins, 2004). Notably, Edling et al. (1985)) reported numbness in the lips as an effect. Also, the World Health Organization published a summary of the literature and noted a study of 23 laboratory workers involved in field trials. In this study, the most frequent symptom was a facial sensation described as tingling or burning. This did not occur when permethrin alone was involved but when exposures included cypermethrin, fenvalerate, or fenpropathrin. These findings correlate with the results of animal studies used in this assessment. The general symptoms reported also suggests that permethrin products are more likely to cause a direct irritative effect rather than an allergic reaction. The World Health Organization reported another study cited tested permethrin impregnated clothing on 10 male volunteers and they did not complain of any irritation. A third study tested permethrin for up to nine days using a patch test and 2 out of 17 volunteers developed mild erythema (flushing). A test of permethrin against head lice in 10 adults found 3 with mild, patchy erythema which faded away after 4-7 days. *The overall reported adverse effect rate is 2.5 per 1,000 patients.*

5.2 Animal Incident Reports

HED performed an animal incident data review in 2002 and reviewed that database again in April 2004 to note any changes or additions. This section reflects the most updated information concerning animal incident data from use of permethrin. (Internal communication: Kit Farwell, April 2004.) Permethrin is registered for use on many species of domestic animals (dogs, cats, cattle, horses, swine) for control of a variety of insects, including fleas, ticks, lice, mites, etc. Single ingredient products contain 0.25-65% active ingredient. Multiple ingredient products contain permethrin combined with other insecticides, insect growth regulators and synergists. Formulations include sprays, dusts, shampoos, dips, collars, concentrated spot-on preparations, pour-ons and ear tags. Concentrated (45%-65%) permethrin spot-on preparations are registered for use only on dogs; there are extremely toxic to cats.

HED requests that the registrants submit aggregate incident summary reports concerning injury/poisoning to domestic animals for individual permethrin products. Incidents reported are categorized in a range of severity from domestic animal death (DA) to clinical signs are unknown or not specified. Registrants are only required to report the number of animals in each

category, however, if OPP has concern about the number of incidents reported for a products, the Agency may request more detailed information. For Permethrin containing products, there were 18,343 incidents involving domestic animals reported from April 1, 1998 to March 31, 2002. The products included in this data base were both those used directly on animals and for other uses such as household ant or roach killer. A review of the data showed two products were responsible for the majority of the incidents with domestic animals: Hartz One Spot Repellant for Dogs (2596-137) and Hartz Control One Spot for Dogs and Puppies (2596-146). HED notes that the incidents reported for the Ortho-Ant Killer Spray (239-2678) in the *Review of Domestic Animal Incident Data for Reregistration Eligibility Decision (RED). V. Dobozy. DP Barcode D279521. TXR 0050902. July 9, 2002* was incorrectly identified.

There is evidence that a majority of the incidents for Hartz Control One Spot for Dogs and Puppies involve cats. Care reports for the incidents recorded for this product show that the majority of domestic animal deaths reported for this product, 59%, involved cats which were accidently or intentionally treated with the product and some of the deaths of cats (7%) involved exposure to treated dogs. Symptoms in cats reported before death include tremors, seizures and ataxia. Exposure of cats to permethrin can cause life-threatening toxicosis because cats, as compared to other domestic animals, are relatively deficient in their ability to conjugate xenobiotics with glucuronic acid, which is the most important step in the metabolism of certain substances. Therefore, they metabolize many chemicals more slowly than other species.

EPA/RD has previously suggested label changes to make it more clear to domestic animal owners/caretakers of the potential for adverse affects occurring to cats as a result of either direct or indirect permethrin exposure. At the time of this writing, the suggested label changes have not been made by the registrants. As a result, HED has the following recommendations regarding the conclusions of the domestic animal incident report:

1. Some permethrin products for use on domestic animals may have been registered prior to the uniform requirement of a companion animal safety study. It is recommended that these studies be required for the reregistration of such products.

2. Severe adverse reactions, including deaths, in cats intentionally or mistakenly exposed directly to concentrated (45 and 65%) permethrin products or secondarily exposed to treated dogs are a major concern. HED recommends that OPP consult with the ASPCA/APCC about the overall magnitude of permethrin toxicity in cats and whether label revisions are a reasonable solution both to direct and secondarily exposures.

6.0 Exposure Assessment and Characterization

6.1 Dietary Exposure Pathway

6.1.1 Residue Profile

The qualitative nature of permethrin residues in plants and animals is adequately understood based on the adequate soybean, cabbage, and sweet corn metabolism studies and the oral and dermal ruminant and poultry metabolism studies. In the most recent review of metabolism data, the Metabolism Assessment Review Committee (MARC memo by S. Kinard, Y. Yang, and J. Melendez dated July 6, 2004) concluded that the residues of concern in plants and animals include *cis*- and *trans*-permethrin for purposes of both tolerance reassessment and risk assessment.

With the exception of cottonseed, tolerances for permethrin residues in/on plant raw agricultural commodities (RACs) are currently expressed in terms of the combined residues of permethrin and its metabolites, 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylic acid (DCVA) and (3-phenoxyphenyl) methanol (MPBA) [40 CFR §180.378 (b) and (d)]. Tolerances for residues of permethrin in/on cottonseed (0.5 ppm) are expressed in terms of permethrin *per se* [40 CFR §180.378 (a)]. Tolerances for permethrin residues in/on animal RACs are currently expressed in terms of the combined residues of permethrin, DCVA, MPBA, and 3-phenoxybenzoic acid (3-PBA) [40 CFR §180.378 (c)].

Adequate GC electron capture detection (GC/ECD) methods are available for enforcing tolerances of permethrin *per se* and are listed in PAM Vol. II (Section 180.378). Method I is a GC/ECD method for determining permethrin in plant matrices and has a limit of quantitation (LOQ) of 0.05 ppm for each isomer. Method II is a GC/ECD method for determining permethrin in animal matrices that has a LOQ of 0.01 ppm for each isomer. In addition, permethrin is completely recovered using FDA Multiresidue Methods (PAM Vol. I Sections 302 and 304).

In addition to the uses on crops and livestock, permethrin is registered for use in food-handling establishments. Although residue data on representative foods have not been submitted to support this use, the current label restrictions for uses in food-handling establishments are such that residues of permethrin are unlikely to occur in/on food commodities when permethrin is applied in accordance with the amended label directions. However, confirmatory food residue data are still required at the present time to ensure no detectable residues in food when permethrin is applied in residential areas while food is present. The registrant should submit a protocal on the determination of residues in food when permethrin is applied at maximum application rates to areas containing uncovered and covered food products.

Reregistration requirements for magnitude of the residues in animals are fulfilled provided supporting storage stability data for representative animal commodities are submitted and deemed adequate. Data are available from studies depicting residues in animal commodities following direct treatment of cattle, swine, and poultry and their premises with permethrin. Data are also available from several cattle and poultry feeding studies. Based upon residue data from

these studies, dietary exposure to permethrin residues is the route that can result in the highest potential residues in animal commodities. Therefore, data from the ruminant and poultry feeding studies were used as the basis for reassessing tolerances for animal commodities. Based on the reassessed tolerances for livestock feed items, the maximum theoretical dietary burdens (MTDB) of permethrin residues for livestock are 34.1 ppm for beef cattle, 40.3 ppm for dairy cattle, 4.56 ppm for poultry, and 0.06 ppm for swine.

Reregistration requirements for magnitude of the residue in plants are fulfilled for the following crops: alfalfa, almonds, apples, artichokes, asparagus, avocados, broccoli, Brussels sprouts, cauliflower, celery, cherries, corn, cucurbit vegetables, filberts, horseradish, lettuce (head), onions (dry bulb), papayas, peppers (bell), pistachios, potatoes, spinach, turnips, and walnuts. Adequate field trial data depicting permethrin residues following applications made according to the maximum use patterns have been submitted for these crops. Although complete sets of data are not available on all crops depicting use of permethrin formulated as a WP, these data are not required as bridging data from side-by-side trials using EC and WP formulations indicate that permethrin residues resulting from application of an EC are consistently higher or no different than permethrin residues resulting from application of a WP.

The adequate data from bell peppers will be translated to supplement the residue data on eggplants. Adequate data are also available on soybeans, provided use directions for soybeans are amended to specify a minimum volume of 2 gal/A for aerial applications; otherwise, residue data supporting ULV applications to soybeans are required. Additional field trail data are required on cabbage, collards, grasses (rangeland), leaf lettuce, tomatoes and sweet corn (FL only), and information is also required to upgrade the existing mushroom, peach, and pear field trials.

The reregistration requirements for magnitude of the residue in processed food/feed commodities are also fulfilled for apple, corn, potatoes, soybeans, and tomatoes. Based on the available processing studies, tolerances for permethrin are not required on apple, corn (field), potato, soybean, and tomato processed commodities. However, data from the corn grain processing study indicate that a separate tolerance is necessary for aspirated grain fractions. Residues of permethrin concentrated by 19.3x in corn aspirated grain fractions. Based on the highest average field trial (HAFT) residues for field corn grain and the above concentration factor, the maximum expected residues in corn aspirated grain fractions would be 0.386 ppm.

Adequate confined and limited field rotational crop studies are available for assessing the potential of inadvertent residues occurring in rotational crops following applications of permethrin to primary crops totaling 2.0 lb ai/A/season, which is 1x the maximum seasonal use rate on any rotated crops. The metabolism in rotational crops is similar to the primary crops. For purposes of tolerance enforcement and risk assessment the residues of concern consist of the *cis*-and *trans*-permethrin isomers. The limited rotational field trial data indicate that tolerances for residues of permethrin in rotational crops are not required, provided labels specify a 60-day plant-back interval (PBI) for crops not listed on the labels.

6.1.2 Acute and Chronic Dietary Exposure and Risk

Acute, chronic, and cancer dietary (food and water) exposure risk assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The acute, chronic, and cancer dietary risk assessments were conducted for all supported permethrin food uses and were performed to support the reregistration eligibility decision.

Highly refined acute (probabilistic), chronic, and cancer dietary exposure assessments were conducted to estimate the dietary risks associated with the reregistration of permethrin. Permethrin residue estimates used in these assessments include cis- and trans-permethrin calculated as total permethrin along with the percent crop treated (%CT) estimates reported by the Biological and Economic Analysis Division (BEAD). The anticipated residue (AR) estimates are based primarily on the USDA PDP food sampling data. Processing data was also used on a number of crops if available.

The estimated surface drinking water concentrations (EDWCs) for permethrin were calculated using Tier II PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modeling System) for use in the human health risk assessment. The EDWCs for permethrin were calculated based on a maximum application rate of 2.0 lb ai/A and were incorporated into the DEEM-FCID analyses.

Acute dietary risk estimates are provided for the general U.S. population and various population subgroups, with the major emphasis placed on the exposure estimates for infants and children. This assessment concludes that for all supported registered commodities, the acute risk estimates do not exceed HED's level of concern (less than 100%) at the 99.9th exposure percentile for the U.S. population (4% aPAD) and all population subgroups, with the highest exposed population subgroup being infants at 16% aPAD.

Chronic dietary risk estimates are provided for the general U.S. population and various population subgroups, with the major emphasis placed on the exposure estimates for infants and children. This assessment also concludes that for all supported registered commodities, the chronic risk estimates do not exceed HED's level of concern for the U.S. population and all population subgroups (all populations were less than 1% cPAD).

Cancer dietary risk estimates are provided for the general U.S. population and resulted in a estimated cancer risk of 1.1×10^{-6}. The estimated dietary cancer risk for the general U.S. population exceeds HED's level of concern (greater than $1.0 \times 10^{-6)}$. The significant cancer risk contributors have been identified as water (direct and indirect, all sources), spinach, and egg (whole).

Table 6.1. Summary of Food and Water Dietary Exposure and Risk for Permethrin						
	Acute Dietary (99.9^{th} Percentile)		Chronic Dietary		Cancer	
Population Subgroup	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	0.010971	4	0.000121	<1	**0.000117**	**1.1×10^{-6}**
All Infants (< 1 year old)	**0.039416**	**16**	**0.000283**	**<1**		
Children 1-2 years old	0.024494	10	0.000263	<1		
Children 3-5 years old	0.017287	7	0.000194	<1		
Children 6-12 years old	0.009144	4	0.000114	<1		
Youth 13-19 years old	0.009979	4	0.000078	<1		
Adults 20-49 years old	0.009660	4	0.000107	<1		
Adults 50+ years old	0.011689	5	0.000123	<1		
Females 13-49 years old	N/A	N/A	0.000112	<1	N/A	N/A

6.2 Water Exposure Pathway

This assessment presents Tier II Estimated Surface Drinking Water Concentrations (EDWCs), calculated using PRZM/EXAMS (surface water) and employing the Index Reservoir (IR) water body with a Percent Crop Area (PCA) adjustment. Groundwater concentrations were estimated using the Tier 1 model SCI-GROW.

The EDWCs for permethrin were calculated based on a maximum application rate of 2.0 lb a.i./A. The acute concentration in surface water is 4.79 ppb of permethrin. The cancer and chronic concentrations are 0.751 ppb and 0.901 ppb, respectively, using the Georgia onion scenario. These values represent the mean value over a 30-year period. The SCI-GROW generated EDWC for lettuce, almonds, or onions (highest application rate) is 0.012 ppb of permethrin, which is recommended for use, both for acute and chronic exposures.

These values generally represent upper-bound estimates of the concentrations that might be found in surface water and groundwater due to the use of permethrin on almonds, peppers, onions, peaches, and lettuce which represent the scenarios with the highest application rates, and with the lowest intervals between applications. Both models provide estimates suitable for screening purposes.

Table 6.2. Summary of Estimated Surface and Groundwater Concentrations for Permethrrin		
Exposure Duration	**Permethrin**	
	Surface Water Conc., ppb [a]	**Groundwater Conc., ppb [b]**
Acute	4.79	0.012
Chronic (non-cancer)	0.90	0.012
Chronic (cancer)	0.75	0.012

[a] From the Tier II PRZM-EXAMS - Index Reservoir model. Input parameters are based on a maximum application rate of 2.0 lb a.i./A.
[b] From the Tier I SCI-GROW model assuming a maximum seasonal use rate of 2.0 lb ai/A, a K_{oc} of 170,000, and, aerobic soil half-life of 37 days.

6.3 Residential (Non-Occupational) Exposure/Risk Pathway

At this time, products containing permethrin are intended for both occupational and non-occupational uses. Residential homeowners may use permethrin in a variety of indoor and outdoor residential environments including: lawns, gardens, indoor surfaces and spaces, ornamentals, and on pets. Due to this use profile, adult residential homeowners may experience exposure to permethrin during application of the chemical (i.e., residential handler exposures). Adults and children may experience exposure to permethrin when contacting permethrin-treated areas (i.e., residential postapplication exposure). Risk assessments presented in this section reflect potential exposures to adult residential handlers and potential postapplication exposure to adults and children of varying ages.

In addition to homeowner uses in residential settings, permethrin is labeled for mosquito adulticide use, which is applied by occupational handlers, but may result in postapplication exposures in residential settings. Permethrin is also used in residential automatic misting systems for mosquito control, as well as impregnated into clothing which also may result in occupational handler exposure and residential postapplication exposure. These potential postapplication exposures to adults and children also have been considered in this assessment.

Short-term exposures (defined as exposures from 1 to 30 days in duration) may occur for residents applying permethrin products and for residents exposed to permethrin following applications in residential settings. Intermediate- and long-term exposures are not anticipated for residential handling or postapplication exposures, due to the episodic nature of the applications. The dermal toxicological endpoint of concern (500 mg/kg/day) is the same for short-, intermediate-, and long-term dermal exposures and is based on a 21-day dermal toxicity study in rats. Since the dermal endpoints are based on a dermal study, no dermal absorption factor is necessary to complete the dermal assessments. The inhalation toxicological endpoint of concern (11 mg/kg/day) is also the same for short-, intermediate-, and long-term inhalation exposures and is based on a 15-day inhalation study in rats. Since the inhalation endpoints are based on an inhalation study, no inhalation absorption factor is necessary to complete the inhalation

assessments. The dermal and inhalation risks were combined for this assessment, because the adverse effects for the dermal and inhalation routes of exposure were the same (neurotoxicity).

6.3.1 Home Uses

The permethrin assessment reflects HED's current approaches for completing residential exposure assessments based on the guidance provided in the OPPTS Harmonized Guidelines, Series 875: Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines, the Draft: Standard Operating Procedures (SOPs) for Residential Exposure Assessment, and the Overview of Issues Related to the Standard Operating Procedures for Residential Exposure Assessment presented at the September 1999 meeting of the FIFRA Scientific Advisory Panel (SAP). The Agency is, however, currently in the process of revising its guidance for completing these types of assessments.

6.3.1.1 Residential Handlers - Noncancer

Scenarios used to define risks are based on the *U.S. EPA Guidelines for Exposure Assessment* (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Assessing exposures and risks resulting from residential uses is very similar to assessing occupational exposures and risks, with the following exceptions: 1) residential handler exposure scenarios are considered to be short-term only, due to the infrequent use patterns associated with homeowner products, 2) homeowner handler assessments are based on the assumption that individuals are wearing shorts, short-sleeved shirts, socks, and shoes [no personal protective equipment (PPE)], and 3) homeowner handlers are expected to complete all tasks associated with the use of a pesticide product including mixing/ loading, if needed, as well as the application.

The anticipated use patterns and current labeling indicate several likely residential handler exposure scenarios, based on the types of equipment and techniques that can potentially be used to apply permethrin in residential settings. Due to the scope of the various permethrin residential uses (there are over 900 permethrin products registered), it is extremely difficult to assess each individual exposure scenario. Therefore, HED selected representative exposure scenarios to reflect the major ways in which permethrin can be applied in the residential environment. HED believes this approach is protective of public health as the scenarios likely to result in the greatest exposure are considered. Anticipated use pattern and current labeling indicate 25 likely residential exposure scenarios based on the types of equipment and techniques that can potentially be used to make permethrin applications. Scenarios in this document include the following (scenarios denoted with a "*" could not be evaluated quantitatively, because applicable unit exposure data are not available):

Mixer/Loader/Applicators:
(1) Liquid: Low Pressure Handwand;
(2) Liquid: Backpack Sprayer;
(3) Liquid: Hose-End Sprayer;
(4) Liquid: Watering Can;
(5) Liquid: Paint Brush;

(6) Liquid: Sponge;
(7) Liquid: Automatic Mister Systems
(8) Granulars: Push Type Spreader;
(9) Granulars: Belly Grinder;
(10) Granulars: Spoon or Cup;
(11) Dusts: Spoon or Cup;
(12) Dusts: Shaker Can;
(13) Dusts: Rotary Duster/Dust Gun*;
(14) Dusts: FPO Puffer Can*;
(15) RTU Liquids: Pour-on (using PHED liquid mixing/loading data);
(16) RTU Cream: Applicator Tube*;
(17) RTU Shampoos: Hands;
(18) RTU Wipe Applications (using CMA data);
(19) RTU: Trigger Pump Sprayer Applications;
(20) RTU: Aerosol Cans;
(21) RTU: Fogger (using PHED aerosol can data);
(22) RTU Mattress Liners *;
(23) RTU Tubes (for use on lawns)*;
(24) RTU Chair and Table Coasters*;
(25) RTU Protective Flanges*.

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments. Each assumption and factor is detailed below. In addition to these factors, unit exposure values were used to calculate risk estimates. Unit exposure values were derived from the following exposure data:

- the Pesticide Handler Exposure Database (PHED);
- the Outdoor Residential Task Force (ORETF) studies;
- the Non-Dietary Exposure Task Force (NDETF) Studies;
- the Chemical Manufacturers Association (CMA) Antimicrobial Exposure Assessment Study; and
- four proprietary exposure studies reflecting the following scenarios-
  - handlers applying dusts via shaker can or by hand (MRID # 444399-01),
  - handlers applying granulars via spoon and cup (MRID # 452507-02),
  - handlers applying liquids via trigger sprayer (MRID # 410547-01), and
  - postapplication exposure to dog shampoos (MRID # 466010-01).

The noncancer residential handler exposure risk estimates are included in Table 6.3.1.1. Scenarios that could not be evaluated quantitatively are not presented in the table. The results indicate that all of the residential handler risks do not exceed HED's level of concern [i.e., MOEs are all greater than 100]. In order to refine this residential handler risk assessment, more data on actual use patterns including rates, timing, and areas treated would better characterize risks.

Table 6.3.1.1. Summary of Short-Term Permethrin Residential Handler Noncancer Risk Estimates						
Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Baseline MOEs		
				Dermal	Inhalation	Combined
Mixer/Loader/Applicator						
Mixing/Loading/Applying Emulsifiable Concentrates with Low Pressure Handwand (1)	outdoor surfaces	0.046 lb ai/gallon	5 gallons	10000	1200000	**10000**
	ornamentals: outdoor trees	0.043 lb ai/gallon	5 gallons	11000	1300000	**11000**
	perimeter treatment, outdoor wood surfaces	0.04 lb ai/gallon	5 gallons	12000	1400000	**12000**
	ornamentals: outdoor	0.02 lb ai/gallon	5 gallons	23000	2900000	**23000**
	turf	0.005 lb ai/gallon	5 gallons	93000	11000000	**93000**
	almonds, filberts, pears, pistachios	0.004 lb ai/gallon	5 gallons	120000	14000000	**120000**
	apples, peaches	0.0033 lb ai/gallon	5 gallons	140000	17000000	**140000**
	celery, cherries, eggplant, horseradish, head lettuce, ornamentals: indoor, ornamentals: outdoor (trees, shrubs, roses, flowers, woody plants), potatoes, peppers, sweet corn; animal premises: dogs	0.002 lb ai/gallon	5 gallons	230000	29000000	**230000**
	asparagus, broccoli, brussel sprouts, cabbage, cauliflower, spinach	0.0012 lb ai/gallon	5 gallons	390000	48000000	**390000**
	fire ant mounds	0.1 lb ai/mound	5 mounds	4700	570000	**4600**
	animal: dogs, horses	0.00075 lb ai/animal	2 animals	1600000	190000000	**1500000**
Mixing/Loading/Applying Emulsifiable Concentrates with Backpack Sprayer (2)	outdoor surfaces	0.046 lb ai/gallon	5 gallons	30000	110000	**24000**
	ornamentals: outdoor trees	0.043 lb ai/gallon	5 gallons	32000	120000	**25000**
	perimeter treatment, outdoor wood surfaces	0.04 lb ai/gallon	5 gallons	34000	130000	**27000**
	ornamentals: outdoor	0.02 lb ai/gallon	5 gallons	69000	260000	**54000**
	turf	0.005 lb ai/gallon	5 gallons	270000	1000000	**220000**
	almonds, filberts, pears, pistachios	0.004 lb ai/gallon	5 gallons	340000	1300000	**270000**
	apples, peaches	0.0033 lb ai/gallon	5 gallons	420000	1600000	**330000**
	celery, cherries, eggplant, horseradish, head lettuce, ornamentals: indoor, ornamentals: outdoor (trees, shrubs, roses, flowers, woody plants), potatoes, peppers, sweet corn; animal premises: dogs	0.002 lb ai/gallon	5 gallons	690000	2600000	**540000**
	fire ant mounds	0.1 lb ai/mound	5 mounds	14000	51000	**11000**
	asparagus, broccoli, brussel sprouts, cabbage, cauliflower, spinach	0.0012 lb ai/gallon	5 gallons	1100000	4300000	**900000**
	animal: dogs, horses	0.00075 lb ai/animal	2 animals	4600000	17000000	**3600000**
Mixing/Loading/Applying Emulsifiable Concentrates with Hose-End Sprayer (ORETF data) (3)	turf	0.087 lb ai/acre	0.5 acres	73000	1100000	**69000**
	ornamentals: outdoor trees	0.043 lb ai/gallon	100 gallons	740	11000	**690**
	stored lumber, wood piles	0.04 lb ai/gallon	100 gallons	800	12000	**750**
	ornamentals: outdoor	0.02 lb ai/gallon	100 gallons	1600	24000	**1500**
	almonds, filberts, pears, pistachios	0.004 lb ai/gallon	100 gallons	8000	120000	**7500**
	apples, peaches	0.003 lb ai/gallon	100 gallons	11000	160000	**9900**
	cherries; ornamentals: outdoor herbaceous/ woody plants & shrubs	0.002 lb ai/gallon	100 gallons	16000	240000	**15000**
Mixing/Loading/Applying Emulsifiable Concentrates with a Watering Can (using	fire ant mounds	0.1 lb ai/mound	5 mounds	64000	960000	**60000**
	stored lumber, wood piles	0.04 lb ai/gallon	5 gallons	16000	240000	**15000**
	ornamentals: indoor	0.0017 lb ai/gallon	5 gallons	370000	5700000	**350000**

Table 6.3.1.1. Summary of Short-Term Permethrin Residential Handler Noncancer Risk Estimates						
Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Baseline MOEs		
				Dermal	Inhalation	Combined
ORETF residential hose-end data) (4)						
Mixing/Loading/Applying Emulsifiable Concentrates with a Paint Brush (5)	outdoor wood surfaces; outdoor surfaces	0.04 lb ai/gallon	1 gallon	3800	68000	**3600**
Mixing/Loading/Applying Emulsifiable Concentrates via Sponge (CMA data) (6)	horses	0.005 lb ai/gallon	2 gallons	1200	2800	**850**
Mixing/Loading Emulsifiable Concentrates for Automatic Mister Systems (7)	mosquitos	0.0023 lb ai/gallon	55 gallons	16000	5100000	**16000**
		0.0023 lb ai/gallon	250 gallons	3400	1100000	**3400**
Loading/Applying Granulars via Push Type Spreader (ORETF data) (8)	turf	0.65 lb ai/acre	0.5 acres	160000	2600000	**150000**
	perimeter treatment	0.015 lb ai/1000 sq ft	1000 sq ft	3400000	56000000	**3200000**
Loading/Applying Granulars via Belly Grinder (9)	perimeter treatment	0.015 lb ai/1000 sq ft	1000 sq ft	21000	830000	**21000**
Loading/Applying Granulars via Spoon or Cup (MRID 452507-01) (10)	fire ant mounds	0.00125 lb ai/mound	5 mounds	2800000	2700000	**1400000**
	ant mounds	0.000078 lb ai/mound	5 mounds	45000000	44000000	**22000000**
Loading/Applying Dusts via Spoon or Cup (MRID 444598-01) (11)	fire ant mounds	0.00156 lb ai/mound	5 mounds	30000	110000	**24000**
Mixing/Loading/Applying Dusts via Shaker Can (MRID 444598-01) (12)	indoor surfaces	0.05 lb ai/1000 sq ft	1000 sq ft	4700	18000	**3700**
	apples, asparagus, broccoli, brussel sprouts, cauliflower, cabbage, celery, cucumber, eggplant, garlic, head & leaf lettuce, muskmelon, onion: dry bulb, parsley, peaches, pepper: bell, potato, pumpkin, rhubarb, spinach, squash, sweet corn, tomato, walnuts	0.0025 lb ai/1lb container	1 lb container	95000	350000	**75000**
	animal premises: dogs and cats	0.0025 lb ai/1lb container	1/10 of 1 lb container	950000	3500000	**750000**
	animal: dogs, cats	0.00016 lb ai/animal	2 animals	740000	2800000	**580000**
Mixing/Loading/Applying Dusts via Rotary Duster/Dust Gun (13)	apples, asparagus, broccoli, brussel sprouts, cauliflower, cabbage, celery, cucumber, eggplant, garlic, head & leaf lettuce, muskmelon, onion: dry bulb, parsley, peaches, pepper: bell, potato, pumpkin, rhubarb, spinach, squash, sweet corn, tomato, walnuts	0.0025 lb ai/1lb container	1 lb container	No Data		
Mixing/Loading/Applying Dusts via FPO Puffer Can (14)	garden vegetables, ornamentals	0.00125 lb ai/1lb container	1 lb container	No Data	No Data	No Data
Applying Ready to Use Formulations via Pour-on (using PHED liquid mixer/loader data) (15)	animal: horses	0.005 lb ai/animal	2 animals	1200000	64000000	**1200000**
	clothing: personal	0.002 lb ai/6 oz container	1 container	6000000	320000000	**5900000**
Applying Ready to Use Cream Formulations via Applicator Tube (16)	animal: dogs	0.003 lb ai/animal	2 animals	No Data		
Applying Ready to Use	animal: dogs, cats	0.0014 lb ai/animal	2 animals	No Data		

Table 6.3.1.1. Summary of Short-Term Permethrin Residential Handler Noncancer Risk Estimates						
Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Baseline MOEs		
				Dermal	Inhalation	Combined
Formulations via Hands (17)						
Applying Ready to Use Formulations via RTU Wipe (CMA data) (18)	animal: dogs & horses	0.000077 lb ai/animal	2 animals	79000	180000	**55000**
Applying Ready to Use Formulations via Trigger-Pump Sprayer (using Propoxur study) (19)	ornamentals: outdoors; indoor surfaces	0.043 lb ai/gallon	1 gallon	60000	150000	**43000**
	animal: dogs	0.00034 lb ai/ounce	8 ounces (assume 1/2 16 oz bottle)	950000	2300000	**670000**
	animal: cats	0.000034 lb ai/ounce	8 ounces (assume 1/2 16 oz bottle)	9500000	23000000	**6700000**
	animal: horses, foals	0.016 lb ai/animal	2 animals	81000	200000	**57000**
Applying Ready to Use Formulations with Aerosol Cans (20)	outdoor & indoor surfaces	0.00438 lb ai/16 oz can	1 sixteen-ounce aerosol can	36000	73000	**24000**
	animal: dogs & cats; animal premises: dogs and cats	0.000538 lb ai/16 oz can	1/2 sixteen-ounce aerosol can	590000	1200000	**400000**
	ornamentals: indoor & outdoor	0.00213 lb ai/16 oz can	1 sixteen-ounce aerosol can	75000	150000	**50000**
Applying Ready to Use Formulations with Foggers (using PHED aerosol data) (21)	indoor spaces	0.0023 lb ai/6 oz fogger	2 six ounce fogger treats 6000 cubic feet	35000	70000	**23000**
Applying Ready to Use Mattress Liners (22)	mattress	0.143 lb ai/liner	No Data			
Applying Ready to Use Tubes (23)	outdoor surfaces	0.000733 lb ai/tube	No Data			
Applying Ready to Use Coasters (24)	ants	No Data				
Applying Ready to Use Protective Flanges (25)	ants	No Data				

Footnotes

a Application rates are the maximum application rates provided by for permethrin in all cases.

b Amount handled per day values are HED estimates of area treated or gallons applied based on Exposure SAC SOP #9 "Standard Values for Daily Acres Treated in Agriculture," industry input, and HED estimates.

6.3.1.2 Residential Handlers - Cancer

The residential handler exposure and cancer risk calculations are presented in this section. Cancer risk estimates were calculated using a linear, low-dose extrapolation approach (Q_1*). The same scenarios, assumptions, and unit exposures were used as in the noncancer assessment. HED estimated cancer risk assuming estimates for an annual a maximum of 1 day of exposure per year. In addition, HED calculated the maximum number of days of exposure per year that still would result in cancer risks less than or equal to $1x10^{-6}$ (HED's level of concern for residential cancer).

The revised cancer exposure and risk calculations for permethrin residential handler scenarios are presented in Table 6.3.1.2. There are four scenarios where the number of days to reach the target of $3x10^{-6}$ is 5 days or less. [**Note:** In general, the post-application risk estimates that reached the $\leq 3x10^{-6}$ negligible risk range after 5 or more exposure events per year (over a period of 50 years of a 70-year lifetime) are considered to be below HED's level of concern. For handler scenarios, this was based on data from the *Residential Exposure Joint Venture (REJV)* survey that showed that homeowners use permethrin products on an average of 5 times a year.] These include the following:

- mixing/loading/applying emulsifiable concentrates with low pressure handwand sprayer to fire ant mounds (0.1 lb ai/mound);
- mixing/loading/applying emulsifiable concentrates with hose-end sprayer to outdoor trees (0.043 lb ai/acre);
- mixing/loading/applying emulsifiable concentrates with hose-end sprayer to stored lumber and wood piles (0.04 lb ai/gallon); and
- mixing/loading emulsifiable concentrates for automatic mister systems (0.0023 lb ai/gallon and 250 gallons handled).

Table 6.3.1.2: Summary of Revised Permethrin Residential Handler Cancer Risk Estimates [a]					
Exposure Scenario	Crop or Target	Application Rate [b]	Area Treated Daily [c]	Residential Applicator Baseline Cancer Risk [d]	# of Days to Reach $3x10^{-6}$ Risk Level
Mixer/Loader/Applicator					
Mixing/Loading/Applying Emulsifiable Concentrates with Low Pressure Handwand (1)	outdoor surfaces	0.046 lb ai/gal	5 gal	5.3E-08	56
	ornamentals: outdoor trees	0.043 lb ai/gal	5 gal	4.9E-08	60
	perimeter treatment, outdoor wood surfaces	0.04 lb ai/gal	5 gal	4.6E-08	65
	ornamentals: outdoor	0.02 lb ai/gal	5 gal	2.3E-08	130
	turf	0.005 lb ai/gal	5 gal	5.7E-09	365
	almonds, filberts, pears, pistachios	0.004 lb ai/gal	5 gal	4.6E-09	365
	apples, peaches	0.0033 lb ai/gal	5 gal	3.8E-09	365
	celery, cherries, eggplant, horseradish, head lettuce, ornamentals: indoor, ornamentals: outdoor (trees, shrubs, roses, flowers, woody plants), potatoes, peppers, sweet corn; animal premises: dogs	0.002 lb ai/gal	5 gal	2.3E-09	365
	asparagus, broccoli, brussel sprouts, cabbage, cauliflower, spinach	0.0012 lb ai/gal	5 gal	1.4E-09	365
	fire ant mounds	0.1 lb ai/mound	5 mounds	1.1E-07	26
	animal: dogs, horses	0.00075 lb ai/animal	2 animals	3.4E-10	365
Mixing/Loading/Applying Emulsifiable Concentrates with Backpack Sprayer (2)	outdoor surfaces	0.046 lb ai/gal	5 gal	2.0E-08	152
	ornamentals: outdoor trees	0.043 lb ai/gal	5 gal	1.8E-08	162
	perimeter treatment, outdoor wood surfaces	0.04 lb ai/gal	5 gal	1.7E-08	174
	ornamentals: outdoor	0.02 lb ai/gal	5 gal	8.6E-09	349
	turf	0.005 lb ai/gal	5 gal	2.1E-09	365
	almonds, filberts, pears, pistachios	0.004 lb ai/gal	5 gal	1.7E-09	365
	apples, peaches	0.0033 lb ai/gal	5 gal	1.4E-09	365
	celery, cherries, eggplant, horseradish, head lettuce, ornamentals: indoor, ornamentals: outdoor (trees, shrubs, roses, flowers, woody plants), potatoes, peppers, sweet corn; animal premises: dogs	0.002 lb ai/gal	5 gal	8.6E-10	365
	asparagus, broccoli, brussel sprouts, cabbage, cauliflower, spinach	0.0012 lb ai/gal	5 gal	5.1E-10	365
	fire ant mounds	0.1 lb ai/mound	5 mounds	4.3E-08	69
	animal: dogs, horses	0.00075 lb ai/animal	2 animals	1.3E-10	365
Mixing/Loading/Applying Emulsifiable Concentrates with Hose-End Sprayer (ORETF data) (3)	turf	0.87 lb ai/A	0.5 A	7.5E-08	40
	ornamentals: outdoor trees	0.043 lb ai/gal	100 gal	7.4E-07	4
	stored lumber, wood piles	0.04 lb ai/gal	100 gal	6.9E-07	4
	ornamentals: outdoor	0.02 lb ai/gal	100 gal	3.4E-07	8
	almonds, filberts, pears, pistachios	0.004 lb ai/gal	100 gal	6.9E-08	43
	apples, peaches	0.003 lb ai/gal	100 gal	5.2E-08	58
	cherries; ornamentals: outdoor herbaceous/ woody plants & shrubs	0.002 lb ai/gal	100 gal	3.4E-08	87

Table 6.3.1.2: Summary of Revised Permethrin Residential Handler Cancer Risk Estimates [a]					
Exposure Scenario	Crop or Target	Application Rate [b]	Area Treated Daily [c]	Residential Applicator Baseline Cancer Risk [d]	# of Days to Reach $3x10^{-6}$ Risk Level
Mixing/Loading/Applying Emulsifiable Concentrates with a Watering Can (using ORETF residential hose-end data) (4)	fire ant mounds	0.1 lb ai/mound	5 mounds	8.6E-08	34
	stored lumber, wood piles	0.04 lb ai/gal	5 gal	3.4E-08	87
	ornamentals: indoor	0.0017 lb ai/gal	5 gal	1.5E-09	365
Mixing/Loading/Applying Emulsifiable Concentrates with a Paint Brush (5)	outdoor wood surfaces; outdoor surfaces	0.04 lb ai/gal	1 gal	1.4E-07	20
Mixing/Loading/Applying Emulsifiable Concentrates via Sponge (CMA data) (6)	horses	0.005 lb ai/gal	2 gal	5.1E-07	5
Mixing/Loading Emulsifiable Concentrates for Automatic Mister Systems (7)	mosquitos	0.0023 lb ai/gallon	55 gal	5.6E-09	365
		0.0023 lb ai/gallon	250 gal	2.6E-08	119
Loading/Applying Granulars via Push Type Spreader (ORETF data) (8)	turf	0.65 lb ai/A	0.5 A	3.4E-09	365
	perimeter treatment	0.015 lb ai/1000 sq ft	1000 sq ft	1.6E-10	365
Loading/Applying Granulars via Belly Grinder (9)	perimeter treatment	0.015 lb ai/1000 sq ft	1000 sq ft	2.5E-08	118
Loading/Applying Granulars via Spoon or Cup (MRID 452507-01) (10)	fire ant mounds	0.00125 lb ai/mound	5 mounds	2.6E-10	365
	ant mounds	0.000078 lb ai/mound	5 mounds	1.6E-11	365
Loading/Applying Dusts via Spoon or Cup (MRID 444598-01) (11)	fire ant mounds	0.00156 lb ai/mound	5 mounds	1.9E-08	154
Mixing/Loading/Applying Dusts via Shaker Can (MRID 444598-01) (12)	indoor surfaces	0.05 lb ai/1000 sq ft	1000 sq ft	1.2E-07	24
	apples, asparagus, broccoli, brussel sprouts, cauliflower, cabbage, celery, cucumber, eggplant, garlic, head & leaf lettuce, muskmelon, onion: dry bulb, parsley, peaches, pepper: bell, potato, pumpkin, rhubarb, spinach, squash, sweet corn, tomato, walnuts	0.0025 lb ai/1 lb container	1 lb container	6.2E-09	365
	animal premises: dogs and cats	0.0025 lb ai/1 lb container	1/10th of a 1 lb container	6.2E-10	365
	animal: dogs, cats	0.00016 lb ai/animal	2 animals	8.0E-10	365
Mixing/Loading/Applying Dusts via Rotary Duster or Dust Gun (13)	apples, asparagus, broccoli, brussel sprouts, cauliflower, cabbage, celery, cucumber, eggplant, garlic, head & leaf lettuce, muskmelon, onion: dry bulb, parsley, peaches, pepper: bell, potato, pumpkin, rhubarb, spinach, squash, sweet corn, tomato, walnuts	0.0025 lb ai/1 lb container	1 lb container	No Data	
Mixing/Loading/Applying	garden vegetables, ornamentals	0.00125 lb ai/1 lb	1 lb	No Data	

Table 6.3.1.2: Summary of Revised Permethrin Residential Handler Cancer Risk Estimates [a]					
Exposure Scenario	Crop or Target	Application Rate [b]	Area Treated Daily [c]	Residential Applicator Baseline Cancer Risk [d]	# of Days to Reach $3x10^{-6}$ Risk Level
Dusts via FPO Puffer Can (14)		container	container		
Applying Ready to Use Formulations via Pour-on (using PHED liquid mixer/loader data) (15)	animal: horses	0.005 lb ai/animal	2 animals	4.5E-10	365
	clothing: personal	0.002 lb ai/6 oz container	1 container	8.9E-11	365
Applying Ready to Use Cream Formulations via Applicator Tube (16)	animal: dogs	0.003 lb ai/animal	2 animals	No Data	
Applying Ready to Use Formulations via Hands (17)	animal: dogs, cats	0.0014 lb ai/animal	2 animals	No Data	
Applying Ready to Use Formulations via RTU Wipe (CMA data) (18)	animal: dogs & horses	0.000077 lb ai/animal	2 animals	7.9E-09	365
Applying Ready to Use Formulations via Trigger-Pump Sprayer (using Propoxur study) (19)	ornamentals: outdoors; indoor surfaces	0.043 lb ai/gal	1 gal	1.0E-08	292
	animal: dogs	0.00034 lb ai/oz	8 ounces	6.5E-10	365
	animal: cats	0.000034 lb ai/oz	8 ounces	6.5E-11	365
	animal: horses, foals	0.016 lb ai/animal	2 animals	7.6E-09	365
Applying Ready to Use Formulations with Aerosol Cans (20)	outdoor & indoor surfaces	0.00438 lb ai/16 oz can	1 sixteen-ounce aerosol can	1.8E-08	171
	animal: dogs & cats; animal premises: dogs and cats	0.000538 lb ai/16 oz can	0.5 sixteen-ounce aerosol can	1.1E-09	365
	ornamentals: indoor & outdoor	0.00213 lb ai/16 oz can	1 sixteen-ounce aerosol can	8.5E-09	352
Applying Ready to Use Formulations with Foggers (using PHED aerosol data) (21)	indoor spaces	0.0023 lb ai/6 oz fogger	2 six ounce fogger treats 6000 cubic feet	1.8E-08	163
Applying Ready to Use Mattress Liners (22)	mattress	0.143 lb ai/liner	No Data		
Applying Ready to Use Tubes (23)	outdoor surfaces	0.000733 lb ai/tube	No Data		
Applying Ready to Use Coasters (24)	ants	No Data			
Applying Ready to Use Protective Flanges (25)	ants	No Data			

Footnotes

a Cancer risk calculations utilize the permethrin Q_1^* $(mg/kg/day)^{-1} = 9.567 \times 10^{-3}$.

b Application rates are the maximum label application rates provided by for permethrin in all cases.

c Amount handled per day values are HED estimates of area treated or gallons applied based on Exposure SAC SOP #9 "Standard Values for Daily Acres Treated in Agriculture," industry input, and HED estimates.

d Cancer risk estimates were calculated for an annual frequency of 1 time per year.

6.3.1.3 Residential Noncancer Postapplication Exposures and Risks

HED uses the term "postapplication" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. Permethrin can be used in many areas that can be frequented by the general population including residential areas (e.g., home lawns and gardens). As a result, individuals can be exposed by entering these areas if they have been previously treated. Permethrin can also be used on companion animals, which can lead to exposures by contact with the treated animals. HED generically refers to these exposures as "residential" in nature. The residential populations that were considered in the assessment include:

- **Residential Adults engaged in:**
  - mowing or exercising on a treated lawn,
  - working in a treated garden, and
  - playing/exercising on treated indoor surfaces, such as carpeting or hard floors.

- **Residential Youth (representative age 10-12) engaged in:**
  - working in a treated garden.

- **Residential Children (representative age 1-5) engaged in:**
  - playing on a treated lawn (toddlers are the representative population),
  - playing on treated indoor surfaces, such as carpeting or hard floors (toddlers are the representative population), and
  - playing with treated companion animals.

The *Standard Operating Procedures (R-SOPs) For Residential Exposure Assessment* define several scenarios that apply to uses specified in current permethrin labels. These scenarios served as the basis for the residential postapplication assessment.

Noncancer risks were calculated using the MOE approach, which is a ratio of the body burden to the toxicological endpoint of concern. Exposures were calculated by considering the potential sources of exposure (i.e., DFRs on garden plants, TTRs on lawns, and transferable residues on treated pets), then calculating dermal and non-dietary ingestion exposures.

Adults: For all adult postapplication scenarios, short-term risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application. Table 6.3.1.3a presents the postapplication MOEs for adults following applications of permethrin.

Table 6.3.1.3a. Adult Residential Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Outdoors			
Residential Turf (High Contact Activities)	Dermal	0.87 lb ai/acre	20,000
Residential Turf (Mowing)	Dermal	0.87 lb ai/acre	580,000
Home Garden (Fruit and Nut Tree)	Dermal	0.4 lb ai/acre	6,100
Home Garden (Vegetables)	Dermal	0.23 lb ai/acre	21,000
Indoors			
Indoor Surfaces (High Contact Activities) – Broadcast Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	380
Indoor Surfaces (High Contact Activities) – Baseboard Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	630
Indoor Surfaces (High Contact Activities) – Crack and Crevice Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	1,900
Indoor Surfaces (High Contact Activities) – Broadcast Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	2,600
Indoor Surfaces (High Contact Activities) – Baseboard Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	4,300
Indoor Surfaces (High Contact Activities) – Crack and Crevice Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	13,000
Indoor Surfaces (High Contact Activities) - Aerosol (Carpet) [2]	Dermal	0.5 % a.i.	27,000
Indoor Surfaces (High Contact Activities) - Aerosol (Vinyl) [2]	Dermal	0.5 % a.i.	140,000
Indoor Surfaces (High Contact Activities) - Fogger (Carpet) [3]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	1,000
Indoor Surfaces (High Contact Activities) - Fogger (Vinyl) [3]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	5,300

[1] Deposition values based on data from 2007 Keenan doctoral dissertation.
[2] Surrogate data used from MRID 46188618, "Measurement of Air Concentration, Dermal Exposure, and Deposition of Pyrethrin and Piperonyl Butoxide Following the Use of an Aerosol Spray."
[3] Deposition data used from MRID 41688623, "Post-Application Deposition Measurements for Permethrin and Piperonyl Butoxide Following Use of a Total Release Indoor Fogger." Data showed a mean deposition rate of 4.8 ug/cm^2 when a 0.5% a.i. fogger was used. Deposition was normalized for this example.

Youth-aged children (10 to 12 years old): Short-term postapplication risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) for all scenarios involving youths. Table 6.3.1.3b below summarizes the postapplication MOEs for youth following applications of permethrin.

Table 6.3.1.3b. Youth Residential Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Home Garden (Fruit and Nut Tree)	Dermal	0.4 lb ai/acre	14,000
Home Garden (Vegetables)	Dermal	0.23 lb ai/acre	48,000

Toddler (3 year old): Short-term postapplication risks to toddlers were calculated following the lawncare, indoor, and pet uses of permethrin. The assessments for indoor and pet uses considered dermal and nondietary ingestion exposures. Short-term postapplication risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) for all scenarios involving toddlers

Table 6.3.1.3c. Toddler Residential Risk Estimates for Postapplication Exposure to Permethrin

Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Outdoors			
Hand to Mouth Activity on Turf	Oral	0.87 lb ai/acre	15,000
Object to Mouth Activity on Turf	Oral	0.87 lb ai/acre	250,000
Incidental Soil Ingestion	Oral	0.87 lb ai/acre	570,000
Incidental Ingestion of Granules	Oral	0.65 lb ai/acre	250
Residential Turf (High Contact Activities)	Dermal	0.87 lb ai/acre	12,000
Indoors			
Hand to Mouth Activity on Indoor Surfaces - Broadcast Spray (Carpet) [1]	Oral	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	120
Hand to Mouth Activity on Indoor Surfaces - Baseboard Spray (Carpet) [1]	Oral	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	200
Hand to Mouth Activity on Indoor Surfaces – Crack and Crevice Spray (Carpet) [1]	Oral	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	600
Hand to Mouth Activity on Indoor Surfaces – Broadcast Spray (Vinyl) [1]	Oral	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	470
Hand to Mouth Activity on Indoor Surfaces – Baseboard Spray (Vinyl) [1]	Oral	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	790
Hand to Mouth Activity on Indoor Surfaces – Crack and Crevice Spray (Vinyl) [1]	Oral	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	2,400
Hand to Mouth Activity on Indoor Surfaces - Aerosol (Carpet) [2]	Oral	0.5 % a.i.	8,500
Hand to Mouth Activity on Indoor Surfaces - Aerosol (Vinyl) [2]	Oral	0.5 % a.i.	33,000
Hand to Mouth Activity on Indoor Surfaces - Fogger (Carpet) [3]	Oral	0.0023 lb ai/6 oz fogger (0.58% a.i.)	320
Hand to Mouth Activity on Indoor Surfaces - Fogger (Vinyl) [3]	Oral	0.0023 lb ai/6 oz fogger (0.58% a.i.)	1,300
Indoor Surfaces (High Contact Activities) – Broadcast Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	230
Indoor Surfaces (High Contact Activities) – Baseboard Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	380
Indoor Surfaces (High Contact Activities) – Crack and Crevice Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	1,100
Indoor Surfaces (High Contact Activities) – Broadcast Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	1,600
Indoor Surfaces (High Contact Activities) – Baseboard Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	2,600
Indoor Surfaces (High Contact Activities) – Crack and Crevice Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	7,800
Indoor Surfaces (High Contact Activities) - Aerosol (Carpet) [2]	Dermal	0.5 % a.i.	16,000
Indoor Surfaces (High Contact Activities) - Aerosol (Vinyl) [2]	Dermal	0.5 % a.i.	84,000
Indoor Surfaces (High Contact Activities) - Fogger (Carpet) [3]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	610
Indoor Surfaces (High Contact Activities) - Fogger (Vinyl) [3]	Dermal	0.0023 lb ai/6 oz fogger	3,200

Table 6.3.1.3c. Toddler Residential Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
		(0.58% a.i.)	
Pets			
Hand to Mouth Activity on Pets – Dusts	Oral	0.00016 lb ai/animal	1,300
Hand to Mouth Activity on Pets - Shampoo [4]	Oral	0.0014 lb ai/animal	360
Pet Contact Activities - Spot on [5]	Oral	0.006 lb ai/animal	5,000
Pet Contact Activities – Dusts	Dermal	0.00016 lb ai/animal	1,600
Pet Contact Activities - Shampoo [4]	Dermal	0.0014 lb ai/animal	12,000
Pet Contact Activities - Spot on [5]	Dermal	0.006 lb ai/animal	1,200

[1] Deposition values based on data from 2007 Keenan doctoral dissertation.
[2] Surrogate data used from MRID 46188618, Measurement of Air Concentration, Dermal Exposure, and Deposition of Pyrethrin and Piperonyl Butoxide Following the Use of an Aerosol Spray.
[3] Deposition data used from MRID 41688623, "Post-Application Deposition Measurements for Permethrin and Piperonyl Butoxide Following Use of a Total Release Indoor Fogger." Data showed a mean deposition rate of 4.8 ug/cm^2 when a 0.5% a.i. fogger was used. Deposition was normalized for this example.
[4] Surrogate data used from MRID 466010-01, Human Exposure During and Following Use of a Pyrethrins/Piperonyl Butoxide/MGK 264 Shampoo Formulation on Dogs.
[5] Data used from MRID 465941-03, Stroking Test in Dogs after Topical Application of Imidacloprid 10% (w/v) + Permethrin 50% (w/v) Spot-On."

6.3.1.4 Residential Cancer Postapplication Exposures and Risks

The residential postapplication exposure and cancer risk calculations are presented in this section. Postapplication cancer risk estimates were calculated using a linear, low-dose extrapolation approach (Q_1*). The same scenarios, assumptions, and unit exposures were used as in the noncancer postapplication assessment. HED estimated cancer risk assuming a maximum of 1 day of exposure per year. In addition, HED calculated the maximum number of days of exposure per year that still would result in cancer risks less than or equal to $1x10^{-6}$ (HED's level of concern for residential cancer).

Table 6.3.1.4 below summarizes the postapplication risk estimates calculated for adults after applications of permethrin. It should be noted that these estimates represent one day of postapplication exposure per year and exposure on the day of application (i.e., day 0) for each year of a 50-year exposure period. HED has also calculated the number of exposure-days allowed per year to achieve a $1x10^{-6}$ cancer risk level of concern. HED lacks data to further refine the postapplication cancer assessments for turf and pets in residential settings. Section 6.3.1.4.1 discusses a draft approach for refining indoor cancer assessments. At this time, this draft approach should be viewed as characterization when indoor cancer risks are considered.

For all scenarios, estimated cancer risks do not exceed HED's target level of concern (i.e., risks are below 3×10^{-6}). There are three scenarios (high contact activities treated with broadcast sprays for carpets and vinyl; high contact activities treated with baseboard sprays for carpets) where the number of days to reach the target of $3x10^{-6}$ is 5 days or less. [**Note:** In general, the post-application risk estimates that reached the $\leq 3x10^{-6}$ negligible risk range after 5 or more exposure events per year (over a period of 50 years of a 70-year lifetime) are considered to be below HED's level of concern.]

Table 6.3.1.4. Summary of Permethrin Postapplication Residential Cancer Risks For Adults				
Exposure Scenario	Route of Exposure	Application Rate	Cancer Risk on Day of Application	# of Days to Reach $3x10^{-6}$ Risk Level
Outdoors				
Residential Turf (High Contact Activities)	Dermal	0.87 lb ai/acre	2.6×10^{-8}	114
Residential Turf (Mowing)	Dermal	0.87 lb ai/acre	9.2×10^{-10}	365
Home Garden (Fruit and Nut Tree)	Dermal	0.4 lb ai/acre	1.1×10^{-8}	276
Home Garden (Vegetables)	Dermal	0.23 lb ai/acre	2.6×10^{-8}	114
Indoors				
Hand to Mouth Activity on Indoor Surfaces - Broadcast Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	1.4×10^{-6}	2
Hand to Mouth Activity on Indoor Surfaces - Baseboard Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	8.4×10^{-7}	3
Hand to Mouth Activity on Indoor Surfaces – Crack and Crevice Spray (Carpet) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	2.8×10^{-7}	10
Hand to Mouth Activity on Indoor Surfaces – Broadcast Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	7.1×10^{-7}	4
Hand to Mouth Activity on Indoor Surfaces – Baseboard Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	4.3×10^{-7}	7
Hand to Mouth Activity on Indoor Surfaces – Crack and Crevice Spray (Vinyl) [1]	Dermal	0.5% a.i. (Assuming 3 ug/cm^2 deposition)	1.4×10^{-7}	21
Indoor Surfaces (High Contact Activities) - Aerosol (Carpet) [2]	Dermal	0.5% a.i.	2.0×10^{-8}	150
Indoor Surfaces (High Contact Activities) - Aerosol (Vinyl) [2]	Dermal	0.5% a.i.	1.0×10^{-8}	300
Indoor Surfaces (High Contact Activities) - Fogger (Carpet) [3]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	5.3×10^{-7}	5
Indoor Surfaces (High Contact Activities) - Fogger (Vinyl) [3]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	2.6×10^{-7}	11
Pets				
Pet Contact Activities - Dust	Dermal	0.00016 lb ai/animal	6.9×10^{-8}	43
Pet Contact Activities - Shampoo [4]	Dermal	0.0014 lb ai/animal	1.6×10^{-7}	18

[1] Deposition values based on data from 2007 Keenan doctoral dissertation.
[2] Surrogate data used from MRID 46188618, Measurement of Air Concentration, Dermal Exposure, and Deposition of Pyrethrin and Piperonyl Butoxide Following the Use of an Aerosol Spray."
[3] Deposition data used from MRID 41688623, "Post-Application Deposition Measurements for Permethrin and Piperonyl Butoxide Following Use of a Total Release Indoor Fogger." Data showed a mean deposition rate of 4.8 ug/cm^2 when a 0.5% a.i. fogger was used. Deposition was normalized for this example.
[4] Surrogate data used from MRID 466010-01, Human Exposure During and Following Use of a Pyrethrins/ Piperonyl Butoxide/MGK 264 Shampoo Formulation on Dogs

6.3.1.4.1 Draft Approach for Revising Indoor Cancer Risks

HED has recently developed a draft approach for refining indoor cancer assessments. The draft approach assumes that residues are only available for a certain period of time after an indoor application. During the days after an application, an applied pesticide can be impacted by a number of things including dissipation of residues, residue transfer to clothing, and removal by

vacuum. At some point in time, it can be assumed that residues of the applied pesticide are no longer available. Although residues may not be available, house dust may still provide an outlet for pesticide exposure. This draft approach attempts to provide a person's average combined exposure to the actual pesticide residues and the house dust which contains pesticide over an entire year. This will allow HED to provide a more accurate representation of what individuals may be exposed to over an entire year for performing cancer risk assessments.

Currently, HED has no data to verify what day after application residues are no longer available for transfer. For this draft approach, HED is conservatively assuming a 10% dissipation rate and assuming that residues will be available up to 28 days after application.

The levels of permethrin in house dust have been taken from a study entitled, "Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP)." This study was performed by the EPA's Office of Research and Development and it was designed to determine what commonly used chemicals are found in home and/or day care environments. A total of 129 dust samples were collected in OH and NC homes and 100% of these samples contained some level of permethrin.

HED used the REJV survey to determine the typical number of times per year that permethrin broadcast indoor applications and indoor fogger applications are used. The REJV survey is a 12 month longitudinal survey that examined pesticide use in a residential environment. The data evaluated by the HED in this analysis were information collected in 2001 and 2002. Using REJV, it was determined that 5 applications per year should be assumed for both broadcast and fogger indoor permethrin applications.

HED combined the starting permethrin depositions for broadcast and fogger applications (15 and 5.6 ug/cm^2, respectively) and assumed that these residues dissipated 10% per day for 28 days after application. This resulted in 140 total days of available permethrin residues. HED believes that 28 days of dissipation (after an indoor application) is a very high-end estimate because this assessment does not take into account removal processes such as vacuuming, transfer to clothing, etc. HED assumed that an individual could be exposed to permethrin found in house dust (from the CTEPP study) the other 225 days of the year. To calculate the average daily permethrin exposure value, the surface residues were averaged with permethrin found in house dust (samples labeled as, "home children at home" were used for this approach). This resulted in an average daily permethrin residue for broadcast applications of 1.95 ug/cm^2 and fogger applications of 0.73 ug/cm^2. Further explanation of how these numbers were calculated can be found in Appendix B.

At this time, HED believes that this draft approach should be viewed as characterization when indoor cancer risks are considered.

Table 6.3.1.4.1: Summary of Residential Permethrin Postapplication Cancer Risks For Adults				
Exposure Scenario	Route of Exposure	Application Rate [a]	Cancer Risk on Day of Application	# of Days to Reach $3x10^{-6}$ Risk Level
Indoor Surfaces (High Contact Activities) – Broadcast Spray (Carpet) [b,c,d]	Dermal	0.5% a.i. (Assuming 15 ug/cm^2 deposition)	1.8×10^{-7}	16
Indoor Surfaces (High Contact Activities) – Baseboard Spray (Carpet) [b,c,d]	Dermal	0.5% a.i. (Assuming 9 ug/cm^2 deposition)	1.1×10^{-7}	27
Indoor Surfaces (High Contact Activities) – Fogger (Carpet) [b,d]	Dermal	0.0023 lb ai/6 oz fogger (0.58% a.i.)	6.8×10^{-8}	43

a Application rates are the maximum label application rates provided by for permethrin in all cases.
b Assumes 5 applications occur in one year (from REJV).
c Deposition values based on data from 2007 Keenan doctoral dissertation.
d Deposition data used from MRID 41688623, "Post-Application Deposition Measurements for Permethrin and Piperonyl Butoxide Following Use of a Total Release Indoor Fogger." Data showed a mean deposition rate of 4.8 ug/cm^2 when a 0.5% a.i. fogger was used. Deposition was normalized to 5.6 ug/cm^2 for this scenario.

6.3.2 Other Uses Resulting in Residential Exposure

HED uses the term "postapplication" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. Permethrin can be impregnated in clothing which can lead to exposures during use of the clothing, and also be used as a mosquito adulticide which can result in postapplication exposures to the general population, because it involves wide area, ultra-low volume spraying in residential areas. HED generically refers to these exposures as "residential" in nature. The residential populations that were considered in the assessment include:

- **Residential Adults engaged in:**
  - wearing permethrin-impregnated clothing, and
  - any outdoor activity during a mosquito fogging application.

- **Residential Youth (representative age 10-12) engaged in:**
  - wearing permethrin-impregnated clothing

- **Residential Children (representative age 1-5) engaged in:**
  - wearing permethrin-impregnated clothing and
  - any outdoor activity during a mosquito fogging application.

The *Standard Operating Procedures (R-SOPs) For Residential Exposure Assessment* define several scenarios that apply to uses specified in current permethrin labels. These scenarios served as the basis for the residential postapplication assessment. Noncancer risks were calculated using the MOE approach, which is a ratio of the body burden to the toxicological endpoint of concern. Exposures were calculated by considering the potential sources of exposure (i.e., transferable residues from impregnated clothing), then calculating dermal and

non-dietary ingestion exposures. Inhalation exposures were calculated following truck-mounted mosquito fogger and aerial treatments.

6.3.2.1 Public Health

Permethrin labels allow for wide area applications such as mosquito control (for adulticides) and for the control of other pest species such as black fly. When HED considers these use patterns in risk assessments, the amount deposited on the turf is determined by the using the *AgDrift* model for aerial applications. All other components are similar to a residential turf risk assessment. However, in the case of permethrin, the maximum turf application rate is significantly higher than the maximum occupational mosquito control application rate (0.87 lb ai/acre versus 0.1 lb ai/acre) and thus HED believes that it is not necessary to separately analyze the postapplication dermal and incidental oral exposure risks resulting from mosquito applications.

The permethrin labels present a range of application rates from 0.007 to 0.1 lb ai/acre but the American Mosquito Control Association (AMCA) has stated that virtually all permethrin mosquito application labels allow no more than 0.007 lb/acre for aerial applications, and typical ground ULV applications ranging from 0.0010 lb/acre - 0.0035 lb/acre, with occasional use up to 0.007 lbs/acre. Once the deposition patterns have been defined, a turf-type risk assessment was completed accounting for different deposition patterns, compared to a typical turf risk assessment. Different deposition patterns were accounted for in the calculation of the turf transferable residues to which adults and children are exposed.

Adults: Short-term postapplication risks resulting from the public health mosquito use do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application. Table 6.3.2.1a presents the postapplication MOEs for adults following public health mosquito applications of permethrin.

Table 6.3.2.1a. Adult Public Health Mosquito Risk Estimates for Postapplication Exposure to Permethrin

Exposure Scenario	Route of Exposure	Application Rate[a]	MOE on Day of Application
Mosquitos (ULV Truck Fogger)	Inhalation	0.007 lb ai/acre	57,000
Mosquitos (ULV Aerial)	Inhalation	0.007 lb ai/acre	5.0×10^{11}

Toddler (3 year old): Short-term postapplication risks to toddlers were calculated following the public health mosquito use of permethrin. Table 6.3.2.1b presents a summary of the MOE estimates for toddlers. Short-term MOEs from inhalation exposures to ULV truck fogger and aerial mosquito treatments do not exceed HED's level of concern (i.e., the MOEs are greater than 100).

Table 6.3.2.1b. Toddler Public Health Mosquito Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Mosquitos (ULV Truck Fogger)	Inhalation	0.007 lb ai/acre	28,000
Mosquitos (ULV Aerial)	Inhalation	0.007 lb ai/acre	2.5×10^{11}

Table 6.3.2.1c below summarizes the postapplication risk estimates resulting from the public health mosquito use calculated for adults after applications of permethrin. It should be noted that these estimates represent one day of postapplication exposure per year and exposure on the day of application (i.e., day 0) for each year of a 50-year exposure period. HED lacks data to further refine postapplication cancer assessments in residential settings. For all scenarios, estimated cancer risks do not exceed HED's target level of concern (i.e., risks are below 3×10^{-6}).

Table 6.3.2.1c. Summary of Permethrin Postapplication Public Health Mosquito Cancer Risks For Adults				
Exposure Scenario	Route of Exposure	Application Rate[a]	Cancer Risk on Day of Application[b]	Days/Year to Reach LOC[c]
Mosquitos (ULV Truck Fogger)	Inhalation	0.007 lb ai/acre	3.6×10^{-9}	365
Mosquitos (ULV Aerial)	Inhalation	0.007 lb ai/acre	4.1×10^{-16}	365

Footnotes

a Application rates are the maximum application rates for permethrin in all cases; typical rates were not available.

b Cancer risk estimates were calculated assuming one day of exposure per year.

c HED calculated the maximum number of days of exposure per year that still would result in cancer risks less than or equal to a 1×10^{-6}.

6.3.2.2 Residential Automatic Misting Systems

Postapplication exposures from residential mosquito control applications (i.e., automatic mister systems) have not been previously addressed by HED. HED has recently compiled a draft methodology to assess this type of application equipment which involves defining how much material is deposited on the ground in impacted areas and then using the same methodology that is used for a residential lawn risk assessment. However, in the case of permethrin, the maximum turf application rate is significantly higher than the maximum automatic mister system application rate (0.87 lb ai/acre versus 0.0057 lb ai/acre) and thus HED believes that it is not necessary to separately analyze the postapplication dermal and incidental oral exposure risks resulting from mosquito applications.

Inhalation exposure usually does not factor significantly into postapplication risk. However, due to the use of permethrin in automatic mister systems to control mosquitos around homes, a risk assessment has been developed for residential postapplication inhalation exposure from automatic mister systems. The approach for the automatic mister systems was part of the

recently compiled draft methodology and it is based on the SOP for inhalation exposure to outdoor residential short-term pest control.

Adults: Short-term postapplication risks to adults resulting from the automatic misting system applications do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application. Table 6.3.2.2a presents the postapplication MOE for adults following automatic misting system applications of permethrin.

Table 6.3.2.2a. Adult Mosquito Automatic Misting Systems Risk Estimates for Postapplication Exposure to Permethrin

Exposure Scenario	Route of Exposure	Application Rate[a]	MOE on Day of Application
Mosquitos (Automatic Misting Systems)	Inhalation	1.1E-05 lb ai/1000 cu ft	160,000

Toddler (3 year old): Short-term postapplication risks to toddlers were calculated following the automatic misting system applications of permethrin. Table 6.3.2.2b presents a summary of the MOE estimates for toddlers. Short-term MOE from inhalation exposures to automatic misting system applications do not exceed HED's level of concern (i.e., the MOEs are greater than 100).

Table 6.3.2.2b. Toddler Mosquito Automatic Misting Systems Risk Estimates for Postapplication Exposure to Permethrin

Exposure Scenario	Route of Exposure	Application Rate[a]	MOE on Day of Application
Mosquitos (Automatic Misting Systems)	Inhalation	1.1E-05 lb ai/1000 cu ft	69,000

Table 6.3.2.2c below summarizes the postapplication risk estimates resulting from the automatic misting system application of permethrin calculated for adults. It should be noted that these estimates represent one day of postapplication exposure per year and exposure on the day of application (i.e., day 0) for each year of a 50-year exposure period. HED lacks data to further refine postapplication cancer assessments in residential settings. For all scenarios, estimated cancer risks do not exceed HED's target level of concern (i.e., risks are below 3×10^{-6}).

Table 6.3.2.2c. Summary of Permethrin Postapplication Mosquito Automatic Misting Systems Cancer Risks For Adults

Exposure Scenario	Route of Exposure	Application Rate[a]	Cancer Risk on Day of Application[b]	Days/Year to Reach LOC[c]
Mosquitos (Automatic Misting Systems)	Inhalation	1.1E-05 lb ai/1000 cu ft	1.3×10^{-11}	365

Footnotes

a Application rates are the maximum application rates for permethrin in all cases; typical rates were not available.

b Cancer risk estimates were calculated assuming one day of exposure per year.

c HED calculated the maximum number of days of exposure per year that still would result in cancer risks less than or equal to a 1×10^{-6}.

6.3.2.3 Impregnated Clothing

HED is aware that there is a variety of commercial application/impregnation methods currently being used to produce permethrin impregnated clothing. HED believes that some of the new more technologically advanced application/impregnation methods will result in less exposure to individuals wearing this clothing. Currently, HED's permethrin impregnated clothing assessment utilizes data collected from clothing treated with older and less technologically advanced application/impregnation methods. In 2006, HED received a pilot exposure study based on the impregnation method currently being used by BUZZ OFF Insect Shield LLC to produce permethrin impregnated clothing. This study was reviewed by HED and it was determined to be scientificly valid. However, the study includes a very limited number of biomonitoring and patch replicates and thus is not applicable for use in the assessment of this scenario for permethrin. The Agency believes that the current assessment results in conservative and protective estimates of exposure and risk to permethrin impregnated clothing produced by any currently used application/impregnation method.

When assessing postapplication exposures to impregnated clothing, HED used the latest EPA Antimicrobial Division (AD) approaches to estimate the postapplication exposures.

Adults: Short-term postapplication risks from wearing impregnated clothing do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application. Table 6.3.2.3a presents the postapplication MOEs for adults following applications of permethrin.

Table 6.3.2.3a. Adult Impregnated Clothing Risk Estimates for Postapplication Exposure to Permethrin

Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Impregnated Clothing: Long Sleeve Shirt	Dermal	0.125 mg ai/cm^2	6,200
Impregnated Clothing: Long Sleeve Shirt/Long Pants	Dermal	0.125 mg ai/cm^2	3,800

Youth-aged children (10 to 12 years old): The assessments for youth-aged children's exposure to permethrin impregnated clothing only considered dermal exposures. Short-term postapplication risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) for impregnated clothing scenarios involving youths. Table 6.3.2.3b below summarizes the postapplication MOEs for youth following applications of permethrin.

Table 6.3.2.3b. Youth Impregnated Clothing Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Impregnated Clothing: Long Sleeve Shirt	Dermal	0.125 mg ai/cm^2	5,700
Impregnated Clothing: Long Sleeve Shirt/Long Pants	Dermal	0.125 mg ai/cm^2	3,700

Toddler (3 year old): Short-term postapplication risks to toddlers were calculated following the exposure to clothing impregnated with permethrin. Table 6.3.2.3c presents a summary of the MOE estimates for toddlers. The assessments for exposure to permethrin impregnated clothing considered dermal and non-dietary ingestion exposures. The short-term risks for postapplication risks from exposure to permethrin impregnated clothing do not exceed HED's level of concern (i.e., the MOEs are greater than 100).

Table 6.3.2.3c. Toddler Impregnated Clothing Risk Estimates for Postapplication Exposure to Permethrin			
Exposure Scenario	Route of Exposure	Application Rate	MOE on Day of Application
Impregnated Clothing: Long Sleeve Shirt	Dermal	0.125 mg ai/cm^2	4,100
Impregnated Clothing: Long Sleeve Shirt/Long Pants	Dermal	0.125 mg ai/cm^2	2,700
Object to Mouth Activity on Impregnated Clothing	Oral	0.125 mg ai/cm^2	24,000

Table 6.3.2.3d below summarizes the postapplication risk estimates resulting from the impregnated clothing use calculated for adults after applications of permethrin. HED estimated cancer risk assuming an annual maximum of 1 day of exposure per year for the maximum clothing residue. In addition, HED calculated the maximum number of days of exposure per year that still would result in cancer risks less than or equal to $3x10^{-6}$ (HED's level of concern) using an average clothing residue of 0.029 mg permethrin/cm^2. This average was calculated by assuming the clothing is usable for up to 30 washes and that the first wash results in a 33% permethrin loss, the second wash results in a 6% permethrin loss, washes 3 through 10 each result in a 3% permethrin loss, and washes 11 through 30 each result in a 6.5% permethrin loss (MRID 457519-02). It was also assumed that each individual would wear the clothing for 2 days before a washing event took place to simulate wearing the clothing for a camping weekend. Both the long sleeve shirt and the long sleeve shirt/pants scenario cancer risk estimates do not exceed HED's level of concern (i.e., risks are below 3×10^{-6}).

Table 6.3.2.3d. Summary of Permethrin Postapplication Impregnated Clothing Cancer Risks For Adults				
Exposure Scenario	Route of Exposure	Application Rate[a]	Cancer Risk on Day of Application[b]	Days/Year to Reach LOC[c]
Impregnated Clothing: Long Sleeve Shirt	Dermal	0.125 mg ai/cm^2	8.6×10^{-8}	150
Impregnated Clothing: Long Sleeve Shirt/Long Pants	Dermal	0.125 mg ai/cm^2	1.4×10^{-7}	92

Footnotes

a HED is aware that some manufacturers of clothing impregnated with permethrin have developed a new method for the impregnation process. HED believes that this new process will likely reduce exposure to permethrin; however, at this time there is no exposure data available to evaluate this method.

b Day of application calculations utilize the maximum clothing residue.

c Days per year to reach the LOC calculations utilize the average clothing residue to reflect washings over the life of the garment.

6.3.3 Combined Risk Assessment for Residential Scenarios

HED combines risks resulting from exposures to individual chemicals when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. Within a residential assessment, this can take two forms. The first approach is to add together risks for individual exposure scenarios from all likely sources of exposure such as after an application to turf or use on a pet. For permethrin, HED has combined risks to residential children from exposures to treated lawns (i.e., dermal, hand-to-mouth, object-to-mouth, and soil ingestion), from hugging treated companion animals, (i.e., dermal and hand-to-mouth), and from wearing impregnated clothing scenarios (i.e., dermal and object-to-mouth). These represent the standard set of exposures that are typically combined when chemicals are used on turf, on pets and in impregnated clothing, because it is likely they co-occur. Table 6.3.3 presents a summary of the combined risk estimates.The combined risks for the turf spray scenario, the indoor carpet-aerosol scenario, the indoor carpet-fogger scenario, the pet-dust scenario, the pet-shampoo scenario, and the impregnated clothing scenario are 6400, 5600, 210, 720, 350, and 2400, respectively and do not exceed HED's level of concern.

Table 6.3.3. Permethrin Residential Scenarios for Combined Risk Estimates				
Postapplication Exposure Scenario			Margins of Exposure (MOEs) (UF=100)	
			Short-Term Oral (Non-Dietary)	Total Non-Dietary Risk
Toddler	Turf - sprays	Dermal	12,000	6,400
		Hand to Mouth	15,000	
		Object to Mouth	250,000	
		Incidental Soil Ingestion	570,000	
Toddler	Indoor Carpet - Broadcast	Dermal	230	79
		Hand to Mouth	120	
Toddler	Indoor Carpet - Aerosol	Dermal	8,500	5,600
		Hand to Mouth	16,000	
Toddler	Indoor Carpet - Fogger	Dermal	320	210
		Hand to Mouth	610	
Toddler	Pet - shampoo	Hand to Mouth	360	350
		Dermal	1,200	
Toddler	Pet - dusts	Hand to Mouth	1,300	720
		Dermal	1,600	
Toddler	Pet - spot on	Hand to Mouth	5,000	1,000
		Dermal	1,200	
Toddler	Impregnated Clothing: Long Sleeves/Long Pants	Object to Mouth	24,000	2,400
		Dermal	2,700	

6.3.4 Spray Drift

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 permethrin. 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. 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 the 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 pesticide 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 and risks associated with aerial as well as other application types where appropriate.

7.0 Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures (oral, dermal, and inhalation exposures). In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

In general, exposures from various sources (routes) are aggregated only when the toxic effects, determined by the endpoint selected for that route, are the same. In this case, preliminary results from the *Residential Exposure Joint Venture (REJV)* survey were used to further refine HED's aggregate assessment. The *REJV* survey is a 12 month longitudinal survey that examined pesticide use in a residential environment. The data evaluated by the HED in this analysis were information collected in 2001 and 2002. This information is critical because it can be used for comparison to the deterministic inputs used for the Agency's aggregate risk assessment and it can be used to characterize the results of the companion probabilistic risk assessment that has recently been submitted for permethrin.

HED has also reviewed a permethrin CARES (Cumulative and Aggregate Risk Evaluation System) assessment submitted by Valent BioSciences Corporation (*see Permethrin: Review of Valent BioSciences Corporation's CARES Aggregate Submission entitled "Preliminary Evaluation of Potential Aggregate Human Health Risks Associated with Agricultural and Consumer Uses of Permethrin", DP Barcode 358432*). CARES is a software program which performs single chemical, aggregate, and cumulative (multichemical) exposure and risk assessments. In the permethrin submission, exposures through food, water, and residential pathways were assessed. This submission is briefly described in section 7.2.2.

HED also reviewed residential biomonitoring data produced by the Department of Health and Human Services, Centers for Disease Control and Prevention (CDC) published in July of 2005. The assessment entitled, "Third National Report on Human Exposure to Environmental Chemicals", looked at exposure of the U.S. population to environmental chemicals using biomonitoring. These environmental chemicals included permethrin as well as a number of other pyrethroid pesticides. The study looked for three metabolites (cis DCCA, trans DCCA, and 3-PBA) of permethrin in the urine of individuals ranging in age from 6 to 59 and the data is also broken down into race and gender. This assessment is briefly described in section 7.2.3.

7.1 Acute Aggregate Risk

The acute aggregate risk estimate includes the contribution of risk from dietary (food + drinking water) sources only. Acute risk estimates from exposures to food and water, associated with the use of permethrin do not exceed HED's level of concern. The estimated acute dietary risk for the general U.S. population is 4 %, with the highest exposed population subgroup being infants at 16% aPAD (see Section 6.1.2).

Drinking water expected concentrations (DWECs) were calculated from models, for risk assessment purposes, based on maximum application rates. The deterministic DWECs were combined directly with the acute dietary exposure assessment for all populations to calculate aggregate dietary (food + water) risk. The advantage of this approach, for any population subgroup, 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 DWECs were combined with estimated food exposure for aggregate risk assessment purposes since the calculated surface water estimates exceed the calculated groundwater estimates and therefore, are more conservative.

7.2 Short-Term Aggregate Risk

7.2.1 HED SOP Methodology

Aggregate short-term risk estimates include the contribution of risk from chronic dietary sources (food + water) and short-term residential sources. There are a number of exposure scenarios that could be aggregated. According to the preliminary results of the *REJV* survey, uses on lawns and on indoor crack and crevice sites account for the most use in the residential marketplace. For this assessment, HED used the *REJV* survey to look at the likelihood of a co-occurrent application scenario. This was examined using a conditional probability approach. Table 7.2.1 contains the REJV co-occurrence matrix.

Table 7.2.1a. REJV Co-Occcurrence Matrix

Scenario Description		LC	VGC	OW&H	IC&C	TT	PC	OF	IF	IC	FIK	IC&R	PH
Lawn Care (LC) (spot or broadcast)	**LC**		0.145	0.049	0.024	0.100	0.133	0.000	0.000	0.100	0.044	0.003	0.100
Vegetable Garden Care (VGC)	**VGC**	0.046		0.045	0.015	0.100	0.000	0.000	0.000	0.100	0.040	0.003	0.100
Outdoor Wasp & Hornet (OW&H)	**OW&H**	0.003	0.009		0.002	0.100	0.015	0.000	0.000	0.100	0.100	0.100	0.100
Indoor Crack & Crevice (ICC)	**IC&C**	0.003	0.005	0.003		0.100	0.004	0.000	0.000	0.100	0.003	0.000	0.100
Termite Treatment (TT)	TT	0.100	0.100	0.100	0.100		0.100	0.100	0.100	0.100	0.100	0.100	0.100
Pet Care (PC)	PC	0.031	0.000	0.054	0.008	0.100		0.003	0.000	0.100	0.049	0.003	0.100
Outdoor Fogger (OF)	OF	0.000	0.000	0.051	0.000	0.100	0.000		0.000	0.100	0.046	0.003	0.100
Indoor Fogger (IF)	IF	0.000	0.000	0.051	0.000	0.100	0.000	0.000		0.100	0.046	0.003	0.100
Impregnated Clothing (IC)	IC	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100		0.100	0.100	0.100
Indoor Flying Insect Killer (FIK)	FIK	0.003	0.008	0.100	0.002	0.100	0.014	0.000	0.000	0.100		0.100	0.100
Indoor Carpet & Room Spray (IC&R)	IC&R	0.000	0.001	0.100	0.000	0.100	0.001	0.000	0.000	0.100	0.100		0.100
Public Health Care: Mosquito Control (PH)	PH	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	

* Reproduced from, "Preliminary Evaluation of Potential Aggregate Human Health Risks Associated with Agricultural and Consumer Uses of Permethrin" (dated June 21, 2005). Jeffrey Driver, Dr.P.H.; Muhilan Pandian, Ph.D.; and John Ross, Ph.D. MRID 465785-01.

Adult Aggregate Risk: Chronic food and water exposures for the U.S. general population and for females 13-49 years of age were combined with residential handler and postapplication exposures. Residential handler exposures for mixing/loading/applying emulsifiable concentrates with a low pressure handwand at 0.005 lb ai/gal (max rate) to lawns, dermal and inhalation, were combined, by route, with postapplication exposures (dermal) for vegetable gardens performed at 0.4 lb ai/acre. Residential handler exposures for mixing/loading/applying emulsifiable

concentrates with a low pressure handwand at 0.005 lb ai/gal (max rate) to lawns, dermal and inhalation, were also combined, by route, with postapplication exposures (dermal) for indoor carpet surface sprays performed at 0.0001 lb ai/ft^2.

Toddler Aggregate Risk: Chronic food and water exposures for children 1-2 years of age were combined with postapplication residential hand to mouth activity and dermal contact to lawns (application at 0.87 lb ai/acre) and indoor carpets (application at 0.0001 lb ai/sq ft) resulting from applications of permethrin. Chronic food and water exposures for children 1-2 years of age were combined with postapplication residential hand to mouth activity and dermal contact to lawns (application at 0.87 lb ai/acre) and indoor vinyl floors (application at 0.0001 lb ai/sq ft) resulting from applications of permethrin. Chronic food and water exposures for children 1-2 years of age were combined with postapplication residential hand to mouth activity and dermal contact to lawns (application at 0.87 lb ai/acre) and pets (application at 0.0062 lb ai/animal) resulting from applications of permethrin.

With the exception of indoor carpet broadcast sprays exposure to toddlers, HED can conclude that combined residues of permethrin from food, drinking water, and other potential residential exposures do not result in short-term aggregate risks of concern to population subgroups.

Table 7.2.1b. Short-Term Aggregate Risk

Population	Residential Scenarios Included in Aggregate	Short-Term Scenario					
		HED's Aggregate LOC [1]	MOE food + water [2]	MOE incid oral [3]	MOE dermal [4]	MOE inhalation [5]	Aggregate MOE (food and residential) [6]
U.S. Pop.	Lawn Care, Postapp Vegetable	100	210,000	NA	4,200	1,000,000	4,100
	Lawn Care, Postapp Indoor Surface Spray on Carpet				120	1,000,000	120
Adult Female	Lawn Care, Postapp Vegetable	100	220,000	NA	4,200	1,000,000	4,100
	Lawn Care, Postapp Indoor Surface Crack and Crevice Spray on Carpet				1,700	1,000,000	1,700
Toddler	Lawn Care, Indoor Surface Broadcast Spray on Carpet	100	88,000	120	220	NA	78
	Lawn Care, Indoor Surface Broadcast Spray on Vinyl	100	88,000	460	1,400	NA	340
	Lawn Care, Indoor Surface Baseboard Spray on Carpet	100	88,000	210	370	NA	130
	Lawn Care, Indoor Surface Baseboard Spray on Vinyl	100	88,000	740	2,200	NA	550
	Lawn Care, Indoor Surface Crack and Crevice Spray on Carpet	100	88,000	1,300	1,000	NA	560
	Lawn Care, Indoor Surface Crack and Crevice Spray on Vinyl	100	88,000	2,000	4,700	NA	1,400
	Lawn Care, Pet Shampoo	100	88,000	350	6,000	NA	330

[1] *Level of Concern (LOC) is 100 based on 10X for inter-species extrapolation and 10X for intra-species variation.*

[2] MOE food + water = [(short-term oral NOAEL 25 mg/kg/day)/(chronic dietary exposure)]
Chronic dietary exposure: U.S. Pop.= 0.000121 *mg/kg/day; Females 13-49 yrs* = 0.000112 *mg/kg/day; All Infants <1 yr* = 0.000283 *mg/kg/d*ay.
[3] MOE incidental oral = [(short-term incidental oral NOAEL 25 mg/kg/day)/(child residential exposure)]
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day + Carpet Crack and Crevice Hand to Mouth = 0.042 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day; + Vinyl Crack and Crevice Hand to Mouth = 0.011 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day + Carpet Baseboard Hand to Mouth = 0.12 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day; + Vinyl Baseboard Hand to Mouth = 0.032 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day + Carpet Broadcast Hand to Mouth = 0.21 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day; + Vinyl Broadcast Hand to Mouth = 0.053 mg/kg/day
Child: Lawn Hand-to-mouth = 0.0016 mg/kg/day; + Pet Shampoo Hand to Mouth = 0.011 mg/kg/day
[4] MOE dermal = [(short-term dermal NOAEL 500 mg/kg/day)/(high-end dermal residential exposure)]
Adult: Handler Low Pressure Handwand Turf = 0.036 mg/kg/day + Postapp from Gardens = 0.082 mg/kg/day
Adult: Handler Low Pressure Handwand Turf = 0.036 mg/kg/day + Postapp from Indoor Crack and Crevice = 0.26 mg/kg/day
Child: Lawn = 0.042 mg/kg/day + Carpet Crack and Crevice = 0.44 mg/kg/day
Child: Lawn = 0.042 mg/kg/day; Vinyl Crack and Crevice = 0.064 mg/kg/day
Child: Lawn = 0.042 mg/kg/day + Carpet Baseboard = 1.3 mg/kg/day
Child: Lawn = 0.042 mg/kg/day; Vinyl Baseboard = 0.19 mg/kg/day
Child: Lawn = 0.042 mg/kg/day + Carpet Broadcast = 2.2 mg/kg/day
Child: Lawn = 0.042 mg/kg/day; Vinyl Broadcast = 0.32 mg/kg/day
[5] MOE inhalation = [(inhalation NOAEL 11mg/kg/day)/(high-end inhalation residential exposure)]
Adult: Handler Low Pressure Handwand Turf = 0.000011 mg/kg/day
[6] Aggregate MOE (food + water + residential) = 1÷[(1÷MOE food+water) + (1÷MOE incidental oral) + (1÷MOE dermal) + (1÷MOE inhalation)]

7.2.2 Valent CARES Assessment

Valent reported aggregate MOEs corresponding to the 99.9th percentile for both children 1-2 and adults 20-49. For children 1-2 years old, Valent reported an aggregate MOE at the 99.9th percentile of 433. For adults 20-49, Valent reported an aggregate MOE at the 99.9th percentile of 915. These aggregate results are in reasonable agreement with those generated by HED in the permethrin risk assessment.

HED believes the Valent CARES assessment provides valuable complementary information to HED regarding aggregate exposure to permethrin. The results generated in the permethrin CARES assessment are generally in reasonable agreement with those generated by HED in the current permethrin risk assessment. The Valent permethrin CARES assessment allows HED to provide support and better characterization to HED's deterministic aggregate non-cancer assessment (developed from standard operating procedures for estimating aggregate exposure).

7.2.3 CDC - Third National Report on Human Exposure to Environmental Chemicals

In July of 2005, the Department of Health and Human Services, Centers for Disease Control and Prevention (CDC) published an assessment entitled, "Third National Report on Human Exposure to Environmental Chemicals" which looked at exposure of the U.S. population to environmental chemicals using biomonitoring. This report included looking at permethrin via its three metabolites: cis DCCA, trans DCCA, and 3-PBA. The study looked for these metabolites in the urine of individuals ranging in age from 6 to 59 and the data is also broken down into race and gender. All three metabolites were detected in measurable quantities throughout the sampled population.

The study is population based meaning that none of the monitoring is linked to specific application events. This is an issue because the biomonitoring results do not necessarily correlate to the deterministic estimates of risk (presented above) obtained through the use of HED's Standard Operating Procedures. HED generally agrees that population-based monitoring results likely represent something close to background levels from the diet and drinking water. Another issue with the study is that the three permethrin metabolites looked for in urine are also metabolites for various other pyrethroids. This means that it is all but impossible to determine what portion of the metabolites that were found in the urine actually were a result of permethrin exposure. HED believes the CDC data provides valuable complementary information to HED regarding aggregate exposure to permethrin.

7.3 Intermediate-Term Aggregate Risk

All residential/recreational exposures are expected to be short-term in duration.

7.4 Long-Term Aggregate Risk

Aggregate long-term (noncancer) risk estimates include the contribution of risk from chronic dietary sources (food + water) and residential sources. However, based on the labeled uses, no long-term or chronic residential exposures are expected. Chronic risk estimates from exposures to food and water, associated with the use of permethrin do not exceed HED's level of concern for the U.S. population and all population subgroups (all populations were less than 1% cPAD).

As in the acute aggregate assessment, surface water DWECs were calculated by EFED to estimate the potential contribution to the chronic exposure from drinking water, and the DWECs were combined with chronic food exposures to estimate potential long-term aggregate risks from the uses of permethrin.

7.5 Cancer Risk

Adult Aggregate Risk: Cancer food and water exposures for the U.S. general population were combined with residential handler and postapplication exposures. Residential handler exposures for mixing/loading/applying emulsifiable concentrates with a low pressure handwand at 0.005 lb ai/gal (max rate) to lawns, dermal and inhalation were combined, by route, with postapplication exposures (dermal) for vegetable gardens performed at 0.4 lb ai/acre. Residential handler exposures for mixing/loading/applying emulsifiable concentrates with a low pressure handwand at 0.005 lb ai/gal (max rate) to lawns, dermal and inhalation were also combined, by route, with postapplication exposures (dermal) for indoor carpet surface sprays performed at 0.0001 lb ai/ft^2.

With the exception of indoor carpet sprays exposure to adults, HED can conclude that combined residues of permethrin from food, drinking water, and other potential residential exposures do not result in cancer risks of concern to population subgroups.

Table 7.5. Cancer Aggregate Risk					
Population	Residential Scenarios Included in Aggregate	Short-Term Scenario			
		HED's Cancer Risk Aggregate LOC [1]	Cancer Risk from food + water [2]	Cancer Risk from residential [3]	Aggregate Cancer Risk (food and residential) [4]
U.S. Pop.	Lawn Care, Postapp Vegetable	3.0×10^{-6}	1.1×10^{-6}	4.0×10^{-8}	1.1×10^{-6}
	Lawn Care, Postapp Indoor Surface Crack and Crevice Spray on Carpet			3.1×10^{-7}	1.4×10^{-6}

[1] *Level of Concern (LOC).*
[2] Cancer Risk from food + water = $[(Q_1^*$ of 9.567×10^{-3} $(mg/kg/day)^{-1})^*$(cancer dietary exposure)]
Cancer dietary exposure: U.S. Pop.=0.000117 *mg/kg/day*.
[3] Cancer Risk from residential = $[(Q_1^*$ of 9.567×10^{-3} $(mg/kg/day)^{-1})^*$(residential LADD)]
Adult: Handler Low Pressure Handwand Turf = 3.0×10^{-6} mg/kg/day + Postapp from Gardens = 1.1×10^{-6} mg/kg/day
Adult: Handler Low Pressure Handwand Turf = 3.0×10^{-6} mg/kg/day + Postapp from Indoor Surface Crack and Crevice Spray on Carpet = 7.4×10^{-5} mg/kg/day
[4] Aggregate Cancer Risk (food + water + residential) = $[(Q_1^*$ of 9.567×10^{-3} $(mg/kg/day)^{-1})^*$ (cancer dietary exposure + cancer residential exposure)]

8.0 Cumulative Risk Characterization/Assessment

Permethrin is a member of the pyrethroid class of pesticides. This class also includes cypermethrin, esfenvalerate, cyfluthrin, fluvalinate, bifenthrin, fenpropathrin, and lambda-cyhalothrin among others. The pyrethroids as a group are believed to share a common mechanism of toxicity. A cumulative risk assessment has not been performed as part of this review because further study is needed regarding the assumptions of dose additivity and common mechanism(s) of toxicity to appropriately identify a group or subgroups for such an assessment. EPA's Office of Research and Development and pyrethorid registrants are currently investigating the pharmacokinetics and pharmcodynamics of pyrethroids which will provide a more solid scientific foundation for considering a cumulative assessment of these pesticides in the future.

9.0 Occupational Exposure/Risk Pathway

There is a potential for exposure to permethrin in occupational scenarios from handling permethrin products during the application process (i.e., mixer/loaders, applicators, flaggers, and mixer/loader/applicators) and a potential for postapplication worker exposure from entering into areas previously treated with permethrin. As a result, risk assessments have been completed for occupational handler scenarios as well as occupational postapplication scenarios.

9.1 Short- and Intermediate-Term Noncancer Handler Risk

Exposure scenarios categorize the exposures that occur during the use of a chemical. The use of scenarios in exposure assessments is common and is described in the *U.S. EPA Guidelines for Exposure Assessment* (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Information from the current labels, use and usage information, toxicology data, and exposure

data were all key components in developing the exposure scenarios. For exposure and risk assessment purposes, pesticide handling tasks associated with occupational pesticide use are categorized as one of the following:

- **Mixers and/or Loaders:** these individuals perform tasks in preparation for an application. For example, prior to application, mixer/loaders would mix the permethrin and load it into the holding tank of the airplane or groundboom.

- **Applicators:** these individuals operate application equipment during the release of a pesticide product into the environment. These individuals can make applications using equipment such as airplanes or groundboom sprayers.

- **Mixer/Loader/Applicators and or Loader/Applicators:** these individuals are involved in the entire pesticide application process (i.e., they do all job functions related to a pesticide application event). These individuals would transfer permethrin into the application equipment and then also apply it.

- **Occupational Flaggers:** these individuals guide aerial applicators during the release of a pesticide product onto an intended target.

The risk assessors must understand how exposures to permethrin occur (i.e., frequency and duration) and how the patterns of these occurrences can cause the effects of the chemical to differ (referred to as dose response). Wherever possible, use and usage data determine the appropriateness of certain types of risk assessments. Other parameters are also defined from use and usage data such as application rates and application frequency. HED always completes non-cancer risk assessments using maximum application rates for each scenario because what is possible under the label (the legal means of controlling pesticide use) must be evaluated in order to ensure there are no concerns for each specific use.

The frequency and duration of pesticide handlers' exposures must also be estimated in order to determine which toxicological endpoints of concern are applicable to a handler exposure scenario. HED believes that occupational permethrin exposures can occur over a single day or up to weeks at a time for many use-patterns and also anticipates intermittent exposures can occur over several weeks. Custom or commercial applicators may apply permethrin over a period of weeks completing applications for a number of different clients. HED classifies exposures up to 30 days as short-term and exposures greater than 30 days up to several months as intermediate-term. HED completes both short- and intermediate-term assessments for occupational scenarios in essentially all cases, because these kinds of exposures are likely and often reliable use/usage data are not available to justify deleting intermediate-term scenarios. Long-term handler exposures are not expected to occur for permethrin. The same toxicological endpoint (25 mg/kg/day from an oral study) of concern was selected for short- and intermediate-term dermal permethrin exposures therefore the risk results for all dermal durations of exposure are numerically identical. The HIARC report, dated October 8, 2003, states that a dermal absorption factor of 30% should be used to assess dermal risks, since the dermal noncancer endpoint for permethrin is from an oral study. The same toxicological endpoint (11 mg/kg/day from an

inhalation study) of concern has been selected for short- and intermediate-term inhalation exposures to permethrin therefore the risk results for all inhalation durations of exposure are numerically identical. Since the inhalation endpoint of concern is from an inhalation study, no inhalation absorption factor is necessary.

Occupational handler exposure assessments are completed by HED using different levels of personal protection. HED typically evaluates all exposures with a tiered approach. The lowest tier is represented by the baseline exposure scenario (i.e., long-sleeve shirt, long pants, shoes, socks, and no respirator) followed by increasing the levels of personal protective equipment or PPE (e.g., gloves, double-layer body protection, and respirators), and then by engineering controls (e.g., enclosed cabs and closed mixing/loading systems). This approach is always used by HED in order to be able to define label language using a risk-based approach. In addition, the minimal level of adequate protection for a chemical is generally considered by HED to be the most practical option for risk reduction (i.e., over-burdensome risk mitigation measures are not considered a practical alternative).

The anticipated use patterns and current labeling indicate several likely occupational handler exposure scenarios, based on the types of equipment and techniques that can potentially be used to apply permethrin. Due to the scope of the various permethrin occupational uses (there are over 900 permethrin products registered), it would be difficult to assess each individual exposure scenario. Therefore, HED selected representative worse-case exposure scenarios to represent the major ways permethrin can be handled in the occupational environment. HED believes this approach is protective of public health as the scenarios likely to result in the greatest exposure are considered. Anticipated use pattern and current labeling indicate 39 likely occupational exposure scenarios, based on the types of equipment and techniques that can potentially be used to make permethrin applications. Scenarios in this document include: (Note: scenarios denoted with a "*" could not be evaluated quantitatively, because applicable unit exposure data are not available.)

Mixer/Loaders:

(1a) Liquids for Aerial Applications;
(1b) Liquids for Groundboom Applications;
(1c) Liquids for Airblast Applications;
(1d) Liquids for Truck Mounted ULV Applications;
(1e) Liquids for Dip Applications;
(1f) Liquids for Residential Mister Systems;
(2a) Wettable Powder for Aerial Applications;
(2b) Wettable Powder for Groundboom Applications;
(2c) Wettable Powder for Airblast Applications;
(2d) Dusts for Mechanical Duster Applications (using PHED WP mixer/loader data);
(2e) Dusts for Dust Bag Applications (using PHED WP mixer/loader data);
(3a) Granulars for Aerial Applications;
(3b) Granulars for Tractor Drawn Spreader Applications;

Applicators:

(4) Aerial Applications (Sprays);

(5) Groundboom Applications;
(6) Airblast Applications;
(7) Truck Mounted ULV Applications;
(8) Dip Applications*;
(9) Aerial Applications (Granulars)
(10) Tractor Drawn Spreader Applications (Granulars);
(11) Mechanical Duster Applications*;
(12) Dust Bag Applications*;

Flaggers:
(13) Flagging for Aerial- Sprays;
(14) Flagging for Aerial-Granulars;

Mixer/Loader/Applicators:
(15) Liquid: Low Pressure Handwand Sprayer;
(16) Liquid: Handgun Sprayer;
(17) Liquid: High Pressure Handwand Sprayer;
(18) Liquid: Termiticide Injector;
(19) Liquid: Foam Applicator Equipment (using ORETF low pressure handwand data);
(20) Liquid: Watering Can (using ORETF residential hose end sprayer data);
(21) Liquid: Backpack ULV Sprayer (using ORETF low pressure handwand data);
(22) Liquid: Paint Brush;
(23) Liquid: Cold Fogger;
(24) Wettable Powder: Low Pressure Handwand Sprayer;
(25) Wettable Powder: Handgun Sprayer;
(26) Wettable Powder: High Pressure Handwand Sprayer*;
(27) Water Soluble Bag: Handgun Sprayer;
(28) Wettable Powder: Cold Fogger*;
(29) Dusts: Shaker Can;
(30) Microencapsulated Liquid: Fogger/Mist Generator*;
(31) RTU Liquid: Pour On Applications (using PHED mixing/loading liquid data);
(32) RTU Ear Tag Applications*;
(33) RTU: Hand Applications (Shampoos);
(34) RTU: Wipe Applications;
(35) RTU: Trigger Pump Sprayer Applications;
(36) RTU: Aerosol Cans;
(37) RTU: Fogger (using PHED aerosol can data);
(38) RTU Protective Flanges*;
(39) RTU Vapor Recovery System Tubes*.

Unit exposure values from the following sources were used to calculate risk estimates:

- the Pesticide Handler Exposure Database (PHED);
- the Outdoor Residential Task Force (ORETF) studies;
- the Chemical Manufacturers Association (CMA) Antimicrobial Exposure

Assessment Study; and

- two proprietary exposure studies reflecting the following scenarios:
  - handlers applying shampoo to dogs (MRID # 446584-01) and
  - handlers applying liquids via trigger sprayer (MRID # 410547-01).

The noncancer occupational handler exposure and risk calculations are included in Table 9.1. Scenarios that could not be evaluated quantitatively are not presented in the table. The results indicate that for all scenarios, risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) at some level of risk mitigation.

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates											
Exposure Scenario	**Crop or Target**	**Application Rate [a]**	**Area Treated Daily [b]**	**Combined MOEs [c]**							
				Baseline	**G - NR**	**PPE-G, DL-NR**	**G - 80% R**	**G,DL - 80% R**	**G - 90% R**	**G,DL - 90% R**	**Eng Cont**
Mixer/Loader											
Mixing/Loading Emulsifiable Concentrates for Aerial Applications (1a)	pine seed orchard	1.2 lb ai/A	100 acres	**99**	3800	4100	13000	17000	13000	17000	24000
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	350 acres	85	**3200**	3500	11000	15000	11000	15000	20000
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/A	350 acres	**110**	4300	4700	14000	19000	14000	19000	27000
	corn: sweet (FL only)	0.25 lb ai/A	1200 acres	39	1500	1600	5000	6800	5000	6800	9600
	corn: sweet (FL only)	0.25 lb ai/A	350 acres	**140**	5200	5600	17000	23000	17000	23000	33000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	1200 acres	49	**1900**	2000	6300	8500	6300	8500	12000
	cabbage, chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	350 acres	**170**	6400	7000	22000	29000	22000	29000	40000
	conifers (field grown)	0.2 lb ai/A	100 acres	**590**	23000	24000	75000	100000	76000	100000	140000
	rose: field grown	0.2 lb ai/A	60 acres	**990**	38000	41000	130000	170000	130000	170000	240000
	broccoli, brussel sprouts, cauliflower, chinese broccoli, collards	0.1 lb ai/A	350 acres	**340**	13000	14000	43000	58000	43000	58000	83000
Mixing/Loading Emulsifiable Concentrates for Groundboom Applications(1b)	artichokes, garlic, onions: dry bulb	0.3 lb ai/A	80 acres	**490**	19000	20000	63000	85000	63000	85000	120000
	corn: sweet (FL only)	0.25 lb ai/A	200 acres	**240**	9000	9800	30000	41000	30000	41000	57000
	corn: sweet (FL only)	0.25 lb ai/A	80 acres	**590**	23000	24000	75000	100000	76000	100000	140000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	200 acres	**300**	11000	12000	38000	51000	38000	51000	70000
	cabbage, chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	80 acres	**740**	28000	31000	94000	130000	95000	130000	170000
	chrysanthemum, roses: field grown	0.2 lb ai/A	40 acres	**1500**	56000	61000	190000	250000	190000	260000	360000
	asparagus, broccoli, brussel sprouts, cauliflower, chinese broccoli, collards, turnips	0.1 lb ai/A	80 acres	**1500**	56000	61000	190000	250000	190000	260000	360000
Mixing/Loading Emulsifiable Concentrates for Airblast Applications (1c)	pine seed orchard	1.2 lb ai/A	20 acres	**490**	19000	20000	63000	85000	63000	85000	120000
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	40 acres	**740**	28000	31000	94000	130000	95000	130000	170000
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/A	40 acres	**990**	38000	41000	130000	170000	130000	170000	240000
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/A	40 acres	**1500**	56000	61000	190000	250000	190000	260000	360000
	conifers (field grown), ornamental nursery stock	0.2 lb ai/A	20 acres	**3000**	110000	120000	380000	510000	380000	510000	700000
Mixing/Loading Emulsifiable Concentrates with Truck Mounted ULV Sprayer (using	outdoor spaces	0.007 lb ai/A	3000 acres	**560**	21000	23000	72000	97000	72000	97000	130000

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
PHED airblast data) (1d)											
Mixing/Loading Emulsifiable Concentrates via Dip (1e)	animal: livestock (beef and dairy cattle), horses	0.0023 lb ai/animal	400 animals	**13000**	490000	530000	1600000	2200000	1600000	2200000	3100000
	animal: swine	0.002 lb ai/animal	400 animals	**15000**	560000	610000	1900000	2500000	1900000	2600000	3600000
	animal: dogs	0.005 lb ai/gal	10 gallons	**240000**	9000000	9800000	30000000	41000000	30000000	41000000	57000000
Mixing/Loading Emulsifiable Concentrates for Residential Mister Systems (1f)	mosquitos	0.0023 lb ai/gal	250 gallons	**3500**	320000	390000	430000	430000	570000	580000	NF
		0.0023 lb ai/gal	1000 gallons	**870**	79000	97000	110000	110000	140000	150000	NF
Mixing/Loading Wettable Powders for Aerial Applications (2a)	pine seed orchard	1.2 lb ai/A	100 acres	52	**140**	140	1600	2100	1700	2200	14000
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	350 acres	44	**120**	120	1400	1800	1400	1900	12000
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/A	350 acres	59	**160**	160	1900	2400	1900	2500	16000
	corn: sweet (FL only)	0.25 lb ai/A	1200 acres	21	**55**	56	650	840	670	870	5700
	corn: sweet (FL only)	0.25 lb ai/A	350 acres	71	**190**	190	2200	2900	2300	3000	19000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	1200 acres	26	**69**	70	820	1100	840	1100	7000
	cabbage, chinese cabbage, corn (pop, seed, sweet) cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	350 acres	88	**240**	240	2800	3600	2900	3700	24000
	conifers (field grown)	0.2 lb ai/A	100 acres	**310**	820	840	9800	13000	10000	13000	85000
	rose: field grown	0.2 lb ai/A	60 acres	**520**	1400	1400	16000	21000	17000	22000	140000
	broccoli, brussel sprouts, cauliflower, chinese broccoli, collards	0.1 lb ai/A	350 acres	**180**	470	480	5600	7200	5700	7400	48000
Mixing/Loading Wettable Powders for Groundboom Applications (2b)	artichokes, garlic, onions: dry bulb	0.3 lb ai/A	80 acres	**260**	690	700	8200	11000	8400	11000	70000
	corn: sweet (FL only)	0.25 lb ai/A	200 acres	**120**	330	340	3900	5100	4000	5200	34000
	corn: sweet (FL only)	0.25 lb ai/A	80 acres	**310**	820	840	9800	13000	10000	13000	85000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	200 acres	**150**	410	420	4900	6300	5000	6500	42000
	cabbage, chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	80 acres	**390**	1000	1000	12000	16000	13000	16000	100000
	chrysanthemum, roses: field grown	0.2 lb ai/A	40 acres	**770**	2100	2100	24000	32000	25000	33000	210000
	asparagus, broccoli, brussel sprouts, cauliflower, chinese broccoli, collards, turnips	0.1 lb ai/A	80 acres	**770**	2100	2100	24000	32000	25000	33000	210000
Mixing/Loading Wettable Powders for Airblast	pine seed orchard	1.2 lb ai/A	20 acres	**260**	690	700	8200	11000	8400	11000	70000
	almonds, apples, filberts, pears (dormant &	0.4 lb ai/A	40 acres	**390**	1000	1000	12000	16000	13000	16000	100000

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
Applications (2c)	prebloom combo), pistachios, walnuts										
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/A	40 acres	**520**	1400	1400	16000	21000	17000	22000	140000
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/A	40 acres	**770**	2100	2100	24000	32000	25000	33000	210000
	conifers (field grown), ornamental nursery stock	0.2 lb ai/A	20 acres	**1500**	4100	4200	49000	63000	50000	65000	420000
Loading Dusts via Mechanical Duster (using PHED wettable powders data) (2d)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	**500000**	1300000	1400000	16000000	20000000	16000000	21000000	ND
	animal: poultry	0.0025 lb ai/animal	100000 animals	25	66	67	**780**	1000	800	1000	ND
	animal: swine	0.00016 lb ai/animal	400 animals	**97000**	260000	260000	3100000	3900000	3100000	4100000	ND
Loading Dusts via Dust Bag (using PHED wettable powders data) (2e)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	**500000**	1300000	1400000	16000000	20000000	16000000	21000000	ND
	animal: swine	0.00016 lb ai/animal	400 animals	**97000**	260000	260000	3100000	3900000	3100000	4100000	ND
Loading Granulars for Aerial Applications (3a)	almonds, pistachios	0.4 lb ai/A	350 acres	**2900**	3000	3100	35000	67000	35000	70000	140000
	alfalfa; corn: field, sweet-fresh & processed; corn: field-preplant	0.2 lb ai/A	1200 acres	**1700**	1700	1800	20000	39000	21000	41000	85000
	corn:sweet-fresh & processed	0.2 lb ai/A	350 acres	**5800**	5900	6200	69000	130000	71000	140000	290000
Loading Granulars for Tractor Drawn Spreader Applications (3b)	almonds, pistachios	0.4 lb ai/A	80 acres	**13000**	13000	14000	150000	290000	150000	310000	640000
	corn: sweet (fresh & processed)	0.2 lb ai/A	80 acres	**26000**	26000	27000	300000	580000	310000	610000	1300000
	alfalfa, corn (field, sweet-fresh & processed), corn: field (preplant)	0.2 lb ai/A	200 acres	**10000**	10000	11000	120000	230000	120000	250000	510000
Applicator											
Applying Liquid Sprays via Aerial Equipment (4)	pine seed orchard	1.2 lb ai/A	100 acres	ND	ND	ND	ND	ND	ND	ND	**36000**
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**31000**
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**42000**
	corn: sweet (FL only)	0.25 lb ai/A	1200 acres	ND	ND	ND	ND	ND	ND	ND	**14000**
	corn: sweet (FL only)	0.25 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**50000**
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	1200 acres	ND	ND	ND	ND	ND	ND	ND	**18000**
	cabbage, chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**62000**
	conifers (field grown)	0.2 lb ai/A	100 acres	ND	ND	ND	ND	ND	ND	ND	**220000**
	rose: field grown	0.2 lb ai/A	60 acres	ND	ND	ND	ND	ND	ND	ND	**360000**
	broccoli, brussel sprouts, cauliflower, chinese broccoli, collards	0.1 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**120000**
Applying Liquid Sprays via Groundboom Equipment (5)	artichokes, garlic, onions: dry bulb	0.3 lb ai/A	80 acres	**31000**	31000	33000	100000	130000	100000	130000	210000
	corn: sweet (FL only)	0.25 lb ai/A	200 acres	**15000**	15000	16000	49000	63000	50000	63000	100000

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
	corn: sweet (FL only)	0.25 lb ai/A	80 acres	**37000**	37000	39000	120000	160000	120000	160000	250000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/A	200 acres	**18000**	18000	20000	62000	78000	62000	79000	130000
	cabbage, chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	80 acres	**46000**	46000	49000	150000	200000	160000	200000	310000
	chrysanthemum, roses: field grown	0.2 lb ai/A	40 acres	**92000**	92000	98000	310000	390000	310000	400000	630000
	asparagus, broccoli, brussel sprouts, cauliflower, chinese broccoli, collards, turnips	0.1 lb ai/A	80 acres	**92000**	92000	98000	310000	390000	310000	400000	630000
Applying Liquid Sprays via Airblast Equipment (6)	pine seed orchard	1.2 lb ai/A	20 acres	**2600**	3300	3400	6100	6600	6100	6600	37000
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	40 acres	**3900**	4900	5200	9100	9900	9100	9900	57000
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/A	40 acres	**5200**	6600	6900	12000	13000	12000	13000	72000
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/A	40 acres	**7700**	9800	10000	18000	20000	18000	20000	110000
	conifers (field grown), ornamental nursery	0.2 lb ai/A	20 acres	**15000**	20000	21000	36000	40000	36000	40000	220000
Applying Liquid Sprays with Truck Mounted ULV Sprayer (using PHED airblast data) (7)	outdoor spaces	0.007 lb ai/A	3000 acres	**3000**	3700	3900	6900	7500	6900	7600	42000
Applying Emulsifiable Concentrates via Dip (8)	animal: livestock (beef and dairy cattle), horses	0.0023 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: swine	0.002 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: dogs	0.005 lb ai/gal	10 gallons	ND	ND	ND	ND	ND	ND	ND	ND
	military battle dress			ND	ND	ND	ND	ND	ND	ND	ND
Applying Granulars via Aerial Equipment (9)	almonds, pistachios,	0.4 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**4100**
	alfalfa, corn:field, corn: sweet (fresh & processed), corn: field (preplant)	0.2 lb ai/A	1200 acres	ND	ND	ND	ND	ND	ND	ND	**2400**
	corn: sweet (fresh & processed)	0.2 lb ai/A	350 acres	ND	ND	ND	ND	ND	ND	ND	**8300**
Applying Granulars via Tractor Drawn Spreader (10)	almonds, pistachios,	0.4 lb ai/A	80 acres	**17000**	18000	19000	150000	250000	150000	250000	91000
	alfalfa, corn:field, corn: sweet (fresh & processed), corn: field (preplant)	0.2 lb ai/A	200 acres	**14000**	14000	15000	120000	200000	120000	200000	73000
	corn:sweet (fresh & processed)	0.2 lb ai/A	80 acres	**34000**	35000	37000	290000	490000	300000	510000	180000
Applying Dusts via Mechanical Duster (11)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: poultry	0.0025 lb ai/animal	100 acres000	ND	ND	ND	ND	ND	ND	ND	ND
	animal: swine	0.00016 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
Applying Dusts via Dust Bag (12)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: poultry	0.0025 lb ai/animal	100000 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: swine	0.00016 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
Flagger											
Flagging for Liquid Sprays via	pine seed orchard	1.2 lb ai/A	100 acres	**11000**	ND	11000	ND	29000	ND	29000	130000

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
Aerial Equipment (13)	almonds, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/A	350 acres	**9300**	ND	9600	ND	25000	ND	25000	120000
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/A	350 acres	**12000**	ND	13000	ND	33000	ND	33000	150000
	corn: sweet (FL only)	0.25 lb ai/A	350 acres	**15000**	ND	15000	ND	40000	ND	40000	180000
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans, cabbage, chinese cabbage, cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/A	350 acres	**19000**	ND	19000	ND	50000	ND	50000	230000
	conifers (field grown)	0.2 lb ai/A	100 acres	**65000**	ND	68000	ND	170000	ND	170000	810000
	rose: field grown	0.2 lb ai/A	60 acres	**110000**	ND	110000	ND	290000	ND	290000	1300000
	broccoli, brussel sprouts, cauliflower, chinese broccoli, collards	0.1 lb ai/A	350 acres	**37000**	ND	39000	ND	99000	ND	100000	460000
Flagging for Granulars via Aerial Equipment (14)	almonds, pistachios,	0.4 lb ai/A	350 acres	**26000**	ND	30000	ND	150000	ND	150000	25000
	alfalfa, corn:field, corn: sweet (fresh & processed), corn: field (preplant)	0.2 lb ai/A	350 acres	**52000**	ND	59000	ND	310000	ND	310000	50000
Mixer/Loader/Applicator											
Mixing/Loading/Applying Emulsifiable Concentrates with Low Pressure Handwand (15)	turf	0.87 lb ai/A	8 acres	50	**2800**	2900	12000	13000	12000	13000	NF
	mushroom houses	0.267 lb ai/gal	40 gallons	32	**1800**	1900	7500	8700	7600	8800	NF
	conifers (field grown)	0.2 lb ai/gal	40 gallons	43	**2400**	2500	10000	12000	10000	12000	NF
	indoor surfaces, perimeter treatments	0.08 lb ai/gal	40 gallons	**110**	6100	6300	25000	29000	25000	29000	NF
	ornamentals: outdoor	0.046 lb ai/gal	40 gallons	**190**	11000	11000	44000	51000	44000	51000	NF
	outdoor surfaces, wood, ants & fire ants	0.04 lb ai/gal	40 gallons	**220**	12000	13000	50000	58000	51000	59000	NF
	animal premises	0.039 lb ai/gal	40 gallons	**220**	13000	13000	51000	60000	52000	60000	NF
	rose: field grown	0.02 lb ai/gal	40 gallons	**430**	24000	25000	100000	120000	100000	120000	NF
	animal premises	0.012 lb ai/gal	40 gallons	**720**	41000	42000	170000	190000	170000	200000	NF
	pine seed orchard	0.0105 lb ai/gal	40 gallons	**820**	46000	48000	190000	220000	190000	220000	NF
	agricultural premises	0.0085 lb ai/gal	40 gallons	**1000**	57000	59000	240000	270000	240000	280000	NF
	chrysanthemum	0.005 lb ai/gal	40 gallons	**1700**	98000	100000	400000	470000	400000	470000	NF
	almond, filbert, pear, pistachio (trees at residential sites)	0.004 lb ai/gal	40 gallons	**2200**	120000	130000	500000	580000	510000	590000	NF
	peach (trees at residential sites)	0.003 lb ai/gal	40 gallons	**2900**	160000	170000	670000	780000	670000	780000	NF
	apple & cherry trees at residential sites, ornamentals: greenhouse & other indoor, rose: greenhouse, ornamental nursery stock	0.002 lb ai/gal	40 gallons	**4300**	240000	250000	1000000	1200000	1000000	1200000	NF
	termites	33.2 lb ai/1000 lin ft	1000 lin feet	10	**590**	610	2400	2800	2400	2800	NF
	animal: livestock (beef and dairy cattle), goats, horses, sheep	0.0023 lb ai/animal	400 animals	**380**	21000	22000	87000	100000	88000	100000	NF
	animal: swine	0.002 lb ai/animal	400 animals	**430**	24000	25000	100000	120000	100000	120000	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Handgun Sprayer	turf	0.87 lb ai/A	8 acres	**6600**	9200	16000	10000	20000	10000	20000	NF
	conifers (field grown)	0.2 lb ai/gal	1000 gallons	**230**	320	550	360	700	360	700	NF

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
(ORETF data) (16)	perimeter treatment	0.08 lb ai/gal	500 gallons	**1200**	1600	2800	1800	3500	1800	3500	NF
	ornamentals: outdoor	0.046 lb ai/gal	1000 gallons	**1000**	1400	2400	1600	3000	1600	3000	NF
	outdoor surfaces, ants, and fire ants	0.04 lb ai/gal	500 gallons	**2300**	3200	5500	3600	7000	3600	7000	NF
	rose: field grown	0.02 lb ai/gal	1000 gallons	**2300**	3200	5500	3600	7000	3600	7000	NF
	pine seed orchard	0.0105 lb ai/gal	1000 gallons	**4400**	6100	10000	6900	13000	6900	13000	NF
	agricultural premises	0.0085 lb ai/gal	1000 gallons	**5400**	7500	13000	8600	16000	8600	16000	NF
	chrysanthemum	0.005 lb ai/gal	1000 gallons	**9200**	13000	22000	15000	28000	15000	28000	NF
	almond, filbert, pear, pistachio (trees at residential sites)	0.004 lb ai/gal	1000 gallons	**23000**	32000	55000	36000	70000	36000	70000	NF
	peach (trees at residential sites)	0.003 lb ai/gal	1000 gallons	**31000**	43000	73000	49000	93000	49000	93000	NF
	roses: greenhouse, ornamental nursery stock (non-bearing); ornamentals: greenhouse	0.002 lb ai/gal	1000 gallons	**23000**	32000	55000	36000	70000	36000	70000	NF
	apple & cherry (trees at residential sites)	0.002 lb ai/gal	500 gallons	**46000**	64000	110000	73000	140000	73000	140000	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a High Pressure Handwand (only study in PHED is for greenhouse use) (17)	rose: field grown	0.02 lb ai/gal	1000 gallons	ND	**220**	250	690	1100	700	1100	NF
	animal premises	0.012 lb ai/gal	1000 gallons	ND	**370**	410	1200	1800	1200	1800	NF
	chrysanthemum	0.005 lb ai/gal	1000 gallons	ND	**880**	990	2800	4300	2800	4300	NF
	rose: greenhouse	0.002 lb ai/gal	1000 gallons	ND	**2200**	2500	6900	11000	7000	11000	NF
	animal: poultry	0.00027 lb ai/animal	100000 animals	ND	**160**	180	510	800	520	800	NF
Mixing/Loading/Applying Emulsifiable Concentrate with an Injector (18)	termites	0.08 lb ai/gal	2000 gallons	ND	**480**	630	610	870	610	870	NF
Mixing/Loading/Applying Emulsifiable Concentrates via Foam Applicator Equipment (using PHED low-pressure handwand) (19)	termites	4.25 lb ai/1000 sq ft	1000 sq ft	81	**4600**	4800	19000	22000	19000	22000	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Watering Can (using ORETF residential hose-end data) (20)	fire ant mounds	0.04 lb ai/gal	10 gallons	**7500**	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Emulsifiable Concentrates with Backpack ULV Sprayer (using PHED backpack data) (21)	outdoor spaces	0.007 lb ai/A	5 acres	ND	**260000**	340000	400000	620000	400000	620000	NF
	outdoor spaces: barrier spray	0.1 lb ai/A	5 acres	ND	**18000**	24000	28000	44000	28000	44000	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Paint Brush (22)	indoor surfaces	0.08 lb ai/gal	5 gallons	450	**2400**	2500	3600	4000	3600	4000	NF
	wood, outdoor surfaces	0.04 lb ai/gal	5 gallons	910	**4800**	5000	7300	7900	7300	7900	NF
Mixing/Loading/Applying Emulsifiable Concentrates via Cold Fogger (23) [d]	mushroom houses	0.0078 lb ai/ sq ft	40000 sq ft (8000 sq ft per house)	ND	ND	ND	ND	ND	ND	ND	NF

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Combined MOEs [c]							
				Baseline	G - NR	PPE-G, DL-NR	G - 80% R	G,DL - 80% R	G - 90% R	G,DL - 90% R	Eng Cont
	indoor spaces	0.00036 lb ai/cu ft	200000 cu ft	ND	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Wettable Powders with Low Pressure Handwand (24)	conifers (field grown)	0.2 lb ai/gal	40 gallons	ND	75	78	**500**	680	500	690	NF
	rose: field grown	0.02 lb ai/gal	40 gallons	ND	**750**	780	5000	6800	5000	6900	NF
	indoor surfaces	0.0117 lb ai/gal	40 gallons	ND	**1300**	1300	8500	12000	8600	12000	NF
	pine seed orchard	0.0105 lb ai/gal	40 gallons	ND	**1400**	1500	9400	13000	9600	13000	NF
	mushroom houses, agricultural premises	0.0085 lb ai/gal	40 gallons	ND	**1800**	1800	12000	16000	12000	16000	NF
	chrysanthemum	0.005 lb ai/gal	40 gallons	ND	**3000**	3100	20000	27000	20000	28000	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gal	40 gallons	ND	**7500**	7800	50000	68000	50000	69000	NF
Mixing/Loading/Applying Wettable Powders with a Handgun Sprayer (ORETF data) (25)	conifers (field grown)	0.2 lb ai/gal	1000 gallons	46	49	55	**240**	450	240	450	NF
	rose: field grown	0.02 lb ai/gal	1000 gallons	**460**	490	550	2400	4500	2400	4500	NF
	pine seed orchard	0.0105 lb ai/gal	1000 gallons	**880**	940	1000	4600	8500	4600	8500	NF
	agricultural premises	0.0085 lb ai/gal	1000 gallons	**1100**	1200	1300	5700	10000	5700	10000	NF
	chrysanthemum	0.005 lb ai/gal	1000 gallons	**1800**	2000	2200	9600	18000	9600	18000	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gal	1000 gallons	**4600**	4900	5500	24000	45000	24000	45000	NF
Mixing/Loading/Applying Wettable Powders with a High Pressure Handwand (26)	rose: field grown	0.02 lb ai/gal	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF
	chrysanthemum	0.005 lb ai/gal	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF
	rose: greenhouse	0.002 lb ai/gal	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Water Soluble Bags with Handgun Sprayer (ORETF data) (27)	animal premises	0.0085 lb ai/gal	1000 gallons	**3100**	4000	5900	6100	12000	6100	12000	NF
	chrysanthemum	0.005 lb ai/gal	1000 gallons	**5300**	6900	10000	10000	20000	10000	20000	NF
	pine seed orchard	0.0105 lb ai/gal	1000 gallons	**2500**	3300	4800	5000	9500	5000	9500	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gal	1000 gallons	**13000**	17000	25000	26000	50000	26000	50000	NF
	rose: field grown	0.02 lb ai/gal	1000 gallons	**1300**	1700	2500	2600	5000	2600	5000	NF
	conifers (field grown)	0.2 lb ai/gal	1000 gallons	**130**	170	250	260	500	260	500	NF
Mixing/Loading/Applying Wettable Powders via Cold Fogger (28)	mushroom houses	0.011 lb ai/1000 sq ft	8000 sq ft	ND	ND	ND	ND	ND	ND	ND	NF
Applying Dusts via Shaker Can (MRID 444598-01) (29)	animal: poultry	0.0025 lb ai/animal	100000 animals	0.75	ND	ND	ND	ND	ND	ND	NF
	animal: swine	0.00016 lb ai/animal	400 animals	2900	ND	ND	ND	ND	ND	ND	NF
	animal: dogs, cats	0.00016 lb ai/animal	16 animals	73000	ND	ND	ND	ND	ND	ND	NF
	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	15000	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Microencapsulated Liquids via Fogger/Mist Generator (30)	animal premises	0.012 lb ai/1000 sq ft	1000 sq ft	ND	ND	ND	ND	ND	ND	ND	NF
	indoor spaces	0.00036 1000 cu ft	1000 cu ft	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via Pour-on (using PHED mix/load liquid) (31)	animal: horses	0.005 lb ai/animal	400 animals	5900	**230000**	240000	750000	1000000	760000	1000000	1400000
	animal: dairy and beef cattle, calves, sheep	0.0034 lb ai/animal	400 animals	8700	**330000**	360000	1100000	1500000	1100000	1500000	2100000
	animal: swine	0.002 lb ai/animal	400 animals	15000	**560000**	610000	1900000	2500000	1900000	2600000	3600000

Table 9.1. Summary of Short- and Intermediate-Term Permethrin Occupational Handler Non-cancer Risk Estimates											
Exposure Scenario	**Crop or Target**	**Application Rate [a]**	**Area Treated Daily [b]**	**Combined MOEs [c]**							
				Baseline	**G - NR**	**PPE-G. DL-NR**	**G - 80% R**	**G,DL - 80% R**	**G - 90% R**	**G,DL - 90% R**	**Eng Cont**
	clothing: personal	0.002 lb ai/6 oz container	1 container	5900000	**230000000**	240000000	750000000	1000000000	760000000	1000000000	1400000000
	deer (ticks)	0.0092 lb ai/per post	40 posts	32000	**1200000**	1300000	4100000	5500000	4100000	5600000	7600000
Applying Ready to Use Formulations via RTU Ear-Tag (32)	animal	0.0044 lb ai/2 ear tags	400 animals	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Shampoo Formulations via Hands (33)	animal: dogs	0.0062 lb ai/animal	16 animals	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via RTU Wipe (34)	animal: horses	0.0062 lb ai/animal	40 acres0	ND	ND	ND	ND	ND	ND	ND	NF
	animal: dogs	0.0062 lb ai/animal	16 animals	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via Trigger-Pump Sprayer (using Propoxur Trigger Pump study) (35)	indoor surfaces	0.043 lb ai/gal	2 gallons	**21000**	ND	ND	ND	ND	ND	ND	NF
	animal: horses, foals	0.016 lb ai/animal	400 animals	**290**	ND	ND	ND	ND	ND	ND	NF
	animal: cattle, goats, sheep, swine	0.00067 lb ai/animal	400 animals	**6800**	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations with Aerosol Cans (36)	outdoor surfaces	0.00438 lb ai/16 oz can	2 sixteen-ounce aerosol cans	**16000**	29000	32000	49000	62000	49000	62000	NF
Applying Ready to Use Formulations with Foggers (using PHED aerosol data) (37)	indoor spaces	0.0016 lb ai/6 oz fogger	4 six ounce foggers	**22000**	39000	44000	67000	85000	67000	85000	NF
Applying Ready to Use Protective Flanges (38)	ants	ND	ND	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Vapor Recovery System Tubes (39)	engines	0.000189 lb ai/tube	ND	ND	ND	ND	ND	ND	ND	ND	NF

Footnotes

* MOEs shown in bold indicate the lowest risk mitigation level that does not exceed HED's level of concern.

ND No Data

NF Not Feasible

a Application rates are the maximum application rates determined from EPA registered labels for permethrin.

b Amounts handled per day are HED estimates of acres, square feet, or cubic feet treated or gallons applied based on Exposure SAC SOP #9 "Standard Values for Daily Acres Treated in Agriculture," industry sources, and HED estimates.

c Baseline: Long-sleeve shirt, long pants, no gloves, and no respirator.

PPE-G-NR: Baseline plus chemical-resistant gloves, and no respirator.

PPE-G,DL-NR: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and no respirator.

PPE-G-80% R: Baseline plus chemical-resistant gloves and an 80% PF (quarter-face dust/mist) respirator.

PPE-G,DL-80% R: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and an 80% PF (quarter-face dust/mist) respirator.

PPE-G-90% R: Baseline plus chemical-resistant gloves and a 90% PF (half-face dust/mist) respirator.

PPE-G,DL-90% R: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and a 90% PF (half-face dust/mist) respirator.

Eng Controls: Closed mixing/loading system, enclosed cab, or enclosed cockpit.

9.2 Short- and Intermediate-Term Cancer Handler Risk

The occupational handler exposure and cancer risk calculations are presented in this section. Cancer risk estimates were calculated using a linear, low-dose extrapolation approach (Q_1*). The same scenarios, assumptions, and unit exposures were used as in the noncancer assessment. HED estimated cancer risk assuming estimates for an annual maximum of 10 days of exposure per year. This number is based on a Biological & Economic Analysis Division (BEAD) memo dated March 24, 2004 (Brassard). This memo provided information on the number of days permethrin is applied annually by applicators. The information in this memo showed that for most crops and use-patterns, occupational handlers apply permethrin less than ten days per year. As a result, HED considered one handler population (small, medium, and large scale growers as well as commercial applicators) for the cancer risk assessment.

HED has defined a level of concern range for cancer risk estimates based on a policy memorandum issued in 1996 by then Office of Pesticide Programs (OPP) director, Mr. Dan Barolo. This memo refers to a predetermined quantified "level of concern" for occupational carcinogenic risk. In summary, this policy memo indicates occupational carcinogenic risks that are 3×10^{-6} or lower require no risk management action. For those chemicals subject to reregistration, HED is to carefully examine uses with estimated risks in the 10^{-6} to 10^{-4} range to seek ways of cost-effectively reducing risks. If estimated cancer risks are in this range for occupational handlers, increased levels of personal protection would be warranted as is commonly applied with non-cancer risk estimates (e.g., additional PPE or engineering controls).

Estimated permethrin cancer risks for handlers are summarized below in Table 9.2. For all but a few scenarios, estimated cancer risks do not exceed HED's target level of concern (i.e., risks are below 3×10^{-6}) at some level of risk mitigation. For most scenarios, cancer risk estimates do not exceed HED's level of concern for cancer risks with the single layer clothing, gloves, and no respirator level of personal protection. In order to refine this occupational risk assessment, more data on actual use patterns including rates, timing, and areas treated would better characterize permethrin risks.

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
Mixer/Loader											
Mixing/Loading Emulsifiable Concentrates for Aerial Applications (1a)	pine seed orchard	1.2 lb ai/acre	100 acres	3.7E-05	5.6E-07	4.9E-07	3.5E-07	2.7E-07	3.2E-07	2.4E-07	1.3E-07
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	350 acres	4.4E-05	6.6E-07	5.7E-07	4.1E-07	3.2E-07	3.8E-07	2.9E-07	1.5E-07
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/acre	350 acres	3.3E-05	4.9E-07	4.3E-07	3.0E-07	2.4E-07	2.8E-07	2.1E-07	1.1E-07
	corn: sweet (FL only)	0.25 lb ai/acre	1200 acres	9.4E-05	1.4E-06	1.2E-06	8.7E-07	6.8E-07	8.0E-07	6.1E-07	3.2E-07
	corn: sweet (FL only)	0.25 lb ai/acre	350 acres	2.7E-05	4.1E-07	3.6E-07	2.5E-07	2.0E-07	2.3E-07	1.8E-07	9.4E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	1200 acres	7.5E-05	1.1E-06	9.7E-07	7.0E-07	5.4E-07	6.4E-07	4.9E-07	2.6E-07
	cabbage, Chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	350 acres	2.2E-05	3.3E-07	2.8E-07	2.0E-07	1.6E-07	1.9E-07	1.4E-07	7.5E-08
	conifers (field grown)	0.2 lb ai/acre	100 acres	6.2E-06	9.4E-08	8.1E-08	5.8E-08	4.5E-08	5.4E-08	4.1E-08	2.1E-08
	rose: field grown	0.2 lb ai/acre	60 acres	3.7E-06	5.6E-08	4.9E-08	3.5E-08	2.7E-08	3.2E-08	2.4E-08	1.3E-08
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards	0.1 lb ai/acre	350 acres	1.1E-05	1.6E-07	1.4E-07	1.0E-07	7.9E-08	9.4E-08	7.1E-08	3.8E-08
Mixing/Loading Emulsifiable Concentrates for Groundboom Applications (1b)	artichokes, garlic, onions: dry bulb	0.3 lb ai/acre	80 acres	7.5E-06	1.1E-07	9.7E-08	7.0E-08	5.4E-08	6.4E-08	4.9E-08	2.6E-08
	corn: sweet (FL only)	0.25 lb ai/acre	200 acres	1.6E-05	2.4E-07	2.0E-07	1.5E-07	1.1E-07	1.3E-07	1.0E-07	5.4E-08
	corn: sweet (FL only)	0.25 lb ai/acre	80 acres	6.2E-06	9.4E-08	8.1E-08	5.8E-08	4.5E-08	5.4E-08	4.1E-08	2.1E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	200 acres	1.2E-05	1.9E-07	1.6E-07	1.2E-07	9.1E-08	1.1E-07	8.2E-08	4.3E-08
	cabbage, Chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	80 acres	5.0E-06	7.5E-08	6.5E-08	4.6E-08	3.6E-08	4.3E-08	3.3E-08	1.7E-08
	chrysanthemum, roses: field grown	0.2 lb ai/acre	40 acres	2.5E-06	3.8E-08	3.2E-08	2.3E-08	1.8E-08	2.1E-08	1.6E-08	8.6E-09
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards, turnips	0.1 lb ai/acre	80 acres	2.5E-06	3.8E-08	3.2E-08	2.3E-08	1.8E-08	2.1E-08	1.6E-08	8.6E-09
Mixing/Loading Emulsifiable Concentrates for Airblast Applications (1c)	pine seed orchard	1.2 lb ai/acre	20 acres	7.5E-06	1.1E-07	9.7E-08	7.0E-08	5.4E-08	6.4E-08	4.9E-08	2.6E-08
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	40 acres	5.0E-06	7.5E-08	6.5E-08	4.6E-08	3.6E-08	4.3E-08	3.3E-08	1.7E-08
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/acre	40 acres	3.7E-06	5.6E-08	4.9E-08	3.5E-08	2.7E-08	3.2E-08	2.4E-08	1.3E-08
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	40 acres	2.5E-06	3.8E-08	3.2E-08	2.3E-08	1.8E-08	2.1E-08	1.6E-08	8.6E-09
	conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	20 acres	1.2E-06	1.9E-08	1.6E-08	1.2E-08	9.1E-09	1.1E-08	8.2E-09	4.3E-09
Mixing/Loading Emulsifiable Concentrates with Truck Mounted ULV Sprayer (using PHED airblast data) (1d)	outdoor spaces	0.007 lb ai/acre	3000 acres	6.5E-06	9.9E-08	8.5E-08	6.1E-08	4.8E-08	5.6E-08	4.3E-08	2.3E-08
Mixing/Loading Emulsifiable Concentrates via Dip (1e)	animal: livestock (beef and dairy cattle), horses, swine	0.0023 lb ai/animal	400 animals	2.9E-07	4.3E-09	3.7E-09	2.7E-09	2.1E-09	2.5E-09	1.9E-09	9.9E-10
	animal: dogs	0.005 lb ai/gal	10 gallons	1.6E-08	2.4E-10	2.0E-10	1.5E-10	1.1E-10	1.3E-10	1.0E-10	5.4E-11

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
Mixing/Loading Emulsifiable Concentrates for Residential Mister Systems (1f)	mosquitos	0.0023 lb ai/gal	250 gallons	1.8E-07	2.7E-09	2.3E-09	1.7E-09	1.3E-09	1.5E-09	1.2E-09	6.2E-10
		0.0023 lb ai/gal	1000 gallons	7.2E-07	1.1E-08	9.3E-09	6.7E-09	5.2E-09	6.2E-09	4.7E-09	2.5E-09
Mixing/Loading Wettable Powders for Aerial Applications (2a)	pine seed orchard	1.2 lb ai/acre	100 acres	5.7E-05	1.2E-05	1.1E-05	4.1E-06	3.6E-06	3.1E-06	2.6E-06	1.8E-07
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	350 acres	6.7E-05	1.4E-05	1.3E-05	4.8E-06	4.2E-06	3.7E-06	3.1E-06	2.1E-07
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/acre	350 acres	5.0E-05	1.0E-05	9.9E-06	3.6E-06	3.1E-06	2.8E-06	2.3E-06	1.6E-07
	corn: sweet (FL only)	0.25 lb ai/acre	1200 acres	1.4E-04	3.0E-05	2.8E-05	1.0E-05	9.0E-06	7.9E-06	6.6E-06	4.5E-07
	corn: sweet (FL only)	0.25 lb ai/acre	350 acres	4.2E-05	8.6E-06	8.3E-06	3.0E-06	2.6E-06	2.3E-06	1.9E-06	1.3E-07
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	1200 acres	1.1E-04	2.4E-05	2.3E-05	8.2E-06	7.2E-06	6.3E-06	5.3E-06	3.6E-07
	cabbage, Chinese cabbage, corn (pop, seed, sweet) cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	350 acres	3.3E-05	6.9E-06	6.6E-06	2.4E-06	2.1E-06	1.8E-06	1.5E-06	1.0E-07
	conifers (field grown)	0.2 lb ai/acre	100 acres	9.5E-06	2.0E-06	1.9E-06	6.8E-07	6.0E-07	5.2E-07	4.4E-07	3.0E-08
	rose: field grown	0.2 lb ai/acre	60 acres	5.7E-06	1.2E-06	1.1E-06	4.1E-07	3.6E-07	3.1E-07	2.6E-07	1.8E-08
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards	0.1 lb ai/acre	350 acres	1.7E-05	3.5E-06	3.3E-06	1.2E-06	1.0E-06	9.2E-07	7.7E-07	5.2E-08
Mixing/Loading Wettable Powders for Groundboom Applications (2b)	artichokes, garlic, onions: dry bulb	0.3 lb ai/acre	80 acres	1.1E-05	2.4E-06	2.3E-06	8.2E-07	7.2E-07	6.3E-07	5.3E-07	3.6E-08
	corn: sweet (FL only)	0.25 lb ai/acre	200 acres	2.4E-05	4.9E-06	4.7E-06	1.7E-06	1.5E-06	1.3E-06	1.1E-06	7.5E-08
	corn: sweet (FL only)	0.25 lb ai/acre	80 acres	9.5E-06	2.0E-06	1.9E-06	6.8E-07	6.0E-07	5.2E-07	4.4E-07	3.0E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	200 acres	1.9E-05	3.9E-06	3.8E-06	1.4E-06	1.2E-06	1.0E-06	8.8E-07	6.0E-08
	cabbage, Chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	80 acres	7.6E-06	1.6E-06	1.5E-06	5.5E-07	4.8E-07	4.2E-07	3.5E-07	2.4E-08
	chrysanthemum, roses: field grown	0.2 lb ai/acre	40 acres	3.8E-06	7.9E-07	7.6E-07	2.7E-07	2.4E-07	2.1E-07	1.8E-07	1.2E-08
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards, turnips	0.1 lb ai/acre	80 acres	3.8E-06	7.9E-07	7.6E-07	2.7E-07	2.4E-07	2.1E-07	1.8E-07	1.2E-08
Mixing/Loading Wettable Powders for Airblast Applications (2c)	pine seed orchard	1.2 lb ai/acre	20 acres	1.1E-05	2.4E-06	2.3E-06	8.2E-07	7.2E-07	6.3E-07	5.3E-07	3.6E-08
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	40 acres	7.6E-06	1.6E-06	1.5E-06	5.5E-07	4.8E-07	4.2E-07	3.5E-07	2.4E-08
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/acre	40 acres	5.7E-06	1.2E-06	1.1E-06	4.1E-07	3.6E-07	3.1E-07	2.6E-07	1.8E-08
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	40 acres	3.8E-06	7.9E-07	7.6E-07	2.7E-07	2.4E-07	2.1E-07	1.8E-07	1.2E-08
	conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	20 acres	1.9E-06	3.9E-07	3.8E-07	1.4E-07	1.2E-07	1.0E-07	8.8E-08	6.0E-09
Loading Dusts via Mechanical Duster (using PHED wettable powders data) (2d)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	5.9E-09	1.2E-09	1.2E-09	4.2E-10	3.7E-10	3.2E-10	2.7E-10	NF
	animal: poultry	0.0025 lb ai/animal	100000 animals	1.2E-04	2.5E-05	2.4E-05	8.6E-06	7.5E-06	6.5E-06	5.5E-06	NF
	animal: swine	0.00016 lb ai/animal	400 animals	3.0E-08	6.3E-09	6.0E-09	2.2E-09	1.9E-09	1.7E-09	1.4E-09	NF
Loading Dusts via Dust Bag (using PHED wettable powders data) (2e)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	5.9E-09	1.2E-09	1.2E-09	4.2E-10	3.7E-10	3.2E-10	2.7E-10	#VALUE!
	animal: swine	0.00016 lb ai/animal	400 animals	3.0E-08	6.3E-09	6.0E-09	2.2E-09	1.9E-09	1.7E-09	1.4E-09	#VALUE

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
											!
Loading Granulars for Aerial Applications (3a)	almonds, pistachios	0.4 lb ai/acre	350 acres	5.7E-07	5.5E-07	5.0E-07	1.9E-07	1.4E-07	1.5E-07	9.5E-08	1.1E-08
	alfalfa; corn: field, sweet-fresh & processed; corn: field-preplant	0.2 lb ai/acre	1200 acres	9.8E-07	9.4E-07	8.5E-07	3.3E-07	2.4E-07	2.5E-07	1.6E-07	2.0E-08
	corn: sweet-fresh & processed	0.2 lb ai/acre	350 acres	2.9E-07	2.7E-07	2.5E-07	9.6E-08	7.0E-08	7.4E-08	4.8E-08	5.7E-09
Loading Granulars for Tractor Drawn Spreader Applications (3b)	almonds, pistachios	0.4 lb ai/acre	80 acres	1.3E-07	1.3E-07	1.1E-07	4.4E-08	3.2E-08	3.4E-08	2.2E-08	2.6E-09
	corn: sweet (fresh & processed)	0.2 lb ai/acre	80 acres	6.5E-08	6.3E-08	5.7E-08	2.2E-08	1.6E-08	1.7E-08	1.1E-08	1.3E-09
	alfalfa, corn (field, sweet-fresh & processed), corn: field (preplant)	0.2 lb ai/acre	200 acres	1.6E-07	1.6E-07	1.4E-07	5.5E-08	4.0E-08	4.2E-08	2.7E-08	3.3E-09
Applicator											
Applying Liquid Sprays via Aerial Equipment (4)	pine seed orchard	1.2 lb ai/acre	100 acres	ND	ND	ND	ND	ND	ND	ND	7.9E-08
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	9.3E-08
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	6.9E-08
	corn: sweet (FL only)	0.25 lb ai/acre	1200 acres	ND	ND	ND	ND	ND	ND	ND	2.0E-07
	corn: sweet (FL only)	0.25 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	5.8E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	1200 acres	ND	ND	ND	ND	ND	ND	ND	1.6E-07
	cabbage, Chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	4.6E-08
	conifers (field grown)	0.2 lb ai/acre	100 acres	ND	ND	ND	ND	ND	ND	ND	1.3E-08
	rose: field grown	0.2 lb ai/acre	60 acres	ND	ND	ND	ND	ND	ND	ND	7.9E-09
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards	0.1 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	2.3E-08
Applying Liquid Sprays via Groundboom Equipment (5)	artichokes, garlic, onions: dry bulb	0.3 lb ai/acre	80 acres	ND	ND	ND	ND	ND	ND	ND	1.5E-08
	corn: sweet (FL only)	0.25 lb ai/acre	200 acres	1.4E-07	1.4E-07	1.3E-07	8.9E-08	7.3E-08	8.2E-08	6.6E-08	3.1E-08
	corn: sweet (FL only)	0.25 lb ai/acre	80 acres	5.8E-08	5.8E-08	5.1E-08	3.5E-08	2.9E-08	3.3E-08	2.6E-08	1.2E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans	0.2 lb ai/acre	200 acres	1.2E-07	1.2E-07	1.0E-07	7.1E-08	5.8E-08	6.5E-08	5.2E-08	2.5E-08
	cabbage, Chinese cabbage, corn (pop, seed, sweet), cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	80 acres	4.6E-08	4.6E-08	4.1E-08	2.8E-08	2.3E-08	2.6E-08	2.1E-08	9.8E-09
	chrysanthemum, roses: field grown	0.2 lb ai/acre	40 acres	2.3E-08	2.3E-08	2.0E-08	1.4E-08	1.2E-08	1.3E-08	1.0E-08	4.9E-09
	asparagus, broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards, turnips	0.1 lb ai/acre	80 acres	2.3E-08	2.3E-08	2.0E-08	1.4E-08	1.2E-08	1.3E-08	1.0E-08	4.9E-09
Applying Liquid Sprays via Airblast Equipment (6)	pine seed orchard	1.2 lb ai/acre	40 acres	1.1E-06	8.2E-07	7.7E-07	6.6E-07	6.0E-07	6.3E-07	5.8E-07	3.8E-07
	almonds, apples, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	40 acres	7.5E-07	5.4E-07	5.1E-07	4.4E-07	4.0E-07	4.2E-07	3.9E-07	2.5E-07
	cherries: sweet and sour, nectarines, peaches	0.3 lb ai/acre	40 acres	5.6E-07	4.1E-07	3.8E-07	3.3E-07	3.0E-07	3.2E-07	2.9E-07	1.9E-07
	avocados, papayas, conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	40 acres	3.7E-07	2.7E-07	2.6E-07	2.2E-07	2.0E-07	2.1E-07	1.9E-07	1.3E-07

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
	conifers (field grown), ornamental nursery stock	0.2 lb ai/acre	20 acres	1.9E-07	1.4E-07	1.3E-07	1.1E-07	1.0E-07	1.1E-07	9.7E-08	6.3E-08
Applying Liquid Sprays with Truck Mounted ULV Sprayer (using PHED Airblast data) (7)	outdoor spaces	0.007 lb ai/acre	3000 acres	9.8E-07	7.1E-07	6.7E-07	5.7E-07	5.3E-07	5.6E-07	5.1E-07	3.3E-07
Applying Emulsifiable Concentrates via Dip (8)	animal: livestock (beef and dairy cattle), horses, swine	0.0023 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: dogs	0.005 lb ai/gal	10 gallons	ND	ND	ND	ND	ND	ND	ND	ND
	military battle dress	0.00000011 lb ai/cm2 of fabric		ND	ND	ND	ND	ND	ND	ND	ND
Applying Granulars via Aerial Equipment (9)	almonds, pistachios,	0.4 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	3.7E-07
	alfalfa, corn: field, corn: sweet (fresh & processed), corn: field (preplant)	0.2 lb ai/acre	1200 acres	ND	ND	ND	ND	ND	ND	ND	6.3E-07
	corn: sweet (fresh & processed)	0.2 lb ai/acre	350 acres	ND	ND	ND	ND	ND	ND	ND	1.8E-07
Applying Granulars via Tractor Drawn Spreader (10)	almonds, pistachios,	0.4 lb ai/acre	80 acres	1.1E-07	9.6E-08	8.6E-08	3.9E-08	2.9E-08	3.2E-08	2.2E-08	2.0E-08
	alfalfa, corn: field, corn: sweet (fresh & processed), corn: field (preplant)	0.2 lb ai/acre	200 acres	1.3E-07	1.2E-07	1.1E-07	4.9E-08	3.6E-08	4.0E-08	2.7E-08	2.5E-08
	corn: sweet (fresh & processed)	0.2 lb ai/acre	80 acres	5.3E-08	4.8E-08	4.3E-08	1.9E-08	1.4E-08	1.6E-08	1.1E-08	1.0E-08
Applying Dusts via Mechanical Duster (11)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: poultry	0.0025 lb ai/animal	100000 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: swine	0.00016 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
Applying Dusts via Dust Bag (12)	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: poultry	0.0025 lb ai/animal	100000 animals	ND	ND	ND	ND	ND	ND	ND	ND
	animal: swine	0.00016 lb ai/animal	400 animals	ND	ND	ND	ND	ND	ND	ND	ND
Flagger											
Flagging for Liquid Sprays via Aerial Equipment (13)	pine seed orchard	1.2 lb ai/acre	100 acres	2.2E-07	ND	2.1E-07	ND	1.4E-07	ND	1.4E-07	7.4E-08
	almonds, filberts, pears (dormant & prebloom combo), pistachios, walnuts	0.4 lb ai/acre	350 acres	2.6E-07	ND	2.4E-07	ND	1.7E-07	ND	1.6E-07	8.6E-08
	artichokes, garlic, nectarines, onions: dry bulb, peaches	0.3 lb ai/acre	350 acres	1.9E-07	ND	1.8E-07	ND	1.3E-07	ND	1.2E-07	6.4E-08
	corn: sweet (FL only)	0.25 lb ai/acre	350 acres	1.6E-07	ND	1.5E-07	ND	1.0E-07	ND	9.9E-08	5.4E-08
	alfalfa, corn (field, pop, seed, sweet), corn: field (preplant), range grasses, soybeans, cabbage, Chinese cabbage, cucurbits, eggplant, leafy vegetables, peppers: bell, potatoes, tomatoes, tomatillos	0.2 lb ai/acre	350 acres	1.3E-07	ND	1.2E-07	ND	8.4E-08	ND	7.9E-08	4.3E-08
	conifers (field grown)	0.2 lb ai/acre	100 acres	3.7E-08	ND	3.4E-08	ND	2.4E-08	ND	2.3E-08	1.2E-08
	rose: field grown	0.2 lb ai/acre	60 acres	2.2E-08	ND	2.1E-08	ND	1.4E-08	ND	1.4E-08	7.4E-09
	broccoli, Brussel sprouts, cauliflower, Chinese broccoli, collards	0.1 lb ai/acre	350 acres	6.4E-08	ND	6.0E-08	ND	4.2E-08	ND	4.0E-08	2.1E-08
Flagging for Granulars via Aerial Equipment (14)	almonds, pistachios,	0.4 lb ai/acre	350 acres	8.1E-08	ND	6.3E-08	ND	3.2E-08	ND	2.8E-08	8.9E-08
	alfalfa, corn: field, corn: sweet (fresh &	0.2 lb ai/acre	350 acres	4.1E-08	ND	3.2E-08	ND	1.6E-08	ND	1.4E-08	4.5E-08

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
	processed), corn: field (preplant)										
Mixer/Loader/Applicator											
Mixing/Loading/Applying Emulsifiable Concentrates with Low Pressure Handwand (15)	turf	0.87 lb ai/acre	5 acres	4.7E-05	4.4E-07	4.2E-07	2.5E-07	2.2E-07	2.2E-07	2.0E-07	NF
	mushroom houses	0.267 lb ai/gallon	40 gallons	1.1E-04	1.1E-06	1.0E-06	6.1E-07	5.4E-07	5.5E-07	4.8E-07	NF
	conifers (field grown)	0.2 lb ai/acre	40 gallons	8.6E-05	8.2E-07	7.7E-07	4.6E-07	4.1E-07	4.1E-07	3.6E-07	NF
	indoor surfaces, perimeter treatments	0.08 lb ai/gallon	40 gallons	3.4E-05	3.3E-07	3.1E-07	1.8E-07	1.6E-07	1.6E-07	1.4E-07	NF
	ornamentals: outdoor	0.046 lb ai/gallon	40 gallons	2.0E-05	1.9E-07	1.8E-07	1.1E-07	9.3E-08	9.5E-08	8.3E-08	NF
	animal premises, outdoor surfaces, wood, ants & fire ants	0.04 lb ai/gallon	40 gallons	1.7E-05	1.6E-07	1.5E-07	9.1E-08	8.1E-08	8.2E-08	7.2E-08	NF
	rose: field grown	0.02 lb ai/gallon	40 gallons	8.6E-06	8.2E-08	7.7E-08	4.6E-08	4.1E-08	4.1E-08	3.6E-08	NF
	pine seed orchard	0.0105 lb ai/gallon	40 gallons	4.5E-06	4.3E-08	4.0E-08	2.4E-08	2.1E-08	2.2E-08	1.9E-08	NF
	agricultural premises	0.0085 lb ai/gallon	40 gallons	3.6E-06	3.5E-08	3.3E-08	1.9E-08	1.7E-08	1.8E-08	1.5E-08	NF
	chrysanthemum	0.005 lb ai/gallon	40 gallons	2.1E-06	2.0E-08	1.9E-08	1.1E-08	1.0E-08	1.0E-08	9.0E-09	NF
	almond, filbert, pear, pistachio (trees at residential sites)	0.004 lb ai/gallon	40 gallons	1.7E-06	1.6E-08	1.5E-08	9.1E-09	8.1E-09	8.2E-09	7.2E-09	NF
	peach (trees at residential sites)	0.003 lb ai/gallon	40 gallons	1.3E-06	1.2E-08	1.1E-08	6.9E-09	6.1E-09	6.2E-09	5.4E-09	NF
	apple & cherry trees at residential sites, ornamentals: greenhouse & other indoor, rose: greenhouse, ornamental nursery stock	0.002 lb ai/gallon	40 gallons	8.6E-07	8.2E-09	7.7E-09	4.6E-09	4.1E-09	4.1E-09	3.6E-09	NF
	termites	33.2 lb ai/1000 linear feet	1000 linear feet	3.6E-04	3.4E-06	3.2E-06	1.9E-06	1.7E-06	1.7E-06	1.5E-06	NF
	animal: livestock (beef and dairy cattle), goats, horses, sheep, swine	0.0023 lb ai/animal	400 animals	9.9E-06	9.4E-08	8.8E-08	5.3E-08	4.7E-08	4.7E-08	4.1E-08	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Handgun Sprayer (ORETF data) (16)	turf	0.87 lb ai/acre	5 acres	6.5E-07	4.6E-07	2.5E-07	4.4E-07	2.3E-07	4.4E-07	2.3E-07	NF
	conifers (field grown)	0.2 lb ai/gallon	1000 gallons	3.8E-07	2.7E-07	1.5E-07	2.6E-07	1.4E-07	2.6E-07	1.3E-07	NF
	perimeter treatment	0.08 lb ai/gallon	500 gallons	1.5E-07	1.1E-07	5.9E-08	1.0E-07	5.4E-08	1.0E-07	5.4E-08	NF
	ornamentals: outdoor	0.046 lb ai/gallon	1000 gallons	1.1E-07	8.1E-08	4.4E-08	7.8E-08	4.1E-08	7.7E-08	4.0E-08	NF
	outdoor surfaces, ants, and fire ants	0.04 lb ai/gallon	500 gallons	1.5E-07	1.1E-07	5.9E-08	1.0E-07	5.4E-08	1.0E-07	5.4E-08	NF
	rose: field grown	0.02 lb ai/gallon	1000 gallons	7.6E-08	5.4E-08	2.9E-08	5.2E-08	2.7E-08	5.2E-08	2.7E-08	NF
	pine seed orchard	0.0105 lb ai/gallon	1000 gallons	4.4E-05	3.9E-05	3.1E-05	2.0E-05	1.3E-05	1.8E-05	1.0E-05	NF
	agricultural premises	0.0085 lb ai/gallon	1000 gallons	4.4E-06	3.9E-06	3.1E-06	2.0E-06	1.3E-06	1.8E-06	1.0E-06	NF
	chrysanthemum	0.005 lb ai/gallon	1000 gallons	2.3E-06	2.0E-06	1.6E-06	1.1E-06	6.7E-07	9.3E-07	5.5E-07	NF
	almond, filbert, pear, pistachio (trees at residential sites)	0.004 lb ai/gallon	500 gallons	1.9E-06	1.6E-06	1.3E-06	8.5E-07	5.4E-07	7.5E-07	4.4E-07	NF
	peach (trees at residential sites)	0.003 lb ai/gallon	500 gallons	1.1E-06	9.6E-07	7.8E-07	5.0E-07	3.2E-07	4.4E-07	2.6E-07	NF
	roses: greenhouse, ornamental nursery stock (non-bearing); ornamentals: greenhouse	0.002 lb ai/gallon	1000 gallons	4.4E-07	3.9E-07	3.1E-07	2.0E-07	1.3E-07	1.8E-07	1.0E-07	NF
	apple & cherry (trees at residential sites)	0.002 lb ai/gallon	500 gallons	9.9E-07	7.3E-07	4.4E-07	6.3E-07	3.4E-07	6.2E-07	3.3E-07	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a High Pressure Handwand (only study in PHED is for greenhouse use) (17)	rose: field grown	0.02 lb ai/gallon	1000 gallons	ND	9.8E-06	7.9E-06	6.2E-06	4.3E-06	5.8E-06	3.9E-06	NF
	animal premises	0.012 lb ai/gallon	1000 gallons	ND	5.9E-06	4.7E-06	3.7E-06	2.6E-06	3.5E-06	2.3E-06	NF
	chrysanthemum	0.005 lb ai/gallon	1000 gallons	ND	2.5E-06	2.0E-06	1.6E-06	1.1E-06	1.4E-06	9.7E-07	NF
	rose: greenhouse	0.002 lb ai/gallon	1000 gallons	ND	9.8E-07	7.9E-07	6.2E-07	4.3E-07	5.8E-07	3.9E-07	NF
	animal: poultry	0.00027 lb ai/animal	4000 animals	ND	1.3E-05	1.1E-05	8.4E-06	5.8E-06	7.8E-06	5.2E-06	NF

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
Mixing/Loading/Applying Emulsifiable Concentrate with an Injector (18)	termites	0.08 lb ai/gallon	2000 gallons (Carbaryl)	ND	6.8E-06	4.9E-06	6.3E-06	4.4E-06	6.2E-06	4.3E-06	NF
Mixing/Loading/Applying Emulsifiable Concentrates via Foam Applicator Equipment (using PHED low-pressure handwand) (19)	termites	4.25 lb ai/1000 sq ft	1000 sq ft	4.6E-05	4.3E-07	4.1E-07	2.4E-07	2.2E-07	2.2E-07	1.9E-07	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Watering Can (using ORETF residential hose-end data) (20)	fire ant mounds	0.04 lb ai/gallon	10 gallons	4.8E-07	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Emulsifiable Concentrates with Backpack ULV Sprayer (using PHED backpack data) (21)	outdoor spaces	0.007 lb ai/acre	5 acres	ND	1.1E-08	7.9E-09	9.7E-09	6.4E-09	9.5E-09	6.2E-09	NF
	outdoor spaces: barrier spray	0.1 lb ai/acre	5 acres	ND	1.6E-07	1.1E-07	1.4E-07	9.1E-08	1.4E-07	8.8E-08	NF
Mixing/Loading/Applying Emulsifiable Concentrates with a Paint Brush (22)	indoor surfaces	0.08 lb ai/gallon	5 gallons	7.9E-06	1.2E-06	1.1E-06	1.1E-06	9.8E-07	1.0E-06	9.6E-07	NF
	wood, outdoor surfaces	0.04 lb ai/gallon	5 gallons	3.9E-06	6.2E-07	5.7E-07	5.3E-07	4.9E-07	5.2E-07	4.8E-07	NF
Mixing/Loading/Applying Emulsifiable Concentrates via Cold Fogger/ (23)	mushroom houses	0.0078 lb ai/ sq ft	40000 sq ft (8000 sq ft per house)	ND	ND	ND	ND	ND	ND	ND	NF
	indoor spaces	0.00036 lb ai/cu ft	200000 cu ft	ND	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Wettable Powders with Low Pressure Handwand (24)	conifers (field grown)	0.2 lb ai/gallon	40 gallons	ND	2.4E-05	2.2E-05	1.1E-05	8.6E-06	9.0E-06	6.9E-06	NF
	rose: field grown	0.02 lb ai/gallon	40 gallons	ND	2.4E-06	2.2E-06	1.1E-06	8.6E-07	9.0E-07	6.9E-07	NF
	indoor surfaces	0.0117 lb ai/gallon	40 gallons	ND	1.4E-06	1.3E-06	6.2E-07	5.0E-07	5.3E-07	4.1E-07	NF
	pine seed orchard	0.0105 lb ai/gallon	40 gallons	ND	1.3E-06	1.1E-06	5.6E-07	4.5E-07	4.7E-07	3.6E-07	NF
	mushroom houses, agricultural premises	0.0085 lb ai/gallon	40 gallons	ND	1.0E-06	9.3E-07	4.5E-07	3.6E-07	3.8E-07	2.9E-07	NF
	chrysanthemum	0.005 lb ai/gallon	40 gallons	ND	6.0E-07	5.4E-07	2.7E-07	2.1E-07	2.2E-07	1.7E-07	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gallon	40 gallons	ND	2.4E-07	2.2E-07	1.1E-07	8.6E-08	9.0E-08	6.9E-08	NF
Mixing/Loading/Applying Wettable Powders with a Handgun Sprayer (ORETF data) (25)	conifers (field grown)	0.2 lb ai/gallon	40 gallons	4.4E-05	3.9E-05	3.1E-05	2.0E-05	1.3E-05	1.8E-05	1.0E-05	NF
	rose: field grown	0.02 lb ai/gallon	40 gallons	4.4E-06	3.9E-06	3.1E-06	2.0E-06	1.3E-06	1.8E-06	1.0E-06	NF
	pine seed orchard	0.0105 lb ai/gallon	40 gallons	2.3E-06	2.0E-06	1.6E-06	1.1E-06	6.7E-07	9.3E-07	5.5E-07	NF
	agricultural premises	0.0085 lb ai/gallon	40 gallons	1.9E-06	1.6E-06	1.3E-06	8.5E-07	5.4E-07	7.5E-07	4.4E-07	NF
	chrysanthemum	0.005 lb ai/gallon	40 gallons	1.1E-06	9.6E-07	7.8E-07	5.0E-07	3.2E-07	4.4E-07	2.6E-07	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gallon	40 gallons	4.4E-07	3.9E-07	3.1E-07	2.0E-07	1.3E-07	1.8E-07	1.0E-07	NF
Mixing/Loading/Applying Wettable Powders with a High Pressure Handwand (26)	rose: field grown	0.02 lb ai/gallon	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF
	chrysanthemum	0.005 lb ai/gallon	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF
	rose: greenhouse	0.002 lb ai/gallon	1000 gallons	ND	ND	ND	ND	ND	ND	ND	NF

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
Mixing/Loading/Applying Water Soluble Bags with Handgun Sprayer (ORETF data) (27)	conifers (field grown)	0.2 lb ai/gallon	1000 gallons	9.9E-07	7.3E-07	4.4E-07	6.3E-07	3.4E-07	6.2E-07	3.3E-07	NF
	rose: field grown	0.02 lb ai/gallon	1000 gallons	5.8E-07	4.3E-07	2.6E-07	3.7E-07	2.0E-07	3.6E-07	1.9E-07	NF
	pine seed orchard	0.0105 lb ai/gallon	1000 gallons	1.2E-06	9.0E-07	5.4E-07	7.8E-07	4.2E-07	7.7E-07	4.1E-07	NF
	animal premises	0.0085 lb ai/gallon	1000 gallons	2.3E-07	1.7E-07	1.0E-07	1.5E-07	8.0E-08	1.5E-07	7.8E-08	NF
	chrysanthemum	0.005 lb ai/gallon	1000 gallons	2.3E-06	1.7E-06	1.0E-06	1.5E-06	8.0E-07	1.5E-06	7.8E-07	NF
	rose: greenhouse, ornamental nursery stock (non-bearing)	0.002 lb ai/gallon	1000 gallons	2.3E-05	1.7E-05	1.0E-05	1.5E-05	8.0E-06	1.5E-05	7.8E-06	NF
Mixing/Loading/Applying Wettable Powders via Cold Fogger (28)	mushroom houses	0.011 lb ai/1000 sq ft	8000 sq ft	ND	ND	ND	ND	ND	ND	ND	NF
Applying Dusts via Shaker Can (MRID 444598-01) (29)	animal: poultry	0.0025 lb ai/animal	4000 animals	1.7E-04	ND	ND	ND	ND	ND	ND	NF
	animal: swine	0.00016 lb ai/animal	400 animals	1.1E-06	ND	ND	ND	ND	ND	ND	NF
	animal: dogs, cats	0.00016 lb ai/animal	8 animals	2.2E-08	ND	ND	ND	ND	ND	ND	NF
	animal: dairy and beef cattle, horses	0.000031 lb ai/animal	400 animals	2.2E-07	ND	ND	ND	ND	ND	ND	NF
Mixing/Loading/Applying Microencapsulated Liquids via Fogger/Mist Generator (30)	animal premises	0.012 lb ai/1000 sq ft	1000 sq ft	ND	ND	ND	ND	ND	ND	ND	NF
	indoor spaces	0.00036 lb ai/1000 cu ft	1000 cu ft	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via Pour-on (using PHED mix/load liquid) (31)	animal: horses	0.005lb ai/animal	400 animals	6.2E-07	9.4E-09	8.1E-09	5.8E-09	4.5E-09	5.4E-09	4.1E-09	NF
	animal: dairy and beef cattle, calves, sheep	0.0034 lb ai/animal	400 animals	4.2E-07	6.4E-09	5.5E-09	3.9E-09	3.1E-09	3.6E-09	2.8E-09	NF
	animal: swine	0.002 lb ai/animal	400 animals	2.5E-07	3.8E-09	3.2E-09	2.3E-09	1.8E-09	2.1E-09	1.6E-09	NF
	clothing: personal	0.002 lb ai/6 oz container	1 container	6.2E-10	9.4E-12	8.1E-12	5.8E-12	4.5E-12	5.4E-12	4.1E-12	NF
	deer: ticks	40	posts (per treatment device)	1.1E-07	1.7E-09	1.5E-09	1.1E-09	8.3E-10	9.9E-10	7.5E-10	NF
Applying Ready to Use Formulations via RTU Ear-Tag (32)	animal	0.0044 lb ai/2 ear tags	400 cattle (2 tags/cattle)	ND	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via Hands (MRID 446584-01) (33)	animal: dogs	0.0062 lb ai/animal	8 animals	9.5E-06	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via RTU Wipe (34)	animal: dogs, horses	0.0062 lb ai/animal	8 animals	1.8E-05	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations via Trigger-Pump Sprayer (using Propoxur Trigger Pump study) (35)	animal: horses, foals	0.61 lb ai/gallon	2 gallons	1.4E-07	ND	ND	ND	ND	ND	ND	NF
	indoor surfaces; animals cattle, goats, sheep, swine	0.043 lb ai/gallon	2 gallons	2.0E-06	ND	ND	ND	ND	ND	ND	NF
Applying Ready to Use Formulations with Aerosol Cans (36)	outdoor surfaces	0.00438 lb ai/16 oz can	2 sixteen-ounce aerosol cans	2.0E-07	9.7E-08	8.1E-08	8.0E-08	6.4E-08	7.8E-08	6.2E-08	NF
Applying Ready to Use Formulations with Foggers (using PHED aerosol data) (37)	indoor spaces	0.0016 lb ai/6 oz fogger	4 six ounce fogger treats 6000 cubic feet	1.5E-07	7.1E-08	5.9E-08	5.8E-08	4.7E-08	5.7E-08	4.5E-08	NF
Applying Ready to Use	ants	ND	ND	ND	ND	ND	ND	ND	ND	ND	NF

Table 9.2. Summary of Permethrin Occupational Handler Cancer Risk Estimates

Exposure Scenario	Crop or Target	Application Rate [a]	Area Treated Daily [b]	Cancer Risk Estimates							
				Baseline	PPE-G-NR	PPE-G, DL-NR	PPE-G-80% R	PPE-G, DL-80% R	PPE-G-90% R	PPE-G, DL- 90% R	Eng Control
Protective Flanges (38)											
Applying Ready to Use Vapor Recovery System Tubes (39)	engines	0.000189 lb ai/tube	ND	ND	ND	ND	ND	ND	ND	ND	NF

Footnotes

- Handler exposure was considered to be 10 days per year for 35 years over a 70 year lifetime.

ND No Data

NF Not Feasible

a Application rates are the maximum application rates provided by for permethrin in all cases. Typical rates provided by BEAD differed very little from the maximum rates.

b Amount handled per day values are HED estimates of acreage treated or gallons applied based on Exposure SAC SOP #9 "Standard Values for Daily Acres Treated in Agriculture," industry input, and HED estimates.

c Baseline: Long-sleeve shirt, long pants, no gloves, and no respirator.

PPE-G-NR: Baseline plus chemical-resistant gloves, and no respirator.

PPE-G,DL-NR: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and no respirator.

PPE-G-80% R: Baseline plus chemical-resistant gloves and an 80% PF (quarter-face dust/mist) respirator.

PPE-G,DL-80% R: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and an 80% PF (quarter-face dust/mist) respirator.

PPE-G-90% R: Baseline plus chemical-resistant gloves and a 90% PF (half-face dust/mist) respirator.

PPE-G,DL-90% R: Coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, and a 90% PF (half-face dust/mist) respirator.

Eng Controls: Closed mixing/loading system, enclosed cab, or enclosed cockpit.

9.3 Short- and Intermediate-Term Noncancer Postapplication Risks

HED uses the term "postapplication" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide (also referred to as reentry exposure). HED believes that there are distinct job functions or tasks related to the kinds of activities that occur in previously treated areas. Job requirements (e.g., the kinds of jobs to cultivate a crop), the nature of the crop or target that was treated, and the how chemical residues degrade in the environment can cause exposure levels to differ over time. Each factor has been considered in this assessment.

9.3.1 Agricultural Scenarios

To assess postapplication exposures and risks, HED attempts to identify the types of tasks and activities that postapplication workers will be performing in permethrin-treated areas. Examples include: agricultural harvesters, scouting activities in agriculture, crop maintenance tasks (e.g., irrigating, hoeing and weeding), and turf maintenance (golf course mowing). Then HED uses a *transfer coefficient* (cm^2/hr) to estimate the amount of contact with a treated surface a person likely would have while doing a specific postapplication task or activity. HED has developed a series of standard *transfer coefficients* that are unique for variety of job tasks or activities that are used in lieu of chemical- and scenario-specific data.

HED estimates the amount of pesticide residue that can transfer from different treated surfaces to a person's skin using techniques that specifically determine the amount of residues on treated surfaces (e.g., foliage, fruit), rather than the total residues on the surface and absorbed into treated plants. These surface- available residues are called *transferable residues* or *dislodgeable foliar residues*. In order to estimate the transferable residues to which individuals can be exposed, HED relies, whenever possible, on chemical- and crop-specific studies as described in HED guidelines for exposure data collection (*Series 875, Occupational and Residential Exposure Test Guidelines: Group B - Postapplication Exposure Monitoring Test Guidelines*). Permethrin-specific studies measured initial transferable surface residues and subsequent surface residue dissipation over time following applications to cotton, peaches, and turfgrass. The DFR/TTR component of those studies has been extracted for chemical-specific use in this risk assessment. The studies which have been used in this assessment are identified below followed by a brief summary of each:

- **"Dislodgeable Insecticide Residues on Cotton Foliage: Fenvalerate, Permethrin, Sulprofos, Chloryrifos, Methyl Parathion, EPN, Oxamyl, and Profenofos"** MRID 455705-25; Report dated 1980. Authors N.A. Buck, B.J. Estesen, and G.W. Ware; Submitted by Dow Chemical Company U.S.A.

- **"Dissipation of Dislodgeable Foliar Residues of Permethrin Applied to Orchards (Peaches)"** EPA MRID 437557-01; Report dated July 20, 1995; Authors; Tami Belcher, Larissa Schuster; Sponsor: Zeneca Ag Products, Inc.: C/O permethrin Task Force; Performing Laboratories: Analytical - ABC Laboratories, Pan-Ag Division.

- **"Transferable Turf Residue Study: Permethrin Residues in Turf Following Application of Dragnet SFR Insecticide"** EPA MRID 449555-01; Report dated October 1, 1999; Author; Jill C. Holihan; Sponsor: FMC Corporation: Agricultural Products Group; Performing Laboratories: Analytical - FMC Corporation and Maxim Technologies, Inc.

In cases where no chemical-specific residue dissipation data are available, HED typically uses a generic dissipation model to complete risk calculations. In this case, HED determined that it is more appropriate however, to extrapolate using permethrin-specific dissipation data in the risk assessment for other currently labeled crops than it is to use the generic dissipation model. This approach is consistent with current HED policies for generating transferable/dislodgeable residue data. The existing residue data were extrapolated to each of the currently labeled crops. This extrapolation was completed because of similarities in application methods between the study and selected crop groups, the crop canopy, and application rates (i.e., between the study and current labels). (Note: agronomic crop groups are defined in HED's revised transfer coefficient policy 003)

- **Cotton DFR Data:** These data have been used to complete assessments for low/medium field/row crop, tall field/row crop, cucurbit vegetable, fruiting vegetable, head and stem vegetable, leafy vegetable, root vegetable, stem and stalk vegetable, and cut flowers.

- **Peach DFR Data:** These data have been used to complete assessments for tree fruit (deciduous and evergreen), nut crop, and ornamentals.

The frequency and duration of occupational postapplication exposures must also be estimated in order to determine which toxicological endpoints of concern are applicable to each postapplication scenario. Two dermal non-cancer risk calculations were required for each postapplication scenario: short-term (≤30 days) and intermediate-term (30 days up to several months). In addition, long-term exposures were determined for persons wearing or working with permethrin-impregnated fabric. Since the short-, intermediate-, and long-term dermal toxicological endpoints of concern are the same endpoint, short-, intermediate-, and long-term dermal risks for a specific postapplication scenario are numerically identical. Inhalation exposures are thought to be negligible in outdoor postapplication scenarios because of the low vapor pressure and due to the infinite dilution expected outdoors. As such, inhalation postapplication exposures are not considered in this assessment.

The use of personal protective equipment or other types of equipment to reduce exposures for postapplication workers is not considered a viable alternative for the regulatory process. This is described in some detail in EPA's Worker Protection Standard (40CFR170). As such, an administrative approach is used by HED to reduce the risks and is referred to as the *Restricted Entry Interval* or REI. The REI is time period follow a pesticide application during which entry into the treated area is restricted. At this time, the REI on the permethrin labels is 12 hours set by the highest acute toxicity category among acute dermal toxicity, eye irritation potential, or skin irritation potential) of the active ingredient.

For all agricultural postapplication exposure scenarios, postapplication occupational risks do not exceed HED's level of concern (i.e., the MOEs are greater than 100) on the day of application – approximately 12 hours following application. A summary of the results for each crop/activity combination considered for each time-frame is also provided in Table 9.3.1.

Table 9.3.1. Summary of Permethrin Non-cancer Postapplication Worker Risk Estimates from Agricultural Scenarios

Crop	Activity	TC cm^2/hr	Maximum Application Rate (lb ai/A)	DAT (days)	DFR ug/cm^2 normalized	Short/ Intermediate-Term MOE
Short/Intermediate-Term Postapplication Risks (Calculated with Peach DFR Study MRID# 437557-01)						
conifer seed orchard	seed cone harvesting	3000	1.2	0	2.56	**570**
apples, pears	thinning	3000	0.4	0	0.85	**1,700**
	hand-harvesting, hand-pruning, propping, training	1500	0.4	0	0.85	**3,400**
	hand-weeding, irrigating, scouting	1000	0.4	0	0.85	**5,100**
almonds, filberts, pistachios, walnuts	hand-harvesting, hand-pruning	2500	0.4	0	0.85	**2,100**
	irrigating, scouting, thinning	500	0.4	0	0.85	**10,000**
cherries: sweet and sour, nectarines, peaches	thinning	3000	0.3	0	0.64	**2,300**
	hand-harvesting, hand-pruning	1500	0.3	0	0.64	**4,600**
	hand-weeding, irrigating, scouting	1000	0.3	0	0.64	**6,800**
avocados, conifer (field grown-christmas trees), papayas	thinning	3000	0.2	0	0.43	**3,400**
	hand-pruning	1500	0.2	0	0.43	**6,800**
	hand-weeding, scouting	1000	0.2	0	0.43	**10,000**
ornamentals	hand-pruning	400	0.2	0	0.43	**26,000**
	hand-pinching	175	0.2	0	0.43	**59,000**
	hand-harvesting	110	0.2	0	0.43	**93,000**
Short/Intermediate-Term Postapplication Risks (Calculated with Cotton DFR Study No MRID)						
alfalfa, soybeans	hand-harvesting	2500	0.20	0	0.22	**8,100**
	irrigating, scouting (full development)	1500	0.20	0	0.22	**13,000**
	irrigating, scouting (min development)	100	0.20	0	0.22	**200,000**

Table 9.3.1. Summary of Permethrin Non-cancer Postapplication Worker Risk Estimates from Agricultural Scenarios						
Crop	Activity	TC cm^2/hr	Maximum Application Rate (lb ai/A)	DAT (days)	DFR ug/cm^2 normalized	Short/ Intermediate-Term MOE
corn	detasseling, hand-harvesting	17000	0.20	0	0.22	**1,200**
	irrigating, scouting (full development)	1000	0.20	0	0.22	**20,000**
	scouting (min development)	400	0.20	0	0.22	**51,000**
cucurbits	hand-harvesting, hand-pruning	2500	0.20	0	0.22	**8,100**
	irrigating, scouting	1500	0.20	0	0.22	**13,000**
	thinning	500	0.20	0	0.22	**40,000**
onions: dry bulb, garlic	hand-harvesting	2500	0.30	0	0.32	**5,400**
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.30	0	0.32	**9,000**
	hand-weeding, irrigating, scouting, thinning (min development)	300	0.30	0	0.32	**45,000**
potatoes	hand-harvesting	2500	0.20	0	0.22	**8,100**
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.20	0	0.22	**13,000**
	hand-weeding, irrigating, scouting, thinning (min development)	300	0.20	0	0.22	**67,000**
turnips	hand-harvesting	2500	0.10	0	0.11	**16,000**
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.10	0	0.11	**27,000**
	hand-weeding, irrigating, scouting, thinning (min development)	300	0.10	0	0.11	**130,000**
eggplant, peppers: bell, tomatoes	hand-harvesting, hand-pruning	1000	0.20	0	0.22	**20,000**
	irrigating, scouting	700	0.20	0	0.22	**29,000**
	hand-weeding, thinning	500	0.20	0	0.22	**40,000**
cabbage	hand-harvesting, hand-pruning, irrigating	5000	0.20	0	0.22	**4,000**
	scouting	4000	0.20	0	0.22	**5,100**
	hand-weeding	2000	0.20	0	0.22	**10,000**
broccoli, brussel sprouts, cauliflower, chinese broccoli	hand-harvesting, hand-pruning, irrigating	5000	0.10	0	0.11	**8,100**
	scouting	4000	0.10	0	0.11	**10,000**
	hand-weeding	2000	0.10	0	0.11	**20,000**
collards	hand-harvesting	2500	0.10	0	0.11	**16,000**
	irrigating, scouting (all at medium development)	1500	0.10	0	0.11	**27,000**
	irrigating, scouting, thinning (all at min development)	500	0.10	0	0.11	**81,000**

Table 9.3.1. Summary of Permethrin Non-cancer Postapplication Worker Risk Estimates from Agricultural Scenarios						
Crop	Activity	TC cm^2/hr	Maximum Application Rate (lb ai/A)	DAT (days)	DFR ug/cm^2 normalized	Short/ Intermediate-Term MOE
chinese cabbage, leafy vegetables	hand-harvesting	2500	0.20	0	0.22	**8,100**
	irrigating, scouting (all at medium development)	1500	0.20	0	0.22	**13,000**
	irrigating, scouting, thinning (all at min development)	500	0.20	0	0.22	**40,000**
artichokes	hand-harvesting, hand-pruning	1000	0.30	0	0.32	**13,000**
	irrigating, scouting (all at medium development)	500	0.30	0	0.32	**27,000**
	irrigating, scouting, thinning (all at min development), hand weeding	300	0.30	0	0.32	**45,000**
cut flowers	Old Brouwer data - for comparative purposes only	7000	0.30	0	0.32	**1,900**
	cut roses	2600	0.30	0	0.32	**5,200**
	all flowers	500	0.30	0	0.32	**27,000**
Short/Intermediate-Term Postapplication Risks (Calculated with Turf TTR Study MRID# 449555-01)						
turf	mowing	500	0.87	0	0.06	**120,000**

9.3.2 Impregnated Clothing Scenarios

HED estimated exposures to permethrin-impregnated clothing occur by considering exposure frequency and duration, as well as degree of contact. HED identified two types of occupational postapplication exposures:

- military personnel who *wear* battle dress impregnated with permethrin on a daily basis (i.e., approximately 250 days/year) and
- factory workers who *work with* fabric or clothing after impregnation during making of garments or packaging of clothing on a work-day basis (i.e., 250 days per year).

Since both postapplication occupational exposures are more than 180 days per year, the duration of exposure considered for this noncancer assessment is long-term. Inhalation exposures are thought to be negligible for postapplication scenarios involving exposure to permethrin-impregnated clothing because of the low vapor pressure. As such, inhalation postapplication exposures are not considered in this assessment.

To assess postapplication exposures to impregnated clothing, HED used the latest EPA Antimicrobial Division (AD) approaches for estimating similar postapplication exposures. The data required for estimating postapplication potential doses via AD's methods include the:

- clothing residue concentration (assumed to be equivalent to the application rate on a mass per area basis, as determined from the label),

- surface area of the skin that is in contact with the fabric,
- transfer factor, and
- body weight.

Dermal exposures to military personnel are based on the clothing contact surface area of adults exposed to permethrin-impregnated clothing (0.85 m^2). This number is based on the assumption that military personnel wear briefs and undershirts underneath the battle dress and therefore the surface area of arms and legs (but not the torso) for an adult are used. Dermal exposures to garment workers are based on the contact surface area of adults exposed to permethrin impregnated clothing in a factory after the impregnation process (0.22 m^2). This number is based on the hands and forearms of an adult garment worker.

All postapplication exposure scenarios for permethrin-impregnated clothing do not exceed HED's level of concern (i.e., the MOEs are greater than 100). A summary of the results for each population considered is provided in Table 9.3.2.

Table 9.3.2. Summary of Permethrin Long-Term Non-cancer Postapplication Worker Risk Estimates from Impregnated Clothing Scenarios

Population	Clothing residue (mg ai/cm2)	Surface area (m2/day)	Transfer factor (%/day)	PDR (mg ai/kg/day)	Long-Term MOE
Military adults	0.125	0.85	0.49%	0.074	**6,700**
Garment workers	0.125	0.221	0.49%	0.019	**26,000**

9.4 Short- and Intermediate-Term Cancer Postapplication Risk

The occupational postapplication worker exposure and cancer risk calculations are presented in this section. Postapplication cancer risk estimates were calculated using a linear, low-dose extrapolation approach (Q_1*).

9.4.1 Agricultural Scenarios

Cancer risk estimates for the agricultural scenarios are summarized in Table 9.4.1 below. Two different occupational postapplication exposure scenarios were assessed – individuals employed solely by one establishment (i.e., "hired hands") were assumed to be exposed 10 days per year and individuals employed by multiple establishments (i.e., commercial or migratory farmworkers) were assumed to be exposed 30 days per year. Within each crop group, separate transfer coefficients were used to represent various types of cultural practices. Data from the permethrin-specific studies were used along with the transfer coefficients to calculate the LADDs. For specific crop groupings, permethrin-specific DFRs or TTRs were averaged over time depending on the retreatment interval listed on the labels. These averages were calculated beginning the day after the postapplication non-cancer risk exceeded HED's level of concern of 100 up to the day when it was possible to retreat the crop. All of the postapplication cancer risks for both "hired hands" and commercial/migratory farmworkers are are in the 10^{-6} to 10^{-8} range.

Table 9.4.1. Summary of Revised Permethrin Cancer Postapplication Worker Risk Estimates for Various Agricultural Scenarios									
Crop	Activity	TC (cm^2/hr)	Maximum Application Rate	DAT (days)	DFR (ug/cm^2 normalized)	10 Days Per Year		30 Days Per Year	
						LADD (mg/kg/day)	Cancer risk	LADD (mg/kg/day)	Cancer risk
Postapplication Cancer Risks (Calculated with Peach DFR Study MRID# 437557-01)									
conifer seed orchard	seed cone harvesting	3000	1.2	AVG DAT 1-7	0.709	1.9E-04	1.8E-06	5.7E-04	5.4E-06
apples, pears	thinning	3000	0.4	AVG DAT 1-7	0.709	1.9E-04	1.8E-06	5.7E-04	5.4E-06
	hand-harvesting, hand-pruning, propping, training	1500	0.4	AVG DAT 1-7	0.709	9.5E-05	9.1E-07	2.8E-04	2.7E-06
	hand-weeding, irrigating, scouting	1000	0.4	AVG DAT 1-7	0.709	6.3E-05	6.1E-07	1.9E-04	1.8E-06
almonds, filberts, pistachios, walnuts	hand-harvesting, hand-pruning	2500	0.4	AVG DAT 1-7	0.709	1.6E-04	1.5E-06	4.7E-04	4.5E-06
	irrigating, scouting, thinning	500	0.4	AVG DAT 1-7	7.1E-01	3.2E-05	3.0E-07	9.5E-05	9.1E-07
cherries: sweet and sour, nectarines, peaches	thinning	3000	0.3	AVG DAT 1-7	5.3E-01	1.4E-04	1.4E-06	4.3E-04	4.1E-06
	hand-weeding, irrigating, scouting	1000	0.3	AVG DAT 1-7	5.3E-01	4.7E-05	4.5E-07	1.4E-04	1.4E-06
avocados, conifer (field grown-Christmas trees), papayas	thinning	3000	0.2	AVG DAT 1-7	3.5E-01	9.5E-05	9.1E-07	2.8E-04	2.7E-06
	hand-pruning	1500	0.2	AVG DAT 1-7	3.5E-01	4.7E-05	4.5E-07	1.4E-04	1.4E-06
ornamentals	hand-pruning	400	0.2	AVG DAT 1-7	3.5E-01	1.3E-05	1.2E-07	3.8E-05	3.6E-07
	hand-pinching	175	0.2	AVG DAT 1-7	3.5E-01	5.5E-06	5.3E-08	1.7E-05	1.6E-07
	hand-harvesting	110	0.2	AVG DAT 1-7	3.5E-01	3.5E-06	3.3E-08	1.0E-05	1.0E-07
Postapplication Cancer Risks (Calculated with Cotton DFR Study No MRID)									
alfalfa, soybeans	irrigating, scouting (full development)	1500	0.20	DAT AVG 1-7	0.08	1.1E-05	1.0E-07	3.2E-05	3.1E-07
	irrigating, scouting (min development)	100	0.20	DAT AVG 1-7	0.08	7.2E-07	6.9E-09	2.2E-06	2.1E-08
corn	detasseling, hand-harvesting	17000	0.20	DAT AVG 1-7	0.08	1.2E-04	1.2E-06	3.7E-04	3.5E-06
	irrigating, scouting (full development)	1000	0.20	DAT AVG 1-7	0.08	7.2E-06	6.9E-08	2.2E-05	2.1E-07
	scouting (min development)	400	0.20	DAT AVG 1-7	0.08	2.9E-06	2.8E-08	8.6E-06	8.3E-08
cucurbits	hand-harvesting, hand-pruning	2500	0.20	DAT AVG 1-7	0.08	1.8E-05	1.7E-07	5.4E-05	5.2E-07
	irrigating, scouting	1500	0.20	DAT AVG 1-7	0.08	1.1E-05	1.0E-07	3.2E-05	3.1E-07

Table 9.4.1. Summary of Revised Permethrin Cancer Postapplication Worker Risk Estimates for Various Agricultural Scenarios									
Crop	Activity	TC (cm^2/hr)	Maximum Application Rate	DAT (days)	DFR (ug/cm^2 normalized)	10 Days Per Year		30 Days Per Year	
						LADD (mg/kg/day)	Cancer risk	LADD (mg/kg/day)	Cancer risk
	thinning	500	0.20	DAT AVG 1-7	0.08	3.6E-06	3.4E-08	1.1E-05	1.0E-07
onions: dry bulb, garlic	hand-harvesting	2500	0.30	DAT AVG 1-7	0.12	2.7E-05	2.6E-07	8.2E-05	7.8E-07
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.30	DAT AVG 1-7	0.12	1.6E-05	1.5E-07	4.9E-05	4.6E-07
	hand-weeding, irrigating, scouting, thinning (min development)	300	0.30	DAT AVG 1-7	0.12	3.2E-06	3.1E-08	9.7E-06	9.3E-08
potatoes	hand-harvesting	2500	0.20	DAT AVG 1-7	0.08	1.8E-05	1.7E-07	5.4E-05	5.2E-07
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.20	DAT AVG 1-7	0.08	1.1E-05	1.0E-07	3.2E-05	3.1E-07
turnips	hand-harvesting	2500	0.10	DAT AVG 1-7	0.04	9.0E-06	8.6E-08	2.7E-05	2.6E-07
	hand-weeding, irrigating, scouting, thinning (full development)	1500	0.10	DAT AVG 1-7	0.04	5.4E-06	5.2E-08	1.6E-05	1.5E-07
eggplant, peppers: bell, tomatoes	hand-harvesting, hand-pruning	1000	0.20	DAT AVG 1-7	0.08	7.2E-06	6.9E-08	2.2E-05	2.1E-07
	irrigating, scouting	700	0.20	DAT AVG 1-7	0.08	5.0E-06	4.8E-08	1.5E-05	1.4E-07
cabbage	hand-harvesting, hand-pruning, irrigating	5000	0.20	DAT AVG 1-7	0.08	3.6E-05	3.4E-07	1.1E-04	1.0E-06
	scouting	4000	0.20	DAT AVG 1-7	0.08	2.9E-05	2.8E-07	8.6E-05	8.3E-07
	hand-weeding	2000	0.20	DAT AVG 1-7	0.08	1.4E-05	1.4E-07	4.3E-05	4.1E-07
broccoli, brussel sprouts, cauliflower, Chinese broccoli	hand-harvesting, hand-pruning, irrigating	5000	0.10	DAT AVG 1-7	0.04	1.8E-05	1.7E-07	5.4E-05	5.2E-07
	scouting	4000	0.10	DAT AVG 1-7	0.04	1.4E-05	1.4E-07	4.3E-05	4.1E-07
	hand-weeding	2000	0.10	DAT AVG 1-7	0.04	7.2E-06	6.9E-08	2.2E-05	2.1E-07
collards	hand-harvesting	2500	0.10	DAT AVG 1-7	0.04	9.0E-06	8.6E-08	2.7E-05	2.6E-07
	irrigating, scouting, thinning (all at medium development)	1500	0.10	DAT AVG 1-7	0.04	5.4E-06	5.2E-08	1.6E-05	1.5E-07
	irrigating, scouting, thinning (all at min development)	500	0.10	DAT AVG 1-7	0.04	1.8E-06	1.7E-08	5.4E-06	5.2E-08
Chinese cabbage, leafy vegetables	hand-harvesting	2500	0.20	DAT AVG 1-7	0.08	1.8E-05	1.7E-07	5.4E-05	5.2E-07
	irrigating, scouting, thinning (all at medium development)	1500	0.20	DAT AVG 1-7	0.08	1.1E-05	1.0E-07	3.2E-05	3.1E-07
	irrigating, scouting, thinning (all at min	500	0.20	DAT AVG 1-7	0.08	3.6E-06	3.4E-08	1.1E-05	1.0E-07

Table 9.4.1. Summary of Revised Permethrin Cancer Postapplication Worker Risk Estimates for Various Agricultural Scenarios									
Crop	Activity	TC (cm^2/hr)	Maximum Application Rate	DAT (days)	DFR (ug/cm^2 normalized)	10 Days Per Year		30 Days Per Year	
						LADD (mg/kg/day)	Cancer risk	LADD (mg/kg/day)	Cancer risk
	development)								
artichokes	hand-harvesting, hand-pruning	1000	0.30	DAT AVG 1-7	0.12	1.1E-05	1.0E-07	3.2E-05	3.1E-07
	irrigating, scouting, thinning (all at medium development)	500	0.30	DAT AVG 1-7	0.12	5.4E-06	5.2E-08	1.6E-05	1.5E-07
	irrigating, scouting, thinning (all at min development), hand weeding	300	0.30	DAT AVG 1-7	0.12	3.2E-06	3.1E-08	9.7E-06	9.3E-08
cut flowers	Old Brouwer data - for comparative purposes only	7000	0.30	DAT AVG 1-7	0.12	7.6E-05	7.2E-07	2.3E-04	2.2E-06
	cut roses	2600	0.30	DAT AVG 1-7	0.12	2.8E-05	2.7E-07	8.4E-05	8.1E-07
	all flowers	500	0.30	DAT AVG 1-7	0.12	5.4E-06	5.2E-08	1.6E-05	1.5E-07
Postapplication Cancer Risks (Calculated with Turf TTR Study MRID# 449555-01)									
turf	mowing	500	0.87	DAT AVG 1-14	0.03	1.2E-06	1.2E-08	3.6E-06	3.5E-08

9.4.2 Impregnated Clothing Scenarios

Cancer risk estimates for impregnated clothing scenarios are summarized in Table 9.4.2 below. HED identified two types of occupational postapplication exposures:

- military personnel who *wear* battle dress impregnated with permethrin on a daily basis (i.e., approximately 250 days/year) and
- factory workers who *work with* fabric or clothing after impregnation during making of garments or packaging of clothing on a work-day basis (i.e., 250 days per year).

Dermal exposures to military personnel are based on the clothing contact surface area of adults exposed to permethrin-impregnated clothing (0.85 m^2). This number is based on the assumption that military personnel wear briefs and undershirts underneath the battle dress and therefore the surface area of arms and legs (but not the torso) for an adult are used. Dermal exposures to garment workers are based on the contact surface area of adults exposed to permethrin impregnated clothing in a factory after the impregnation process (0.22 m^2). This number is based on the hands and forearms of an adult garment worker.

For the cancer assessment, risks were calculated for wearing impregnated military clothing calculated to have an average exposure level of 0.038 mg permethrin/cm^2. This average was calculated by assuming the uniform is usable for up to 30 washes and that the first wash results in a 33% permethrin loss, the second wash results in a 6% permthrin loss, washes 3 through 10 each result in a 3% permethrin loss, and washes 11 through 30 each result in a 6.5% permethrin loss (MRID 457519-02). It was also assumed that each individual would wear a uniform for 7 days before a washing event took place to take into account military personnel being in the field for extended periods of time.

Table 9.4.2. Summary of Permethrin Cancer Postapplication Worker Risk Estimates for Impregnated Clothing Scenarios								
Population	Clothing residue (mg ai/cm2)	Surface area (m2/day)	Transfer factor (%/day)	Exposure duration (years)	Exposure Frequency (days/year)	Averaging time (years)	LADD (mg ai/kg/day)	Cancer Risk
Military adults [2]	0.038	0.85	0.49%	10	250	70	0.0001	1.2e-06
Garment workers	0.125	0.221	0.49%	35	250	70	0.0004	3.6e-06

[1] HED is aware that some manufacturers of clothing impregnated with permethrin have developed a new method for the impregnation process. HED believes that this new process will reduce exposure, however, at this time there is no exposure data available to evaluate this method.
[2] Clothing residues for military adults are based on an average exposure assuming 30 washes and that the uniforms are worn 7 days between washes.

10.0 Data Needs and Label Requirements

10.1 Toxicology

870.6300: Developmental Neurotoxicity Study

- A developmental neurotoxicity study (DNT) is required for additional assurance as to the dose-response in characterizing neurotoxic effects.

870.1300: Acute Inhalation Toxicity Study

- An acute inhalation toxicity study is required as there is currently no acceptable data on acute inhalation toxicity for the permethrin technical.

10.2 Residue Chemistry

860.1380: Storage Stability

- Data depicting the stability of permethrin in frozen mushrooms and representative animal commodities are required to upgrade the existing animal feeding studies and mushroom studies.

860.1500: Magnitude the Residue in Crop Plants

- Additional field trial data are required to support the existing uses of permethrin on cabbage, collards, grasses (rangeland), leaf lettuce, and tomatoes.

- Additional field trial data on sweet corn are also required to support the use of a higher application rate (0.25 lb ai/A) for sweet corn grown in FL.

- Information on sample storage intervals and conditions is required to upgrade pear and older tomato field studies.

10.3 Occupational and Residential Exposure

Occupational Handler:

875.1200: Dermal Exposure Indoors (ULV Cold Fogger)

875.1400: Inhalation Exposure Indoors (ULV Cold Fogger)

References

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Appendix A: Permethrin Toxicity

1.0 TOXICOLOGY DATA REQUIREMENTS

The requirements (CFR 158.340) for food use of permethrin are in Table 1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table 1. Data requirements (CFR 158.340) for food use of permethrin

Test	Technical	
	Required	**Satisfied**
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Primary Eye Irritation	yes	yes
870.2500 Primary Dermal Irritation	yes	yes
870.2600 Dermal Sensitization	yes	yes
870.3100 Oral Subchronic (rodent)	yes	yes[1]
870.3150 Oral Subchronic (nonrodent)	yes	yes[1]
870.3200 21-Day Dermal	yes	yes
870.3250 90-Day Dermal	no	NA
870.3465 90-Day Inhalation	no	NA
870.3700a Developmental Toxicity (rodent)	yes	yes
870.3700b Developmental Toxicity (nonrodent)	yes	yes
870.3800 Reproduction	yes	yes
870.4100a Chronic Toxicity (rodent)	yes	yes
870.4100b Chronic Toxicity (nonrodent)	yes	yes
870.4200a Oncogenicity (rat)	yes	yes
870.4200b Oncogenicity (mouse)	yes	yes
870.4300 Chronic/Oncogenicity	yes	yes
870.5100 Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300 Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375 Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5xxx Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a Acute Delayed Neurotox. (hen)	no	yes
870.6100b 90-Day Neurotoxicity (hen)	no	no
870.6200a Acute Neurotox. Screening Battery (rat)	yes	yes
870.6200b 90 Day Neuro. Screening Battery (rat)	yes	yes
870.6300 Develop. Neuro	yes	no[2]
870.7485 General Metabolism	yes	yes
870.7600 Dermal Penetration	yes	yes
Special Studies for Ocular Effects		
Acute Oral (rat)	no	no
Subchronic Oral (rat)	no	no
Six-month Oral (dog)	no	no

1. Requirements are satisfied by chronic oral toxicity studies.
2. The HIARC determined that a developmental neurotoxicity study is required (Data gap).

2.0 NON-CRITICAL TOXICOLOGY STUDIES

Executive summaries for studies not used for toxicity endpoint selection or FQPA assessment are as follows.

2.1 21/28-Day Dermal Toxicity – Rat (870.3200)

In a 21-day repeated dose dermal toxicity study (MRIDs 41143801, 42653301), groups of Wistar Alpk:Apfsd SPF rats (5/sex/group) were treated with undiluted Permethrin (95.6%, Batch No. Y00040/85, RS/38F). Animals were treated by dermal occlusion for 6 hours/day for 21 days at doses of 0, 50, 150, or 500 mg/kg/day.

There were no treatment-related deaths and no effects on body weight, food consumption, hematology, clinical chemistry, or gross or microscopic lesions. Increases in absolute ($p<0.05$; 10.3% increase) and relative ($p<0.05$; 10.6% increase) liver weight were noted in high-dose females only. No histopathological evidence of adaptive liver change was seen in any treatment group. Therefore, the increase of liver weight in females was not considered biologically significant. Skin irritation was observed at the application site of all treatment groups.

The systemic NOAEL was 500 mg/kg/day (the highest dose tested), the systemic LOAEL was not established. The dermal LOAEL was 50 mg/kg/day based on skin irritation. A dermal NOAEL was not identified.

This study is classified as **Acceptable/Guideline** and does satisfy the guideline requirements for a repeated-dose dermal study [OPPTS 870.3200 (§82-2)] in rats.

2.2 Chronic Toxicity - Dog (870.4100b)

In a chronic oral toxicity study (MRID 00129600), permethrin (92.5%, a.i., cis/trans 32.3/60.2) was administered to beagle dogs (6/sex/group) in corn oil by gelatin capsule at dose levels of 0, 5, 100, or 1000 mg/kg/day for one year. The high dose was lowered from 2000 mg/kg/day after 2 days due to overt toxic reaction to the test material.

There were no mortalities. Neurological clinical signs (tremors, uncoordinated gait, nervousness and convulsions, also excessive salivation and vomiting) were observed in the high-dose group. At the high-dose, decreased body weight gain (37% for males and 33% for females less than control, respectively), decreased food consumption (increased food left uneaten), increased liver weight (+30% and +36% for males and females, respectively) and alkaline phosphatase level (+377% and +220% for males and females, respectively) were reported. At mid-dose, increased liver weight (+25% both sexes) and alkaline phosphatase levels (+134% for males and +99% for females) were observed. Microscopic evaluation of the adrenals showed focal degeneration and necrosis in the cortex with variable inflammatory cell infiltration along with swelling and vacuolization of the cells in the inner cortex at high-dose males and females and at mid-dose males. The liver also showed hepatic cellular swelling at mid- and high-dose males and females.

On April 18, 2002, the HIARC evaluated the toxicology database of permethrin and determined

that the observations of increased liver weight, alkaline phosphatase levels, and hepatic cellular swelling are adaptive and reversible effects and are not considered adverse effects (HED Doc# 0050731). **Therefore, the systemic toxicity LOAEL is 1000 mg/kg/day based on clinical neurotoxic signs and decreased body weight gain and food consumption. The NOAEL is 100 mg/kg/day.**

This one-year dog study is classified **Acceptable/Guideline** and satisfies the guideline requirement for a chronic toxicity study in dogs.

2.3 Metabolism - Rat (870.7485)

(1) In a series of metabolism and disposition experiments (MRID 00089006, 00054719, and MRID 92142041 [summary of MRID 00089006], and MRID 92142042 [summary of MRID 00054719]), male and female Wistar-derived rats were placed on various oral treatment regimens with [^{14}C-alcohol]permethrin ([^{14}C-cyclopropyl]permethrin) or [^{14}C-acid]permethrin ([^{14}C-benzyl]permethrin). For MRID 00054719, [^{14}C-acid]permethrin (>98% purity, 53:47, cis trans ratio; no lot or batch no.) or [^{14}C-alcohol]permethrin (99% purity, 40.5:59.5 cis:trans ratio; no lot or batch no.) were diluted as needed with nonlabeled permethrin (93.6% purity, 40.5:59.5, cis:trans ratio; no lot or batch no.) and given by gavage to two male and two female rats at a dose of 6.5 mg/kg for quantitative and qualitative assessment of excretion. In MRID 00089006, tissue distribution and blood kinetics were assessed in male and female Wistar-derived rats given repeated or single oral doses of [^{14}C-acid]permethrin (>98% purity; 53:47, cis:trans ratio; no lot or batch no.) or [^{14}C-alcohol]permethrin (99% purity, 38:62 cis:trans ratio; no lot or batch no.)

These studies provided information on the excretion and tissue burdens of permethrin in rats following single or multiple oral doses of either alcohol ([^{14}C-cyclopropyl]permethrin) or acid [^{14}C-benzyl]permethrin). Based upon a limited number of rats, overall recovery was 93.7% to 101% regardless of label position. Following a single oral dose of 6.5 mg/kg, most radioactivity (58-65%) from a single dose of the [^{14}C-alcohol] permethrin was eliminated via the urine over a 7-day period with much of the remainder (29-43%) being excreted in the feces. Urinary excretion of radioactivity following a single dose of [^{14} C-acid] permethrin was slightly less and fecal excretion correspondingly greater. Results of tissue distribution and autoradiographic experiments showed that most radioactivity was associated with adipose tissue and, initially, with the gastrointestinal tract and organs/tissue associated with excretory function. Following oral administration to rats, most permethrin-associated radioactivity appears to be excreted within 48 hours. Following multiple doses, radioactivity in adipose tissue appears to be greater for [^{14}C-alcohol] permethrin than for [^{14}C-acid] permethrin. This is also consistent with blood kinetics data showing lower radioactivity (C_{max}) in the blood of rats receiving [^{14}C-acid] permethrin. Upon cessation of dosing, radioactivity levels in adipose tissues declined. There was no attempt to identify the metabolites in these studies.

This metabolism study in the rat is classified **Unacceptable/Guideline** and does not satisfy the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in rats. The unacceptability is the result of deficiencies in level of detail provided which prevent verification/validation of findings (e.g., unreadable data, environmental conditions not reported,

no dose confirmation, no lot/batch numbers for the test article).

(2) In a metabolism study (MRID 00102185), male Wistar-derived rats were given a single low dose (2.0 mg/rat) or single high dose (20 mg/rat) of permethrin ([^{14}C-cyclopropane]permethrin, 40:60 cis-trans ratio and non-labeled permethrin, 38.2:59.3 cis-trans ratio; no purity or lot/batch nos. for either) intragastrically. Feces and urine collected one day prior to dosing and for three days postdose were analyzed for radioactivity and metabolites.

These experiments provided an initial and cursory effort at identification and quantitation of major metabolites in the urine and feces of rats following single oral doses (2 or 20 mg/rat) of [^{14}C-cyclopropane]permethrin. Approximately 78.5% of the administered radioactivity was recovered over the 3-day experimental period (dose group not specified). A conjugated metabolite, 3-(2,2-dichlorovinyl)-1-methylcyclopropane-1,2-dicarboxylic acid, was identified in both the urine and feces that reportedly accounted for approximately 2.2% of the administered dose. No additional data were provided regarding characterization of the remaining recovered radioactivity.

This metabolism study in the rat is classified **Unacceptable/Guideline** and does not satisfy the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in rats. The unacceptability is the result of deficiencies in level of detail provided which prevent verification/validation of findings (e.g., insufficient data regarding characterization of recovered radioactivity, no dose confirmation, no lot/batch numbers for the test article).

(3) In a metabolism study (MRID 00065903), groups of rats were given oral doses (1.6-4.8 mg/kg) of radiolabeled isomers ([^{14}C-acid] or [^{14}C-alcohol] labeled) of permethrin (radiochemical purity >99%; no lot/batch nos.) in dimethylsulfoxide vehicle. Metabolism and disposition was assessed over a 4 to12-day period

Recovery of administered radioactivity was 97-100% at 12 days after administration of the test article. The test material appeared to be rapidly absorbed and excreted in the urine and feces. Quantitative differences in excretion profile were characterized by greater amounts of *trans*-permethrin in the urine suggesting greater metabolism of the *trans* isomer than the *cis* isomer. Most of the urinary metabolites and some fecal metabolites appeared to be hydroxylation products, and glucuronide and sulfate conjugates of these products. Qualitative differences in metabolite profiles were also noted for the two isomers. Excretion of radioactivity via expired air was negligible. Fat tissue, liver, and kidney contained the highest levels of radioactivity, although there did not appear to be potential for sequestration at the dose regimens studied. The study authors concluded that the metabolism in rats of the *cis* and *trans* isomers of permethrin was characterized by ester cleavage, oxidation at the *cis* or *trans* methyl group of the dimethyl moiety, and oxidation at the 2' or 4' position of the phenoxy group.

This review is conducted on a best available copy of the report. However, most data tables and some text were not legible and, therefore, verification of the study authors' interpretations and conclusions was not possible. This metabolism study in the rat (MRID 00065903), apparently a draft manuscript for submission to the J. of Agricultural and Food Chemistry, is classified **Unacceptable/Guideline** and does not satisfy the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in rats. *Although the study appeared to be an in-depth examination of the metabolism of the *cis* and *trans* isomers of permethrin in the rat and could potentially achieve guideline requirements, the resulting study report was generally unreadable and exhibited notable deficiencies.

2.4 Metabolism - Dog (870.7485)

Two metabolism studies were conducted using adult Beagle dogs. In MRID 0054721, groups of four male and four female beagle dogs were given [^{14}C-alcohol]permethrin (PP557; no lot/batch nos.; 59.7 mCi/mM; purity not reported) or [^{14}C-acid]permethrin (PP557; no lot/batch nos.; 1.87 mCi/mM; purity 99%) as a single oral dose (6.5 mg/kg and 6.2 mg/kg, respectively) in a gelatin capsule. Excreta were collected over a 7-day period and tissues collected and analyzed at termination. In MRID 00042160, two beagle dogs (gender not specified) were given 10 daily doses (1.0 mg/kg via gelatin capsules) of [^{14}C-alcohol]permethrin (PP557; no lot/batch nos.; 59.7 mCi/mM; purity not reported). Excreta were collected after seven days and adipose tissues analyzed at termination.

These experiments provided preliminary information regarding the metabolism and disposition of permethrin in dogs. Data were insufficient for determination of definitive mass balance for administered radioactivity. Following oral administration of a single dose of [^{14}C-alcohol]permethrin (6.5 mg/kg) or [^{14}C-acid]permethrin (6.2 mg/kg), approximately 84-87% of administered radioactivity was eliminated via the feces and urine in 24-48 hours (MRID 000054721). Fecal excretion (~45-56% of dose) was somewhat greater than urinary excretion (~30-38% of dose) and the rate of excretion was slightly less for the [^{14}C-alcohol]permethrin. At seven days postdose, radioactivity was detected in the tissues selected for analysis (peri-renal and subcutaneous fat, liver, kidney, lung, heart, blood, and brain). The highest tissue levels (0.5-0.7 µg eq./g) were found in the fat tissues. Although radioactivity was detected in all tissues seven days following the single oral dose, levels were minimal and there was no evidence for significant sequestration. Following a single oral dose, TLC analysis of organic solvent extracts revealed up to four metabolites in the urine and six in the feces, none of which were characterized. The excretory pattern for dogs given multiple doses of [^{14}C-alcohol]permethrin (1.0 mg/kg/day for 10 days) (MRID 00042160) was similar to that observed for the single dose study. The repeat-dose study also provided preliminary data showing a shift in the cis:trans ratio (an increase in the cis isomer) of residues in peri-renal and subcutaneous fat, and noted that this shift was indicative of a preferential metabolism of the trans isomer.

These metabolism/disposition studies in the dog are classified **Unacceptable/Non-Guideline** and do not satisfy the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in dogs. The unacceptability is the result of deficiencies in level of detail provided which prevent verification/validation of findings (e.g., insufficient data regarding characterization of recovered radioactivity, no dose confirmation, no lot/batch numbers for the test article, mass balance data lacking in MRID 00042160). Furthermore, the studies were conducted prior to GLP Guidelines and lacked quality assurance statements.

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Appendix B: Average Yearly Indoor Permethrin Residue Using CTEPP Data

Appendix B/Table B1: Permethrin Dust Data from CTEPP Study						
Sample Site	% Detected	Average cis-Permethrin (ng/m2)	Average cis-Permethrin (ug/cm2)	Average trans-Permethrin (ng/m2)	Average trans-Permethrin (ug/cm2)	Sum cis- and trans-Permethrin (ug/cm2)
CTEPP cis-Permethrin in NC						
All children at home	100	9750	0.000975	9420	0.000942	0.001917
Home children at home	100	9630	0.000963	9030	0.000903	0.001866
Day care children at home	100	9900	0.00099	9890	0.000989	0.001979
Day care children at day care	100	54400	0.00544	55900	0.00559	0.01103
CTEPP cis-Permethrin in OH						
All children at home	100	8250	0.000825	7640	0.000764	0.001589
Home children at home	100	3740	0.000374	3260	0.000326	0.0007
Day care children at home	100	13200	0.00132	12500	0.00125	0.00257
Day care children at day care	100	7750	0.000775	7260	0.000726	0.001501
Average cis- and trans- permethrin OH and NC						
All children at home	0.001753					
Home children at home	0.001283					
Day care children at home	0.0022745					
Day care children at day care	0.0062655					

Appendix B/Table B2: Average Yearly Indoor Permethrin Residues			
Assumes 5 apps per year…10% dissipation, residues available 28 DAT		Assumes 5 apps per year…10% dissipation, residues available 28 DAT	
DAT	Residue (ug/cm^2)	DAT	Residue (ug/cm^2)
1	5.6	1	15
2	5.04	2	13.5
3	4.536	3	12.15
4	4.0824	4	10.935
5	3.67416	5	9.8415
6	3.306744	6	8.85735
7	2.9760696	7	7.971615
8	2.67846264	8	7.1744535
9	2.410616376	9	6.45700815
10	2.169554738	10	5.811307335
11	1.952599265	11	5.230176602
12	1.757339338	12	4.707158941
13	1.581605404	13	4.236443047
14	1.423444864	14	3.812798742
15	1.281100377	15	3.431518868
16	1.15299034	16	3.088366981
17	1.037691306	17	2.779530283
18	0.933922175	18	2.501577255
19	0.840529958	19	2.251419529
20	0.756476962	20	2.026277577
21	0.680829266	21	1.823649819
22	0.612746339	22	1.641284837
23	0.551471705	23	1.477156353
24	0.496324535	24	1.329440718
25	0.446692081	25	1.196496646
26	0.402022873	26	1.076846982
27	0.361820586	27	0.969162283
28	0.325638527	28	0.872246055
29	5.6	29	15
30	5.04	30	13.5
31	4.536	31	12.15
32	4.0824	32	10.935
33	3.67416	33	9.8415
34	3.306744	34	8.85735
35	2.9760696	35	7.971615
36	2.67846264	36	7.1744535
37	2.410616376	37	6.45700815
38	2.169554738	38	5.811307335
39	1.952599265	39	5.230176602

40	1.757339338	40	4.707158941
41	1.581605404	41	4.236443047
42	1.423444864	42	3.812798742
43	1.281100377	43	3.431518868
44	1.15299034	44	3.088366981
45	1.037691306	45	2.779530283
46	0.933922175	46	2.501577255
47	0.840529958	47	2.251419529
48	0.756476962	48	2.026277577
49	0.680829266	49	1.823649819
50	0.612746339	50	1.641284837
51	0.551471705	51	1.477156353
52	0.496324535	52	1.329440718
53	0.446692081	53	1.196496646
54	0.402022873	54	1.076846982
55	0.361820586	55	0.969162283
56	0.325638527	56	0.872246055
57	5.6	57	15
58	5.04	58	13.5
59	4.536	59	12.15
60	4.0824	60	10.935
61	3.67416	61	9.8415
62	3.306744	62	8.85735
63	2.9760696	63	7.971615
64	2.67846264	64	7.1744535
65	2.410616376	65	6.45700815
66	2.169554738	66	5.811307335
67	1.952599265	67	5.230176602
68	1.757339338	68	4.707158941
69	1.581605404	69	4.236443047
70	1.423444864	70	3.812798742
71	1.281100377	71	3.431518868
72	1.15299034	72	3.088366981
73	1.037691306	73	2.779530283
74	0.933922175	74	2.501577255
75	0.840529958	75	2.251419529
76	0.756476962	76	2.026277577
77	0.680829266	77	1.823649819
78	0.612746339	78	1.641284837
79	0.551471705	79	1.477156353
80	0.496324535	80	1.329440718
81	0.446692081	81	1.196496646
82	0.402022873	82	1.076846982
83	0.361820586	83	0.969162283
84	0.325638527	84	0.872246055
85	5.6	85	15

86	5.04	86	13.5
87	4.536	87	12.15
88	4.0824	88	10.935
89	3.67416	89	9.8415
90	3.306744	90	8.85735
91	2.9760696	91	7.971615
92	2.67846264	92	7.1744535
93	2.410616376	93	6.45700815
94	2.169554738	94	5.811307335
95	1.952599265	95	5.230176602
96	1.757339338	96	4.707158941
97	1.581605404	97	4.236443047
98	1.423444864	98	3.812798742
99	1.281100377	99	3.431518868
100	1.15299034	100	3.088366981
101	1.037691306	101	2.779530283
102	0.933922175	102	2.501577255
103	0.840529958	103	2.251419529
104	0.756476962	104	2.026277577
105	0.680829266	105	1.823649819
106	0.612746339	106	1.641284837
107	0.551471705	107	1.477156353
108	0.496324535	108	1.329440718
109	0.446692081	109	1.196496646
110	0.402022873	110	1.076846982
111	0.361820586	111	0.969162283
112	0.325638527	112	0.872246055
113	5.6	113	15
114	5.04	114	13.5
115	4.536	115	12.15
116	4.0824	116	10.935
117	3.67416	117	9.8415
118	3.306744	118	8.85735
119	2.9760696	119	7.971615
120	2.67846264	120	7.1744535
121	2.410616376	121	6.45700815
122	2.169554738	122	5.811307335
123	1.952599265	123	5.230176602
124	1.757339338	124	4.707158941
125	1.581605404	125	4.236443047
126	1.423444864	126	3.812798742
127	1.281100377	127	3.431518868
128	1.15299034	128	3.088366981
129	1.037691306	129	2.779530283
130	0.933922175	130	2.501577255
131	0.840529958	131	2.251419529

132	0.756476962	132	2.026277577
133	0.680829266	133	1.823649819
134	0.612746339	134	1.641284837
135	0.551471705	135	1.477156353
136	0.496324535	136	1.329440718
137	0.446692081	137	1.196496646
138	0.402022873	138	1.076846982
139	0.361820586	139	0.969162283
140	0.325638527	140	0.872246055
141-365	0.001283	141-365	0.001283
365 Day Average	0.73	365 Day Average	1.95