Permethrin & Resmethrin (Pyrethroids)

TEACH Chemical Summary



U.S. EPA, Toxicity and Exposure Assessment for Children's Health

This TEACH Chemical Summary is a compilation of information derived primarily from U.S. EPA and ATSDR resources, and the TEACH Database. The TEACH Database contains summaries of research studies pertaining to developmental exposure and/or health effects for each chemical or chemical group. TEACH does not perform any evaluation of the validity or quality of these research studies. Research studies that are specific for adults are not included in the TEACH Database, and typically are not described in the TEACH Chemical Summary.

I. INTRODUCTION

Pyrethroids are a group of synthetic (man-made) chemicals which are used as pesticides in a variety of commercial, agricultural, and home uses (1-3). Pyrethroids are a more stable form of pyrethrins (natural insecticides derived from the chrysanthemum plant) (2, 3). Permethrin and resmethrin are two examples of pyrethroid insecticides which are used to control a wide variety of insects in agricultural, veterinary, and domestic uses. Generally, permethrin and resmethrin are used in sprays, pet flea shampoos, lice shampoos, municipal mosquito abatement products, and aerosol bombs (household foggers) that may result in exposure of children (1-3). Permethrin is also used on agricultural crops, particularly fruits and vegetables (2). Other pyrethroids include allethrin, cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, fluvalinate, fenpropathrin, fenvalerate, and tralomethrin, used in similar applications as permethrin and resmethrin (1); details pertaining to these pyrethroids will not be discussed in this Chemical Summary. Formulations of permethrin and resmethrin include granules, powders, emulsifiable concentrates, and aerosols (1-3).

Children are likely to be exposed to permethrin or resmethrin following use of products containing these insecticides, including pet flea control products (i.e. pet flea shampoos) on pets, lice shampoos, and community spraying with mosquito abatement products (1).

Studies in adult humans and experimental animals have demonstrated that permethrin, like other pyrethroids, alters nerve function by altering the biochemistry of nerve membrane sodium channels (2, 4). Acute exposure to permethrin or resmethrin in adults has been shown to result in skin irritation, dizziness, twitching, and nervous disorders (i.e., movement problems) (1-3). There are some developmental studies of the health effects of permethrin and resmethrin exposure. Reported effects include increased incidence of anti-nuclear antibodies which are markers of potential autoimmune disease (5), skin irritation (6), and respiratory irritation (6). One study demonstrated changes in neurologically-active proteins (c-*fos* and Brain-Derived Neurotropic Factor, or BDNF) in young mice exposed to permethrin from birth via breast milk (7). Evidence is accumulating that pyrethroid exposure may also be neurotoxic during development (8).

II. EXPOSURE MEDIA AND POTENTIAL FOR CHILDREN'S EXPOSURE¹

Exposure Media	Relative Potential for Children's Exposure ^{2,3}	Basis ⁴
Indoor Air	Higher	Use of pyrethroid-containing pesticidal sprays and foggers indoors in the home is a concern for potential exposure of children.
Commercially- Available Products	Higher	Dermal exposure of children via pyrethroid-containing pet flea collars, pet flea shampoos, and lice shampoos, is a route of concern for exposure. Dermal exposure of toddlers is a concern from contact with lawns, carpets, and floors following applications containing permethrin. Yard permethrin sprayers or misters on timers are a
		concern for increased inhalation exposures, and contact exposures from touching sprayed surfaces.
Ambient Air	Medium	Concentrations of pyrethroids in ambient air may be higher in agricultural areas and after broadcast spraying applications.
Diet	Medium	Permethrin is used on some fruit and vegetable crops, and ingestion of these foods is considered by the U.S. EPA to be an important route of exposure for the general population. The USDA Pesticide Data Program and U.S. FDA reported on permethrin concentrations in foods (see Considerations for Decision Making). Ingestion exposure for toddlers is a concern from hand-to-mouth activity after contact with lawns, carpets, and floors after permethrin treatments.
Soil	Lower	Pyrethroids bind tightly to soil and are moderately persistent; the half life in soil is approximately 30 days. Pyrethroid breakdown is facilitated by microbes in soil.
Dust	Lower	Exposure via house dust after indoor applications of pesticides can occur, though generally is of lower concern than indoor air. Infants and toddlers may be more susceptible to dermal and ingestion exposure via house dust than older children and adults because of hand-to-mouth activity.
Sediment	Lower	Pyrethroids are not likely to accumulate to a great extent in sediment.
Drinking Water	Lower	Pyrethroids have very low solubility in water and are not likely to be found at levels of concern.
Groundwater	Lower	Pyrethroids have very low solubility in water and are not likely to be found at levels of concern.

¹ For more information about child-specific exposure factors, please refer to the Child-Specific Exposure Factors Handbook (<u>http://www.epa.gov/NCEA/jmcsefh2.htm</u>).

² The Relative Potential for Children's Exposure category reflects a judgment by the TEACH Workgroup, U.S. EPA, that incorporates potential exposure pathways, frequency of exposure, level of exposure, and current state of knowledge. Site-specific conditions may vary and influence the relative potential for exposure. For more information on how these determinations were made, go to http://www.epa.gov/teach/teachprotocols_chemsumm.html.

³Childhood represents a lifestage rather than a subpopulation, the distinction being that a subpopulation refers to a portion of the population, whereas a lifestage is inclusive of the entire population.

⁴Information described in this column was derived from several resources (e.g., 1-3) including studies listed in the TEACH Database (<u>http://www.epa.gov/teach</u>). Marisa I don't know what you want to do about cutting some text in the above table to fit this in the footnote???

Supporting references and summaries are provided in the TEACH database at <u>*http://www.epa.gov/teach/.*</u> *Last revised 1/18/2007: includes research articles through 2005, and other information through 2006.*

III. TOXICITY SUMMARY^{5, 6}

Exposures to pyrethroids in adult humans have resulted in skin irritant effects, dizziness, twitching, and nervous disorders; and the dose ranges at which symptoms occur vary widely for the different pyrethroids (1-4). Recent studies of children reported immunotoxic effects following exposure to pyrethroids, with increased incidence of anti-nuclear antibodies associated with autoimmune disease (5), and dermal irritation (including urticaria, which is red, itchy patches on the skin) (6). Respiratory irritation was also reported (6).

In experimental animal studies, adult rats experienced behavioral (e.g., increased aggression and pawing) and neurological effects (e.g., tremors and seizures) following exposure to permethrin or resmethrin (1-3). Neurological effects were noted starting at an oral permethrin dose of 75 mg/kg/day (1, 2). Permethrin exposure also resulted in significantly increased liver and lung weights in adult animals (1). Resmethrin exposure has resulted in thyroid and liver weight increases in adult dogs and rats (1). Permethrin exposure resulted in significant decreases in neurologically-active proteins, c-*fos* and BDNF, in young rats (7). Following permethrin exposure, increased lethality (death) of newborn rats at lower doses (lethal dose for 50% of rats treated (LD50) of 340 mg/kg), as compared to adult rats (LD50 of 1,500 mg/kg), was reported (9).

Carcinogenicity Weight of Evidence Classification⁷: The U.S. EPA Office of Pesticide Programs (OPP) Cancer Assessment Review Committee (CARC), in 2006, classified permethrin as "likely to be carcinogenic in humans" following oral, dermal, and inhalation exposure based on two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in rats, and supporting structural activity relationship information with a Q1*=9.6x10⁻³ (mg/kg/day)⁻¹ (2). The U.S. EPA OPP CARC, in 2006, classified resmethrin as "likely to be carcinogenic to humans" based on male mouse liver combined adenoma and/or carcinoma tumor rates with oral Q1*=5.621x10⁻² (mg/kg/day)⁻¹ (3). There is no carcinogenicity assessment listed in U.S. EPA IRIS for either permethrin (http://www.epa.gov/iris/subst/0185.htm) or resmethrin (http://www.epa.gov/iris/subst/0343.htm). In 1991, the World Health Organization International Agency for Research on Cancer (IARC) evaluated permethrin as "nonclassifiable" as to carcinogenicity

(http://monographs.iarc.fr/ENG/Monographs/vol53/volume53.pdf); resmethrin was not evaluated.

⁵Please refer to research article summaries listed in the TEACH Database for details about study design considerations (e.g., dose, sample size, exposure measurements).

⁶This toxicity summary is likely to include information from workplace or other studies of mature (adult) humans or experimental animals if child-specific information is lacking for the chemical of interest. Summaries of articles focusing solely on adults are not listed in the TEACH Database because the TEACH Database contains summaries of articles pertaining to developing organisms.

⁷ For recent information pertaining to carcinogen risk assessment during development, consult "Guidelines for Carcinogen Risk Assessment and Supplemental Guidance on Risks from Early Life Exposure" at <u>http://www.epa.gov/cancerguidelines</u>.

IV. EXPOSURE AND TOXICITY STUDIES FROM THE TEACH DATABASE

This section provides a brief description of human and animal studies listed in the TEACH Database. For more details about study design parameters, e.g., doses and exposure information, please refer to article summaries in the TEACH Database. Any consideration should include an understanding that exposure levels in animal studies, in many cases, are greater than exposure levels normally encountered by humans.

A. HUMAN EXPOSURE AND EFFECTS

- Potential media of permethrin and resmethrin exposure of infants and children include lice shampoos (2), air in urban areas (10), soil in agricultural areas (6), house dust (11-13), treated turf and carpeting (2), and diet (14, 15). Permethrin was detected in 9% of baby foods and 4% of other foods tested by the U.S. FDA in 2002 (15), but was not detected in a study that tested 25 baby foods in New Zealand (16).
- Children are at risk of exposure to pyrethroids in the home. Infants and toddlers were estimated to have higher rates of dermal exposure to resmethrin than adults through contact with resmethrin-contaminated house dust on household surfaces (17). A study in Minnesota revealed that 24% of families surveyed stored permethrin in the house, and 15% of families used permethrin at home (18). Another study in Minnesota detected permethrin most frequently in personal air samples, but infrequently in drinking water (19). Pyrethroids were the most common chemical of exposure from household products for calls to poison control centers in India (20). Additional information about children's exposures to permethrin and resmethrin are available from the U.S. EPA (2, 3).
- Pyrethroid metabolites have been detected in urine of adults and children (1). A cohort study of 386 pregnant women in New York City were evaluated for indoor pesticide exposure, and detected a pyrethroid metabolite, phenoxybenzoic acid (PBA), in their urine (21). Pyrethroid metabolites have also been detected in urine of children in Germany (14, 22).
- Measuring infant growth parameters at birth, one study found no significant associations between pyrethroid metabolite concentrations in maternal urine, and their infant's size at birth (e.g. head circumference, birth weight) (23). Another study found no significant differences in several measurements of birth outcome (e.g., birth weight, number of miscarriages, etc.) in children born to women who used permethrin for head lice treatment during pregnancy, as compared to women who did not (24).
- Permethrin exposure may impact the immune system in children. The presence of anti-nuclear antibodies in blood, a marker of potential or existing autoimmune disease, in children and adults was associated with estimated exposure (personal questionnaire) to permethrin (5). The incidence of anti-nuclear antibodies between age groups was similar in this study (5). Also, case reports indicated that children exposed to permethrin developed immune-mediated respiratory and dermal irritation (6).

B. EXPERIMENTAL ANIMAL EXPOSURE AND EFFECTS

- Lactational exposure of newborn mice to permethrin, via maternal ingestion, resulted in decreased levels of c-*fos* and Brain-Derived Neurotropic Factor (BDNF), both of which are important for neurological development, in the cerebellum of the brain during the first three weeks of postnatal life (7). This decrease did not persist once permethrin exposure was stopped (7). The consequences of these changes for neurological function in permethrin-exposed mice were not evaluated in this study. A critical review article is available which discussed studies of neurotoxicological effects of pyrethroid exposure during development (8).
- Young rats may be more sensitive to lethal effects of pyrethroids than adult rats. One study reported increased lethality at lower doses of permethrin in neonatal rats as compared to adult rats (9); the lethal dose for 50% of rats treated (LD50) for young rats was 340 mg/kg, as compared to an LD50 of 1,500 mg/kg for adult rats. Based on additional data in that study, the authors concluded that the difference in sensitivity was a consequence of incomplete development of enzymes which contribute to the metabolism, or break-down, of pyrethroids in the liver of young animals (9). Studies of lethal dose sensitivity to pyrethroids at different ages were summarized in a review article (25).
- One study observed increased testicular damage and germ cell apoptosis when adult male rats were exposed to a combination of dermal exposure to permethrin and N,N-diethyltoluamide (DEET), plus oral exposure to pyridostigmine bromide (26). This combination of chemicals has been used together in insect repellents, particularly in the military during the Gulf War (27).
- The TEACH Database contains developmental studies of health effects following exposure to other types of pyrethroids (28-36), but these studies will not be discussed in this Chemical Summary.

V. CONSIDERATIONS FOR DECISION-MAKERS

This section contains information that may be useful to risk assessors, parents, caregivers, physicians, and other decisionmakers who are interested in reducing the exposure and adverse health effects in children for this particular chemical. Information in this section focuses on ways to reduce exposure, assess possible exposure, and, for some chemicals, administer treatment.

- ► The U.S. EPA recommends that home insecticide products that contain permethrin or resmethrin be stored safely (37). Recommendations include storing products in a locked cabinet, never transferring products to another unlabeled container, and washing toys and home surfaces often. Additional fact sheets and recommendations on steps that caregivers can take to prevent or minimize children's exposures to pesticides are available from the U.S. EPA (38).
- Lists of household products that contain permethrin (39) or resmethrin (40) are available from the National Library of Medicine.
- A detailed compilation of information pertaining to exposure and health effects of permethrin, resmethrin, and other pyrethroids is available in the Toxicological Profile for Pyrethrins and Pyrethroids (1). Detailed information on exposure and health effects of permethrin (2) and resmethrin (3) are also available from the U.S. EPA. Fact Sheets are available for permethrin (4, 41), and pyrethrin and pyrethroids (42) from the National Pesticide Telecommunications Network and the U.S. EPA.
- A treatment guide for clinicians, "Recognition and Management of Pesticide Poisonings," is available online from the U.S. EPA (43), and includes a chapter on recognition and treatment of pyrethroid poisonings.
- To reduce children's exposures to pesticides, a program called "Integrated Pest Management" (IPM) is available through the U.S. EPA that provides pest management alternatives to reduce pesticide residues in food (44), on lawns (45) and in schools (46).
- An alternative treatment for head lice that uses a cream cleanser, available over-the-counter, has recently been publicized as an alternative to permethrin-containing lice shampoos (47).
- ► Household uses of pyrethroids can reach exposure levels that result in measurable concentrations of pyrethroids in house dust (2, 12) and metabolites in urine of children and adults (2, 14, 21, 22).
- Exposure of toddlers to permethrin exceeded the U.S. EPA Level of Concern (LOC) when combined chronic exposure via dietary sources (food and drinking water) and short-term exposure via contact with permethrin-treated lawns and indoor surfaces (particularly with carpets in treated rooms) (2); this led to new EPA risk mitigation measures (2, 4). For permethrin, mitigation measures include discontinued use of sponge applications; discontinued use of broadcast, crack and crevice sprays on all residential indoor surfaces (except for aerosol sprays); and concentration limits on aerosol and total release fogger formulations (4).
- The resmethrin Reregistration Eligibility Decision (RED) includes specific instructions to reduce exposures after resmethrin use indoors (3). Following use of broadcast and crevice or crack sprayers, people and pets are to be kept out of the room until the product dries. Following use of room area sprays or foggers, the room is to be closed, with windows and doors shut, for 4 hours after treatment. After the 4 hours, the room is to be well-ventilated for up to 2 hours, depending on room size, before allowing people or pets into the room.

- The U.S. EPA (1), U.S. FDA Pesticide Program (15), and the USDA Pesticide Data Program (48) have tested and regularly monitor food products in the U.S. for pesticide residues, including permethrin and resmethrin. Though levels detected were generally low, the USDA detected permethrin more frequently in fresh and canned spinach and in lettuce, than in other foods (48).
- Consult "Child-Specific Exposure Factors Handbook," EPA-600-P-00-002B, for factors to assess children's inhalation rates (49). An updated External Draft of the 2006 version of this handbook is available (50).

VI. TOXICITY REFERENCE VALUES

PERMETHRIN:

A. Oral/Ingestion

- U.S. EPA Acute Dietary RfD: 0.25 mg/kg/day [oral NOAEL=25 mg/kg/day; UF=100X; FQPA SF=1X], based on observations of clinical signs in acute neurotoxicity studies (i.e., aggression, abnormal and/or decreased movement) and increased body temperature in rats (http://www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf, p. 11). Last revised 4/06.
- U.S. EPA Chronic Dietary RfD: 0.25 mg/kg/day [oral NOAEL=25 mg/kg/day; UF=100X; FQPA SF=1X], based on observations of clinical signs in acute neurotoxicity studies (i.e., aggression, abnormal and/or decreased movement) and increased body temperature in rats (http://www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf, p. 11). Last revised 4/06.
- **U.S. EPA Short- and Intermediate-Term Incidental Oral:** Oral NOAEL = 25 mg/kg/day [UF=100; residential and occupational LOC for MOE=100], based on observations of clinical signs in acute neurotoxicity studies (i.e., aggression, abnormal and/or decreased movement) and increased body temperature in rats (<u>http://www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf</u>, p. 11). Last revised 4/06.
- **U.S. EPA Reference Dose (RfD) for Chronic Oral Exposure:** 5E-2 (or 0.05) mg/kg/day, based on the critical effect of increased liver weight in adult rats (2-year dietary feeding study) with supporting evidence in developmental animal studies (<u>http://www.epa.gov/iris/subst/0185.htm</u>, I.A.1). Last Workgroup verification date 10/28/86, with screening-level literature review in 8/03.
- U. S. ATSDR Minimal Risk Level (MRL): 0.3 mg/kg/day (acute oral), based on neurological effects; 0.2 mg/kg/day (intermediate oral), based on neurological effects (http://www.atsdr.cdc.gov/mrls.html). Last revised 9/03.

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B. Inhalation

U.S. EPA Short-, Intermediate, and Long-Term Inhalation: Inhalation NOAEL = 0.042 mg/L (converts to oral equivalent of 11 mg/kg/day) [UF=100; residential and occupational LOC for MOE=100], based on 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 (http://www.epa.gov/oppsrtd1/REDs/permethrin_red.pdf, p. 11). Last revised 4/06.

C. Dermal

U.S. EPA Short-, Intermediate, and Long-Term Incidental Dermal: Dermal NOAEL = 500 mg/kg/day [UF=100; residential and occupational LOC for MOE=100], based on 21-day dermal toxicity study in rats (<u>http://www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf</u>, p. 11). Last revised 4/06.

RESMETHRIN:

D. Oral/Ingestion

- U.S. EPA Chronic Dietary RfD: 0.035 mg/kg/day [dose for risk assessment=35 mg/kg/day; UF=1000; FQPA SF=10], based on two-generation reproductive studies in rats [rat Reproductive/Offspring LOAEL=70.8 mg/kg/day based on decreased mating index in males and females during the second F1 mating, decreased viability index and decreased pup weight in all generations at birth and during lactation, and possible slight increase in stillborn pups in the F1a and F2a generation; 3-generation reproduction study is co-critical with LOAEL=47mg/kg/day] (http://www.epa.gov/oppsrrd1/REDs/resmethrin_red.pdf, p. 23). Last revised 6/06.
- **U.S. EPA Incidental Oral (Short- and Intermediate-Term):** Oral NOAEL=40 mg/kg/day [maternal LOAEL=80 mg/kg/day; residential LOC for MOE=100; FQPA SF=10X], based on rat developmental toxicity study with reduced weight gain and reduced food consumption during gestation (<u>http://www.epa.gov/oppsrrd1/REDs/resmethrin_red.pdf</u>, p. 23). Last revised 6/06.
- **U.S. EPA Reference Dose (RfD) for Chronic Oral Exposure:** 3E-2 (or 0.03) mg/kg/day, based on the critical effect of reproductive toxicity (increased frequency of neonatal deaths) in a three-generational reproductive study in rats (<u>http://www.epa.gov/iris/subst/0343.htm</u>, I.A.1). Last Workgroup verification date 7/20/88, with screening-level literature review in 8/03.

E. Inhalation

U.S. EPA Short-, Intermediate-, and Long-Term Inhalation: Inhalation NOAEL=0.1 mg/L (28.2 mg/kg/day), based on 90-day Inhalation Toxicity Study [inhalation NOAEL=0.1 mg/L (28.2 mg/kg/day) based on clinical signs within the first month, decreased glucose levels in males, a decrease in body weight gain (-13%) during weeks 1-4 and an increase in blood urea nitrogen (32%) at week 12 in females (<u>http://www.epa.gov/oppsrrd1/REDs/resmethrin_red.pdf</u>, p. 23). Last revised 6/06.

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F. <u>Dermal</u>

U.S. EPA Short-, Intermediate-, and Long-Term Dermal: Oral developmental NOAEL=30 mg/kg/day [dermal absorption rate=2%; residential and occupational LOC for MOE=100; FQPA SF=10X], based on oral rabbit developmental toxicity study (developmental LOAEL=100 mg/kg/day) based on increased incidence of skeletal variations and a possible marginal increase in resorbed litters in the absence of maternal toxicity (http://www.epa.gov/oppsrtd1/REDs/resmethrin_red.pdf, p. 23). Last revised 6/06.

VII. U.S. FEDERAL REGULATORY INFORMATION

- The U.S. EPA issued reregistration eligibility decisions (REDs) in 2006 for permethrin (2) and resmethrin (3), providing current U.S. EPA registration information for these pesticides with instructions for use and labeling requirements. These REDs also include comprehensive reviews of available data pertaining to exposures and health effects for these pesticides, and toxicity values for oral, dermal, and inhalation routes of exposure (see Toxicity Values in this Chemical Summary).
- Many formulations of resmethrin and permethrin, including flea or lice shampoos and turf applications, are available as "General Use Products," meaning that no professional training is necessary to use some products (1-3). Professional applicators are required for some specific uses of permethrin (2) and resmethrin (3). Broadcast spraying of permethrin in agricultural areas, and resmethrin for mosquito abatement, are registered uses that require certified pesticide applicators (2, 3, 51).
- Use of permethrin for the treatment of lice (e.g., Nix Shampoo) is regulated by the U.S. Food and Drug Administration (FDA), and is available in over-the-counter formulations (52).
- The U.S. EPA requires reporting of quantities of certain chemicals that exceed a defined reportable quantity, and the reportable quantity varies for different chemicals (39). Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 "Toxic Chemicals," quantities of permethrin or resmethrin greater than 25,000 pounds manufactured or processed, or greater than 10,000 pounds otherwise used, is required; under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), there are no requirements for reportable releases of permethrin or resmethrin (53).

VIII. BACKGROUND ON CHEMICAL

A. CAS Number: Permethrin 52645-53-1; Resmethrin 10453-86-8

B. Physicochemical Properties: Permethrin and resmethrin are colorless crystals at room temperature, and are usually found as liquid formulations in commercially-available products. Permethrin and resmethrin are poorly soluble in water (54, 55). For more information, go to the National Library of Medicine ChemID Web site (<u>http://chem.sis.nlm.nih.gov/chemidplus</u>) and search for permethrin or resmethrin.

C. Production: According to the U.S. EPA, annual U.S. usage of permethrin is approximately 2 million pounds (2), and usage of resmethrin is approximately 50,000 pounds (3). Total reported U.S. disposals and transfers offsite of permethrin were 17,858 pounds, and of resmethrin were 0 pounds in 2004 (56). These releases are likely representative of only a portion of actual releases because only some facilities (i.e., landfills) are required to report to the U.S. EPA (1, 56).

D. Uses: Permethrin and resmethrin are typically applied as sprays, aerosols, dusts, and dilutable concentrates. The majority of permethrin uses are in non-agricultural applications (2). Permethrin and resmethrin are used in municipal mosquito control sprays, children's lice shampoos, flea control (sprays and dips), indoor insect foggers, control of beetles and cockroaches, garden and turf products, and termite treatments (1-3, 42). Agricultural uses for permethrin include application to a variety of crops including cotton, mushroom, potato, cereal, collard, green pepper, spinach, and nuts (1).

E. Environmental Fate: Permethrin and resmethrin have very low solubility in water (54, 55), and bind tightly to soil and sediment particles, rarely leaching into groundwater. Permethrin and resmethrin are moderately persistent in soil (half-life of 30 days or less), and certain environmental conditions (i.e., greater organic matter, presence of microbes, sunlight) can facilitate the breakdown process (54, 55). Pyrethroids are highly toxic to fish and other aquatic organisms, and do not bioaccumulate (1-3).

F. Synonyms and Trade Names: Some synonyms and trade names for permethrin include: Ambush, Dragnet, Kestrel, Outflank, Pounce, Torpedo. Synonyms and trade names for resmethrin include: benzofuroline, Chryson, Derringer, FOR-SYN, Pynosect, Raid Flying Insect Killer, Respond, Scourge, Sun-Bugger #4. For a more complete list of synonyms and trade names, go to the National Library of Medicine ChemID Web site (<u>http://chem.sis.nlm.nih.gov/chemidplus</u>) and search for permethrin or resmethrin.

Additional information on permethrin and resmethrin is available in the TEACH Database for Pyrethroids and at the following Web sites:

<u>http://www.epa.gov/pesticides/health/mosquitoes/pyrethroids4mosquitoes.htm</u> <u>www.extoxnet.orst.edu/pips/pyrethri.htm</u> www.npic.orst.edu/factsheets/pyrethrins.pdf

REFERENCES

- 1. U.S. Centers for Disease Control (ATSDR). 2003. "Toxicological Profile for Pyrethrins and Pyrethroids." <u>http://www.atsdr.cdc.gov/toxprofiles/tp155.html</u>.
- 2. U.S. Environmental Protection Agency. 2006. "Reregistration Eligibility Decision (RED) for Permethrin." <u>http://www.epa.gov/oppsrrd1/REDs/permethrin_red.pdf</u>.
- 3. U.S. Environmental Protection Agency. 2006. "Reregistration Eligibility Decision for Resmethrin." http://www.epa.gov/oppsrrd1/REDs/resmethrin_red.pdf.
- 4. U.S. Environmental Protection Agency. 2006. "Permethrin Facts (Reregistration Eligibility Decision (RED) Fact Sheet)." <u>http://www.epa.gov/oppsrtd1/REDs/factsheets/permethrin_fs.htm</u>.
- 5. Rosenberg, A.M., et al. 1999. "Prevalence of antinuclear antibodies in a rural population." J.Toxicol.Environ.Health A 57(4):225-236.
- 6. Fuortes, L. 1999. "Urticaria due to airborne permethrin exposure." Vet.Hum.Toxicol. 41(2):92-93.
- 7. Imamura, L., et al. 2002. "Neonatal exposure of newborn mice to pyrethroid (permethrin) represses activity-dependent c-fos mRNA expression in cerebellum." Arch.Toxicol. 76(7):392-397.
- 8. Shafer, T.J., et al. 2005. "Developmental neurotoxicity of pyrethroid insecticides: critical review and future research needs." Environ Health Perspect. 113(2):123-136.
- 9. Cantalamessa, F. 1993. "Acute toxicity of two pyrethroids, permethrin, and cypermethrin in neonatal and adult rats." Arch.Toxicol. 67(7):510-513.
- 10. Whyatt, R.M., et al. 2002. "Residential pesticide use during pregnancy among a cohort of urban minority women." Environ.Health Perspect. 110(5):507-514.
- 11. Heudorf, U., and J. Angerer. 2001. "Metabolites of pyrethroid insecticides in urine specimens: current exposure in an urban population in Germany." Environ.Health Perspect. 109(3):213-217.
- 12. Seifert, B., et al. 2000. "The German Environmental Survey 1990/1992 (GerES II): reference concentrations of selected environmental pollutants in blood, urine, hair, house dust, drinking water and indoor air." J.Expo.Anal.Environ.Epidemiol. 10(6 Pt 1):552-565.
- 13. Matoba, Y., et al. 1998. "Indoor behavior and risk assessment following residual spraying of d-phenothrin and d-tetramethrin." Am.Ind.Hyg.Assoc.J. 59(3):191-199.
- Schettgen, T., et al. 2002. "Pyrethroid exposure of the general population-is this due to diet." Toxicol.Lett. 134(1-3):141-145.
- 15. U.S. Food and Drug Administration. 2005. "FDA Pesticide Program Residue Monitoring 1993-2003." http://www.cfsan.fda.gov/~dms/pesrpts.html.
- 16. Cressey, P.J., and R.W. Vannoort. 2003. "Pesticide content of infant formulae and weaning foods available in New Zealand." Food Addit.Contam 20(1):57-64.
- 17. Matoba, Y., et al. 1998. "Indoor behavior and risk assessment following residual spraying of d-phenothrin and d-tetramethrin." Am.Ind.Hyg.Assoc.J. 59(3):191-199.
- 18. Adgate, J.L., et al. 2000. "Pesticide storage and use patterns in Minnesota households with children." J.Expo.Anal.Environ.Epidemiol. 10(2):159-167.
- 19. Clayton, C.A., et al. 2003. "Distributions, associations, and partial aggregate exposure of pesticides and polynuclear aromatic hydrocarbons in the Minnesota Children's Pesticide Exposure Study (MNCPES)." J.Expo.Anal.Environ Epidemiol. 13(2):100-111.
- 20. Gupta, S.K., et al. 2003. "A study of childhood poisoning at National Poisons Information Centre, All India Institute of Medical Sciences, New Delhi." J.Occup.Health 45(3):191-196.
- 21. Berkowitz, G.S., et al. 2003. "Exposure to indoor pesticides during pregnancy in a multiethnic, urban cohort." Environ.Health Perspect. 111(1):79-84.

- 22. Heudorf, U., et al. 2004. "Current internal exposure to pesticides in children and adolescents in Germany: urinary levels of metabolites of pyrethroid and organophosphorus insecticides." Int.Arch.Occup.Environ.Health 77(1):67-72.
- 23. Berkowitz, G.S., et al. 2004. "In utero pesticide exposure, maternal paraoxonase activity, and head circumference." Environ.Health Perspect. 112(3):388-391.
- 24. Kennedy, D., et al. 2005. "Pregnancy outcome following exposure to permethrin and use of teratogen information." Am.J Perinatol. 22(2):87-90.
- 25. Sheets, L.P. 2000. "A consideration of age-dependent differences in susceptibility to organophosphorus and pyrethroid insecticides." Neurotoxicology 21(1-2):57-63.
- 26. Abou-Donia, M.B., et al. 2003. "Testicular Germ-Cell Apoptosis in Stressed Rats Following Combined Exposure to Pyridostigmine Bromide, N,N-Diethyl-m-Toluamide (DEET), and Permethrin." Journal of Toxicology and Environmental Health, Part A 66(1):57-73.
- 27. Abu-Qare, A.W., and M.B. Abou-Donia. 2003. "Combined exposure to DEET (N,N-diethyl-m-toluamide) and permethrin: pharmacokinetics and toxicological effects." J.Toxicol.Environ.Health B Crit Rev. 6(1):41-53.
- 28. Gomes, M.S., et al. 1991. "Effects of prenatal pyrethroid insecticide exposure on the sexual development of rats." Vet.Hum.Toxicol. 33(5):427-428.
- 29. Gomes, M.S., et al. 1991. "Pyrethroid insecticides and pregnancy: effect on physical and behavioral development of rats." Vet.Hum.Toxicol. 33(4):315-317.
- Husain, R., et al. 1992. "Differential responses of regional brain polyamines following in utero exposure to synthetic pyrethroid insecticides: a preliminary report." Bull.Environ.Contam Toxicol. 49(3):402-409.
- 31. Malaviya, M., et al. 1993. "Perinatal effects of two pyrethroid insecticides on brain neurotransmitter function in the neonatal rat." Vet.Hum.Toxicol. 35(2):119-122.
- 32. Lazarini, C.A., et al. 2001. "Effects of prenatal exposure to deltamethrin on forced swimming behavior, motor activity, and striatal dopamine levels in male and female rats." Neurotoxicol.Teratol. 23(6):665-673.
- 33. Gupta, A., et al. 1999. "Functional impairment of blood-brain barrier following pesticide exposure during early development in rats." Hum.Exp.Toxicol. 18(3):174-179.
- 34. Eriksson, P., and A. Nordberg. 1990. "Effects of two pyrethroids, bioallethrin and deltamethrin, on subpopulations of muscarinic and nicotinic receptors in the neonatal mouse brain." Toxicol.Appl.Pharmacol. 102(3):456-463.
- 35. Eriksson, P. 1997. "Developmental neurotoxicity of environmental agents in the neonate." Neurotoxicology 18(3):719-726.
- 36. Cantalamessa, F., et al. 1998. "Influence of neonatal treatment with the pyrethroid insecticide cypermethrin on the development of dopamine receptors in the rat kidney." Mech.Ageing Dev. 103(2):165-178.
- 37. U.S. Environmental Protection Agency. 2003. "Pesticides: Health and Safety: Protecting Children." <u>http://www.epa.gov/pesticides/health/children.htm</u>.
- 38. U.S. Environmental Protection Agency. 2006. "Pesticides: Topical & Chemical Fact Sheets Health and Safety Fact Sheets." <u>http://www.epa.gov/pesticides/factsheets/health_fs.htm</u>.
- 39. National Institutes of Health. 2005. "Household Products Database: Permethrin." <u>http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=52645-53-</u> <u>1&tbl=TblChemicals&prodcat=all</u>.
- 40. National Institutes of Health. 2005. "Household Products Database: Resmethrin." <u>http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=10453-86-</u> <u>&&tbl=TblChemicals&prodcat=all.</u>

Supporting references and summaries are provided in the TEACH database at <u>http://www.epa.gov/teach/</u>. Last revised 1/18/2007: includes research articles through 2005, and other information through 2006.

Chemical Summary, Permethrin & Resmethrin (Pyrethroids) (continued)

- 41. National Pesticide Telecommunications Network. 1997. "Permethrin." http://npic.orst.edu/factsheets/permethrin.pdf.
- 42. National Pesticide Telecommunications Network. 1998. "Pyrethrins & Pyrethroids." <u>http://npic.orst.edu/factsheets/pyrethrins.pdf</u>.
- 43. Reigart, J.R., and .J.R. Roberts. 1999. "Recognition and Management of Pesticide Poisonings." http://www.epa.gov/oppfead1/safety/healthcare/handbook/handbook.htm.
- 44. U.S. Environmental Protection Agency. 2004. "Integrated Pest Management (IPM) and Food Production." <u>http://www.epa.gov/pesticides/factsheets/ipm.htm</u>.
- 45. U.S. Environmental Protection Agency, Prevention, Pesticides and Toxic Substances. 2004. "Healthy Lawn Healthy Environment: Caring for Your Lawn in an Environmentally Friendly Way." http://www.epa.gov/oppfead1/Publications/lawncare.pdf.
- 46. U.S. Environmental Protection Agency. 2006. "Pesticides: Controlling Pests Integrated Pest Management (IPM) in Schools." <u>http://www.epa.gov/pesticides/ipm/</u>.
- 47. Pearlman, D.L. 2005. "Nuvo Lotion and the Future of Head-Lice Treatment." Pediatrics 115(5):1452-1453.
- 48. U.S. Department of Agriculture (USDA). 2006. "USDA Science and Technology Programs: Pesticide Data Program (PDP)." <u>http://www.ams.usda.gov/science/pdp/</u>.
- 49. U.S. Environmental Protection Agency. 2002. "Child-Specific Exposure Factors Handbook." http://www.epa.gov/NCEA/jmcsefh2.htm.
- 50. U.S. Environmental Protection Agency. 2006. "Child-Specific Exposure Factors Handbook 2006 (External Review Draft)." <u>http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=56747</u>.
- 51. U.S. Environmental Protection Agency. 2003. "Restricted Use Products (RUP) Report." http://www.epa.gov/opprd001/rup/index.htm.
- 52. U.S. Food and Drug Administration, Center for Drug Evaluation and Research. 2000. "Permethrin (Company: Alpharma)." <u>http://www.fda.gov/cder/foi/anda/2000/075014_permethrin_toc.htm</u>.
- 53. U.S. Environmental Protection Agency. 2001. "Lists of Lists: Consolidated List of Chemicals Subject to the Emergency Planning and Right-to-Know Act (EPCRA) and Section 112(r) of the Clean Air Act." <u>http://www.epa.gov/ceppo/pubs/title3.pdf</u>.
- 54. World Health Organization. 1996. "International Program on Chemical Safety, Environmental Health Criteria 94: Resmethrin." <u>http://www.inchem.org/documents/pds/pds/pest83_e.htm</u>.
- 55. World Health Organization. 2006. "International Program on Chemical Safety, Environmental Health Criteria 92: Permethrin." <u>http://www.inchem.org/documents/pds/pds/pest51_e.htm</u>.
- 56. U.S. Environmental Protection Agency. 2002. "TRI Explorer: Providing Access to EPA's Toxic Release Inventory Data." <u>http://www.epa.gov/triexplorer/</u>.