

# RESMETHRIN

## TECHNICAL FACT SHEET

NPIC Technical Fact Sheets provide information that is complex and intended for individuals with a scientific background and/or familiarity with toxicology and risk assessment. This document is intended to promote informed decision-making. Please refer to the General Fact Sheet for less technical information.

### Chemical Class and Type:

- Resmethrin is a broad-spectrum insecticide, and it is a member of the synthetic pyrethroid family of chemicals.<sup>1</sup> The International Union of Pure and Applied Chemistry (IUPAC) name for resmethrin is 5-benzyl-3-furylmethyl (1R,3R;1R,3SR)-2,2-dimethyl-3-(2-methylpropyl-1-enyl) cyclopropanecarboxylate, and the Chemical Abstracts Service (CAS) registry number is 10453-86-8.<sup>1</sup>
- Resmethrin was first registered for use in the United States in 1967.<sup>1</sup>

### Physical / Chemical Properties:

- Resmethrin is a colorless to yellow-brown, waxy solid with an odor similar to chrysanthemums.<sup>2,3</sup>
- Vapor pressure<sup>4</sup>:  $1.13 \times 10^{-8}$  mmHg at 30 °C; 0.01 mPa at 25 °C
- Octanol-Water Partition Coefficient ( $K_{ow}$ )<sup>3</sup>:  $2.63 \times 10^5$ ; ( $\log K_{ow}$ )<sup>3</sup>: 5.43
- Henry's constant<sup>4</sup>:  $1.3 \times 10^{-7}$  atm·m<sup>3</sup>/mol
- Molecular weight<sup>3</sup>: 338.45 g/mol
- Solubility (water)<sup>3</sup>:  $3.79 \times 10^{-2}$  mg/L
- Soil Sorption Coefficient ( $K_{oc}$ )<sup>5</sup>:  $1.00 \times 10^5$

### Uses:

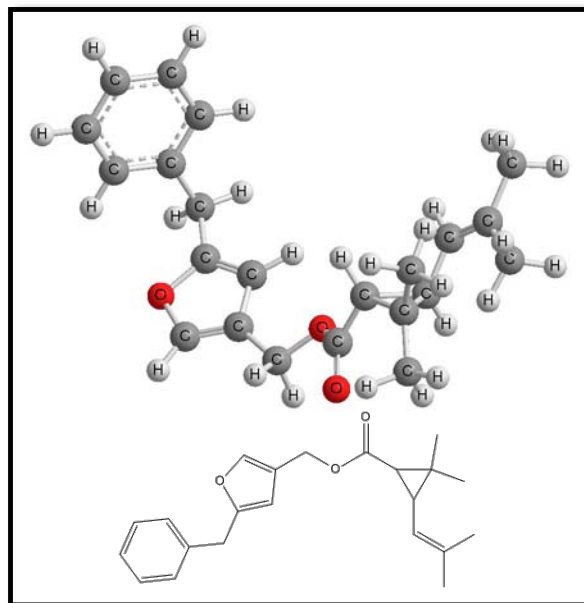
- Resmethrin is registered as a general use pesticide to control flying and crawling insects in and around residential settings, on pets and livestock, and in industrial settings, including food-handling establishments.<sup>1</sup> Uses for products containing resmethrin vary widely. Always read and follow the label when applying pesticide products.
- Resmethrin is also classified as a Restricted Use insecticide for professional use as an ultra-low volume (ULV) application for mosquito abatement programs, due to its acute fish toxicity.<sup>1</sup>
- Signal words for products containing resmethrin may range from Caution to Danger.<sup>6</sup> The signal word reflects the combined toxicity of the active ingredient and other ingredients in the product. See the pesticide label on the product and refer to the NPIC fact sheets on [Signal Words](#) and [Inert or "Other" Ingredients](#).
- To find a list of products containing resmethrin which are registered in your state, visit the website [http://npic.orst.edu/reg/state\\_agencies.html](http://npic.orst.edu/reg/state_agencies.html) and search by "active ingredient."

### Mode of Action:

#### Target Organisms

- Resmethrin kills insects by direct contact.<sup>3</sup> Resmethrin is a Type I pyrethroid that affects the insects nervous system by interfering with sodium channels in the central and peripheral nervous system.<sup>1,7</sup> Following exposure to resmethrin, sodium channels are kept open for prolonged periods of time, causing repetitive nerve discharge and increased excitation.<sup>7,8</sup>

### Molecular Structure - Resmethrin



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### Non-target Organisms

- Resmethrin is lower in toxicity to mammals than insects.<sup>8</sup> Pyrethroid insecticides have a negative temperature dependence, meaning they more strongly interfere with sodium channels at lower temperatures. Insects and other invertebrates are subsequently more susceptible to the toxicity of pyrethroids given that their body temperature is 10°C below that of mammals. Higher mammalian body temperatures also contribute to the increased metabolic degradation of pyrethroids in mammals compared to insects.<sup>8</sup>

### Acute Toxicity:

#### Oral

- Resmethrin is low in toxicity to rats when ingested. The acute oral LD<sub>50</sub> is 6091 mg/kg for male rats and 4639 mg/kg for female rats.<sup>1</sup> See the text boxes on **Toxicity Classification** and **LD<sub>50</sub>/LC<sub>50</sub>**.

#### Dermal

- Resmethrin is low in toxicity to rabbits when applied to the skin. The acute dermal LD<sub>50</sub> in rabbits is >2000 mg/kg.<sup>1</sup>
- Resmethrin is not a skin irritant or a skin sensitizer.<sup>1</sup>
- Resmethrin is not an eye irritant.<sup>1</sup>

**LD<sub>50</sub>/LC<sub>50</sub>:** A common measure of acute toxicity is the lethal dose (LD<sub>50</sub>) or lethal concentration (LC<sub>50</sub>) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD<sub>50</sub> is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC<sub>50</sub> is often expressed as mg of chemical per volume (e.g., liter (L)) of medium (i.e., air or water) the organism is exposed to. Chemicals are considered highly toxic when the LD<sub>50</sub>/LC<sub>50</sub> is small and practically non-toxic when the value is large. However, the LD<sub>50</sub>/LC<sub>50</sub> does not reflect any effects from long-term exposure (i.e., cancer, birth defects or reproductive toxicity) that may occur at levels below those that cause death.

### TOXICITY CLASSIFICATION - RESMETHRIN

	High Toxicity	Moderate Toxicity	Low Toxicity	Very Low Toxicity
Acute Oral LD <sub>50</sub>	Up to and including 50 mg/kg (≤ 50 mg/kg)	Greater than 50 through 500 mg/kg (> 50 – 500 mg/kg)	Greater than 500 through 5000 mg/kg (> 500 – 5000 mg/kg)	Greater than 5000 mg/kg (> 5000 mg/kg)
Inhalation LC <sub>50</sub>	Up to and including 0.05 mg/L (≤ 0.05 mg/L)	Greater than 0.05 through 0.5 mg/L (>0.05 – 0.5 mg/L)	Greater than 0.5 through 2.0 mg/L (> 0.5 – 2.0 mg/L)	Greater than 2.0 mg/L (> 2.0 mg/L)
Dermal LD <sub>50</sub>	Up to and including 200 mg/kg (≤ 200 mg/kg)	Greater than 200 through 2000 mg/kg (> 200 - 2000 mg/kg)	Greater than 2000 through 5000 mg/kg (>2000 – 5000 mg/kg)	Greater than 5000 mg/kg (> 5000 mg/kg)
Primary Eye Irritation	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	Corneal involvement or other eye irritation clearing in 8 – 21 days	Corneal involvement or other eye irritation clearing in 7 days or less	Minimal effects clearing in less than 24 hours
Primary Skin Irritation	Corrosive (tissue destruction into the dermis and/or scarring)	Severe irritation at 72 hours (severe erythema or edema)	Moderate irritation at 72 hours (moderate erythema)	Mild or slight irritation at 72 hours (no irritation or erythema)

The highlighted boxes reflect the values in the “Acute Toxicity” section of this fact sheet. Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7: Precautionary Labeling. <http://www.epa.gov/oppfead1/labeling/lrm/chap-07.pdf>

### Inhalation

- Resmethrin is low in toxicity when inhaled by rats. The 4-hour inhalation LC<sub>50</sub> in rats is 5.28 mg/L.<sup>1</sup>

### Signs of Toxicity - Animals

- Resmethrin, and other Type I pyrethroids, demonstrate acute signs of neurotoxicity when administered to animals in experimental studies via oral or intravenous routes of exposure. Signs of toxicity may include, tremors, convulsive twitching, nasal discharge, tearing, incoordination, restlessness, hyperexcitability, involuntary muscle movements, paralysis, coma, and death.<sup>1,7,9,10</sup>

### Signs of Toxicity - Humans

- A review of human incident reports by the United States Environmental Protection Agency (U.S. EPA) revealed that symptoms were dependent on the pathway of exposure.<sup>1</sup> Reported symptoms were most frequently associated with systemic or respiratory effects.
- Symptoms from exposure to resmethrin and other pyrethroids include stinging, burning, itching and tingling of the skin, which may progress to numbness. Systemic toxicity by inhalation or dermal absorption is low, and less common with exposure to Type I pyrethroids.<sup>11</sup> In cases of severe exposure to pyrethroids, seizures have been reported, but are more common with exposure to the Type II pyrethroids (those containing a cyano- group).<sup>11,12</sup> Other symptoms from exposure include abnormal facial sensations, dizziness, nausea, fatigue, and irritability to sound and touch. Signs from exposure include salivation, vomiting and diarrhea, as well as pulmonary edema and muscle fasciculations in severe cases of exposure.<sup>11</sup>
- Always follow label instructions and take steps to avoid exposure. If any exposures occur, be sure to follow the First Aid instruction on the product label carefully. For additional treatment advice, contact the Poison Control Center at 1-800-222-1222. If you wish to report an incident to NPIC, please call 1-800-858-7378.

### Chronic Toxicity:

#### Animals

- Liver toxicity is the “most sensitive endpoint” in subchronic and chronic oral exposure to resmethrin.<sup>1</sup>
- In a 90-day subchronic oral toxicity study in rats, investigators determined a LOAEL of 1250 ppm based on increased liver weights, increased blood urine nitrogen, and vacuolization of thyroid follicular cells in female rats, and hepatocellular vacuolization and hypertrophy in male and female rats.<sup>13,14</sup> See the text box on **NOAEL, NOEL, LOAEL, and LOEL**.
- Researchers administered resmethrin to dogs by gavage at doses of 0, 12.5, 125.0, 500.0, and 2000.0 mg/kg/day for one year. Investigators found decreased body weight gain and decreased food consumption in both male and female dogs, and observed bilateral cataracts in a male dog.<sup>14</sup>
- Researchers applied resmethrin to the skin of rabbits at doses up to 1000 mg/kg/day for three weeks and found no evidence of systemic toxicity.<sup>14</sup>

**NOAEL: No Observable Adverse Effect Level**

**NOEL: No Observed Effect Level**

**LOAEL: Lowest Observable Adverse Effect Level**

**LOEL: Lowest Observed Effect Level**

#### Humans

- No human data were found on the chronic health effects of resmethrin. See the text box on **Exposure**.

**Exposure: Effects of resmethrin on human health and the environment depend on how much resmethrin is present and the length and frequency of exposure. Effects also depend on the health of a person and/or certain environmental factors.**

### Endocrine Disruption:

- Resmethrin is included in the draft list of initial chemicals for screening under the U.S. EPA Endocrine Disruptor Screening Program (EDSP). The list of chemicals was generated based upon exposure potential, not based on whether the pesticide is a known or likely potential cause of endocrine effects.<sup>15</sup>
- In a 90-day rat feeding study with resmethrin investigators observed thyroid follicular cell vacuolization in the presence of liver toxicity. However, in acceptable mouse and rat feeding studies submitted to the U.S. EPA for the purpose of reregistration, resmethrin did not induce estrogen, androgen, or thyroid-mediated toxicity.<sup>4,11</sup>

**Cancer:** Government agencies in the United States and abroad have developed programs to evaluate the potential for a chemical to cause cancer. Testing guidelines and classification systems vary. To learn more about the meaning of various cancer classification descriptors listed in this fact sheet, please visit the appropriate reference, or call NPIC.

## Carcinogenicity:

### Animals

- Scientists fed mice resmethrin in the diet at doses of 0, 250, 500, or 1000 mg/kg for an 85-week period. They observed no evidence of carcinogenicity.<sup>9</sup>
- Scientists fed rats resmethrin in the diet at doses of 0, 500, 2500, and 5000 mg/kg for a 112-week period. They observed no evidence of carcinogenicity at any of the dose levels tested.<sup>9</sup>
- Researchers often use studies designed to test for mutagenicity to screen chemicals for carcinogenicity. Researchers concluded that resmethrin is not mutagenic based on its failure to induce gene mutations, chromosomal aberrations, or unscheduled DNA synthesis in genotoxicity studies.<sup>13</sup>

### Humans

- Resmethrin is classified by the U.S. EPA as “likely to be carcinogenic to humans” based on “increased incidences of benign and malignant liver tumors in female rats and male mice.”<sup>13</sup> See the text box on **Cancer**.
- No human data were found on carcinogenic effects of resmethrin.

## Reproductive or Teratogenic Effects:

### Animals

- In a two-generation reproductive study, researchers fed rats resmethrin at doses of 0, 17.4, 34.8, or 70.8 mg/kg/day during gestation. At the highest dose tested investigators found a slight decrease in female body weight and weight gain during gestation, and no weight gain during the first 4 days of lactation. At the highest dose tested investigators also found decreased second generation mating, decreased pup weight, and a slight increase in stillborn pups. The reproductive NOAEL is 34.8 mg/kg/day (500 ppm).<sup>14</sup>
- In a developmental toxicity study, researchers administered resmethrin to rabbits by oral gavage at doses of 0, 34, 138, or 345 mg/kg/day on days 6-18 of gestation. Researchers observed abortion and complete resorption at the highest dose tested. The developmental NOAEL is 138 mg/kg/day.<sup>14</sup>
- In a teratogenicity study, researchers administered resmethrin to rabbits by oral gavage at doses of 0, 10, 30, or 100 mg/kg on days 6 to 18 of gestation. Researchers observed skeletal abnormalities and a minimal increase of resorbed litters at the highest dose tested.<sup>14</sup>

### Humans

- No human data were found on the reproductive or developmental effects of resmethrin.

## Fate in the Body:

### Absorption

- Pyrethroids are rapidly absorbed by the gastrointestinal tract following ingestion, likely to be efficiently absorbed from the respiratory tract following inhalation, and poorly absorbed through the skin following dermal exposure.<sup>10</sup> Pyrethroids formulated in emulsifiable concentrates exhibit 3-fold greater dermal absorption than pyrethroids in a dust formulation.<sup>10</sup>

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### Distribution

- Pyrethroids are lipophilic. Following absorption they are distributed throughout the body primarily to lipid-rich tissue, such as body fat and elements of the nervous system.<sup>10</sup>
- Following oral administration, pyrethroids are quickly absorbed from the intestinal tract and distributed among all body tissue with peak concentrations occurring at three hours after dosing and gradually disappearing thereafter.<sup>16</sup>

### Metabolism

- Resmethrin is metabolized by ester bond cleavage, oxidation, and glucuronidation or conjugation.<sup>1</sup>
- Researchers fed rats single low (1 mg/kg) and high (200 mg/kg) oral doses of resmethrin, as well as multiple low (1 mg/kg) oral doses of resmethrin, and found that resmethrin was completely metabolized within 48-72 hours.<sup>1</sup>
- In a metabolism study in rats, more than 30 resmethrin metabolites were found, generally in low amounts. The major urinary metabolites of resmethrin included 5-benzyl-3-furancarboxylic acid (BFCA) and  $\alpha$ -(4-carboxy-2-furyl)-benzyl alcohol ( $\alpha$ -OH-BFCA).<sup>1</sup>
- In metabolism studies in hens and goats, investigators determined that resmethrin metabolites are present in low levels compared to the parent compound, and metabolites are not likely to be as toxic or more toxic than the parent compound.<sup>1</sup>

### Excretion

- In metabolism studies, investigators determined that significant excretion of resmethrin occurs in both the feces and the urine, and it is typically eliminated within 48-72 hours of exposure.<sup>1</sup>
- Excessive accumulation and persistence of pyrethroids in the body is not expected to occur.<sup>10</sup>

### Medical Tests and Monitoring:

- Analytical methods have been developed to detect pyrethroids in blood and urine. These methods have been used in research studies to better understand human exposure to pyrethroids.<sup>17</sup>
- Most clinical laboratories do not offer testing services for pyrethroids in human body fluids. Finding a measurable amount of pyrethroids in blood or urine does not mean that the level will result in an adverse health effect. Further research is needed to better understand the relationship between these measurements and a person's health status.<sup>18</sup>
- The relevant biomarker of exposure for resmethrin in human urine is *trans*-chrysanthemumdicarboxylic acid (*trans*-CD-CA).<sup>16</sup>
- Resmethrin was not among the group of pyrethroids included for biomonitoring assessment in the third National Health and Nutrition Examination Survey (NHANES).<sup>19</sup>

### Environmental Fate:

#### Soil

- Resmethrin is degraded in the environment primarily by photolysis.<sup>1</sup> The typical half-life of resmethrin in the soil is 30 days.<sup>5</sup> See the text box on **Half-life**.

The "half-life" is the time required for half of the compound to break down in the environment.

1 half-life = 50% remaining

2 half-lives = 25% remaining

3 half-lives = 12% remaining

4 half-lives = 6% remaining

5 half-lives = 3% remaining

Half-lives can vary widely based on environmental factors. The amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied. It should be noted that some chemicals may degrade into compounds of toxicological significance.

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- Resmethrin has low water solubility and high adsorption potential to organic material and sediment. Therefore, resmethrin has low soil mobility and is unlikely to contaminate groundwater.<sup>1,5</sup>
- Resmethrin is degraded by photooxidation in the environment resulting in several metabolites, including (+)-trans-chrysanthemic acid, which is more toxic to mice compared to resmethrin when administered intraperitoneally.<sup>20</sup>

### Water

- Resmethrin is not efficiently degraded by hydrolysis with a half-life >89 days at pH 5-9.<sup>1</sup>
- Resmethrin is rapidly degraded in aqueous solutions through photodegradation with a half-life of 22 minutes in seawater and 47 minutes in fresh (distilled) water.<sup>1</sup>
- Resmethrin has a low potential to reach groundwater.<sup>1</sup>

### Air

- Resmethrin has a low vapor pressure ( $1.1 \times 10^{-8}$  at 30 °C) and Henry's Law Constant ( $1.3 \times 10^{-7}$  atm·m<sup>3</sup>/mol), and is not expected to significantly volatilize from water or soil surfaces.<sup>4</sup>
- Researchers exposed solutions of resmethrin on a surface to forenoon and midday sunlight conditions. Half-lives ranged from 20 to 90 minutes.<sup>2</sup>

### Plants

- Researchers applied resmethrin to tomato and lettuce plants and observed that 55-82% of the compound degraded within two hours. No resmethrin residues remained after five days, although researchers observed low amounts of degradation products on the plants.<sup>9</sup>
- Resmethrin poses no phytotoxic concern for plants.<sup>1</sup>

### Indoor

- Under indoor conditions with exposure to natural light (facing south), resmethrin decomposed within a few hours.<sup>16</sup>

### Food Residue

- Resmethrin is registered for use as a crack and crevice and space spray in food handling establishments and storage areas. Therefore, the U.S. EPA has established a general tolerance of 3.0 ppm for resmethrin in or on food.<sup>21</sup>
- The United States Food and Drug Administration (FDA) Pesticide Residue Monitoring Program conducts regulatory and incidence/level monitoring for pesticide residues in domestic and imported foods (except meat, poultry, dairy, and eggs). In 2000, the FDA analyzed 2525 domestic and 3998 import agricultural samples for tolerance compliance.<sup>22</sup> Investigators analyzed one domestic sample for detectable levels of resmethrin and found that residues exceeded the established regulatory tolerance.<sup>22</sup>
- In 2006, the United States Department of Agriculture (USDA) Pesticide Data Program (PDP) analyzed more than 9700 agricultural commodity samples, and 655 poultry breast and poultry thigh samples for residue levels of resmethrin and/or resmethrin isomers. No samples had detectable residues.<sup>23</sup>

### Ecotoxicity Studies:

#### Fish and Aquatic Life

- Resmethrin is "very highly toxic" to freshwater and estuarine fish. The LC<sub>50</sub> for resmethrin is 0.28 µg/L in rainbow trout, (*Oncorhynchus mykiss*) and 11.0 µg/L in sheepshead minnow (*Cyprinodon variegatus*).<sup>1</sup>
- Resmethrin is "very highly toxic" to freshwater and estuarine invertebrates with a respective LC<sub>50</sub> of 3.10 µg/L in *Daphnia* and 1.30 µg/L in pink shrimp (*Pandalus borealis*).<sup>1</sup>

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- Field conditions are expected to reduce the impact of resmethrin to fish due to rapid photodegradation, microbial breakdown, and low water solubility of resmethrin in the environment.<sup>9</sup>

### Birds

- Resmethrin is moderately toxic to birds with an acute oral LD<sub>50</sub> of 75 mg/kg in the red-winged black bird.<sup>1</sup>
- Resmethrin was practically non-toxic to birds in a subacute dietary study in bobwhite quail (*Colinus virginianus*) with an LC<sub>50</sub> >5000 ppm.<sup>1</sup>
- In chronic toxicity studies, resmethrin demonstrated a No Observable Adverse Effect Concentration (NOAEC) of 12 ppm based on “increased incidence of early embryonic death” in mallard ducks (*Anas platyrhynchos*).<sup>1</sup>

**Reference Dose (RfD):** The RfD is an estimate of the quantity of chemical that a person could be exposed to every day for the rest of their life with no appreciable risk of adverse health effects. The reference dose is typically measured in milligrams (mg) of chemical per kilogram (kg) of body weight per day.

### Terrestrial Invertebrates

- Resmethrin is highly toxic to honey bees. The LD<sub>50</sub> is 0.063 µg/bee.<sup>4</sup>

U.S. Environmental Protection Agency, Office of Water. 2002 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-02-038.

<http://www.epa.gov/ost/drinking/standards/dwstandards.pdf>

### Regulatory Guidelines:

- The chronic reference dose (RfD) for resmethrin is 0.035 mg/kg/day.<sup>14</sup> See the text box on **Reference Dose (RfD)**.
- The U.S. EPA has classified resmethrin as “likely to be carcinogenic to humans” based on “increased incidences of benign and malignant liver tumors in female rats and male mice.”<sup>13</sup> See the text box on **Cancer** (page 4).
- The Acceptable Daily Intake (ADI) for resmethrin is 0.1250 mg/kg/day.<sup>3</sup>

### Date Reviewed: July 2008

Please cite as: Jackson, D.; Luukinen, B.; Buhl, K.; Stone, D. 2008. *Resmethrin Technical Fact Sheet*; National Pesticide Information Center, Oregon State University Extension Services. <http://npic.orst.edu/factsheets/ResTech.pdf>.

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