LINDANE

Lindane, like DDT and in the organochlorine family, has been controversial for decades because of its cancer causing and neurotoxic properties. Despite its toxicity, lindane is commonly prescribed as a pharmaceutical to treat lice and scabies, and is used as a seed treatment.

While the U.S. Environmental Protection Agency (EPA) regulates pesticide use, it is the Food and Drug Administration (FDA) that regulates medicinal use of lindane to treat lice and scabies. Over 2 million lindane prescriptions for head lice and scabies are issued every year. (NPA, 2000)

Over the past ten years, all uses of lindane have been voluntarily canceled by lindane registrants, except 13 seed treatment uses and prescription-only treatments for lice and scabies, (Howard, 2000). Despite this, FDA residue monitoring in 1999 found lindane to be the 12th most commonly found pesticide residue in food samples tested (FDA, 1999).

Lindane Bans

In September 2000, California Governor Davis signed a bill that prohibits the use or sale of any lindane containing products for treatment of human head lice or scabies by January 1, 2002.

At least 14 countries have banned all uses of lindane and 16 countries have severely restricted its use. In July 2000, the European Union's Standing Committee on Plant Health voted to ban all agricultural and gardening applications of lindane. The European Commission is expected to ratify the decision, which should take effect by 2002 (Schafer, 2000).

Routes of Exposure

Exposure to lindane is a concern, especially considering its inclusion in creams and shampoos for lice and scabies. Lindane is efficiently absorbed across the skin, with a documented 9.3% dermal absorption rate. It is absorbed even more efficiently across abraded skin, which is of high concern considering the severe dermatitis associated with scabies. Absorption across the skin as well as in the gut is enhanced by the presence of fat and fat solvents. Although lindane is not highly volatile, pesticide-laden aerosol or dust particles trapped in respiratory mucous and subsequently swallowed may lead to significant absorption in the gut (Reigart, 1999).

Following absorption, lindane is partially dechlorinated and oxidized, promptly yielding a series of conjugated chlorophenols and other oxidation products in the urine. Excretion of lindane occurs within a few days, primarily through the feces. While exposure to most organochlorines results in significant storage of the unchanged parent compound in fat tissue, the rapid metabolic breakdown of lindane reduces the likelihood that it will be detected in body fat, blood or milk (Reigart, 1999).

Health Effects

EPA classifies lindane as moderately toxic, or a class II, chemical and bears the signal word "warning." The chief toxic action is on the nervous system where lindane, like other organochlorines, interferes with the flux of cations across nerve cell membranes. Adverse health effects include: apprehension, agitation, mental/motor impairment, excitation vomiting, stomach upset, abdominal pain, central nervous system depression, convulsions, muscle weakness and spasm, loss of balance, grinding of the teeth, hyperirritability, violent seizures, increased respiratory rate and/or failure, dermatitis, immunotoxicity, and fetotoxicity.

Lindane is more acutely toxic than DDT and may modify brain function for days and even weeks after a single exposure (Gosselin, 1983). Data from animal tests indicate that lindane may affect the liver, kidney, pancreas, testes, and nasal mucous membrane (Dalsenter, 1997; Sircar, 1989; ETN, 1996, US EPA, 1985; US EPA, 1998). Lindane is an endocrine disruptor and was found to be slightly estrogenic to female rats and mice, and caused the testes of male rats to become atrophied (PAN, 1998; ETN, 1996). Lindane has been shown to induce drug-metabolizing enzymes in the liver (Gosselin, 1983). This tends to accelerate excretion of the pesticides themselves, but may also stimulate biotransformation of critical natural substances, such as steroid hormones and therapeutic drugs (Reigart, 1999).

Diet and age can affect sensitivity to lindane's toxic action. Children are more sensitive, doses of 1.6 and 45 grams are capable of producing seizures in young children and adults, respectively. A low protein diet may render an individual more susceptible as well. Rats on low protein diets were twice as susceptible to the acute toxic effects of lindane compared with animals on a normal diet (Gosselin, 1983).

There is a great deal of anecdotal evidence in medical literature linking chronic lindane exposure to rare blood disorders including aplastic anemia (West, 1967; PAN, 1998). Pulmonary edema has been reported after intentional lindane ingestion (US EPA, 1998), but the exact role of aspiration in producing these changes is not clear. The development of myoglobin in the urine, acute kidney failure, and muscle weakness in the limbs after ingestion of 15-20 ml of lindane suggests that it may be a direct muscle toxin (Gosselin, 1983).

A laboratory study found that a single topical application of 1% lindane on weanling rabbits caused convulsions. Gosselin et al. report six human cases of alleged neurotoxicity associated with the use of this type of product. At least five of these were judged the result of accidental ingestion or inappropriate application. "Some children exhibited seizures after total body applications or after applications that were left on longer than the recommended 24 hours."

Carcinogenicity

The International Agency for Research on Cancer (IARC) has concluded that lindane is a possible human carcinogen (class 2B), and EPA has classified it similarly as a class B2/C possible human carcinogen based on liver and lung tumors in mice (US EPA, 2000a). The State of California has listed lindane as known carcinogen (CalEPA, 1999).

Lindane is linked to breast cancer (Wolff, 1985; Schafer, 2000). There is a significant body of evidence that suggests that where lindane is used extensively, and particularly in areas where cattle were treated, the incidence of breast cancer is elevated (PAN, 1998). The presence of lindane in human and cow milk has been reported in countries throughout the world (Moses, 1993; Schafer, 2000).

Regulatory History

In 1977, lindane was put into EPA Special Review because of concerns over its ability to cause cancer, fetotoxicity/teratogenicity, reproductive effects, blood dyscrasia, and its acute toxicity to aquatic wildlife. In 1980, EPA proposed canceling most uses of lindane because "lindane continues to meet or exceed the risk criteria for oncogenicity and reproductive and fetotoxic effects," noting children's particular risk (US EPA, 1980). However, in its final 1983 decision, EPA continued most registrations with various restrictions. At the time, the Scientific Advisory Panel supported bans on household, pet and homeowner ornamental applications (US EPA, 1983). In 1985, lindane again came under EPA scrutiny because of its link with kidney effects (US EPA, 1985). Over the past 10 years, most uses, including wood treatment, foliar, termiticide, home insecticidal and military use of lindane, have been voluntarily canceled by the chemical's registrants (Howard, 2000).

In 1996, FDA's Dermatologic Drugs Advisory Committee reviewed claims that lindane causes neurological damage in children and required additional advisories on packaging, and a warning against repeated treatment with lindane products, because repeated treatments have been clearly linked to neurotoxicity. FDA stated, "The reason for the product's misuse may be connected with pruritus - itching that continues after ... treatment - due to the residual inflammation in the skin. When treated children continue to scratch, some parents may continue to medicate beyond the recommended procedure" (Kupec, 1996).

Currently, EPA is working on the preliminary risk assessment for lindane as required under the *Federal Insecticide, Fungicide and Rodenticide Act* and the *Food Quality Protection Act* (Howard, 2000). Lindane's preliminary risk assessment and registration eligibility is expected to be released for public comment period in 2001, at which time registered uses will be reviewed and decisions on continued registration for each use will be made (US EPA, 2000b).

Ecological Effects

Lindane is moderately toxic to bird species and can be stored in the fat of birds. Residues can also find their way into egg yolks at measurable concentrations for 32 days after dosing. Lindane is highly toxic to fish and aquatic invertebrate species. Lindane is also highly toxic to bees and certain beneficial parasites and predacious insects (ETN, 1996; US EPA, 1994).

Plants may pick up residues from not only direct application, but through water and vapor phases. Persistence is seen when plants are rich in lipid content, and crops like cauliflower and spinach will build up less residue than crops like carrots (ETN, 1996).

Environmental Fate

Lindane is highly persistent in most soils, with a field half-life of approximately 15 months. It may be mobile in soils and may pose a risk of groundwater contamination. Lindane is very stable in both fresh and salt water and is resistant to photodegradation (ETN, 1996). EPA's Office of Water established the maximum contaminant level for lindane in drinking water at 0.2 parts per billion (US EPA, 1998). From 1987 to 1993, according to EPA's Toxics Release Inventory, lindane releases to land and water totaled 1,115 pounds (US EPA, 1998). Lindane has been found in 239 sites listed on EPA's National Priorities List (ATSDR, 1995).

Resistance

The Centers for Disease Control and Prevention, and the World Health Organization, among others, cite widespread insect resistance to lindane in the U.S. and other parts of the world (NPA, 2000; Downs, 1999; Brainerd, 1998).

LINDANE ChemicalWATCH Fact Sheet References

Agency for Toxic Substances and Disease Registry (ATSDR). 1995. ToxFAQs: Hexachlorocyclohexane. <www.atsdr.cdc.gov/tfacts43.html>.

Brainerd, E. 1998. "Eradication to resistance: five continuing concerns about pediculosis." *Journal of School Health* 68(4):146-150.

CalEPA. 2000. Proposition 65: Chemicals known to the state to cause cancer or reproductive toxicity. Office of Environmental Health Hazard Assessment. <http://www.oehha.org/prop65/prop65_list/Newlist.html>.

Centers for Disease Control and Prevention. 1998. Ectoparasitic Infections. 47(RR-1). <www.cdc.gov/nchstp>.

Dalsenter, P.R., et al. 1997. "Reproductive toxicity and toxicokinetics of lindane in the male offspring of rats exposed during lactation." *Human & Experimental Toxicology* 16:146-153.

Downs, A., et al. 1999. "Head Lice: Prevalence in school children and insecticide resistance." *Parasitology Today* 15(1):1-3.

Extension Toxicology Network (ETN). 1996. Chlorpyrifos: Pesticide Information Profiles. <http://ace.orst.edu/cgi-bin/mfs/01/pips/lindane.htm>.

FDA. 1999. Food and Drug Administration Pesticide Program: Residue Monitoring 1999. Washington, DC. <www.cfsan.fda.gov>.

Gosselin, R.E. et al. 1983. *Clinical Toxicology of Commercial Products*. 5th ed. Williams & Wilkins. Baltimore, MD.

Howard, Mark. 2000. Personal communication. Lindane chemical review manager, Office of Pesticide Programs. Washington, DC.

Kupec, I.F. 1996. FDA Requires Labeling Change on Lindane-Containing Lice Treatments. T96-24. Food & Drug Administration. Washington, DC.

Moses, M. 1993. "Pesticides and breast cancer." *Pesticide News* 22:3-5.

National Pediculosis Association (NPA). 2000. The No Nit Policy. <www.headlice.org/publications/nonit.html>.

Pesticide Action Network United Kingdom (PAN). 1998. Lindane Fact Sheet.

Reigart, J.R. et al. 1999. *Recognition & Management of Pesticide Poisonings*. 5th ed. US EPA. Washington, DC.

Schafer, K. 2000. "Going, Going, Gone: Lindane moves closer to elimination." *Global Pesticide Campaigner*. San Fransisco, CA.

Sircar, S. et al. 1989. "Lindane causes reproductive failure and fetotoxicity in mice." *Toxicology* 59:171-177.

US EPA. 2000a. List of Chemicals Evaluated for Carcinogenic Potential. Office of Pesticide Programs. Washington, DC.

US EPA. 2000b. Reregistration Eligibility Decisions Projected for FY2000-FY2001. Office of Pesticide Programs. Washington, DC.

US EPA. 1998. National Primary Drinking Water Regulations: Consumer Factsheet on Lindane. Office of Water. Washington, DC.

US EPA. 1994. Pesticide Fact Sheet: Lindane, Decision not to initiate Special Review (Proposed Rule). EPA 738-F-84-001.Office of Pesticide Programs. Washington DC.

US EPA. 1985. Guidance for the Reregistration of Pesticide Products Containing Lindane as the Active Ingredient. Office of Pesticide Programs. Washington, DC.

US EPA. 1983. Lindane: Special Review Position Document 4. Office of Pesticide Programs. Washington, DC.

US EPA. 1980. Preliminary Notice of Determination Concluding the Rebuttable Presumption Against Registration of Products Containing Lindane. Notice of Availability of PD 2/3. Office of Pesticide Programs. Washington, DC.

West, I. 1967. "Lindane and hematologic reactions." Archives of Environmental Health 15:97-101.

Wolffe, M. 1985. "Blood levels of organochlorineresidues and risk of breast cancer." *Journal of the National Cancer Institute* 85(8):648-652.

ChemicalWATCH Factsheet
A BEYOND PESTICIDES/NCAMP FACTSHEET

SYNTHETIC PYRETHROIDS

Despite their toxicity, pesticide products containing pyrethroids are often described by pest control operators and community mosquito managers as "safe as chrysanthemum flowers." While pyrethroids are a synthetic version of an extract from the chyrsanthemum, they were chemically designed to be more toxic with longer breakdown times, and are often formulated with synergists, increasing potency and compromising the human body's ability to detoxify the pesticide.

What are Synthetic Pyrethroids?

Synthetic pyrethroids are synthesized derivatives of naturally occurring pyrethrins, which are taken from pyrethrum, the oleoresin extract of dried chrysanthemum flowers. The insecticidal properties of pyrethrins are derived from ketoalcoholic esters of chrysanthemic and pyrethroic acids. These acids are strongly lipophilic and rapidly penetrate many insects and paralyze their nervous system (Reigart et al., 1999). Both pyrethrins and synthetic pyrethroids are sold as commercial pesticides used to control pest insects in agriculture, homes, communities, restaurants, hospitals, schools, and as a topical head lice treatment. Various formulations of these pesticides are often combined with other chemicals, known as synergists, to increase potency and persistence in the environment.

While chemically and toxicologically similar, pyrethrins are extremely sensitive to light, heat and moisture. In direct sunlight, half-lives can be measured in hours. However, the pyrethroids, the synthetic analogues of naturally occurring pesticides, were developed to capture the effective insecticidal activity of this botanical insecticide, with increased stability in light, yielding longer residence times (Gosselin et al., 1984).

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Pyrethroids and Health Effects

Pyrethroids have irritant and/or sensitizing properties. They are not easily absorbed through the skin, but are absorbed through the gut and pulmonary membrane. Tests of some pyrethroids on laboratory animals reveal striking neurotoxicity when administered by injection or orally. Systemic toxicity by inhalation and dermal absorption is low. The acute toxicity, calculated by LD_{50}'s, ranges from low to high, depending on the specific formulation. Low toxicity is attributed to two factors: limited absorption of some pyrethroids, and rapid biodegradation by mammalian liver enzymes (ester hydrolysis and oxidation). Insects, without this liver function, exhibit greater susceptibility to the chemicals (Reigart et al., 1999).

Pyrethroids interfere with the ionic conductance of nerve membranes by prolonging the sodium current. This stimulates nerves to discharge repeatedly causing hyper-excitability in poisoned animals. The World Health Organization explains that synthetic pyrethroids are neuropoisons acting on the axons in the peripheral and central nervous systems by interacting with sodium channels in mammals and/or insects. The main systems for metabolism include breakage of the ester bond by esterase action and oxidation at various parts of the molecule. Induction of liver microsomal enzymes has also been observed (WHO, 1999).

Signs and symptoms of poisoning by pyrethroids may take several forms. Because of the similarities to crude pyrethrum, pyrethroids may act as dermal and respiratory allergens. Exposure to pyrethroids has resulted in contact dermatitis and asthma-like reactions. Persons, especially children, with a history of allergies or asthma, are particularly sensitive, and a strong cross-reactivity with ragweed pollen has been recognized. Severe anaphylactic (allergic) reactions with peripheral vascular collapse and respiratory difficulty are rare. Other symptoms of acute toxicity due to inhalation include sneezing, nasal stuffiness, headache, nausea, incoordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensations. The most severe poisonings have been reported in infants, who are not able to efficiently break down pyrethroids (ETN, Pyrethroids, 1994). With orally ingested doses, nervous symptoms may occur, which include excitation and convulsions leading to paralysis, accompanied by muscular fibrillation and diarrhea (ETN, Pyrethroids, 1994). Death in these cases is due to respiratory failure. Symptoms of acute exposure last about 2 days.

Endocrine Disruption and Breast Cancer

Many pyrethroids have also been linked to disruption of the endocrine system, which can adversely affect reproduction and sexual development, interfere with the immune system and increase chances of breast cancer. Pyrethroids contain human-made, or xenoestrogens, which can increase the amount of estrogen in the body (Garey et al., 1998). When tested, certain pyrethroids demonstrate significant estrogenicity and increase the levels of estrogen in breast cancer cells (Go et al., 1999). Because increased cell division enhances the chances for the formation of a malignant tumor in the breast, artificial hormones, like those found in pyrethroids, may increase breast cancer risk (PCBR, 1996). Some pyrethroids are classified by EPA as possible human carcinogens.

Pyrethroids and the Environment

While the development of the synthetic pyrethroids was heralded with claims of selective toxicity to insects, both pyrethroids and

pyrethrins are extremely toxic to aquatic organisms, including fish such as the bluegill and lake trout, with LC_{50} values less than 1.0 parts per billion. These levels are similar to those for mosquito, blackfly and tsetse fly larvae, often the actual target of the pyrethroid application. Lobster, shrimp, mayfly nymphs and zooplankton are the most susceptible non-target aquatic organisms (Mueller-Beilschmidt, 1990). The nonlethal effects of pyrethroids on fish include damage to the gills and behavioral changes.

Pyrethroids are moderately toxic to birds, with most LD_{50} values greater than 1000 mg/kg. Birds can also be indirectly affected by pyrethroids, because of the threat to their food supply. Waterfowl and small insectivorous birds are the most susceptible (Mueller-Beilschmidt, 1990). Because pyrethroids are toxic to all insects, both beneficial insects and pests are affected by pyrethroid applications. In some cases, predator insects may be susceptible to a lower dose than the pest, disrupting the predator-prey relationship.

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Pyrethroids Residues / Persistence

As mentioned, pyrethroids are designed to breakdown more slowly than the naturally occurring pyrethrins. While pyrethrins, extremely sensitive to light, heat and moisture, break down in a few hours, the synthetic pyrethroids are stable and persist in the environment much longer. As a general rule, pyrethroids break down most quickly in direct sunlight, usually just a few days after application, with a few exceptions. However, in areas with limited sunlight, such as grain silos and subway tunnels, pyrethroids can persist for months. For more specific breakdown times see the sections below on resmethrin, permethrin and sumithrin.

Synergists

Both pyrethroids and pyrethrins are often formulated with oils or petroleum distillates and packaged in combination with synergists, such as piperonyl butoxide (PBO) and n-octyl bicycloheptene dicarboximide (Gosselin et al., 1984). Synergists are added to increase the potency of the pesticide. A range of products, from repellants to foggers to pediculicides (lice killers) to garden sprays, contain synergists. Many formulations of permethrin, resmethrin and sumithrin, including Scourge™ and Anvil™, used along the east coast for mosquito control to combat the West Nile Virus, contain the synergist PBO.

PBO inhibits important liver enzymes responsible for breakdown of some toxins, including the active ingredients of pesticides. Specifically, it has been shown to inhibit hepatic microsomal oxidase enzymes in laboratory rodents and interfere in humans. Because these enzymes act to detoxify many drugs and other chemicals, a heavy exposure to an insecticidal synergist may make a person temporarily vulnerable to a variety of toxic insults that would normally be easily tolerated. Symptoms of PBO poisoning include anorexia, vomiting, diarrhea, intestinal inflammation, pulmonary hemorrhage and perhaps mild central nervous system depression. Repeated contact may cause slight skin irritation. Chronic toxicity studies have shown increased liver weights, even at the lowest doses, 30 mg/kg/day. While not classified as a carcinogen by EPA, animal studies have shown hepatocellular carcinomas, even treatments as low as 1.2% (Takahashi et al., 1994).

Permethrin (Pounce™, Torpedo™, Dragnet™)

Prior to 1978, permethrin was registered for use on cotton crops only. During the early 1980's, registration was expanded to include use on livestock and poultry, eggs, vegetables and fruit. Today, uses also include lice treatments and urban/suburban pest control. Permethrin resembles pyrethrins chemically, but is chlorinated to increase its stability. There are four isomeric forms, two *cis* and two *trans* of technical permethrin. Although the acute toxicity of the mixture (oral rat LD_{50} > 5000 mg/kg, oral mouse LD_{50} = 500) is less than that of natural pyrethrins, the cis-isomer is considerably more toxic (oral mouse LD_{50} = 100), and in rats, the metabolites of the cis-isomer are more persistent biologically. (The *cis* and *trans* isomers differ in the spatial arrangement of the atoms.) Formulations of permethrin can vary greatly in isomeric content. Compared to other pyrethroids, permethrin is very stable, even when exposed to ultraviolet light. Permethrin is strongly absorbed to soil and other organic particles, with half-lives in soil of up to 43 days. When used as a termiticide, permethrin can persist up to five years.

Permethrin receives an EPA toxicity class rating of II or III, (I = most toxic, IV = least toxic) and carries either the word WARNING or CAUTION on its label, depending on the formulation. While it is not extremely toxic to humans, there are numerous reports of transient skin, eye and respiratory irritation. Like all pyrethroids, permethrin is a central nervous system poison. Workers and researchers report tingling in face and hands, and some report allergic reactions. Based on studies demonstrating carcinogenicity, EPA ranks permethrin as a class C, or possible human carcinogen (U.S. EPA, 1997). Other studies have shown effects on the immune system, enlarged livers and at high doses, decreased female fertility. Permethrin is extremely toxic to aquatic life, bees and other wildlife. It should not be applied in crops or weeds where foraging may occur (ETN, Permethrin, 1996).

Resmethrin (Scourge™, Raid Flying Insect Killer™)

Resmethrin is used for control of flying and crawling insects in homes, greenhouses, processing plants, commercial kitchens, airplanes and for public mosquito control. Resmethrin is considered slightly toxic to humans and is rated EPA toxicity class III, bearing the word CAUTION on its label. The oral rat LD_{50} is about 2500 mg/kg. Although resmethrin has a very short half-life (under an hour in direct sunlight), it persists much longer in soil with a half-life of 30 days (ETN, Resmethrin, 1996). Resmethrin breaks down into a smelly byproduct, phenylacetic acid, which binds strongly to textiles and dissipates slowly, smelling like urine.

Resmethrin is absorbed rapidly and distributed to all tissues, including the brain. Skin absorption is low, although it should be noted that some individuals manifest allergic responses, including dermatitis, asthma, runny nose and watery eyes after ini-

tial contact. In laboratory animals, chronic toxicity studies have shown hypertrophy of the liver, proliferative hyperplasia and benign and cancerous liver tumors. EPA reviewers noted slight, but significant, increases in the number of offspring born dead and with decreased viability, which they thought might be secondary to trans-placental toxicity. Tests for neurotoxicity have been negative. Resmethrin is extremely toxic to fish, other aquatic life and bees. The domestic manufacturer of resmethrin, Penick Company, will not identify the inert ingredients in its product, but recommends that it is not sprayed on paint, plastic or varnished surfaces, and that treatment of living areas or areas with large amounts of textiles be avoided.

Because these enzymes act to detoxify many drugs and other chemicals, a heavy exposure to an insecticidal synergist may make a person temporarily vulnerable to a variety of toxic insults that would normally be easily tolerated.

Sumithrin (Anvil™, d-Phenothrin)

Sumithrin has been registered for use since 1975. It is used to control adult mosquitoes and as an insecticide in transport vehicles, commercial, industrial and institutional non-food areas, in homes, gardens, greenhouses and on pets. Chemically, it is an ester of chrysanthemic acid and alcohol. It is a combination of two *cis* and two *trans* isomers. Sumithrin is slightly toxic and is rated EPA toxicity class IV, bearing the word CAUTION on its label. The oral rat LD_{50} is greater than 5,000 mg/kg, and the LC_{50} for inhalation is greater than 1210 mg/m^3. Sumithrin degrades rapidly, with a half-life of 1-2 days under dry, sunny conditions. Under flooded conditions, the half-life increases to 2-4 weeks for the *trans* isomer and 1-2 months for the *cis* isomer. In grain silos, with no sunlight and little air circulation, most of the product still remains after one year (WHO, 1990).

Symptoms of acute sumithrin poisoning include hyperexcitability, prostration, slow respiration, salivation, tremor, ataxia and paralysis. Chronic feeding studies resulted in increased liver weights in both males and females. In rat studies, sumithrin was completely excreted in 3-7 days (WHO, 1990). Studies have shown that sumithrin demonstrates significant estrogenicity and increases the level of estrogen in breast cancer cell, suggesting that sumithrin may increase the risk of breast cancer (Go et al., 1999).

SYNTHETIC PYRETHROIDS ChemicalWATCH Fact Sheet References

Cassagrande, R.A. 1989. "Considerations for state label for Permanone™." RI Pesticide Relief Advisory Board. Providence, RI.

"EPA's Recent Bets." 1981. *Science*, vol. 218, December 3.

Extension Toxicology Network (ETN). 1996. Permethrin." *Pesticide Information Profiles*. <http://ace.orst.edu/cgi-bin/mfs/01/pips/permethr.htm>.

Extension Toxicology Network (ETN). 1994. Pyrethroids." *Pesticide Information Profiles*. <http://ace.orst.edu/cgi-bin/mfs/01/pips/pyrethri.htm>.

Extension Toxicology Network (ETN). 1996. Resmethrin." *Pesticide Information Profiles*. <http://ace.orst.edu/cgi-bin/mfs/01/pips/resmethr.htm>.

Garey, J. and M. Wolff. 1998. "Estrogenic and Antiprogestagenic Activities of Pyrethroid Insecticides." *Biochem Biophys Res Commun* 251 (3): 855-9.

Go, V. et al. 1999. "Estrogenic Potential of Certain Pyrethroid Comounds in the MCF-7 Human Breast Carcinoma Cell Line." *Environmental Health Perspectives* 107(3): 173-177.

Gosselin, R.E. 1984. *Clinical Toxicology of Commercial Products*. Williams and Wilkins. Baltimore, MD.

Hallenbeck, W.H. and K.M. Cunningham-Burns. *Pesticides and Human Health*. Springer-Verlag. New York, NY.

Hayes, W.H. 1982. *Pesticides Studied in Man*. Williams & Wilkins. Baltimore, MD.

"Hormonal and Environmental Factors Affecting Cell proliferation and Neoplasia in the Mammary Gland." 1996. *Progress in Clinical and Biological Research (PCBR)* 394:211-53.

Kaloyanova, F. and S. Tarkowski, eds. 1982. *Toxicology of Pesticides - Interm Document 9*. World Health Organization. Copenhagen.

Klaassen, C.D. et al., eds. 1986. *Casarett and Doull's Toxicology*. Macmillan Publishing Co. New York, NY.

Kolmodin-Hedman, B., et al. 1982. "Occupational exposure to some synthetic pyrethroids (permethrin and fenvalerate)." *Arch Toxicol* 50:27-33.

Mueller-Beilschmidt, Doria. 1990. "Toxicology and Environmental Fate of Synthetic Pyrethroid." *Journal of Pesticide Reform* 10 (3):32-37.

National Research Council. 1987. *Regulating Pesticides in Food: The Delaney Paradox*. National Academy Press. Washington, DC.

Olkowski, W. 1989. "Natural and synthetic pyrethrum insecticides: Finding your way through the maze." *Common Sense Pest Quarterly* 5(1)8-12.

Reigart, J., M.D. et al. 1999. *Recognition and Management of Pesticide Poisonings*, EPA. Office of Pesticide Programs. Washington, DC.

Scourge Insecticide Product Label with SBP-1382/Piperonyl Butoxide 18% + 54% MF. U.S. EPA Reg. No. 432-667. AgrEvo, Montvale, NJ.

Takahashi, O., et al. 1994. "Chronic toxicity studies of piperonyl butoxide in F344 rats: induction of hepatocellular carcinoma." *Fund Appl Toxicol* 22: 293-303.

Thomson, W.T. 1984. *Agricultural Chemicals: Insecticides*. Thompson Publications. Fresno, CA.

U.S. EPA. 1979. Environmental Fate Review of Permethrin (activated sludge metabolism study). Office of Pesticide Programs. Washington, DC. November 29.

U.S. EPA. 2000. For Your Information, Synthetic Pyrethroids for Mosquito Control. Office of Pesticide Programs. Washington, DC. May.

U.S. EPA. 1997. Office of Pesticide Programs list of chemicals evaluated for carcinogenic potential. Memo from W.L. Burnman, HED, to HED branch chiefs. Washington, DC. February 19.

World Health Organization (WHO). 1990. d-Phenothrin. *Environmental Health Criteria*. Geneva.

Wright, C., et al. 1981. "Insecticides in the ambient air of rooms following their application of control of pests." *Bull Environ Contam Toxicol* 26:548-553.