PERMETHRIN

1. Exposure Data

1.1 Chemical and physical data

Permethrin is typically a mixture of (+) *cis* and (+) *trans* esters of the general structure shown below, in either a 40:60 or 25:75 ratio.

1.1.1 *Synonyms, structural and molecular data*

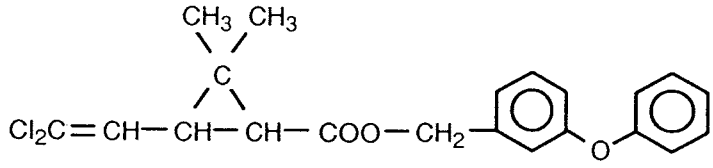
Table 1. Chemical Abstract Services Registry numbers, names and synonyms of permethrin

Name	CAS Reg. Nos[a]	Chem. Abstr. names[b] and synonyms
Permethrin	52645-53-1 (57608-04-5; 60018-94-2; 63364-00-1; 75497-64-2; 93388-66-0)	**3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; *meta*-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate; 3-phenoxybenzyl (1RS)-*cis*,*trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (IUPAC); 3-phenoxybenzyl (1RS,3RS;1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (IUPAC); 3-phenoxybenzyl-2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarboxylate; FMC 33297; FMC 41655; ICI-PP 557; NRDC 143; OMS 1821; WL 43479
trans-Permethrin	61949-77-7	***trans*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; *trans-meta*-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
cis-Permethrin	61949-76-6	***cis*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; *cis-meta*-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate; *cis*-permethrin
(-)-*trans*-Permethrin	54774-47-9	**(1S-*trans*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; 1S-*trans*-permethrin
(-)-*cis*-Permethrin	54774-46-8	**(1S-*cis*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; 1S-*cis*-permethrin
(+)-*cis*-Permethrin	54774-45-7	**(1R-*cis*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; 1R-*cis*-permethrin; NRDC 167
(±)-*cis*-Permethrin	52341-33-0	***cis*-(±)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; (±)-*cis*-FMC 33297; FMC 35171; NRDC 148; 1RS-*cis*-permethrin

Table 1 (contd)

Name	CAS Reg. Nos[a]	Chem. Abstr. names[b] and synonyms
(±)-*trans*-Permethrin	52341-32-9	***trans*-(±)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; NRDC 146; 1RS-*trans*-permethrin
(+)-*trans*-Permethrin	51877-74-8	Biopermethrin; **(1R-*trans*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester**; NRDC 147; 1R-*trans*-permethrin; RU 22090

[a]Replaced CAS Registry number(s) in parentheses
[a]In bold



$C_{21}H_{20}Cl_2O_3$ Mol. wt: 391.3

1.1.2 *Chemical and physical properties*

(*a*) *Description*: Colourless to white, odourless crystalline solid (pure); viscous brown liquid or crystalline solid with a sweet odour (technical) (Swaine & Tandy, 1984; Roussel Bio Corp., undated)

(*b*) *Boiling-point*: 220°C at 0.05 mm Hg [6.7 × 10^{-3} kPa] (Roussel Bio Corp., undated);

(*c*) *Melting-point*: 34-39°C (technical), 63-65°C (*cis*-isomers), 44-47°C (*trans*-isomers) (Worthing & Walker, 1987; WHO, 1990)

(*d*) *Solubility*: Insoluble in water (0.2 mg/l at 30°C); soluble in or miscible with most organic solvents (acetone (450 g/l), chloroform, cyclohexanone, ethanol, ether, hexane (> 1 kg/kg at 25°C), methanol (258 g/kg at 25°C), dichloromethane, xylene (> 1 kg/kg at 25°C) (Swaine & Tandy, 1984; Worthing & Walker, 1987; The Royal Society of Chemistry, 1989; WHO, 1990; Roussel Bio Corp., undated)

(*e*) *Volatility*: Vapour pressure, 3.4 × 10^{-7} mm Hg [0.45 × 10^{-7} kPa] at 25°C (technical) (FMC Corp., 1984); 15 × 10^{-9} mm Hg [2.0 × 10^{-9} kPa] at 20°C (*cis*-isomer), 7.5 × 10^{-9} mm Hg [1.0 × 10^{-9} kPa] at 20°C (*trans*-isomer) (Swaine & Tandy, 1984)

(*f*) *Stability*: Stable in neutral and weak acidic media, but hydrolysis can occur under alkaline or strongly acidic conditions (Swaine & Tandy, 1984).

(*g*) *Half-time*: 10-25 days at 25°C in soil, depending on soil type (Roussel Bio Corp., undated)

(*h*) *Octanol/water partition coefficient (P)*: log P, 6.5 (WHO, 1990)

(*i*) *Conversion factor for airborne concentrations*[1]: $mg/m^3 = 16.0 \times ppm$

1.1.3 *Trade names, technical products and impurities*

Some examples of trade names are: Adion; Ambush; Ambushfog; Anomethrin N; Antiborer 3768; Atroban; BW-21-Z; Cellutec; Chinetrin; Coopex; Corsair; Diffusil H; Dragon; Ecsumin; Ectiban; Efmethrin; Eksmin; Exmin; Imperator; Indothrin; Ipitox; Kafil; Kavil; Kestrel; LE 79-519; MP 79; NIA 33297; Outflank; Perigen; Permanone; Permasect; Permit; Perthrine; Picket; Pounce; PP 557; Pramex; Pynosect; Qamlin; S 3151; SBP 1513; SBP 15131TEC; Spartan; Stockade; Stomoxin; Talcord; Torpedo

Technical-grade permethrin contains from a minimum of 35% to a maximum of 55% (±)-*cis* isomer and from a minimum of 45% to a maximum of 65% (±)-*trans* isomer (Roussel Bio Corp., 1987; Anon., 1989). In the common technical-grade products, the *cis*:*trans* ratio is either 2:3 (WHO, 1990) or 1:3 (Worthing & Walker, 1987).

Permethrin is available in the USA as a technical-grade product containing 91.0-95.0% w/w of the pure chemical and 5.0-9.0% impurities (Fairfield American Corp., 1989; Roussel Bio Corp., 1989; ICI Americas, 1990).

Several of the minor components have been identified in technical permethrin. These were principally: ethyl (±)-*cis*,*trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylate, 3-phenoxytoluene, 4-phenoxybenzyl (±)-*cis*,*trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylate, and 6-bromo-3-phenoxybenzyl (±)-*cis*,*trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylate. Other minor components were found to be xylene (see IARC, 1989), 3-phenoxybenzyl alcohol, *N*,*N*-diethyl-3-phenoxybenzylamine, 3-phenoxybenzaldehyde and 4-(2,2-dichlorovinyl)-5,5-dimethyloxacyclopentane-2-one (Horiba *et al.*, 1977).

Permethrin is formulated as granules, emulsifiable concentrates, wettable powders, dusts, smokes, ultra-low-volume sprays, fumigants, aerosols, fogging solutions and water-dispersible granules. In one European country, registered permethrin products also include capsule suspensions and lacquer formulations (Papadopoulou-Mourkidou, 1983; Swaine & Tandy, 1984; The Royal Society of Chemistry, 1986, 1989; Meister, 1990). In Europe, permethrin is also registered in combination with piperonyl butoxide (see IARC, 1983, 1987), tetramethrin, plifenate and other pyrethrins (Royal Society of Chemistry, 1986).

1.1.4 *Analysis*

Selected methods for the analysis of permethrin in various matrices are given in Table 2. Permethrin can be determined in pesticide formulations using gas chromatography with flame ionization detection (Association of Official Analytical Chemists, 1986; WHO, 1990).

Several other methods for the determination of permethrin (and its individual isomers) in various matrices, including high-performance liquid chromatography and gas chromatography, have been reviewed (Horiba *et al.*, 1977; Miyamoto *et al.*, 1981; Baker & Bottomley, 1982; Papadopoulou-Mourkidou, 1983; Nehmer & Dimov, 1984; Swaine & Tandy, 1984).

---

[1]Calculated from: mg/m^3 = (molecular weight/24.45) × ppm, assuming standard temperature (25°C) and pressure (760 mm Hg [101.3 kPa])

Table 2. Methods for the analysis of permethrin

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Water	Extract with dichloromethane; isolate extract; dry; concentrate with methyl *tert*-butyl ether	GC/ECD	0.5 µg/l (for isomers)	US Environmental Protection Agency (1989a)
Waste-water	Extract with dichloromethane; dry; exchange into hexane	GC/ECD	0.2 µg/l (for isomers)	US Environmental Protection Agency (undated)
Soil	Extract with methanol:water (9:1); partition into dichloromethane; clean-up on activated Florisil column	GC/CCD[b]	0.05 ppm (mg/kg)	US Food and Drug Administration (1989)
Crops	Extract with hexane; remove oil by gel permeation chromatography; clean-up on activated Florisil column	GC/CCD[b] GC/ECD[b]	0.05 ppm (mg/kg)	US Food and Drug Administration (1989)
Milk, animal tissue	Extract with acetone:hexane (1:1); partition into dimethylformamide (in 1% aqueous sodium sulfate solution); back-extract into hexane; clean-up on activated Florisil column	GC/ECD[b]	0.01 ppm (mg/l or mg/kg)	US Food and Drug Administration (1989)
Eggs	Extract with acetone/hexane (1:1); wash with 10% sodium chloride solution; partition into dimethylformamide (in 1% aqueous sodium sulfate solution); back-extract into hexane; clean-up on activated Florisil column plus Merckogel or Fractosil	GC/ECD[b]	0.02 ppm (mg/kg) (0.01 ppm for isomers)	US Food and Drug Administration (1989)

[a]Abbreviations: GC/CCD, gas chromatography/Coulson conductivity detection; GC/ECD, gas chromatography/electron capture detection
[b]Method is suitable for determining total permethrin or the individual *cis*- and *trans*-permethrin isomers

1.2 Production and use

1.2.1 *Production*

Permethrin was first synthesized in 1973 (Swaine & Tandy, 1984) and first marketed in 1977 (WHO, 1990).

The starting acid is prepared by a variation of the conventional chrysanthemic acid synthesis using ethyldiazoacetate in which 1,1-dichloro-4-methyl-1,3-pentadiene is reacted with ethyldiazoacetate in the presence of a copper catalyst and the resulting ethyl (±)-*cis,trans*-2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarboxylate hydrolysed to the free acid. The *cis*- and *trans*-isomers can be separated from one another by selective crystallization from *n*-hexane in which the *cis*-isomer is more soluble. The starting acid is then reacted with 3-phenoxybenzyl alcohol to give permethrin (Sittig, 1980).

Permethrin is produced currently in Japan, the United Kingdom and the USA (Meister, 1990).

1.2.2 *Use*

Permethrin is a synthetic contact pyrethroid insecticide with a high level of activity against a wide range of insects, including *Lepidoptera*, *Hemiptera*, *Diptera* and *Coleoptera*. It is used mainly in agriculture, where it is fast acting and effective against all growth stages, particularly larvae. About 60% of the permethrin produced is used on cotton plants. Other crops to which permethrin is applied are maize, soya beans, coffee, tobacco, rape seed oil, wheat, barley, alfalfa, vegetables and fruit (WHO, 1990).

Permethrin is also used for control of insects in household and animal facilities and in forest pest control, as a fog in mushroom houses, and as a wood preservative. Other applications are in public health, particularly for insect control in buildings and in aircraft, treatment of mosquito nets and control of human lice (WHO, 1990). It is also used for termite control as a barrier treatment on building foundations (Anon., 1989).

Approximately 600 tonnes of permethrin are used annually worldwide. The major countries or regions that were using permethrin in 1980 were (tonnes): the USA (263), Brazil (38), Mexico (36) and Central America (27) (WHO, 1990). In Finland, about 3.5 tonnes (active ingredient) permethrin were used in 1988 (Agrochemical Producers' Association of Finland, 1989)

1.3 Occurrence

1.3.1 *Food*

Samples (1954) of fruits, vegetables, grains, meats, dairy products and wine were analysed as part of the Canadian national surveillance programme in 1984-89. A total of 29 samples contained permethrin residues; of these 25 of 118 were in lettuce, 2 of 100 in pears and 2 of 97 in tomatoes. The residue levels ranged from 0.01 to 1.67 mg/kg (Government of Canada, 1990).

Cows were fed *cis*:*trans* (40:60)-permethrin at rates of 0.2-150 mg/kg diet for 28-31 days. Residues plateaued in milk, with means of < 0.01 μg/g and 0.3 μg/g at dietary levels of 0.2 and 150 mg/kg, respectively. Milk levels declined to < 0.01 μg/g within five days after permethrin administration ceased. Residue levels of < 0.01-0.04 and 2.8-6.2 μg/g fat were found in perirenal fat of cows given dietary levels of 0.2 and 150 mg/kg, respectively (as reported by WHO, 1990). Levels of radioactivity retained in tissues and secreted in milk were appreciably higher in goats treated with *cis*-permethrin than with *trans*-permethrin (Hunt & Gilbert, 1977). In goats dosed orally with 40:60 *cis*:*trans* permethrin equivalent to 10 mg/kg in the diet for seven days, residues in milk also plateaud at 0.02-0.03 μg permethrin equivalents/g after five days (FAO/WHO, 1982).

In supervised trials in Spain and the USA with citrus fruits, permethrin residues in the edible parts did not exceed 0.01 mg/kg and 0.05 mg/kg, respectively, when applied at the recommended rates. The residues were found almost exclusively in the peel (FAO/WHO, 1982).

1.3.2 *Occupational exposure*

Four of five workers in Sweden who packed conifer seedlings for 6 h in a tunnel that had been sprayed 1 h earlier with a 2% aqueous solution of permethrin, resulting in atmospheric concentrations of permethrin of 0.011-0.085 mg/m^3 in the breathing zone, did not excrete detectable amounts of acid pyrethrin metabolites in the urine. One very short person whose face was close to the plants and who had the highest concentration of permethrin in the breathing zone excreted 0.26 μg/ml permethrin acid metabolites in the urine the following morning; in the afternoon, excretion was below the detection limit of the method. A group of five workers who planted the treated conifer seedlings were exposed to non-detectable to low permethrin levels in the breathing zone (mean, 0.002 mg/m^3; range, not detected-0.006 mg/m^3) and excreted no detectable amount of permethrin metabolites in the urine (Kolmodin-Hedman *et al.*, 1982).

1.4 Regulations and guidelines

The FAO/WHO Joint Meeting on Pesticide Residues evaluated permethrin at its meetings in 1979, 1980, 1981, 1982, 1983, 1984, 1985, 1987, 1988 and 1989 (FAO/WHO, 1980, 1981, 1982, 1983, 1985a,b, 1986, 1987, 1988, 1990). In 1987, an acceptable daily intake of 0.05 mg/kg bw was established (40% *cis*:60% *trans* and 25% *cis*:75% *trans* material) (FAO/WHO, 1987).

Maximum residue levels have been established by the Codex Alimentarius Commission for permethrin in or on the following agricultural commodities (in mg/kg): coffee beans, pistachio nuts, potatoes, rape seeds, soya beans and sugar beets, 0.05; almonds, carrots, crude soya bean oil, dried beans, edible cottonseed oil, eggs, Japanese radishes, kohlrabi, melons (except watermelon), milks (fat), mushrooms, peanuts, shelled peas and sweet corn, 0.1; cauliflower, citrus fruits, cottonseed, cucumbers, gherkins, horseradish, leeks, spring onions, summer squash, wheat flour (post-harvest treatment) and winter squash, 0.5; asparagus, blackberries, Brussels' sprouts, common beans, dewberries (boysenberries and loganberries), eggplants, olives, peppers, raspberries (red and black), strawberries, sunflower seeds, sunflower seed oil (crude and edible) and tomatoes, 1; broccoli, celery, cereal grains (post-harvest treatment), currants (black, red and white), gooseberries, grapes, head lettuce, kiwifruit, pome fruit, spinach, stone fruit and wholemeal wheat (post-harvest treatment), 2; cabbage (Chinese, head and savoy) and kale, 5; unprocessed wheat bran (post-harvest treatment), 10; dry sorghum straw and fodder and tea (green and black), 20; dried apple pomace, dried hops and soya bean fodder, 50; alfalfa and maize fodder, 100 (Codex Committee on Pesticide Residues, 1990).

Maximum residue levels have been established by the Codex Alimentarius Commission for permethrin in or on the following animal commodities (in mg/kg): edible offal (mammalian; accommodates veterinary uses) and poultry meat, 0.1; meat (fat; accommodates veterinary uses), 1 (Codex Committee on Pesticide Residues, 1990).

National and regional pesticide residue limits for permethrin in foods are presented in Table 3.

Table 3. National and regional pesticide residue limits for permethrin in foods[a]

Country or region	Residue limit (mg/kg)	Commodities
Australia	10	Bran
	5	Celery, lettuce
	2	Brussels' sprouts, cereal grains, kiwifruit, mushrooms
	1	Cole crops (except Brussels' sprouts)
	0.5	Edible offal of goat, green beans
	0.4	Tomatoes
	0.2	Cottonseed, rapeseed, sunflower seeds
	0.1	Beans (mung, navy), cattle, goats, pigs, poultry, and sheep (fat of meat), eggs, linseed, lupins, soya beans, sugar-cane
	0.05	Cattle and goat milk (in the fat), milk products (fat basis), potatoes, sweet corn
Austria[b]	50	Hops
	1.0	Meat, cereals, fruits, vegetables
	0.1	Eggs (without shell), milk
Belgium[b]	2	Grains, kiwi fruit
	1	Other fruit, other vegetables
	0.05	Animal fats, meat (poultry, hares, fowl, game), meat products, milk, milk products, mushrooms, potatoes
	0 (0.05)[c]	Other foodstuffs of vegetable origin
	0 (0.01)[c]	Other foodstuffs of animal origin
Brazil	0.5	Cottonseed, rice
	0.3	Tomatoes
	0.1	Cabbage, cauliflower, corn, kale
	0.02	Wheat
	0.01	Coffee (shelled), soya beans
Canada	2.0	Grapes
	1.0	Apples, lettuce, peaches, pears
	0.5	Beans, broccoli, Brussels sprouts, cabbage, celery, cucumbers, peppers, plums, tomatoes
	Negligible	Asparagus, cattle (meat and milk), beetroot, blueberries, cauliflower, corn, flax, horseradish, kiwi fruits, onion, potatoes, poultry (meat and eggs), radishes, rapeseed (canola oil), sugar beets (sugar), sunflowers, turnips, wheat
Chile	0.05	Carcasses, eggs, milk, poultry
Denmark[b]	5	Leafy vegetables
	2	Berries, fruit (pome, small, stone, other), other vegetables
	0.5	Citrus fruit
	0.1	Carrots
Finland[b]	2.0	Citrus fruit
	0.5	Other foodstuffs (except cereal grains)
France[b]	2.0	Kiwifruit
	1.0	Cabbage, fruit, vegetable greens (salad)
	0.5	Other vegetables
	0.1	Maize

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Germany	50	Hops
	10	Bran
	2	Cereals (except maize), cereal products (except bran), currants, kiwi-fruit, lettuce
	1.0	Other fruit, other leafy and sprout vegetables
	0.5	Fruit used as vegetables
	0.2	Maize, oilseed
	0.1	Root vegetables
	0.05	Citrus juices, kiwifruit (without peel), raw coffee, spices, tea, tea-like products, other foodstuffs of plant origin
Italy	1.0	Apples, cabbage, carrots, cereals, citrus fruit, cucurbitaceae, drupes, grapes, leeks, lettuce, mushrooms (cultivated), olives, pears, potatoes, solanaceae, spinach, sugar beets, tobacco, turnips
Japan[d]	20	Tea
	15	Exocarp of summer oranges
	5	Fruit (except exocarp of summer oranges)
	3	Vegetables
	0.5	Sugar beets
	0.2	Potatoes, etc.
Netherlands[b]	2	Kiwifruit, leafy vegetables
	1	Other fruit, other vegetables
	0.05[e]	Mushrooms, potatoes, animal products
	0 (0.05)[f]	Other foodstuffs
New Zealand	2.0	Kiwifruit
	1.0	*Brassica* vegetables, fruit (berry, pome)
	0.5	Fruiting vegetables, grapes, legumes
South Africa[b]	0.5	Apples, grapes, lucerne, mealies (green), pears, sorghum
	0.1	Beans, peas, tomatoes
	0.05	Cottonseed, groundnuts, potatoes
Spain[b]	20	Hops (dried)
	10	Alfalfa (dried)
	1.0	Fruit, fruit vegetables
	0.5	Cottonseed, sunflower seeds
	0.05	Beetroot, maize, potatoes, rapeseed, sorghum grains, soya beans
	0.01	Other plant products
Sweden[b]	2.0	Fruit, vegetables
	0.05	Potatoes
Switzerland	2.0[g]	Kiwifruit (whole)
	0.8	Cabbage
	0.5	Other foodstuffs
	0.4	Fruit (except grapes and kiwifruit), vegetables (except cabbage and potatoes)
	0.1[g]	Kiwifruit (pulp)
	0.05	Milk
	0.01	Potatoes

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Taiwan	2.0	Leafy vegetables with large wrapper leaves, leafy vegetables with small leaves
	1.0	Fruit vegetables
	0.5	Rice
USA[h]	60	Maize (fodder, forage)
	55	Alfalfa (hay)
	25	Alfalfa (fresh)
	20	Almond hulls, head lettuce, leafy vegetables (except *Brassica*), spinach, collards, turnip greens
	15	Range grasses
	10	Artichokes
	6.25	Milk fat (reflecting 0.25 ppm in whole milk)
	6	Cabbage, mushrooms
	5	Celery, peaches, watercress
	3	Cherries, pears, cucurbit vegetables, fat (cattle, goats, hogs, horses, sheep), meat by-products (hogs)
	2	Kiwifruit, tomatoes, meat by-products (cattle, goats, horses, sheep)
	1.0	Asparagus, avocados, bell peppers, broccoli, Brussels' sprouts, cauliflower, eggplant, eggs, horseradish, papayas (limited to Florida), turnip roots (regional registration)
	0.5	Cottonseed
	0.25	Meat (cattle, goats, hogs, horses, poultry, sheep)
	0.15	Fat (poultry)
	0.1	Garlic, onions (dry bulb), pistachios, sweet maize (kernel plus cob with husks removed)
	0.05	Almonds, apples, maize grain (field, pop), filberts, potatoes, soya beans, walnuts, meat (poultry)

[a]From Health and Welfare Canada

[b]Sum of isomers

[c]The figure in parentheses is the lower limit for determining residues in the corresponding product according to the standard method of analysis.

[d]Standard for withholding registration of agricultural chemicals

[e]A pesticide may be used on an eating or drinking ware or raw material without a demonstrable residue remaining; the value listed is considered the highest concentration at which this requirement is deemed to have been met.

[f]Residues shall be absent; the value in parentheses is the highest concentration at which this requirement is still deemed to have been met.

[g]These upper 'limit values' are maximum concentrations which, if exceeded, mean that the food is judged unfit for human consumption.

[h]From US Environmental Protection Agency (1989b); includes its metabolites, 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylic acid and (3-phenoxybenzyl)methanol

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Oral administration

Mouse: Four groups of 70 male and 70 female Swiss-derived mice, four to five weeks old, were fed 0, 250, 1000 or 2500 mg/kg of diet permethrin (*cis:trans* isomer, 40:60; > 93.9% pure) for 98 weeks. Survival in control and experimental groups was comparable; more than 75% of animals survived beyond 52 weeks and 20% or more survived until the termination of experiment. In male mice, there was a slight increase in the incidence of pulmonary adenomas: 11/70 control, 6/69 low dose, 13/70 mid dose and 17/70 high dose ($p = 0.04$ test for trend) (Ishmael & Litchfield, 1988).

Rat: Four groups of 60 male and 60 female pathogen-free Alpk:AP (Wistar-derived) rats, aged four to five weeks, were fed 0, 500, 1000 or 2500 mg/kg of diet permethrin (*cis:trans* isomer, 40:60; > 93.9% pure) for 104 weeks, at which time the experiment was terminated. Survival in control and experimental groups was similar; more than 92% survived beyond 52 weeks and 42% or more survived until termination of the experiment. There was no difference in the incidence of tumours between the control and experimental groups (Ishmael & Litchfield, 1988).

4. Other relevant data

The toxicity of permethrin has been reviewed (FAO/WHO, 1980, 1982, 1988; WHO, 1990).

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

Ten scabies patients (five men and five women) had about 25 g (range, 21-32 g) of a 5% permethrin cream applied to the skin of the whole body, with the exception of the head and neck. Dermal absorption of permethrin was calculated from the quantity of conjugated and nonconjugated *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (CVA) metabolites of permethrin determined in the urine. In samples of urine collected by seven patients one and two days after application of the permethrin cream, 414 and 439 μg mean total CVA were found, respectively. The mean total CVA in the urine of three patients who collected their urine in the same container for two days was 1435 μg. The urinary concentration of *trans*-CVA varied during the first 48 h from 0.11 to 1.07 μg/ml and that of the *cis*-isomer from 0.02 to 0.21 μg/ml. CVA was still detectable in the urine of three patients after a week and in the urine of one patient, reported to be an alcoholic, after two weeks. The absorption of permethrin over the first 48 h after application was estimated from the urinary CVA excretion levels to be 6 mg (range, 3-11 mg), i.e., 0.5% of the dose applied (van der Rhee *et al.*, 1989).

Among approximately 350 people who were individually dusted against body lice with 30-50 g of powders containing 2.5 or 5.0 g/kg permethrin (*cis:trans*, 25:75), the mean amount of permethrin absorbed during the first 24 h after treatment was estimated to be 14 μg/kg bw

among 19 of the subjects using the powder containing 2.5 g/kg permethrin and 39 μg/kg bw among 15 of the subjects using the 5 g/kg powder. No residue was found in samples of urine taken 30 and 60 days after treatment (Nassif *et al.*, 1980).

4.1.2 *Experimental systems*

Pyrethroids are absorbed through the skin and the respiratory and digestive tracts, although absorption from the gastrointestinal tract appears to be incomplete. Pyrethroids undergo metabolic degradation at numerous sites (Miyamoto, 1976). In mammals, they are generally metabolized through ester hydrolysis, oxidation and conjugation (WHO, 1990).

The metabolism of permethrin has been studied in great detail in various species of mammals using isomers labelled in the alcohol or acid moiety. The metabolic pathways of permethrin in mammals are given in Figure 1 (WHO, 1990). It is metabolized and almost completely eliminated from the body within approximately 12 days in rats, goats and cows following oral administration; *trans*-permethrin is eliminated more rapidly than is *cis*-permethrin, and trace tissue residue levels of the *cis* isomer were higher than those of the *trans* isomer in these species (Elliot *et al.*, 1976, Gaughan *et al.*, 1977, 1978; Ivie & Hunt, 1980). Absorption through the skin has been demonstrated in mice (Shah *et al.*, 1981), rats (Shah *et al.*, 1987; Sidon *et al.*, 1988) and monkeys (Sidon *et al.*, 1988). Dermal absorption was greater in rats than in monkeys (Sidon *et al.*, 1988). After an intramuscular injection of ^{14}C-labelled permethrin, the urinary half-time values were similar for the *cis* and *trans* isomers in rats and monkeys. Radiocarbon from *trans*-permethrin was excreted mostly in the urine, whereas that from the *cis*-permethrin was eliminated in both urine and faeces (Sidon *et al.*, 1988).

4.2 Toxic effects

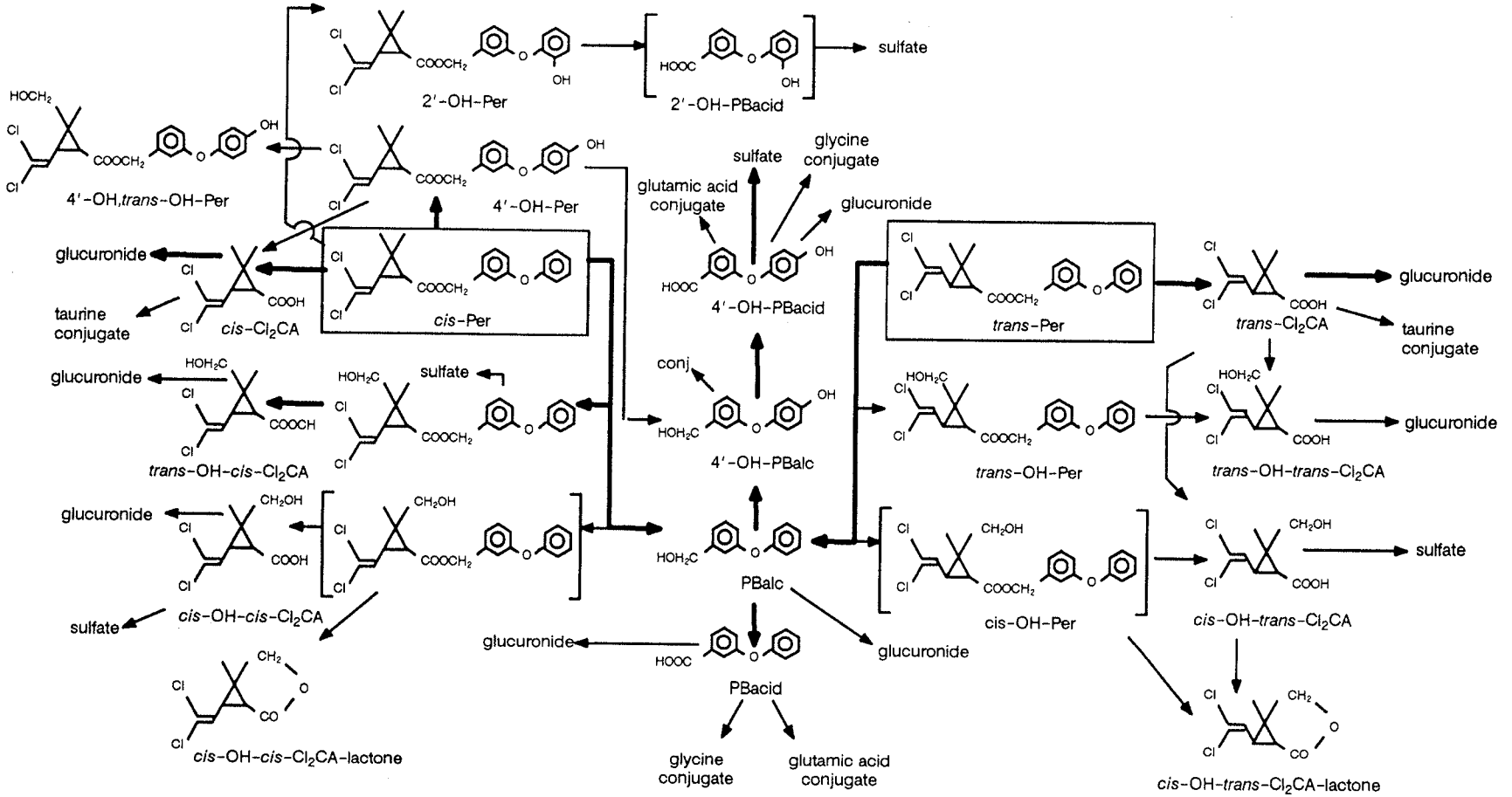
4.2.1 *Humans*

Volunteers received applications to an area of 4 cm^2 on an ear lobe of 0.05 ml of a field-strength preparation of technical (94-96% active ingredients) or formulated (32-36%) permethrin (0.13 mg/cm^2) or of the inert ingredients; 0.05 ml of the vehicle (ethanol as the control for technical permethrin and water as the control for formulated permethrin) was applied to the other lobe. The intensity of paraesthesia induced by permethrin was four-fold stronger than that induced by a similar application of fenvalerate, permethrin being the least active compound for both the technical and formulated preparations. No cutaneous sensation was elicited by the inert ingredients. Paraesthesia appeared after a latent period of about 30 min, peaked between 8 and 12 h and disappeared after about 24 h. Further studies using a range of doses demonstrated that the response was dose-related (Flannigan *et al.*, 1985).

Workers who handled seedlings treated with permethrin (*cis:trans*, 25:75 wettable powder or *cis:trans*, 40:60) reported irritation on the skin (63% of subjects) and in the upper respiratory tract (33%) (Kolmodin-Hedman *et al.*, 1982).

A group of 435 patients, most of them children, were treated for pediculosis capitis; approximately half of the group were treated with a single, 10-min application of 25-50 ml of a permethrin (1%) and isopropanol (20%) cream rinse after towel drying of washed hair, and the remainder were treated with a liquid product containing pyrethrins (0.3%), piperonyl

Fig. 1. Metabolic pathways of permethrin in mammals[a]



[a]From WHO (1990); Per, permethrin; Cl_2CA, chrysanthemic acid; PBacid, 3-phenoxybenzoic acid; PBalc, 3-phenoxybenzyl alcohol

butoxide (3%), petroleum distillate (1.2%) and benzyl alcohol (2.4%). Cutaneous side-effects (pruritus, mild transient skin burning, stinging sensations, skin tingling, erythema and scalp rash) were reported by 7% of the patients in the first group and by 16% of those in the second (DiNapoli *et al.*, 1988). Similar results and side-effects were reported by Brandenburg *et al.* (1986).

One of 28 subjects with pediculosis pubis treated with a 1% permethrin rinse developed mild scrotal erythema and irritation 12 h after application (Kalter *et al.*, 1987).

Of 10 scabies patients treated with one application of 25 g (range, 21-32 g) of a 5% permethrin cream, followed by a thorough washing approximately 8-20 h after treatment, six had limited, mild-to-moderate not pre-existing eczema on the scabies-affected skin at one or more examinations (van der Rhee *et al.*, 1989).

4.2.2 *Experimental systems*

Synthetic pyrethroids act on axons in the peripheral and central nervous system by interacting with sodium channels in mammals and/or insects. The mechanism of toxicity of synthetic pyrethroids and their classification into two types were reviewed by WHO (1990). Permethrin does not contain an α-cyano-group and is a type I pyrethroid.

Oral LD_{50}s in aqueous suspension generally ranged from approximately 3000 to > 4000 mg/kg bw, while the use of corn oil as the vehicle generally gave LD_{50} values of about 500 mg/kg bw (WHO, 1990). *cis*-Permethrin is considerably more toxic than *trans*-permethrin when given orally to rats (in WHO, 1990) or intraperitoneally or intravenously to mice (Glickman *et al.*, 1982). After oral administration of 40:60 *cis:trans* permethrin to rats, signs of poisoning became apparent after 2 h and persisted for up to three days; these included whole-body tremors, sometimes accompanied by salivation. Other signs were hyperactivity, hyperexcitability, urination, defaecation and ataxia (WHO, 1990).

In several subacute and subchronic studies by oral administration of permethrin to mice, rats and dogs, repeated findings were increases in absolute and relative liver weights, proliferation of smooth endoplasmic reticulum and increased activity of microsomal oxidative enzymes. In 90-day studies in rats, increased absolute and relative liver weights were reported to be evident with doses of 100 mg/kg of diet; in dogs, such effects were reported to be apparent with doses of 50 mg/kg bw and upwards for 90 days. In some but not all studies, high doses of permethrin were reported to damage peripheral nerves in rats (WHO, 1990). In rats fed diets of 20, 100 or 500 ppm (mg/kg) permethrin [isomeric composition unspecified] for two years or in rats from the third generation in a three-generation study with dietary exposure to 20 or 100 ppm, however, there was no evidence of morphological damage to nervous tissue when compared to control groups (Dyck *et al.*, 1984).

Long-term studies with rats and mice fed diets containing up to 2500 ppm (mg/kg) permethrin (40:60 *cis:trans*) indicated effects on the central nervous system, such as tremors and hypersensitivity to noise, in rats only and only during the first two weeks. Liver hypertrophy, increased microsomal enzyme activity and proliferation of smooth endoplasmic reticulum occurred in both species but was less pronounced in mice (Ishmael & Litchfield, 1988).

Permethrin (80:20 *cis:trans*) (50 mg/kg bw per day orally to rats) increased the levels of cytochrome P450 in liver after four, eight or 12 days of administration and NADPH cytochrome c reductase after eight or 12 days. A mixture containing less of the *cis* form (40:60 *cis:trans*) increased the levels of the two enzymes only after eight or 12 days of administration (Carlson & Schoenig, 1980). Treatment of rats with 190 mg/kg bw permethrin (25:75 *cis:trans* permethrin) intraperitoneally for three days decreased antipyrine half-time, and γ-glutamyl-transpeptidase activity in plasma was significantly increased within 21 and 14 days at doses of 95 and 190 mg/kg bw per day, respectively (Anadon *et al.*, 1988).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Following immersion of fertile mallard eggs (30 per dose group) for 30 sec in an aqueous solution of permethrin, the LC_{50} for embryonic death was > 40 lb/acre at 100 gal/acre (> 45 kg/ha at 935 l/ha; more than 100 times the usual field application rate); no malformation was observed in mallard chicks (Hoffman & Albers, 1984).

Sprague-Dawley rats, weighing 180-200 g, were treated with permethrin in water at concentrations ranging from 500 to 4000 ppm (mg/l) or with drinking-water (control) on days 6-15 of gestation. At concentrations of 2500 ppm or more, the protein and glycogen content of the placenta was reduced (actual weight not given). The resorption index was increased at all doses, but there was no change in the number of live fetuses at day 20 of gestation in any treatment group (Spencer & Berhane, 1982).

4.4 Genetic and related effects (see also Table 5 and Appendices 1 and 2)

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems*

Several unpublished studies were cited in a recent review (WHO, 1990).

Permethrin did not induce mutation in either bacteria or cultured Chinese hamster V79 cells. It did not induce mutation or aneuploidy in *Drosophila melanogaster,* nor did it inhibit gap-junctional intercellular communication in V79 cells.

[The Working Group noted that the studies by Páldy (1981) and by Hoellinger *et al.* (1987) on rodent bone marrow *in vivo* could not be evaluated because of inadequacies in the experimental design and reporting of the studies.]

5. Summary of Data Reported and Evaluation

5.1 Exposure

Permethrin is a highly active contact insecticide, which was first marketed in 1977. It is used mainly on cotton and food crops. Other uses are in forestry and for public health purposes, in public buildings, residences and aircraft.

Table 5. Genetic and related effects of permethrin

Test system	Result[a]		Dose[b]	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	490.0000	Bartsch *et al.* (1980)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	150.0000	Pluijmen *et al.* (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluct. test)	–	–	10.0000	Pluijmen *et al.* (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2730.0000	Pednekar *et al.* (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	3000.0000	Herrera & Laborda (1988)
SA4, *Salmonella typhimurium* TA104, reverse mutation (spot test)	–	–	3000.0000	Herrera & Laborda (1988)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)
SA5, *Salmonella typhimurium* TA1535, reverse mutation (spot test)	–	–	500.0000	Herrera & Laborda (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)
SA7, *Salmonella typhimurium* TA1537, reverse mutation (spot test)	–	–	500.0000	Herrera & Laborda (1988)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)
SA8, *Salmonella typhimurium* TA1538, reverse mutation (spot test)	–	–	500.0000	Herrera & Laborda (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	490.0000	Bartsch *et al.* (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	150.0000	Pluijmen *et al.* (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation (fluct. test)	–	–	10.0000	Pluijmen *et al.* (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2730.0000	Pednekar *et al.* (1987)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	3000.0000	Herrera & Laborda (1988)
SAS, *Salmonella typhimurium* TA97a, reverse mutation	–	–	2730.0000	Pednekar *et al.* (1987)
SAS, *Salmonella typhimurium* TA97, reverse mutation	–	–	3000.0000	Herrera & Laborda (1988)
EC2, *Escherichia coli* WP2 *hcr*, reverse mutation	–	–	2500.0000	Moriya *et al.* (1983)

Table 5 (contd)

Test system	Result[a]		Dose[b]	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
DMN, *Drosophila melanogaster*, chromosome loss	–	0	5.0000 (feeding solution)	Woodruff *et al.* (1983)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutation	–	0	1.0000 (feeding solution)	Gupta et al (1990)
G9O, Gene mutation, Chinese hamster V79 cells, ouabain resistance	–	0[c]	40.0000	Pluijmen *et al.* (1984)
G9H, Gene mutation, Chinese hamster V79 cells, *hprt* locus	–	0[c]	40.0000	Pluijmen *et al.* (1984)
ICR, Inhibition of intercellular communication, V79 cells *in vitro*	–	0	8.0000	Flodström *et al.* (1988)

[a]–, negative; 0, not tested
[b]In-vitro tests, μg/ml; in-vivo tests, mg/kg bw
[c]Data obtained in the presence of an exogenous metabolic system were inadequate for an evaluation

Permethrin has been formulated as granules, powders, emulsifiable concentrates, aerosols and other forms.

Exposure can occur during its production and application and, at much lower levels, from consumption of food containing residues.

5.2 Carcinogenicity data in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

One preparation of permethrin (*cis:trans*, 40:60) was tested for carcinogenicity in one study in mice and in one study in rats by oral administration in the diet. In mice, a marginal increase in the incidence of pulmonary adenomas was observed in males. No increased tumour incidence was observed in treated rats.

5.4 Other relevant data

Permethrin has caused dermal irritation after topical exposure. It induced microsomal enzymes in rats and mice.

No data were available on the genetic and related effects of permethrin in humans. No effect was observed in the limited number of short-term tests available.

5.5 Evaluation[1]

No data were available from studies in humans.

There is *inadequate evidence* for the carcinogenicity of permethrin in experimental animals.

Overall evaluation

Permethrin *is not classifiable as to its carcinogenicity to humans (Group 3).*

6. References

Agrochemical Producers' Association of Finland (1989) 1988 Finnish pesticide sales. *AGROW, 97*, 11-12

Anadon, A., Diez, M.J., Sierra, M., Sanchez, J.A. & Teran, M.T. (1988) Microsomal enzyme induction by permethrin in rats. *Vet. hum. Toxicol., 30*, 309-312

Anon. (1989) *CPCR® Crop Protection Chemicals Reference*, 5th ed., New York, Chemical and Pharmaceutical Press, pp. 1224-1234, 1268-1277, 1431-1434

Association of Official Analytical Chemists (1986) Permethrin in pesticide formulations. Gas chromatographic method. First action. CIPAC-AOAC method. In: *Changes in Official Methods of Analysis*, 14th ed., 2nd Suppl., Washington DC, pp. 351-352

[1]For definition of the italicized terms, see Preamble, pp. 26-28.

Baker, P.G. & Bottomley, P. (1982) Determination of residues of synthetic pyrethroids in fruit and vegetables by gas-liquid and high-performance liquid chromatography. *Analyst, 107*, 206-212

Bartsch, H., Malaveille, C., Camus, A.-M., Martel-Planche, G., Brun, G., Hautefeuille, A., Sabadie, N., Barbin, A., Kuroki, T., Drevon, C., Piccoli, C. & Montesano, R. (1980) Validation and comparative studies on 180 chemicals with *S. typhimurium* strains and V79 Chinese hamster cells in the presence of various metabolizing systems. *Mutat. Res., 76*, 1-50

Brandenburg, K., Deinard, A.S., DiNapoli, J., Englender, S.J., Orthoefer, J. & Wagner, D. (1986) 1% permethrin cream rinse vs 1% lindane shampoo in treating pediculosis capitis. *Am. J. Dis. Child., 140*, 894-896

Carlson, G.P. & Schoenig, G.P. (1980) Induction of liver microsomal NADPH cytochrome c reductase and cytochrome P-450 by some new synthetic pyrethroids. *Toxicol. appl. Pharmacol., 52*, 507-512

Codex Committee on Pesticide Residues (1990) *Guide to Codex Maximum Limits for Pesticide Residues*, Part 2, (CAC/PR 2—1990; CCPR Pesticide Classification No. 120), The Hague

DiNapoli, J.B., Austin, R.D., Englender, S.J., Gomez, M.P. & Barrett, J.F. (1988) Eradication of head lice with a single treatment. *Am. J. public Health, 78*, 978-980

Dyck, P.J., Shimono, M., Schoening, G.P., Lais, A.C., Oviatt, K.F. & Sparks, M.F. (1984) The evaluation of a new synthetic pyrethroid pesticide (permethrin) for neurotoxicity. *J. environ. Pathol. Toxicol. Oncol., 5*, 109-117

Elliot, M., Janes, N.F., Pulman, D.A., Gaughan, L.C., Unai, T. & Casida, J.E. (1976) Radiosynthesis and metabolism in rats of the 1*R*-isomers of the insecticide permethrin. *J. agric. Food Chem., 24*, 270-276

Fairfield American Corp. (1989) *Material Safety Data Sheet: Permethrin Technical*, Rutherford, NJ

FAO/WHO (1980) *Pesticide Residues in Food: 1979 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 20 Sup.), Rome

FAO/WHO (1981) *Pesticide Residues in Food: 1980 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 26 Sup.), Rome

FAO/WHO (1982) *Pesticide Residues in Food: 1981 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 42), Rome

FAO/WHO (1983) *Pesticide Residues in Food: 1982 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 49), Rome

FAO/WHO (1985a) *Pesticide Residues in Food: 1983 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 61), Rome

FAO/WHO (1985b) *Pesticide Residues in Food: 1984 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 67), Rome

FAO/WHO (1986) *Pesticide Residues in Food: 1985 Evaluations. The Monographs* (FAO Plant Production and Protection Paper 68), Rome

FAO/WHO (1987) *Pesticide Residues in Food: 1987 Evaluations. The Monographs. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues* (FAO Plant Production and Protection Paper 84), Rome

FAO/WHO (1988) *Pesticide Residues in Food—1988 Evaluations. Part I—Residues* (FAO Plant Production and Protection Paper 93/1), Rome

FAO/WHO (1990) *Pesticide Residues in Food—1989 Evaluations. Part I—Residues* (FAO Plant Production and Protection Paper 100), Rome

Flannigan, S.A., Tucker, S.B., Key, M.M., Ross, C.E., Fairchild, E.J., II, Grimes, B.A. & Harrist, R.B. (1985) Synthetic pyrethroid insecticides: a dermatological evaluation. *Br. J. ind. Med., 42*, 363-372

Flodström, S., Wärngård, L., Ljungquist, S. & Ahlborg, U.G. (1988) Inhibition of metabolic cooperation *in vitro* and enhancement of enzyme altered foci incidence in rat liver by the pyrethroid insecticide fenvalerate. *Arch. Toxicol., 61*, 218-223

Gaughan, L.C., Unai, T. & Casida, J.E. (1977) Permethrin metabolism in rats. *J. agric. Food Chem., 25*, 9-17

Gaughan, L.C., Ackerman, M.E., Unai, T. & Casida, J.E. (1978) Distribution and metabolism of *trans*- and *cis*-permethrin in lactating Jersey cows. *J. agric. Food Chem., 26*, 613-618

Glickman, A.H., Weitman, S.D. & Lech, J.J. (1982) Different toxicity of *trans*-permethrin in rainbow trout and mice. I. Role of biotransformation. *Toxicol. appl. Pharmacol., 66*, 153-161

Government of Canada (1990) *Report on National Surveillance Data from 1984/85 to 1988/89*, Ottawa

Gupta, R.K., Mehr, Z.A., Korte, D.W., Jr & Rutledge, L.C. (1990) Mutagenic potential of permethrin in the *Drosophila melanogaster* (Diptera: Drosophilidae) sex-linked recessive lethal test. *J. Econ. Entomol., 83*, 721-724

Health and Welfare Canada (1990) *National Pesticide Residue Limits in Foods*, Ottawa, Bureau of Chemical Safety, Food Directorate, Health Protection Branch

Herrera, A. & Laborda, E. (1988) Mutagenic activity of synthetic pyrethroids in *Salmonella typhimurium*. *Mutagenesis, 3*, 509-514

Hoellinger, H., Lecorsier, A., Sonnier, M., Leger, C., Do, C.-T. & Nguyen, H.-N. (1987) Cytotoxicity, cytogenotoxicity and allergenicity tests on certain pyrethroids. *Drug chem. Toxicol., 10*, 291-310

Hoffman, D.J. & Albers, P.H. (1984) Evaluation of potential embryotoxicity and teratogenicity of 42 herbicides, insecticides, and petroleum contaminants to mallard eggs. *Arch. environ. Contam. Toxicol., 13*, 15-27

Horiba, M., Kobayashi, A. & Murano, A. (1977) Gas-liquid chromatographic determination of a new pyrethroid, permethrin (S-3151) and its optical isomers. *Agric. biol. Chem., 41*, 581-586

Hunt, L.M. & Gilbert, B.N. (1977) Distribution and excretion rates of ^{14}C-labelled permethrin isomers administered orally to four lactating goats for 10 days. *J. agric. Food Chem., 25*, 673-676

IARC (1983) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 30, *Miscellaneous Pesticides*, Lyon, pp. 183-195

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, p. 70

IARC (1989) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 45, *Occupational Exposures in Petroleum Refining; Crude Oil and Major Petroleum Fuels*, Lyon, pp. 125-156

ICI Americas (1990) *Material Safety Data Sheet: Permethrin*, Wilmington, DE

Ishmael, J. & Litchfield, M.H. (1988) Chronic toxicity and carcinogenic evaluation of permethrin in rats and mice. *Fundam. appl. Toxicol., 11*, 308-322

Ivie, G.W. & Hunt, L.M. (1980) Metabolism of *cis*- and *trans*-permethrin in lactating goats. *J. agric. Food Chem., 28*, 1131-1138

Kalter, D.C., Sperber, J., Rosen, T. & Matarasso, S. (1987) Treatment of pediculosis pubis. Clinical comparison of efficacy and tolerance of 1% lindane shampoo vs 1% permethrin cream rinse. *Arch. Dermatol., 123*, 1315-1319

Kolmodin-Hedman, B., Swensson, Å. & Åkerbolm, N. (1982) Occupational exposure to some synthetic pyrethroids (permethrin and fenvalerate). *Arch. Toxicol., 50*, 27-33

Meister, R.T., ed. (1990) *Farm Chemicals Handbook '90*, Willoughby, OH, Meister Publishing Co., pp. C222-C223

Miyamoto, J. (1976) Degradation, metabolism and toxicity of synthetic pyrethroids. *Environ. Health Perspect.*, *14*, 15-28

Miyamoto, J., Beynon, K.I., Roberts, T.R., Hemingway, R.J. & Swaine, H. (1981) The chemistry, metabolism and residue analysis of synthetic pyrethroids. *Pure appl. Chem.*, *53*, 1967-2022

Moriya, M., Ohta, T., Watanabe, K., Miyazawa, T., Kato, K. & Shirasu, Y. (1983) Further mutagenicity studies on pesticides in bacterial reversion assay systems. *Mutat. Res.*, *116*, 185-216

Nassif, M., Brooke, J.P., Hutchinson, D.B.A., Kamel, O.M. & Savage, E.A. (1980) Studies with permethrin against bodylice in Egypt. *Pestic. Sci.*, *11*, 679-684

Nehmer, U. & Dimov, N. (1984) High-performance liquid chromatographic determination of kadethrin, permethrin and piperonyl butoxide in spray solutions. *J. Chromatogr.*, *288*, 227-229

Páldy, A. (1981) Examination of the mutagenic effect of synthetic pyrethroids on mouse bone-marrow cells. In: *Proceedings of the 21st Hungarian Annual Meeting on Biochemistry*, Budapest, National Institute of Public Health, pp. 227-228

Papadopoulou-Mourkidou, E. (1983) Analysis of established pyrethroid insecticides. *Residue Rev.*, *89*, 179-208

Pednekar, M.D., Gandhi, S.R. & Netrawali, M.S. (1987) Evaluation of mutagenic activities of endosulfan, phosalone, malathion and permethrin, before and after metabolic activation in the Ames *Salmonella* test. *Bull. environ. Contam. Toxicol.*, *38*, 925-933

Pluijmen, M., Drevon, C., Montesano, R., Malaveille, C., Hautefeuille, A. & Bartsch, H. (1984) Lack of mutagenicity of synthetic pyrethroids in *Salmonella typhimurium* strains and in V79 Chinese hamster cells. *Mutat. Res.*, *137*, 7-15

van der Rhee, H.J., Farquhar, J.A. & Vermeulen, N.P.E. (1989) Efficacy and transdermal absorption of permethrin in scabies patients. *Acta dermatol. venerol.*, *69*, 170-182

Roussel Bio Corp. (undated) *Technical Information Sheet: Pramex® (Permethrin) Synthetic Pyrethroid Insecticide*, Englewood Cliffs, NJ

Royal Society of Chemistry (1986) *European Directory of Agrochemical Products*, Vol. 3, *Insecticides, Acaricides, Nematicides*, Cambridge, pp. 453-465

Royal Society of Chemistry (1989) *The Agrochemicals Handbook* [Dialog Information Services (File 306)], Cambridge

Shah, P.V., Monroe, R.J. & Guthrie, F.E. (1981) Comparative rates of dermal penetration of insecticides in mice. *Toxicol. appl. Pharmacol.*, *59*, 414-423

Shah, P.V., Fisher, H.L., Sumler, M.R., Monroe, R.J., Chernoff, N. & Hall, L.L. (1987) Comparison of the penetration of 14 pesticides through the skin of young and adult rats. *J. Toxicol. environ. Health*, *21*, 353-366

Sidon, E.W., Moody, R.P. & Franklin, C.A. (1988) Percutaneous absorption of *cis*- and *trans*-permethrin in rhesus monkeys and rats: anatomic site and interspecies variation. *J. Toxicol. environ. Health*, *23*, 207-216

Sittig, M., ed. (1980) *Pesticide Manufacturing and Toxic Materials Control Encyclopedia*, Park Ridge, NJ, Noyes Data Corp., pp. 603-604

Spencer, F. & Berhane, Z. (1982) Uterine and fetal characteristics in rats following a post-implantational exposure to permethrin. *Bull. environ. Contam. Toxicol.*, *29*, 84-88

Swaine, H. & Tandy, M.J. (1984) Permethrin. In: Zweig, G. & Sherma, J., eds, *Analytical Methods for Pesticides and Plant Growth Regulators*, Vol. XIII, *Synthetic Pyrethroids and Other Pesticides*, New York, Academic Press, pp. 103-120

US Environmental Protection Agency (1989a) Method 508. Determination of chlorinated pesticides in water by gas chromatography with an electron capture detector. In: *Methods for the Determination of Organic Compounds in Drinking Water* (EPA Report No. EPA-600/4-88-039; US NTIS PB89-220461), Cincinnati, OH, Environmental Monitoring Systems Laboratory, pp. 171-198

US Environmental Protection Agency (1989b) Permethrin; tolerances for residues. *US Code fed. Regul., Title 40*, Part 180.378, pp. 356-357

US Environmental Protection Agency (undated) *Method 608.2: Analysis of Certain Organochlorine Pesticides in Wastewater by Gas Chromatography*, Cincinnati, OH, Environmental Monitoring and Support Laboratory

US Food and Drug Administration (1989) Permethrin. In: *Pesticide Analytical Manual*, Vol. II, *Methods Which Detect Multiple Residues*, Washington DC, US Department of Health and Human Services

WHO (1990) *Permethrin* (Environmental Health Criteria 94), Geneva

Woodruff, R.C., Phillips, J.P. & Irwin, D. (1983) Pesticide-induced complete and partial chromosome loss in screens with repair-defective females of *Drosophila melanogaster*. *Environ. Mutagenesis, 5*, 835-846

Worthing, C.R. & Walker, S.B., eds (1987) *The Pesticide Manual: A World Compendium*, 8th ed., Thornton Heath, British Crop Protection Council, pp. 647-648