DELTAMETHRIN

1. Exposure Data

1.1 Chemical and physical data

Prior to 1980, deltamethrin was known as decamethrin. Of the eight possible stereoisomers with the general structure shown below (three asymmetric centres), only two isomers, 1R,3R,S(benzyl) and 1R,3S,S(benzyl) have insecticidal activity. The commercial product, deltamethrin, contains only the former (*cis*) isomer; products containing the latter are known as *trans*-deltamethrin. Deltamethrin has an α-cyanogroup on the 3-phenoxybenzyl alcohol and is a type II pyrethroid.

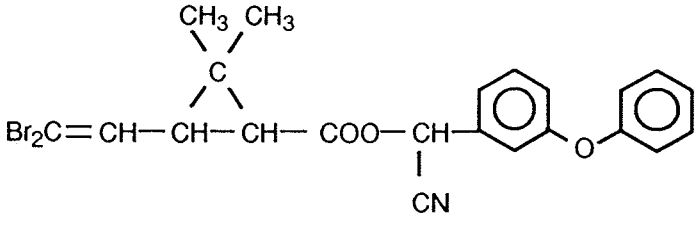
1.1.1 *Synonyms, structural and molecular data*

Deltamethrin

Chem. Abstr. Serv. Reg. No.: 52918-63-5
Replaced CAS Reg. Nos.: 55700-96-4; 62229-77-0
Chem. Abstr. Name: (1R-(1α(S*),3α))-3-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid, cyano(3-phenoxyphenyl)methyl ester
IUPAC Systematic Name: (S)-α-Cyano-3-phenoxybenzyl, (1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
Synonyms: Decamethrin; Decamethrine; FMC 45498; NRDC 161; OMS 1998; RU 22974; RUP 987; *cis*-deltamethrin

***trans*-Deltamethrin**

Chem. Abstr. Serv. Reg. No.: 64363-96-8
Chem. Abstr. Name: (1R-(1α(S*),3β))-3-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid, cyano(3-phenoxyphenyl)methyl ester
IUPAC Systematic Name: (S)-α-Cyano-3-phenoxybenzyl, (1R,3S)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
Synonym: RU 26979



$C_{22}H_{19}Br_2NO_3$ Mol. wt: 505.2

1.1.2 *Chemical and physical properties of deltamethrin*

(*a*) *Description*: White, odourless orthorhombic needles (Roussel-Uclaf, 1982; WHO, 1990)
(*b*) *Boiling-point*: Decomposes above 300°C (WHO, 1990)
(*c*) *Melting-point*: 101-102°C (Roussel-Uclaf, 1982); 98-101°C (Vaysse *et al.*, 1984; WHO, 1990)
(*d*) *Spectroscopy data*: Infrared, nuclear magnetic resonance, ultraviolet and mass spectral data have been reported (Roussel-Uclaf, 1982).
(*e*) *Solubility* at 20°C: Slightly soluble in water (< 0.002 mg/l); ethylene glycol, glycerol and isopropanol (< 0.01 g/100 ml); acetonitrile, cyclohexane and ethanol (0.01-0.1 g/100 ml); acetone, benzene, dimethyl sulfoxide, toluene and xylene (0.1-0.5 g/100 ml); cyclohexanone, dimethylformamide and tetrahydrofuran (> 0.5 g/100 ml) (Roussel-Uclaf, 1982; Vaysse *et al.*, 1984; WHO, 1990)
(*f*) *Volatility*: Vapour pressure, 1.5×10^{-8} mm Hg [0.2×10^{-8} kPa] at 25°C (WHO, 1990)
(*g*) *Stability*: Gradually undergoes photoisomerization to *trans*-deltamethrin and the 1S,3R stereoisomer; photodegrades on exposure to sunlight (Roussel-Uclaf, 1982); stable to heat (for six months at 40°C) and air but unstable in alkaline media (WHO, 1990)
(*h*) *Octanol/water partition coefficient (P)*: log P, 5.43 (WHO, 1990)
(*i*) *Conversion factor for airborne concentrations*[1]: $mg/m^3 = 20.66 \times ppm$

1.1.3 *Trade names, technical products and impurities*

Some common trade names for deltamethrin are Butox, Butoflin, Cislin, Crackdown, Decis and K-Othrine.

Technical-grade deltamethrin has a purity greater than 98% (WHO, 1990). The WHO (1985) specification for technical-grade deltamethrin intended for use in public health programmes requires that it contain a minimum of 98% deltamethrin and a maximum of 1% *trans*-deltamethrin.

Deltamethrin is formulated as solutions, emulsifiable concentrates, flowable powders, wettable powders, ultra-low volume concentrates, dusts, aerosols, granules and concentrated suspensions (Roussel-Uclaf, 1982; WHO, 1985; Royal Society of Chemistry, 1986; Collaborative International Pesticides Analytical Council Ltd, 1988). Deltamethrin is also registered in combination with dimethoate, heptenophos and sulfur (Royal Society of Chemistry, 1986).

1.1.4 *Analysis*

Selected methods for the analysis of deltamethrin in various matrices are given in Table 1. Several analytical methods have been developed for the qualitative determination of deltamethrin residues and formulations, including thin-layer chromatography, gas chromatography and high-performance liquid chromatography (Baker & Bottomley, 1982;

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

Papadopoulou-Mourkidou, 1983; Vaysse *et al.*, 1984; Meinard *et al.*, 1985; Izmerov, 1986; Worthing & Walker, 1987; Martijn & Dobrat, 1988; WHO, 1990).

Table 1. Methods for the analysis of deltamethrin[a]

Sample matrix	Sample preparation	Assay procedure[b]	Reference
Crops (non oily)	Extract with acetonitrile; wash with petroleum ether; extract with petroleum ether/ethyl ether; clean-up on Florisil	GC/ECD	Vaysse *et al.* (1984)
Crops (oily and moist)	Extract with petroleum ether/ethyl ether; concentrate; dissolve extract in dimethyl sulfoxide (DMSO); wash with petroleum ether; partition between DMSO/water and ethyl acetate; clean-up on Florisil	GC/ECD	Vaysse *et al.* (1984)
Formulations	Extract with isooctane/dioxane (80:20); filter	HPLC/UV	Vaysse *et al.* (1984)
Fruit (low fat content)	Extract with acetonitrile or hexane; filter; rewash filter; rewash; purify by liquid-liquid separation	GC/ECD	Roussel-Uclaf (1982)
Fruit (high fat content), milk	Extract with petroleum ether:ethyl ether (50:50); filter; rewash; filter; rewash; purify by liquid-liquid separation	GC/ECD	Roussel-Uclaf (1982)
Meat	Extract; purify by liquid-liquid separation	LG/GP-ECD	Roussel-Uclaf (1982)
Milk	Extract with hexane; partition with acetonitrile; clean-up on Florisil	GC/ECD	Vaysse *et al.* (1984)
Soil	Extract with acetone/hexane; partition extracts between water and hexane; clean-up on acid alumina column	GC/ECD	Vaysse *et al.* (1984)
Tissue	Extract with petroleum ether/ethyl ether; take up in acetonitrile; wash with petroleum ether; clean-up by gel permeation chromatography	GC/ECD	Vaysse *et al.* (1984)

[a]No limit of detection reported

[b]Abbreviations: GC/ECD, gas chromatography/electron capture detection; HPLC/UV, high performance liquid chromatography/ultraviolet detection; LC/GP-ECD, liquid chromatography/gel permeation-electron capture detection

1.2 Production and use

1.2.1 *Production*

Deltamethrin was first synthesized in 1974 and first marketed in 1977 (Vaysse *et al.*, 1984). Chemically, it is the [1R,3R (or *cis*); αS]-isomer of eight stereoisomeric esters of the dibromo analogue of chrysanthemic acid, 2,2-dimethyl-3-(2,2-dibromovinyl)cyclopropanecarboxylic acid, with α-cyano-3-phenoxybenzyl alcohol (WHO, 1990).

In 1987, worldwide production was about 250 tonnes. Production of deltamethrin increased steadily to this level from 75 tonnes in 1979 (WHO, 1990).

1.2.2 *Use*

Deltamethrin is a synthetic pyrethroid insecticide which possesses an extremely high level of activity against a wide range of insects (Worthing & Walker, 1987), including *Lepidoptera*, *Hemiptera*, *Diptera* and *Coleoptera* (Roussel-Uclaf, 1982). It acts by both direct contact and ingestion (Worthing & Walker, 1987).

It is used mostly for crop protection (85% of total production), of which 45% is used on cotton, 25% on fruit and vegetable crops, 20% on cereals, maize and soya beans and the remaining 10% on miscellaneous crops (WHO, 1990), such as coffee, maize (Health and Welfare Canada, 1990) and hops (Codex Committee on Pesticide Residues, 1990). It is also used in public health programmes (against Chagas' disease and malaria) and to protect stored crops, primarily cereal grains, coffee beans and dry beans. It can be used in animal facilities (WHO, 1990).

Deltamethrin is recommended for crop use at 10-15 g/ha (Roussel-Uclaf, 1982).

In the USSR, deltamethrin is approved for commercial application on sunflowers, cotton, potatoes and sugar beets (Izmerov, 1986).

1.3 Occurrence

1.3.1 *Soil*

When deltamethrin was applied to a sandy clay loam soil at 17.5 g/ha in an indoor incubation study and in two field experiments, its half-times were 4.9 and 6.9 weeks, respectively (Hill, 1983).

Chapman *et al.* (1981) examined the relative persistence of five pyrethroids, including deltamethrin, in sand and organic soil under laboratory conditions. All the insecticides (1 mg/kg) were degraded more rapidly in natural soils than in sterilized soils, suggesting the importance of microbial degradation. About 52% of the deltamethrin applied was recovered from sand and 74% from organic soil eight weeks after treatment of natural soil.

The degradation of deltamethrin was investigated by Zhang *et al.* (1984) in an organic soil over a 180-day period. The half-time was found to be 72 days, indicating that deltamethrin is likely to be less susceptible to degradation in organic soils than in mineral soils. The degradation of deltamethrin was also studied in two German soils: the half-times for sandy soil and sandy loam soil were reported to be 35 and 60 days, respectively (WHO, 1990).

1.3.2 *Food*

Some 598 samples of food were analysed as part of the Canadian national surveillence programme in 1984-89. Three samples contained residues (2/25 samples of apples and 1/21 of strawberries) at levels of 0.004-0.006 mg/kg (Government of Canada, 1990).

A trial in Tunisia in 1987 involving one application at a rate of 50 g active ingredient/ha of formulated product (0.1% concentrate) on pears resulted in average residue of 0.04 mg/kg after 14 days. When stored potatoes were dusted with one application of a dust powder formulation of deltamethrin at a rate of 100 g/100 kg potatoes, samples collected at 113 days showed residue levels averaging 0.07 mg/kg (FAO/WHO, 1988).

The level in wheat grain treated with deltamethrin at the rate of 2 mg/kg was 1.08 mg/kg after storage for 9 months. When the wheat was milled and baked, the residue level in white bread was 0.11 mg/kg (as reported by WHO, 1990).

1.3.3 *Occupational exposure*

Workers packaging deltamethrin in a small importing factory in China were reported to have been exposed to airborne levels of 0.5-12 μg/m^3, with resulting skin contact (He *et al.*, 1988).

1.4 Regulations and guidelines

The FAO/WHO Joint Meeting on Pesticide Residues evaluated deltamethrin at its meetings in 1980, 1981, 1982, 1984, 1985, 1986 and 1987 (FAO/WHO, 1981, 1982, 1983a,b, 1985, 1986a,b, 1987, 1988). In 1982, an acceptable daily intake of 0.01 mg/kg bw was established (Codex Committee on Pesticide Residues, 1990; WHO, 1990).

Maximum residue levels have been established by the Codex Alimentarius Commission for deltamethrin in or on the following agricultural commodities (in mg/kg): tea (black, green), 10; hops (dry) and wheat bran (unprocessed), 5; coffee beans, 2; beans (dry), cereal grains, field peas (dry), lentils (dry) and wheat wholemeal, 1; leafy vegetables, legume animal feeds (dry) and straw and fodder (dry) of cereal grains, 0.5; *Brassica* vegetables (head cabbages, flowerhead brassicas), fruiting vegetables (cucurbits) and fruiting vegetables (except cucurbits), 0.2; bulb vegetables (except fennel (bulb)), legume vegetables, oilseed, oilseed (except peanut), olives, pome fruit and wheat flour, 0.1; artichokes (globe), bananas, cocoa beans, grapes, kiwifruit, mandarins, oranges (sweet, sour), stone fruit and strawberries, 0.05; figs, legume oilseeds, melons (except watermelon), milks, mushrooms, peanuts, pineapples and vegetables (root, tuber), 0.01 (Codex Committee on Pesticide Residues, 1990).

The US Environmental Protection Agency (1987) proposed that a tolerance of 0.2 ppm (mg/kg) be established for the combined residues of deltamethrin and a tolerance of 1.0 ppm for its *trans*-isomer in or on imported tomatoes and concentrated tomato products.

National and regional pesticide residue limits for deltamethrin in foods are present in Table 2.

Table 2. National and regional pesticide residue limits for deltamethrin in foods[a]

Country or region	Residue limit (mg/kg)	Commodities
Argentina	1	Stored cereal grains in general
	0.1	Apples, beans, cabbage, cauliflower, maize, cotton, eggplant, flax, peaches, peanuts, pears, peas, peppers, sorghum, soya, sunflower, sweet corn, Swiss chard, tomatoes
	0.05	Artichokes
	0.01	Potatoes
Australia	10 (provisional)	Wheat bran, wheat pollard
	2	Cereal grains (whole grain)
	0.2	Milk (fat basis)
	0.1	Berry vegetables, meat fat (cattle, goats, sheep), oilseeds, sweet maize, vegetables (pod, seed)
	0.05[b]	Cole crops

Table 2 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Austria	5.0	Hops
	0.5	Artichokes, asparagus, beans (broad, green), bulb vegetables, cabbage, cardoon, cereals, chard, cucumber, eggplant, fennel, fruit used as vegetables, garden celery, kitchen herbs, lettuce, melons, mushrooms, parsley (without root), peas (green), pepper cress, peppers, potatoes, pumpkin, rapeseed, rhubarb stalks, spinach, squash, sweet maize, tomatoes, zucchini
	0.2	Fruit, other vegetables
Belgium	0.2	Pome fruit, vegetables
	0.1	Other fruit
	0.05	Potatoes, strawberries
	0 (0.05)[c]	Other foodstuffs of vegetable origin
Brazil	1.0	Coffee, maize (stored in bulk, on cob, in sacks), rice (stored in sacks), wheat
	0.1	Kale
	0.05	Broccoli, citrus fruit (peel), rice, sorghum
	0.04	Peaches
	0.03	Cauliflower, cucumbers, eggplant, garlic, onions, tomatoes
	0.02	Apples, cottonseed, plums
	0.01	Peppers, wheat
	0.005	Cabbage, maize, peanuts, potatoes
	0.002	Figs, honeydew melons, soya beans
	0.001	Citrus fruit (edible parts), string beans, watermelons
Canada	Negligible	Apples, asparagus, barley, blueberries, broccoli, Brussels' sprouts, cabbages, cauliflower, cucumbers, flax, lentils, mustard, oats, pears, peaches, peppers, potatoes, rapeseed (canola oil), Saskatoon berries, sunflowers, strawberries, wheat
Denmark	0.5	Leafy vegetables
	0.1	Fruit (pome, stone)
Finland	0.5	Food products
France	1	Cereal grains
	0.5	Vegetable greens (salad)
	0.2	Fruit, other vegetables
Germany	10	Hops, tea
	2	Raw coffee
	0.5	Green cabbage, legumes
	0.2	Fruit used as vegetables (except mushrooms), pome fruit, vegetables (leaf, sprout (except green cabbage, onions, shallots)), wheat bran
	0.1	Berries (except strawberries), cereals, cereal products (except wheat bran), grapes, oilseeds, olives, onions, shallots, stone fruit
	0.05	Spices, tea-like products, other foods of plant origin
Hungary	0.1	Crops and food

Table 2 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Italy	0.5	Broad beans, cabbages, carrots, citrus fruit, maize, cucumbers, drupes, eggplants, figs, grapes, kidney beans, lettuce, olives, peas, pomes, potatoes, strawberries, sugar beets, tobacco, tomatoes, wheat
Netherlands	0.2	Leafy vegetables
	0.1	Other fruit
	0.05[d]	Meat, milk, other vegetables, potatoes, strawberries
	0 (0.05)[e]	Other foodstuffs
South Africa	1.0	Oats, rye, wheat
	0.1	Apples, beans, cruciferae, grapes, lucerne, mealies (green), peaches, pears, plums
	0.05	Groundnuts, peas, prickly pears, sorghum, sweet potatoes, tomatoes
Spain	2	Hops (dried)
	0.5	Grains (cereal, legume), leafy vegetables
	0.2	Other vegetables (except bulbs, roots, tubers)
	0.05	Fruit
	0.01	Vegetables (bulb, root, tuber), other plant products
Sweden	0.05[b]	Potatoes
Switzerland	0.1	Fruit (except grapes)
	0.05	Cereal, grapes, mushrooms, rapeseed, vegetables (except potatoes)
	0.03	Milk
	0.01	Maize, potatoes
Taiwan	1.0	Tea leaves
	0.5	Leafy vegetables with large wrapper leaves, leafy vegetables with small leaves
	0.2	Berries, fruit vegetables
	0.1	Melons
	0.05	Rice
	0.01	Tropical fruit
Yugoslavia	0.2	Cabbage, cabbage-like plants
	0.1	Fruit, vegetables (except cabbage)

[a]From Health and Welfare Canada (1990)

[b]The maximum residue limit has been set at or about the limit of analytical determination.

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

[d]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.

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

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Oral administration

Mouse: Groups of 30 male and 30 female C57Bl/6 mice, six weeks of age, were given 1 or 4 mg/kg bw deltamethrin (99.5% pure) dissolved in arachis oil by gavage daily on five days a week for 104 weeks. Further groups of 50 males and 50 females received 8 mg/kg bw deltamethrin daily for 104 weeks. Control groups of 50 males and 50 females were given arachis oil or left untreated. The experiment was terminated when the mice were 120 weeks of age. The survival rate was similar in treated and control groups (40-64%), except in high-dose females, of which only 32% were alive at 120 weeks. There was no increase in the incidence of tumours at any site in experimental groups (Cabral *et al.*, 1990).

Rat: Groups of 50 male and 50 female BD VI rats, six weeks of age, were given 0, 3 or 6 mg/kg bw deltamethrin (99.5% pure) in arachis oil by gavage daily on five days a week for 104 weeks. Control rats received arachis oil alone. The experiment was terminated when the rats were 120 weeks of age. The survival pattern was comparable in all groups; 60% or more rats were alive at 120 weeks. The incidence of thyroid adenomas in males (19/50) that received 3 mg/kg bw and in females (14/49) that received 6 mg/kg bw was significantly higher than that in controls (6/48 males, $p = 0.003$; 4/47 females, $p = 0.011$) (Cabral *et al.*, 1990). [The Working Group noted that the type of thyroid adenoma was not specified.]

4. Other Relevant Data

The toxicity of deltamethrin has been reviewed (FAO/WHO, 1981, 1982, 1983a,b; WHO, 1990). For a general introduction to the toxicokinetics of pyrethroids, see the monograph on permethrin.

4.1 Absorption, distribution, metabolism and excretion

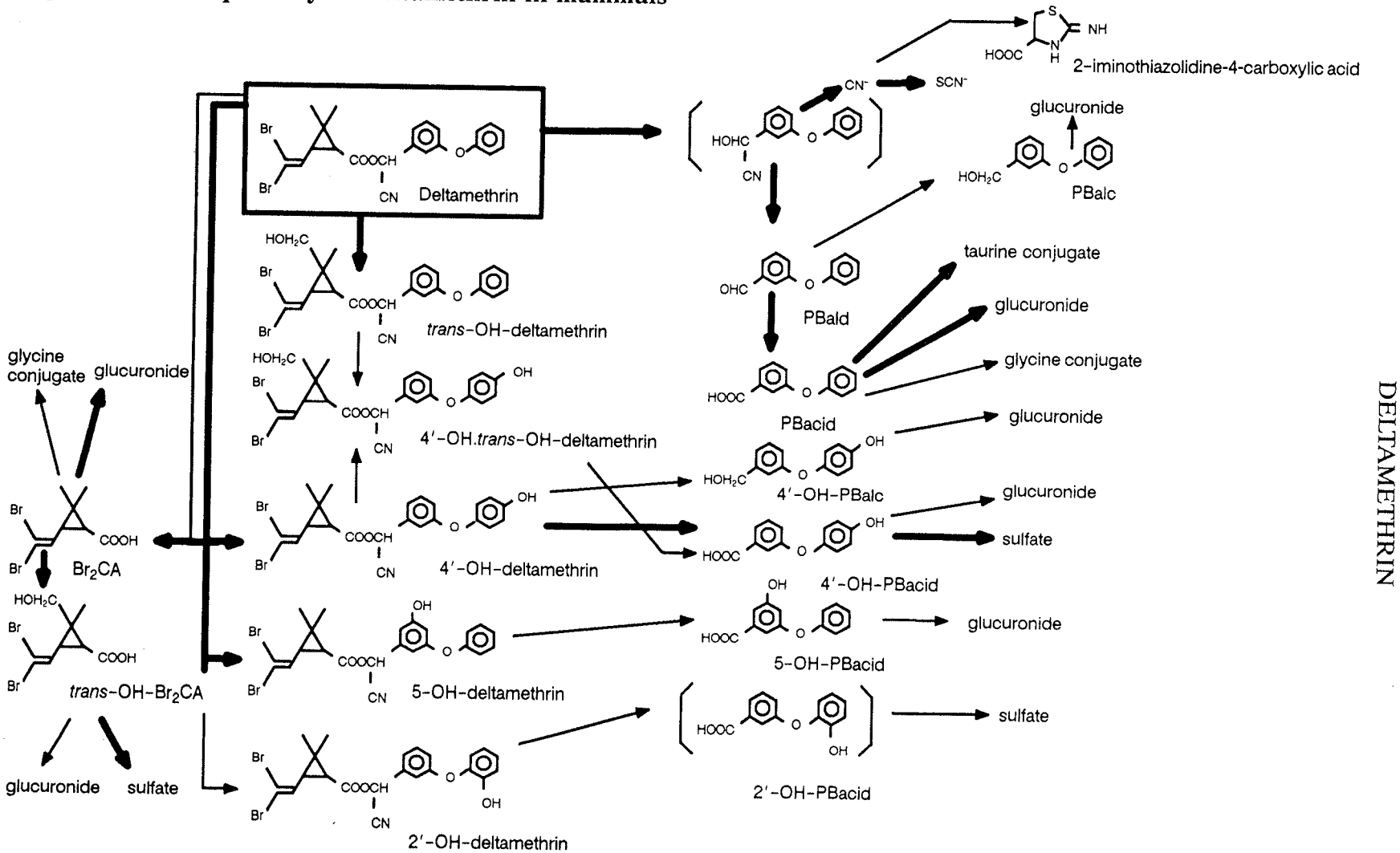
4.1.1 *Humans*

The cutaneous and gastrointestinal absorption of deltamethrin in humans has been demonstrated after acute poisonings due to occupational overexposure or ingestion of deltamethrin products. The presence of a deltamethrin metabolite (3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid) (see Fig. 1) has been reported in the urine of people with acute deltamethrin intoxication (He *et al.*, 1989), confirming the absorption and metabolic degradation of this insecticide in the human body.

4.1.2 *Experimental systems*

The metabolic pathways of deltamethrin in mammals are shown in Figure 1. The metabolism of this compound has been studied in rats *in vivo* (Ruzo *et al.*, 1978, 1979) and

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



[a]From WHO (1990); Br_2CA, 3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid; PBacid, 3-phenoxybenzoic acid; PBald, 3-phenoxybenzaldehyde; PBalc, 3-phenoxybenzyl alcohol

in vitro (Soderlund & Casida, 1977; Shono *et al.*, 1979) and shown to occur *via* ester hydrolysis, oxidation, hydroxylation and conjugation.

Deltamethrin was labelled with ^{14}C in the dibromovinyl substituent or in the benzylic carbon and administered orally to rats and mice. Eight days later, the highest concentrations were retained in fat tissue, regardless of the labelling position, suggesting that unmetabolized deltamethrin is retained in fat. When the ^{14}C-label was in the cyano group, the greatest radiocarbon activity was found in skin and stomach and, in the rat, also in the intestines and blood, due to remaining thiocyanate. In rats, 80-90 % of the radiolabel was eliminated within 24 h. When the ^{14}C-label was in the cyano group, elimination was slower, owing to retention of thiocyanate. In general, unmetabolized deltamethrin and hydroxylated metabolites were excreted in the faeces, while more polar hydrolysis products and conjugates were eliminated in the urine. Mice had a somewhat slower rate of elimination than rats (48-60% within 24 h) (Ruzo *et al.*, 1978, 1979).

4.2 Toxic effects

4.2.1 *Humans*

He *et al.* (1989) reviewed 325 cases of deltamethrin intoxication from the Chinese medical literature. Common findings included paraesthesia, particularly involving the face, dizziness, headache, nausea, anorexia and fatigue. Less common findings included chest tightness, palpitations, blurred vision, increased sweating and low-grade fever. Muscular fasciculations, convulsions and coma were reported in some of the more severely poisoned cases. Two deaths from convulsions were reported.

4.2.2 *Experimental systems*

The acute toxicity of deltamethrin is high, with an oral LD_{50} (in an oily vehicle) of approximately 50 mg/kg bw for adult male and 30 mg/kg bw for adult female rats (Kavlock *et al.*, 1979; Gaines & Linder, 1986). A suspension of deltametrin in 10% gum-arabic solution reduced the oral toxicity in rats by more than 100-fold (Pham *et al.*, 1984).

Signs of acute intoxication in rats and mice included salivation, ataxia and choreoathetotic movements (Kavlock *et al.*, 1979; Pham *et al.*, 1984).

Deltamethrin has been demonstrated to bind covalently to mammalian hepatic proteins *in vitro*, although the binding was less pronounced than that of cismethrin (Catinot *et al.*, 1989).

The following studies were reported in a review (WHO, 1990). In Sprague-Dawley rats given up to 10 mg/kg bw deltamethrin by gavage daily for 13 weeks, slight hyperexcitability was noted in some animals at the highest dose. Lower body weight gain was noted in males at 2.5 and 10 mg/kg. No other treatment-related effect was reported. In dogs treated at similar doses (by gelatin capsule) over 13 weeks, dilated pupils were seen at doses of 2.5 and 10 mg/kg bw per day. The incidence of vomiting increased dose-dependently at doses from 1 mg/kg bw. The central nervous system was the main target of toxicity, with various neurological symptoms at the higher doses. No histopathological lesion was found, neither was any other toxic effect found.

In 24-month studies, no treatment-related non-neoplastic effect was found in mice fed dietary levels of up to 100 mg/kg (CD-1 mice) or in mice given up to 8 mg/kg bw by gavage on

five days a week (C57Bl/6 mice). In Charles River CD rats fed up to 50 mg/kg of diet deltamethrin for 24 months, no significant treatment-related non-neoplastic effect was noted, except for slightly less weight gain at the 50 mg/kg dose level. In dogs given up to 40 mg/kg deltamethrin in the diet for 24 months, no treatment-related non-neoplastic effect was noted.

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Deltamethrin dissolved in corn oil was given to CD-1 mice at 0, 3, 6 or 12 mg/kg by gavage on days 7-16 of gestation and to Sprague-Dawley rats at 0, 1.25, 2.5 or 5.0 mg/kg by gavage on days 7-20 of gestation. Mice and rats were sacrificed on day 18 or 20 of gestation, respectively. In mice, there was a dose-dependent decrease in maternal weight and an increase in supernumary ribs; however, there was no effect on number of implantation sites, perinatal mortality, fetal weight, ossification centres or visceral abnormalities. In rats, there was a dose-dependent decrease in maternal body weight with no effect on fetal parameters (Kavlock *et al.*, 1979).

In a screening study for developmental toxicity, 25 CD-1 mice were treated with deltamethrin at 10 mg/kg [dose reported correctly in follow-up study] in corn oil by gavage on days 8-12 of gestation, and 24 controls were treated with corn oil. There was no effect on the number of pregnancies, maternal weight gain during pregnancy, number of pups born alive or pup weights on postnatal days 1 or 3 (Chernoff & Kavlock, 1982). An extension of the experiment up to 250 days of life to assess growth, viability, morphology and reproductive function of the offspring showed no effect of deltamethrin on these parameters (Gray & Kavlock, 1984).

In a similar screening test in ICR/SIM mice, animals were treated with a minimally toxic maternal dose (14 mg/kg bw per day) by oral intubation (in corn oil) on days 8-12 of gestation. Although maternal weight gain was decreased, there was no effect on neonatal survival or weight gain (Seidenberg *et al.*, 1986). A repetition using similar procedures with deltamethrin at 10 mg/kg bw per day suggested an effect on neonatal survival (Kavlock *et al.*, 1987).

Quail embryos received an intravitelline injection of purified technical-grade or a commercial preparation of deltamethrin (25 g deltamethrin/litre excipient, essentially xylene). The number of germ cells was decreased by both preparations, but the commercial preparation was more potent than the purified deltamethrin, being active independently of the route of treatment (injection, spraying, treatment of parents *via* feed). Both xylene and deltamethrin appeared to be responsible for the decrease in germ cell number (David, 1982).

Treatment of quail eggs with deltamethrin by immersion in aqueous emulsions (equivalent to 0-1.5 g active ingredient in 110 litres applied per hectare) on days 0, 4 or 14 of incubation had no effect on hatchability or developmental malformation. An effect on incubation time was seen at the highest concentration when given at the preincubation stage (Martin, 1990).

4.4 Genetic and related effects (see also Table 3 and Appendices 1 and 2)

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems*

Deltamethrin did not induce point mutation in bacteria or cultured mammalian cells or DNA damage in yeast, but it induced chromosomal aberrations in root meristem cells of *Allium cepa*.

In vivo, deltamethrin induced chromosomal aberrations and micronucleus formation in bone-marrow cells of mice. In a study by oral administration, no chromosomal aberration was observed in mouse bone marrow, but morphological sperm abnormalities were induced in mice. [The Working Group noted that the studies by Páldy (1981) and Hoellinger *et al.* (1987) could not be evaluated because of inadequacies of experimental design and reporting.]

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Deltamethrin is a highly active contact insecticide. It was first marketed in 1977 and is used mostly on cotton and on crops such as coffee, maize, cereals, fruit, vegetables and hops. It is also used in public health programmes and for the protection of stored crops.

Deltamethrin has been formulated as solutions, concentrates, granules, powders and aerosols, alone and in combination with other pesticides.

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

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Deltamethrin was tested for carcinogenicity in one experiment in mice and in one experiment in rats by oral administration. In mice, no increase in tumour incidence was seen. In rats, a statistically significant increase in the incidence of unspecified thyroid adenomas was observed in low-dose males and high-dose females.

5.4 Other relevant data

No data were available on the genetic and related effects of deltamethrin in humans.

Deltamethrin induced micronucleus formation and chromosomal aberrations in bone marrow and abnormal sperm morphology in mice treated *in vivo*. The only other indication of genotoxic potential was induction of chromosomal aberrations in plants.

Table 3. Genetic and related effects of deltamethrin

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic sytem		
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2500.0000	Kavlock *et al.* (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation (plate incorporation)	–	–	300.0000	Pluijmen *et al.* (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluctuation test)*	–	–	10.0000	Pluijmen *et al.* (1984)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	2500.0000	Kavlock *et al.* (1979)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	2500.0000	Kavlock *et al.* (1979)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	2500.0000	Kavlock *et al.* (1979)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2500.0000	Kavlock *et al.* (1979)
SA9, *Salmonella typhimurium* TA98, reverse mutation (plate incorporation)	–	–	300.0000	Pluijmen *et al.* (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation (fluctuation test)*	–	–	10.0000	Pluijmen *et al.* (1984)
EC2, *Escherichia coli* WP2, reverse mutation	–	–	500.0000	Kavlock *et al.* (1979)
SSB, *Saccharomyces cerevisiae* D3, DNA damage	–	–	50000.0000	Kavlock *et al.* (1979)
ACC, *Allium cepa*, chromosomal aberrations	+	0	0.5000 (6–8 h)	Chauhan *et al.* (1986)
G9O, Gene mutation, Chinese hamster V79 cells, ouabain resistance	–	–	40.0000	Pluijmen *et al.* (1984)
G9H, Gene mutation, Chinese hamster V79 cells, *hprt* locus	–	–	40.0000	Pluijmen *et al.* (1984)
CBA, Chromosomal aberrations, Swiss albino mouse bone marrow	+	0	10.0000 × 1, i.p.	Bhunya & Pati (1990)
CBA, Chromosomal aberrations, Swiss albino mouse bone marrow	+	0	20.0000 × 1, p.o.	Bhunya & Pati (1990)
CBA, Chromosomal aberrations, Swiss albino mouse bone marrow	+	0	20.0000 × 1, s.c.	Bhunya & Pati (1990)
CBA, Chromosomal aberrations, Swiss albino mouse bone marrow	–	0	6.8000 × 5, p.o.	Polaková & Vargová (1983)
MVM, Micronucleus test, Swiss albino mouse bone marrow	+	0	10.0000 × 2, i.p.	Bhunya & Pati (1990)
SPM, Sperm morphology, Swiss albino mouse	+	0	10.0000 × 5, i.p.	Bhunya & Pati (1990)
ICR, Inhibition of intercellular communication, V79 cells	–	0	8.0000	Flodström *et al.* (1988)

*Not displayed on profile

[a] +, positive; (+), weakly positive; –, negative; 0, not tested; ?, inconclusive (variable response in several experiments within an adequate study)

[b] In-vitro tests, μg/ml; in-vivo tests, mg/kg bw

5.5 Evaluation[1]

No data were available from studies in humans.

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

Overall evaluation

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

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

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