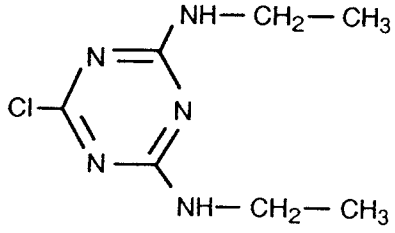
SIMAZINE

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Synonyms, structural and molecular data*

Chem. Abstr. Serv. Reg. No.: 122-34-9
Replaced CAS Reg. Nos: 11141-20-1; 12764-71-5; 39291-64-0; 119603-94-0 *Chem. Abstr. Name*: 6-Chloro-*N*,*N*′-diethyl-1,3,5-triazine-2,4-diamine
IUPAC Systematic Name: 6-Chloro-N^2,N^4-diethyl-1,3,5-triazine-2,4-diamine
Synonyms: 4,6-Bis(ethylamino)-2-chlorotriazine; 2,4-bis(ethylamino)-6-chloro-*s*-triazine; 2-chloro-4,6-bis(ethylamino)-*s*-triazine



$C_7H_{12}ClN_5$ Mol. wt: 201.66

1.1.2 *Chemical and physical properties*

(*a*) *Description*: Colourless-to-white, odourless crystals (US Environmental Protection Agency, 1984a; Royal Society of Chemistry, 1989)

(*b*) *Melting-point*: 225-227°C (Royal Society of Chemistry, 1989)

(*c*) *Spectroscopy data*: Infrared (prism [35711]; grating [13705]) and ultraviolet [16140] spectral data have been reported (Sadtler Research Laboratories, 1980).

(*d*) *Solubility*: Practically insoluble in water (3.5 mg/l at 20°C), petroleum ether (2 mg/l at 20°C) and *n*-pentane (3 mg/l at 25°C); slightly soluble in dioxane and ethyl Cellosolve; soluble in chloroform (900 mg/l at 20°C), methanol (400 mg/l at 20°C) and diethyl ether (300 mg/l at 25°C) (Budavari, 1989; Royal Society of Chemistry, 1989; Meister, 1990)

(*e*) *Vapour pressure*: 6.1×10^{-9} mm Hg [0.8×10^{-9} kPa] at 20°C (US Environmental Protection Agency, 1988a; Royal Society of Chemistry, 1989)

(*f*) *Stability*: Stable in neutral, weakly acidic and weakly alkaline media; hydrolysed by stronger acids and bases; decomposed by ultraviolet irradiation (Royal Society of Chemistry, 1989)

(g) Conversion factor for airborne concentrations[1]: $mg/m^3 = 8.25 \times ppm$

1.1.3 *Trade names, technical products and impurities*

Some examples of trade names are: Aktinit S; Aquazine; Azotop; Bitemol S 50; CAT; CDT; CET; Geigy 27,692; Gesatop; H 1803; Herbazin; Herbex; Herbatoxol S; Herboxy; Hungazin DT; Premazine; Princep; Radocon; Radokor; Simanex; Simatsin-neste; Simazin; Symazine; Tafazine; Taphazine; Triazine A 384; W 6658; Yrodazin

Simazine is registered in the USA as a technical material with 95-99.9% active ingredient (US Environmental Protection Agency, 1984b). It is available there in wettable powder, granular, liquid, flowable concentrate, soluble concentrate and dry flowable forms. The usual carrier is water, oil or clay (US Environmental Protection Agency, 1984a). In Europe, it is available as dustable powders, emulsifiable concentrates, liquid creams, granules, microgranules, suspension concentrates, soluble concentrates, ultra-low volume suspensions, water-dispersible granules and wettable powders (Royal Society of Chemistry, 1986). In the USSR, simazine is manufactured as a wettable powder or dust (Izmerov, 1983).

Simazine can be formulated with most other herbicides and fertilizers (Royal Society of Chemistry, 1986, 1989). It is formulated in the USA in combination with amitrole (see IARC, 1987a), atrazine (see monograph, p. 441), prometon, trietazine, sodium chlorate and sodium metaborate (Anon., 1989; Meister, 1990). It has also been formulated in various countries in combination with metoxuron, diquat, sodium trichloroacetate, secbumeton, MCPA (see IARC, 1987b), ametryne, paraquat dichloride, diquat dichloride, paraquat dibromide, sodium 2-(2,4-dichlorophenoxy)ethyl sulfate, 2,4-D (see IARC, 1987b), diuron, propyzamide, nonflurazon, dalapon sodium and picloram (Worthing & Walker, 1987).

1.1.4 *Analysis*

Selected methods for the analysis of simazine in various matrices are given in Table 1.

Table 1. Methods for the analysis of simazine

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Formulation (80% wettable powder)	Dissolve in chloroform; centrifuge	GC/FID	Not reported	Williams (1984)
Formulation (wettable powder)	Add morpholine; boil; add 50% sulfuric acid; titrate with silver nitrate	Potentiometry	Not reported	Knüsli *et al.* (1964)
Drinking-water	Extract by passing sample through liquid-solid extractor; elute with dichloromethane; concentrate by evaporation	GC/MS	0.2 µg/l	US Environmental Protection Agency (1988b)

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

Table 1 (contd)

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Drinking-water (contd)	Extract with dichloromethane; isolate extract; dry; concentrate with methyl *tert*-butyl ether	GC/NPD	0.075 µg/l	US Environmental Protection Agency (1989a)
	Extract with hexane; inject extract	GC/ECD	6.8 µg/l	US Environmental Protection Agency (1989b)
Crop samples, animal tissues	Extract with chloroform; evaporate to dryness; redissolve in carbon tetrachloride; clean-up on alumina column; convert to hydroxytriazine by treatment with acid	UV	0.05-0.1 ppm (mg/kg)	US Food and Drug Administration (1989a)
Crop samples	Extract with acetonitrile: water (70:30); clean-up on alumina column; elute with benzene: hexane (1:1); analyse benzene solution	GC/MCD	0.05 ppm (mg/kg)	US Food and Drug Administration (1989a,b)
Milk	Add methanol and sodium oxalate; extract with ethyl ether: petroleum ether (1:1); wash with water; dry with sodium sulfate and evaporate to dryness; dissolve in petroleum ether; extract with acetonitrile; backwash combined extracts with petroleum ether and evaporate to dryness	GC/MCD	0.05 ppm (mg/l)	US Food and Drug Administration (1989c)
Fish	Extract with dichloromethane-methanol; clean-up with acetonitrile/hexane partition and alumina column chromatography	GC/MCD	0.01 ppm (mg/kg)	US Food and Drug Administration (1989a,d)

[a]Abbreviations: GC/ECD, gas chromatography/electron capture detection; GC/FID, gas chromatography/flame ionization detection; GC/MCD, gas chromatography/microcoulometric detection; GC/MS, gas chromatography/mass spectrometry; GC/NPD, gas chromatography/nitrogen-phosphorous detection; UV, ultraviolet spectrophotometry

1.2 Production and use

1.2.1 *Production*

Simazine was first introduced in 1957 (US Environmental Protection Agency, 1984a). It is produced by the reaction of cyanuric chloride and monomethylamine in water or aqueous acetone (Izmerov, 1983).

It is produced currently by four companies in Israel, Switzerland and the USA (Meister, 1990). Estimated production in 1978-80 in the USA was approximately 5000 tonnes per annum, of which about 1000 tonnes were exported (Vlier Zygadlo, 1982). A major US

producer reported producing an average of 4000 tonnes per annum in 1981-84 and an average of 8000 tonnes per annum in 1985-89.

1.2.2 *Use*

Simazine is a pre-emergent systemic herbicide that inhibits photosynthesis. It has been used for the control of germinating annual grasses and broad-leaved weeds in a variety of vegetables and fruit, turf and ornamental plants, and in forestry (Meister, 1990); its major use is on maize (US Environmental Protection Agency, 1984b). It is also used for total weed control on non-crop land and as an aquatic herbicide and algicide for control of algae and submerged weeds in ponds (Royal Society of Chemistry, 1989).

Methods of application include broadcast, band, soil incorporated and soil surface using ground or aerial equipment (US Environmental Protection Agency, 1984a). It is also registered for use in the USA in swimming pools, ponds and cooling towers (US Environmental Protection Agency, 1984b).

It was estimated that in the USA during the period 1978-80, yearly usage of simazine (active ingredient) was as follows: maize, 1000-1300 tonnes; aquatic uses, 700-900 tonnes; industrial sites, 600-800 tonnes; grapes, 220-290 tonnes; oranges, 220-290 tonnes; apples, 100-120 tonnes; and various other fruits, 300 tonnes (Vlier Zygadlo, 1982).

In the USSR, simazine is used on vineyards, strawberries and winter wheat sowings; it is also used to suppress couchgrass, Bermuda grass and some other perennial weeds (Izmerov, 1983).

1.3 Occurrence

1.3.1 *Water*

Simazine has been found in groundwater in California, Pennsylvania and Maryland, USA, at levels in the range of 0.2 to 3.0 μg/l. It was found in 922 of 5873 surface water samples and 202 of 2654 groundwater samples in the USA. The 85th percentile was 2.18 μg/l in surface water and 1.60 μg/l in groundwater; the maximal concentration in surface water was 1.3 mg/l and that in groundwater, 0.8 mg/l. Simazine was found in surface water in 16 states and in groundwater in eight states (US Environmental Protection Agency, 1988a).

Simazine did not hydrolyse in sterile aqueous solutions buffered at pH 5, 7 or 9 at 20 °C, over a 28-day test period. Dissipation studies in pond and lake water with simazine gave variable results, with half-times ranging from 50 to 700 days. 2-Chloro-4-ethylamino-6-amino-*s*-triazine was identified in lake water but was no more persistent than simazine (US Environmental Protection Agency, 1988a).

1.3.2 *Soil*

The half-time of simazine varies depending on the soil microbial population, moisture, temperature and farming practice. Under aerobic conditions, the degradation of simazine in soil depends largely on the soil moisture and temperature (Walker, 1976). In a sandy loam soil, half-times ranged from 36 to 234 days. When applied to a loamy sand and silt loam soils and incubated (25-30 °C) for 48 weeks, simazine dissipated with half-times of 16.3 and 25.5 weeks, respectively. Under anaerobic conditions, ^{14}C-simazine had a half-time of 8-12 weeks in a loamy sand soil. Degradation products included 2-chloro-4-ethylamino-6-amino-*s*-

triazine, 2-chloro-4,6-bis(amino)-*s*-triazine, 2-hydroxy-4,6-bis(ethylamino)-*s*-triazine and 2-hydroxy-4-ethylamino-6-amino-*s*-triazine (US Environmental Protection Agency, 1988a).

Studies of column leaching and adsorption/desorption indicated that simazine would be expected to be slightly to very mobile in soils ranging in texture from clay to sandy loam. Its adsorption was correlated with the content of organic matter in the soil and to a lesser degree with the cation exchange capacity and clay content (US Environmental Protection Agency, 1988a).

In field studies, simazine had a half-time of about 30-139 days in sandy loam and silt loam soils (US Environmental Protection Agency, 1988a). In a study with four New Zealand soils, with acid pH (5.4-5.5) and organic carbon levels of 4.6 and 9.4%, the half-times were 25 and 32 days, respectively (Rahman & Holland, 1985).

Field studies with simazine on Taichung (Taiwan) clay loam in different seasons and Taipei loam soils showed a significant effect of climate on degradation rate. Simazine had a half-time of 18 days in summer and 24 days in winter at Taichung; the more moderate temperature and precipitation of the autumn in Taipei resulted in a half-time of 14 days (Chen *et al.*, 1983).

1.3.3 *Food*

In the national surveillence programme in Canada, 1664 samples were analysed for simazine during the period 1984/85 to 1988/89. No residue was detected in fruit, meat, vegetables or wine (Government of Canada, 1990). No simazine residue (< 0.05 ppm [mg/kg]) was reported in a survey of 19 851 samples of various foods and feeds in the USA over 1982-86 (Luke *et al.*, 1988).

1.4 Regulations and guidelines

WHO (1987) recommended a drinking-water guideline of 17 µg/l for simazine. The maximal allowable concentration of simazine in drinking-water in Canada is 10 µg/l (Ritter & Wood, 1989). The US Environmental Protection Agency proposed to establish the 'maximal contaminant level' (feasible and enforceable limits to protect public health) and 'maximal contaminant level goal' (desirable but not enforceable) for simazine at 1 µg/l (Anon., 1990).

In the USSR, the maximal allowable concentration of simazine in workplace air is 2 mg/m^3. The single and mean daily maximal allowable concentration in the atmosphere of residential areas is 0.02 mg/m^3 (Izmerov, 1983).

National pesticide residue limits for simazine in food are presented in Table 2.

Tolerances are established for residues of simazine in sugar-cane byproducts (molasses and syrup and molasses intended for animal feed), resulting from application of the herbicide to growing sugar-cane, at 1 ppm (mg/kg); that for combined residues of simazine and its metabolites (2-amino-4-chloro-6-ethylamino-*s*-triazine and 2,4-diamino-6-chloro-*s*-triazine) in potable water when present therein as a result of application of the herbicide to growing aquatic weeds is 0.01 ppm (mg/kg) (US Environmental Protection Agency, 1989d,e).

Table 2. National pesticide residue limits for simazine in foods[a]

Country	Residue limit (mg/kg)	Commodities
Australia[b]	0.1	Asparagus, fruit, nuts
	0.05	Lupins
	0.01	Eggs, meat, milk, milk products, poultry, meat
Austria	1.0	Asparagus
	0.5	Maize
	0.1	Fish
	0.05	Other
Belgium	1.0	Asparagus
	0.1	Fruit, other vegetables, grains
	0.05	Potatoes
	0[c] (0.05)	Other foodstuffs of vegetable origin
Brazil[d]	10	Asparagus
	1.0	Conifers, rubber plants, sisal
	0.2	Maize, apples, citrus fruits, grapes, pears, sugar-cane, sorghum, pineapples, bananas, black pepper, cocoa, coffee
	0.02	Babassu palm
Canada	Negligible	Apples, alfalfa (meat, milk and eggs), asparagus, blackberries, blueberries, maize, filberts/hazelnuts, fruit tree orchards (fruit), grapes, loganberries, raspberries, strawberries, trefoil (meat, milk and eggs)
France	1.0	Asparagus
	0.1	Blackcurrants, pome fruit, raspberries, sweet maize
Germany	1.0	Asparagus
	0.1	Hops, other vegetable foodstuffs, fish, seafood and their products
Hungary	0.1	Crops and food
Italy	0.1	Citrus fruit, drupes, pomes, strawberries, grapes, olives, minor fruit, hazelnuts, artichokes, asparagus, maize, sorghum
Kenya	10	Asparagus
	0.5	Artichokes
	0.25	Almonds, apples, avocados, cherries, fresh maize including sweet (kernels plus cobs with husks removed), maize grain, cranberries, currants, dewberries, filberts, grapefruit, grapes, lemons, loganberies, macadamia nuts, olives, oranges, peaches, pears, plums, raspberries, strawberries, walnuts
	0.02	Eggs, milk, meat, fat and meat products of cattle, goats, hogs, horses, poultry and sheep
Netherlands	0.1	Cereals, fruit, vegetables
	0.05	Potatoes
	0[c] (0.05)	Other
Spain	1.0	Asparagus
	0.1	Fruit, maize grain, beans and alfalfa
	0.02	Other plant products
Switzerland	0.1	Maize, cereals, asparagus
	0.05	Berries, pome fruit

Table 2 (contd)

Country	Residue limit (mg/kg)	Commodities
USA[e]	15	Alfalfa, alfalfa forage and hay; Bermuda grass, Bermuda grass forage and hay, grass, grass forage and hay
	10	Asparagus
	0.5	Artichokes, sugar-cane
	0.25	Almonds, almonds (hulls), apples, avocados, blackberries, blueberries, boysenberries, cherries, maize (fodder, forage, fresh, grain), cranberries, currants, dewberries, filberts, grapefruit, grapes, lemons, loganberries, macadamia nuts, olives, oranges, peaches, pears, plums, raspberries, strawberries, sugar-cane
	0.2	Walnuts
	0.1	Pecans
	0.02	Fat, meat by-products, and meat of cattle, goats, hogs, horses, poultry and sheep, eggs, milk
	12[f]	Fish
	0.2[f]	Bananas
USSR[g]	1.0	Cereals
	0.2	Fruit, potatoes
	0.05	Grapes
Yugoslavia	0.5	Maize

[a]From Health and Welfare Canada (1990)
[b]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]Provisional
[e]From US Environmental Protection Agency (1989c)
[f]Simazine and its metabolites
[g]From Izmerov (1983)

2. Studies of Cancer in Humans

One case-control study that suggested an association between ovarian cancer and exposure to herbicides in Italy mentioned simazine among the triazine herbicides to which subjects were exposed (Donna *et al.*, 1989) (see monograph on atrazine, p. 449).

3. Studies of Cancer in Experimental Animals[1]

The Working Group was aware of studies by the US National Technical Information Service (1968), Innes *et al.* (1969) and Pliss and Zabezhinsky (1970), in which simazine was tested in mice or rats by oral or subcutaneous administration and in mice by skin application. These studies were considered to be uninformative for an evaluation of carcinogenicity.

[1]The Working Group was aware of a study in progress in rats in which simazine was administered by oral administration (IARC, 1990).

4. Other Relevant Data

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

The primary route of metabolism of simazine in rats, rabbits and other species *in vivo* and *in vitro* is *N*-dealkylation (Böhme & Bär, 1967; Adams *et al.*, 1990). [The Working Group noted that, while minor metabolites (other than some oxidation products of the alkyl side-chains) have not been identified, it is probable that the aromatic chlorine group is a site for glutathione conjugation, as occurs with atrazine (Timchalk *et al.*, 1990).]

Simazine is readily nitrosated by nitrogen oxides at an air:solid interface (Janzowski *et al.*, 1980).

4.2 Toxic effects

4.2.1 *Humans*

Simazine has been implicated as a cause of occupational contact dermatitis (Elizarov, 1972).

4.2.2 *Experimental systems*

The oral LD_{50} was reported to be > 5000 mg/kg bw in rats (Ben-Dyke *et al.*, 1970) and 973, 971 and 2367 mg/kg bw in adult female, male and weanling male rats, respectively. The dermal LD_{50} was > 2500 mg/kg bw in rats of each sex (Gaines & Linder, 1986). The lethal single dose of simazine in sheep has been estimated at 500 mg/kg bw (Hapke, 1968).

The liver and biliary system were identified as the targets for toxicity in rats given simazine by gavage at 15 mg/kg bw per day for three or 28 days (Olędzka-Słotwinska, 1974). Hypothyroidism was the most sensitive indicator of simazine toxicity in sheep at daily dose rates of 1.4-6 mg/kg bw; higher doses produced frank goitres and diffuse hepatic and cerebral damage. Necrotic and dystrophic changes of the testicular germinal epithelium were noted in rams given 6-25 mg/kg bw per day (Dshurov, 1979).

4.3 Reproductive and prenatal effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Simazine perturbed development of gonads *in ovo* and *in vitro* and reduced fertility in chicks and quail (Didier & Lutz-Ostertag, 1972). [The Working Group noted that doses and concentrations were not clearly defined.] It was reported in an abstract that simazine administered at 2.0 and 20 ppm (mg/kg) in the diet to laying mallard ducks throughout the egg production cycle caused no reproductive impairment (Fink, 1975).

Inhalation by rats of simazine at concentrations of up to 317 mg/m^3 on days 7-14 of gestation resulted in no developmental toxicity (Dilley *et al.*, 1977, abstract; Newell & Dilley, 1978). In contrast, a Bulgarian triazine herbicide (Polyzin 50) [impurities unspecified] was embryotoxic when pregnant rats were exposed by inhalation to 2 mg/m^3 in air; it was teratogenic following exposure to 0.2 and 2 mg/m^3 throughout pregnancy and to 2 mg/m^3 during the first trimester of pregnancy. Postnatal liver insufficiency occurred in the offspring (Mirkova & Ivanov, 1981). [The Working Group noted that the apparent discrepancy in effects between these studies might be due to unspecified impurities in the latter study.]

Administration of simazine to rats during the organogenetic period (gestational days 6-15) caused embryolethality at > 312 mg/kg bw, decreased fetal body weight at 2500 mg/kg bw and retarded ossification at ≥ 78 mg/kg bw. No teratogenic effect was observed (Chen *et al.*, 1981).

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*

Simazine did not induce gene mutation in bacteria or in *Saccharomyces cerevisiae*, whereas there were mixed responses in mutation assays with plants. Simazine induced sex-linked recessive lethal mutation in *Drosophila melanogaster*.

Mutations were induced at the *tk* locus in mouse lymphoma L5178Y cells, but DNA damage, as indicated by unscheduled DNA synthesis, was not induced in cultured human fibroblasts.

Neither gene conversion nor mitotic recombination was induced in *S. cerevisiae* or aneuploidy in *Neurospora crassa*. Chromosomal aberrations were induced consistently in plants.

Dominant lethal effects, but not aneuploidy, were induced in *D. melanogaster* in a single study.

In a single study with cultured human lymphocytes, simazine induced a small increase in the frequency of sister chromatid exchange, but it had no such effect in cultured Chinese hamster cells, even at very high concentrations.

It did not induce micronucleus formation in bone-marrow cells of mice *in vivo*.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Simazine was introduced in 1957 as a systemic herbicide for use on grasses and weeds in food crops, especially maize, and for general weed control. It is available in many types of formulation, including wettable powders, granules, concentrates, suspensions and liquids. Exposure can occur during its production and application and *via* contamination of ground- and surface water.

Table 3. Genetic and related effects of simazine

Test system	Result[a]		Dose[b] LED/HID	
	Without exogenous metabolic system	With exogenous metabolic system		
ECB, *Escherichia coli* PQ37, SOS chromotest	0	–	0.0000	Mersch-Sundermann *et al.* (1989)
SAD, *Salmonella typhimurium* TA1978/TA1538 differential toxicity	–	0	2000.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SAD, *Salmonella typhimurium* SL525/SL4700	–	0	2000.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	0	–	2500.0000	Simmon *et al.* (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation	0	+[c]	0.0000	Means *et al.* (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	500.0000	Mersch-Sundermann *et al.* (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2500.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SA2, *Salmonella typhimurium* TA102, reverse mutation	–	–	500.0000	Mersch-Sundermann *et al.* (1988)
SA3, *Salmonella typhimurium* TA1530, reverse mutation (spot test)	–	0	0.0000	Seiler (1973)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	500.0000	US National Technical Information Service, Environmental Protection Agency (1977)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	0	–	2500.0000	Simmon *et al.* (1977)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	500.0000	US National Technical Information Service, Environmental Protection Agency (1977)
SA8, *Salmonella typhimurium* TA98, reverse mutation	–	–	500.0000	US National Technical Information Service, Environmental Protection Agency (1977)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	0	–	2500.0000	Simmon *et al.* (1977)

Table 3 (contd)

Test system	Result[a]		Dose[b] LED/HID	
	Without exogenous metabolic system	With exogenous metabolic system		
SA9, *Salmonella typhimurium* TA98, reverse mutation	0	–	2500.0000	Simmon *et al.* (1977)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2500.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	1000.0000	Mersch-Sundermann *et al.* (1988)
SAS, *Salmonella typhimurium*, reverse mutation	–	0	0.0000	Andersen *et al.* (1972)
SAS, *Salmonella typhimurium his* G46, reverse mutation (spot test)	–	0	0.0000	Seiler (1973)
SAS, *Salmonella typhimurium* TA1531, reverse mutation (spot test)	–	0	0.0000	Seiler (1973)
SAS, *Salmonella typhimurium* TA1532, reverse mutation (spot test)	–	0	0.0000	Seiler (1973)
SAS, *Salmonella typhimurium*, TA1534 reverse mutation (spot test)	–	0	0.0000	Seiler (1973)
SAS, *Salmonella typhimurium* TA97, reverse mutation	–	–	500.0000	Mersch-Sundermann *et al.* (1988)
ECF, *Escherichia coli*, forward mutation	–	0	0.0000	Fahrig (1974)
ECW, *Escherichia coli* WP2 *uvr*, reverse mutation	–	–	500.0000	US National Technical Information Service, Environmental Protection Agency (1984)
**Serratia marcescens*, reverse mutation	–	0	0.0000	Fahrig (1974)
SCG, *Saccharomyces cerevisiae*, gene conversion	–	0	0.0000	Fahrig (1974)
SCG, *Saccharomyces cerevisiae*, gene conversion	–	0	1000.0000[d]	Siebert & Lemperle (1974)
SCH, *Saccharomyces cerevisiae* D3, homozygosis by recombination	–	–	50000.0000	US National Technical Information Service, Environmental Protection Agency (1977)
SCR, *Saccharomyces cerevisiae* D7, reverse mutation	–	–	25000.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SCG, *Saccharomyces cerevisiae* D7, gene conversion	–	–	25000.0000	US National Technical Information Service, Environmental Protection Agency (1984)

Table 3 (contd)

Test system	Result[a]		Dose[b] LED/HID	
	Without exogenous metabolic system	With exogenous metabolic system		
**Saccharomyces cerevisiae* D7, mitotic recombination	–	–	25000.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SCR, *Saccharomyces cerevisiae*, reverse mutation	–	0	5.0000	Emnova *et al.* (1987)
NCN, *Neurospora crassa*, aneuploidy	–	0	0.0000	Griffiths (1979)
HSM, *Hordeum vulgare*, mutation	+	0	1000.0000	Wuu & Grant (1966)
HSM, *Hordeum vulgare*, mutation	–	0	200.0000	Stroyev (1968a)
PLM, *Rizobium meliloti*, mutation	–	0	5000.0000	Kaszubiak (1968)
PLM, *Zea mays*, chlorophyll mutation	+	0	200.0000	Morgun *et al.* (1982)
PLM, *Zea mays*, mutation	+	0	0.0000	Plewa *et al.* (1984)
PLM, *Fragaria ananassa*, mutation	+	0	0.0200	Malone and Dix (1990)
TSI, *Tradescantia paludosa*, micronuclei	–	0	200.0000	Ma *et al.* (1984)
HSC, *Hordeum vulgare*, chromosomal aberrations	+	0	500.0000	Wuu & Grant (1966)
HSC, *Hordeum vulgare*, chromosomal aberrations	+	0	500.0000 spray	Wuu & Grant (1967a)
HSC, *Hordeum vulgare*, chromosomal aberrations	(+)	0	500.0000	Stroyev (1968b)
HSC, *Hordeum vulgare*, chromosomal aberrations	(+)	0	500.0000[d]	Kahlon (1980)
VFC, *Vicia faba*, chromosomal aberrations	+	0	200.0000[d]	Wuu & Grant (1967b)
VFC, *Vicia faba*, chromosomal aberrations	+	0	5.0000	Hakeem & Shehab (1974)
VFC, *Vicia faba*, chromosomal aberrations	(+)	0	1000.0000	de Kergommeaux et al. (1983)
PLC, *Allium cepa*, chromosomal aberrations	+	0	20.0000	Chubutia & Ugulava (1973)
PLC, *Crepis capillaris*, chromosomal aberrations	+	0	1000.0000	Voskanyan & Avakyan (1984)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutation	–	0	50.0000	Benes & Sram (1969)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutation	+	0	80.0000	Murnik & Nash (1977)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutation	+	0	200.0000	US National Technical Information Service, Environmental Protection Agency (1984)
DML, *Drosophila melanogaster*, dominant lethal test	+	0	6000.0000	Murnik & Nash (1977)
DMN, *Drosophila melanogaster*, aneuploidy	–	0	6000.0000	Murnik & Nash (1977)

Table 3 (contd)

Test system	Result[a]		Dose[b] LED/HID	
	Without exogenous metabolic system	With exogenous metabolic system		
G5T, Gene mutation, mouse lymphoma L5178Y cells *in vitro*, *tk* locus	–	(+)	300.0000	US National Technical Information Service, Environmental Protection Agency (1984)
SIC, Sister chromatid exchange, Chinese hamster cells *in vitro*	–	–	1700.0000	US National Technical Information Service, Environmental Protection Agency (1984)
UHF, Unscheduled DNA synthesis, human lung WI 38 fibroblasts *in vitro*	–	–	200.0000	Jones *et al.* (1984)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	(+)	0	0.0000	Ghiazza *et al.* (1984)
MVM, Micronucleus test, mouse *in vivo*	–	0	500.0000	Jones *et al.* (1984)

[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
[c] Tested with extracts of simazine-treated *Zea mays*
[d] Commercial pesticide tested

Exposure could also occur through consumption of foods containing residues. Simazine residues were not detected in large-scale surveys of food products in Canada and the USA.

5.2 Carcinogenicity in humans

No adequate data were available to the Working Group.

5.3 Experimental carcinogenicity data

No adequate data were available to the Working Group.

5.4 Other relevant data

No data on the genetic and related effects of simazine in humans were available to the Working Group.

Simazine did not induce micronucleus formation in mice. It induced a small increase in the frequency of sister chromatid exchange in human cells *in vitro* but not in rodent cells. Simazine did not induce genetic damage in any other tests, except in plants where chromosomal aberrations were induced and in *Drosophila melanogaster* where dominant lethal effects and gene mutation were induced.

5.5 Evaluation[1]

There is *inadequate evidence* in humans for the carcinogenicity of simazine.

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

Overall evaluation

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

6. References

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

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