PENTACHLOROETHANE

Data were last reviewed in IARC (1986) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 76-01-7

Systematic name: Pentachloroethane

1.1.2 *Structural and molecular formulae and relative molecular mass*

$CCl_3—CHCl_2$

C_2HCl_5 Relative molecular mass: 202.29

1.1.3 *Physical properties* (for details, see IARC, 1986)

(*a*) *Boiling-point*: 162°C

(*b*) *Melting-point*: –29°C

(*c*) *Conversion factor*: mg/m^3 = 8.27 × ppm

1.2 Production, use and human exposure

Pentachloroethane was produced commercially as a chemical intermediate, and occupational exposure may have occurred. Trace levels have been reported in ambient air and water (IARC, 1986).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Technical-grade pentachloroethane (containing 4.2% hexachloroethane) was tested for carcinogenicity by oral administration by gavage in one experiment in mice and one

experiment in rats. Hepatocellular carcinomas were induced in mice of each sex and hepatocellular adenomas in female mice; a marginally increased incidence of kidney tubule-cell adenomas was observed in male rats but not in female rats (IARC, 1986).

No data were available on the carcinogenicity of pure pentachloroethane (IARC, 1986).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Following subcutaneous administration of 1.1–1.8 mg/kg bw pentachloroethane to female mice, 12–51% of the dose was expired as the parent compound, 2–16% as trichloroethylene and 3–9% as tetrachloroethylene; the major urinary metabolites were trichloroethanol (16–32%) and trichloroacetic acid (9–18%) (IARC, 1986).

Pentachloroethane is dechlorinated in the presence of a rabbit liver reconstituted cytochrome P450 system or by rat liver microsomes, NADPH and oxygen (without oxygen, it is metabolized to 96% trichloroethylene and 4% 1,1,2,2-tetrachloroethane) (IARC, 1986).

Kinetic constants of pentachloroethane metabolism have been determined in male Fischer 344 rats exposed to the vapour phase at a concentration of 2895 mg/m^3 for 6 h and then placed in exhaled breath chambers. The maximum metabolic rate V_{max} was 9.2 mg/kg per hour (45.5 μmol/kg per hour) and the Michaelis constant K_m was 0.9 mg/L (4.45 μM) (Gargas & Andersen, 1989).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

Pentachloroethane given to rats by gavage during a two-year study caused chronic, diffuse kidney inflammation and renal papilla mineralization. A single dose also reduced hepatic cytochrome P450 content and microsomal epoxide hydrolase activities. Inhalation exposure of rabbits to pentachloroethane decreased their total antibody titres (IARC, 1986).

Male and female Fischer 344 rats were dosed with pentachloroethane (purity, 96%) by gavage for 10 days at a dose level of 150 mg/kg bw. The rat strain, dose and dose route were the same as used in the carcinogenicity study (see Section 3). In male rats, there were increases in the renal α_{2u}-globulin protein droplet concentration from 9.1 ± 2.3 mg/kg wet

kidney weight in controls to 25.9 mg/kg in the treated group. Specifically, in the P_2 renal tubule segment, the [^{3}H]thymidine cell-labelling index increased from 11.5 ± 0.7% in controls to 38.8 ± 3.9% in the treated group. The corresponding values for the P_1 and P_3 segments, respectively, were 8.7 ± 0.6% and 8.5 ± 1.5% in controls and 9.2 ± 1.6% for both segments in the treated group. The labelling index in the P_2 segment in female rats was 1.8 ± 0.7% in controls and 0.8 ± 0.2% in the treated group (Goldsworthy *et al*., 1988).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

Pentachloroethane is not mutagenic to *Salmonella typhimurium*. In the presence of an exogenous metabolic activation system, there was weak induction of mutation and gene conversion in yeast. In Chinese hamster ovary CHO cells, there was induction of sister chromatid exchanges, but not of chromosomal aberrations. In Chinese hamster lung CHL cells, chromosomal aberrations and aneuploidy were induced. Mutations were induced at the *tk* locus of mouse lymphoma L5178Y cells.

[U-^{14}C]Pentachloroethane injected into the peritoneal cavity of male Wistar rats and BALB/c mice was found to bind to DNA (as well as RNA and proteins) in liver, stomach, lung and kidney. Adducts were not identified (Turina *et al*., 1989).

5. Evaluation

No epidemiological data relevant to the carcinogenicity of pentachloroethane were available.

There is *limited evidence* in experimental animals for the carcinogenicity of pentachloroethane.

Overall evaluation

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

6. References

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Table 1. Genetic and related effects of pentachloroethane

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	38	Haworth *et al*. (1983)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	38	Haworth *et al*. (1983)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	38	Haworth *et al*. (1983)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	38	Haworth *et al*. (1983)
SCG, *Saccharomyces cerevisiae* D7, gene conversion *trp* locus	–	(+)	506	Bronzetti *et al*. (1989)
ANG, *Aspergillus nidulans* P1, mitotic segregation	–	NT	336	Crebelli *et al*. (1988)
SCR, *Saccharomyces cerevisiae* D7, forward mutation *ilv* locus	–	(+)	1517	Bronzetti *et al*. (1989)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	–[c]		800 ppm inj	Foureman *et al*. (1994)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	–	100	Galloway *et al*. (1987)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	–	–	206	Galloway *et al*. (1987)
CIC, Chromosomal aberrations, Chinese hamster lung CHL cells *in vitro*	+	+	80	Matsuoka *et al*. (1996)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	70	McGregor *et al*. (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus (microwell method) *in vitro*	+[d]	–	80	Sofuni *et al*. (1996)
AIA, Aneuploidy, Chinese hamster lung CHL cells *in vitro*	+	+	80	Matsuoka *et al*. (1996)

[a] +, positive; (+), weak positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, μg/mL; in-vivo tests, mg/kg bw/day; inj, injection

[c] Also negative with 300 ppm in feed

[d] Two laboratories

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