DICHLOROACETONITRILE

Data were last evaluated in IARC (1991).

1. Exposure Data

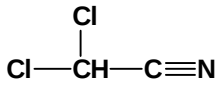
1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 3018-12-0

Chem. Abstr. Name: Dichloroacetonitrile

1.1.2 *Structural and molecular formulae and relative molecular mass*



C_2HNCl_2 Relative molecular mass: 109.94

1.1.3 *Physical properties* (for details, see IARC, 1991)

(*a*) *Boiling point*: 112–113°C

(*b*) *Conversion factor*: $mg/m^3 = 4.5 \times ppm$

1.2 Production and human exposure

Halogenated acetonitriles are not produced on an industrial scale. Several halogenated acetonitriles have been detected in chlorinated drinking-water in a number of countries as a consequence of the reaction of chlorine with natural organic substances present in untreated water. The only known route of human exposure is through chlorinated drinking-water (IARC, 1991).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Dichloroacetonitrile was tested in a limited carcinogenicity study in female SEN mice by skin application, in an initiation/promotion study in female SEN mice by skin application and in a screening assay for lung tumours in female strain A mice by oral administration. No skin tumour was produced after skin application in mice or in the initiation/promotion study, in which dichloroacetonitrile was applied topically as six equal doses over a two-week period, followed by repeated doses of 12-*O*-tetradecanoylphorbol 13-acetate for 20 weeks. There was no increase in either the proportion of mice with lung tumours or the number of lung tumours per mouse (IARC, 1991).

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*

Studies with [1-^{14}C]dichloroacetonitrile in rats and mice and [2-^{14}C]dichloroacetonitrile in rats indicated that the substance is rapidly absorbed after oral administration in water. Excretion of radioactivity following dosing with [1-^{14}C]dichloroacetonitrile is more rapid in mice than in rats. In mice, approximately 84% of the dose was excreted in 24 h (67% in urine, 11% in faeces, 5% as CO_2), compared with 67% in rats in six days (44% in urine, 17% in faeces, 6% as CO_2). Excretion of [2-^{14}C]dichloroacetonitrile radioactivity in rats accounted for about 84% of the dose within 48 h (38% in urine, 12% in faeces, 34% as CO_2). The quantitative differences in the route of excretion of the two labels in rats indicate that dichloroacetonitrile is being cleaved *in vivo*. The 1-^{14}C-labelled compound behaved like cyanide (IARC, 1991).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

Dichloroacetonitrile did not induce γ-glutamyltranspeptidase-positive foci in rat liver. An oral dose by gavage of 65 mg/kg bw per day for 90 days to male and female CD rats reduced body weights, spleen and gonad weights and serum cholesterol levels; other blood chemistry and haematological parameters were generally unchanged. Liver weights relative to body or brain weight were increased in female rats (IARC, 1991).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Dichloroacetonitrile given orally to rats at a dose of 45 mg/kg bw per day on gestation days 6–18 was associated in the full-term fetuses with an increased frequency of malformations of soft tissues, particularly of the cardiovascular and urogenital organs, and some skeletal malformations. This dose was also severely embryotoxic and toxic to the pregnant rats (IARC, 1991).

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)

Dichloroacetonitrile induced DNA damage and mutation in bacteria. Sex-linked recessive lethal mutations were induced in *Drosophila melanogaster*. It weakly induced sister chromatid exchanges and DNA strand breaks in mammalian cell lines. Micronuclei were induced in the erythrocytes of newt (*Pleurodeles waltl*) larvae exposed for 12 days, but in mice dosed for five days, neither micronuclei in bone marrow nor abnormal sperm morphology were induced.

5. Evaluation

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

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

Overall evaluation

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

6. References

Bull, R.J., Meier, J.R., Robinson, M., Ringhand, H.P., Laurie, R.D. & Stober, J.A. (1985) Evaluation of mutagenic and carcinogenic properties of brominated and chlorinated acetonitriles: by-products of chlorination. *Fundam. appl. Toxicol.*, **5,** 1065–1074

Table 1. Genetic and related effects of dichloroacetonitrile

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, SOS chromotest, *Escherichia coli* PQ37	–	(+)	50	Le Curieux *et al.* (1995)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	250	Simmon *et al.* (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	88	Bull *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluctuation test)	+	+	10	Le Curieux *et al.* (1995)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	11	Bull *et al.* (1985)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	NG	Bull *et al.* (1985)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	NG	Bull *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	+	680	Bull *et al.* (1985)
SCH, *Saccharomyces cerevisiae*, mitotic recombination	–	NT	NG	Simmon *et al.* (1977)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	+		200 ppm feed	Valencia *et al.* (1985)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	(+)	+	2.3	Bull *et al.* (1985)
DIH, DNA strand breaks, human lymphoblastic cell line *in vitro*	(+)	NT	NG	Daniel *et al.* (1986)
Micronucleus test, *Pleurodeles waltl* erythrocytes *in vivo*	+		0.25	Le Curieux *et al.* (1995)
MVM, Micronucleus test, CD-1 mouse bone-marrow cells *in vivo*	–		50 po × 5	Bull *et al.* (1985)
SPM, Sperm morphology, B6C3F_1 mice *in vivo*	–		50 po × 5	Meier *et al.* (1985)

[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; NG, not given; po, oral

Daniel, F.B., Schenck, K.M., Mattox, J.K., Lin, E.L.C., Haas, D.L. & Pereira, M.A. (1986) Genotoxic properties of haloacetonitriles: drinking water by-products of chlorine disinfection. *Fundam. appl. Toxicol.,* **6,** 447–453

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Le Curieux, F., Giller, S., Gauthier, L., Erb, F. & Marzin, D. (1995) Study of the genotoxic activity of six halogenated acetonitriles, using the SOS chromotest, the Ames-fluctuation test and the newt micronucleus test. *Mutat. Res.*, **341**, 289–302

Meier, J.R., Bull, R.J., Stober, J.A. & Cimino, M.C. (1985) Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice. *Environ. Mutag.,* **7,** 201–211

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