TRICHLOROACETONITRILE

Data were last evaluated in IARC (1991).

1. Exposure Data

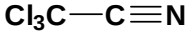
1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 545-06-2

Systematic name: Trichloroacetonitrile

1.1.2 *Structural and molecular formulae and relative molecular mass*



C_2NCl_3 Relative molecular mass: 144.39

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

(*a*) *Boiling point*: 85.7°C

(*b*) *Melting-point*: –42°C

(*c*) *Conversion factor*: $mg/m^3 = 5.91 \times ppm$

1.2 Production, use and human exposure

Halogenated acetonitriles are not produced on an industrial scale. Trichloroacetonitrile has been used on a limited basis in the past as a pesticide. 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. 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

Trichloroacetonitrile 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 trichloroacetonitrile 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. A small, significant increase in the proportion of mice with lung tumours and in the number of tumours per mouse was observed: control, 3/31 and 0.1; treated group (10 mg/kg bw, three times per week, eight weeks), 9/32 and 0.38 ($p < 0.05$) (IARC, 1991).

4. Other Data Relevant to an Evaluation 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*

About 2% of a single oral dose of 108 mg/kg bw trichloroacetonitrile to rats was excreted in urine within 24 h as thiocyanate, the product of released cyanide metabolized by rhodanese (IARC, 1991).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

Trichloroacetonitrile did not induce γ-glutamyltranspeptidase-positive foci in rat liver (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*

Trichloroacetonitrile given orally to rats at doses of 15–55 mg/kg bw per day on gestation days 6–18 was associated in the full-term fetuses with an increased frequency of

malformations, particularly of the cardiovascular and urogenital organs. Embryolethality occurred at dose levels below those which caused maternal toxicity and malformations (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)

Trichloroacetonitrile did not induce DNA damage in bacteria. Conflicting results were obtained in bacterial mutation studies. It 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 trichloroacetonitrile were available.

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

Overall evaluation

Trichloroacetonitrile 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

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

IARC (1991) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 52, *Chlorinated Drinking-water; Chlorination By-products; Some Other Halogenated Compounds; Cobalt and Cobalt Compounds*, Lyon, pp. 269–296

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

Table 1. Genetic and related effects of trichloroacetonitrile

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, SOS chromotest, *Escherichia coli* PQ37	–	–	100	Le Curieux *et al.* (1995)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	844	Bull *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluctuation test)	+	–	30	Le Curieux *et al.* (1995)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	844	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	–	–	844	Bull *et al.* (1985)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	+	2	Bull *et al.* (1985)
DIH, DNA strand breaks, human lymphoblastic line (of T-cell origin) *in vitro*	+	NT	NG	Daniel *et al.* (1986)
MVM, Micronucleus test, CD-1 mouse bone-marrow cells *in vivo*	–		50 po × 5	Bull *et al.* (1985)
Micronucleus test, *Pleurodeles waltl* erythrocytes *in vivo*	+		0.1 µg/mL	Le Curieux *et al.* (1995)
SPM, Sperm morphology, B6C3F$_1$ mice, *in vivo*	–		50 po × 5	Meier *et al.* (1985)

[a] +, 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

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