BROMOCHLOROACETONITRILE

Data were last evaluated in IARC (1991).

1. Exposure Data

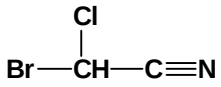
1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Services Reg. No.: 83463-62-1

Systematic name: Bromochloroacetonitrile

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_2HBrClN$ Relative molecular mass: 154.39

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

(*a*) *Boiling-point*: 138–140°C

(*b*) *Conversion factor*: $mg/m^3 = 6.31 \times ppm$

1.2 Production, use 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 and bromide 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

Bromochloroacetonitrile 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/J mice by oral administration. No skin tumour was produced after skin application in mice. In the initiation/promotion study, in which bromochloroacetonitrile 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 a small increase in the number of mice with tumours in the highest dose group: control, 9/105; intermediate dose, 7/37 (non-significant); highest dose (total dose 4800 mg/kg bw), 8/37 ($p < 0.05$). In orally treated mice, an increase in the proportion of animals with lung tumours and 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), 10/32 and 0.34 ($p < 0.05$) (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*

Approximately 13% of a single oral dose to rats of 116 mg/kg bw of bromochloroacetonitrile was excreted in urine within 24 h as thiocyanate, the product of released cyanide metabolized by rhodanese (IARC, 1991).

4.2 Toxic effects

No data were available to the Working Group.

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

There were slight decreases in early postnatal body weights of pups born to rats given bromochloroacetonitrile orally at a dose of 55 mg/kg bw per day on gestation days 7–21 (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)

Bromochloroacetonitrile induced DNA damage and mutation in bacteria. It also 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 orally for five days, neither micronuclei in bone marrow nor abnormal sperm morphology were induced.

5. Evaluation

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

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

Overall evaluation

Bromochloroacetonitrile 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 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

Table 1. Genetic and related effects of bromochloroacetonitrile

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, SOS chromotest, *Escherichia coli* PQ37	+	–	5	Le Curieux *et al.* (1995)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	+	13	Bull *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluctuation test)	+	–	0.6	Le Curieux *et al.* (1995)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	26	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	–	–	105	Bull *et al.* (1985)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	+	0.65	Bull *et al.* (1985)
DIH, DNA strand breaks, human lymphoblast cell line *in vitro*	+	NT	NG	Daniel *et al.* (1986)
Micronucleus test, *Pleurodeles waltl* erythrocytes *in vivo*	(+)		0.125	Le Curieux *et al.* (1995)
MVM, Micronucleus test, CD-1 mouse bone-marrow cells *in vivo*	–		50 po × 5	Bull *et al.* (1985)
SPF, 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