DIBROMOACETONITRILE

Data were last evaluated in IARC (1991).

1. Exposure Data

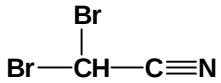
1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 3252-43-5

Chem. Abstr. Name: Dibromoacetonitrile

1.1.2 *Structural and molecular formulae and relative molecular mass*



C_2HNBr_2 Relative molecular mass: 198.84

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

(*a*) *Boiling point*: 169–170°C

(*b*) *Conversion factor*: $mg/m^3 = 8.1 \times ppm$

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 bromine with natural organic substances (and chlorine in the case of chlorinated acetonitriles) 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

Dibromoacetonitrile 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. In the initiation/promotion study, in which dibromoacetonitrile 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 dose-related increase in the number of mice with skin tumours except in the highest-dose group: control, 9/105; low dose (total dose 1200 mg/kg bw), 8/36 ($p < 0.05$); mid dose (total dose 2400 mg/kg bw), 33/70 ($p < 0.01$); high dose (total dose 4800 mg/kg bw), 10/74 (not significant). 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*

Approximately 8% of a single oral dose of 149 mg/kg bw of dibromoacetonitrile 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*

A daily dose of 45 mg/kg bw given by gavage for 90 days to male and female CD rats did not produce any consistent adverse effects (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*

There were slight decreases in early postnatal body weight of pups born to rats given dibromoacetonitrile orally at a dose of 50 mg/kg bw per day on gestation days 7–21. This dose was also toxic to the dams (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)

Dibromoacetonitrile induced DNA damage but not mutations in bacteria. 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 dibromoacetonitrile were available.

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

Overall evaluation

Dibromoacetonitrile 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

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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

Table 1. Genetic and related effects of dibromoacetonitrile

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, SOS chromotest, *Escherichia coli* PQ37	+	–	10	Le Curieux *et al.* (1995)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	58	Bull *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation (fluctuation test)	–	–	30	Le Curieux *et al.* (1995)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	58	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	–	–	58	Bull *et al.* (1985)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	–		200 ppm inj.	Valencia *et al.* (1985)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	+	0.03	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*	+		0.12	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; –, 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; inj., injection

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

Valencia, R., Mason, J.M., Woodruff, R.C. & Zimmering, S. (1985) Chemical mutagenesis testing in *Drosophila*. III. Results of 48 coded compounds tested for the National Toxicology Program. *Environ. Mutag.*, **7**, 325–348