1,2-Dibromoethane

CAS No. 106-93-4

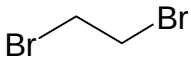

Figure 1: Structure of 1,2-dibromoethane

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA 1999) the Minister of Health may gather information, conduct investigations and evaluations, including screening assessments, relevant for the purpose of assessing whether a substance is entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Screening health assessments focus initially on conservative assessment of hazard or effect levels for critical endpoints and upper-bounding estimates of exposure, after consideration of all relevant identified information. Decisions based on the nature of the critical effects and margins between conservative effect levels and estimates of exposure take into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. Additional background information on screening health assessments conducted under this program is available at http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/index_e.html.

1,2-Dibromoethane (Figure 1) was nominated for inclusion in the pilot phase for preparation of screening assessments under CEPA 1999 as a compound that, based on information available at the time of the compilation of the Domestic Substances List (DSL), is representative of substances on the DSL likely to be prioritized on the basis of greatest potential for exposure.

This draft State of the Science Report for a screening assessment and associated unpublished supporting working documentation were prepared by evaluators within the Existing Substances Division of Health Canada; the content of these documents was reviewed at several meetings of senior Divisional staff. The draft Report was subsequently externally reviewed for adequacy of data coverage and defensibility of the conclusions. The supporting working documentation is available upon request by e-mail from ExSD@hc-sc.gc.ca

Information identified as of September 2003 (effects) and March 2004 (exposure) was considered for inclusion in this Report. The critical information and considerations upon which

this Report is based are summarized below. Additional data identified between these dates and the end of the external peer review period (March 2004) were also scoped and determined not to impact upon the conclusions presented here.

Identity, Uses and Sources of Exposure

In the year 2000, less than 100 tonnes of 1,2-dibromoethane were imported into Canada for use as a fuel additive (Environment Canada, 2001a), which represents a considerable decrease from 11 000 tonnes reported during the period of compilation of the DSL (1984–1986). This decline in use coincides with the ban on the use of leaded gasoline in cars in 1990 under CEPA. As an additive, 1,2-dibromoethane prevents lead oxide build-up in engines running on leaded gasoline Exemptions on the use of leaded gasoline exist for high-performance competition vehicles (cars, boats, snowmobiles) until January 1, 2008 (Environment Canada, 2003a). 1,2-Dibromoethane is still being used in aviation gasoline in North America (Chevron, 2003) but this represents only a small percentage of total aircraft fuel. For example, in 1997, aviation gasoline comprised 1.5% of total aviation fuel and only 0.2% of Ontario's gasoline mix (Patriarche and Campbell, 1999).

1,2-Dibromoethane was also used as a soil and grain fumigant in Canada until 1984, when its application for this purpose was banned (UNEP, 2003). It continues to be used in agricultural applications in a number of countries; as a result, there may be some exposure of the general population in Canada to 1,2-dibromoethane in imported foods and beverages. Use in consumer products has not been identified.

Levels measured in ambient air in Canada are much greater than concentrations predicted by modelling release into air of the total quantity reported to be used in Canada (CEMC, 2003). This comparison suggests that sources of 1,2-dibromoethane in addition to those uses reported are contributing to exposure in Canada, such as long-range transport from other jurisdictions through advection or combustion of aviation fuel.

Exposure Assessment, Hazard Characterization and Risk Evaluation

An upper-bounding estimate of exposure to 1,2-dibromoethane was calculated to be 0.089 µg/kg-bw per day in non-formula-fed infants (0–6 months), based on maximum concentrations reported in ambient air and limits of detection for other media in which the compound was not detected (i.e., indoor air, drinking water and food; see Table 1). However, indoor and ambient air likely contribute proportionally more to overall exposure than indicated in the upper bounding estimates presented in Table 1 and are likely the principal media of exposure to 1,2-dibromoethane, since it is volatile and readily partitions into air and also since the estimated intakes are based on limits of detection for several media.

Given that these upper-bounding estimates are based on detection limits for analyses of all media other than ambient air, and since the use of 1,2-dibromoethane has dropped significantly, confidence that these values overestimate actual exposures in Canada is high.

The International Programme on Chemical Safety (IPCS, 1996) concluded that 1,2-dibromoethane is a carcinogen in rodents and a potential human carcinogen. The International Agency for Research on Cancer (IARC, 1999) concluded that there is *inadequate evidence* in humans and *sufficient evidence* in experimental animals for the carcinogenicity of 1,2-dibromoethane; 1,2-dibromoethane was classified as *probably carcinogenic to humans* (Group 2A). These conclusions were based on significant increases in tumour incidences in rats and mice exposed via multiple routes (see Table 2 for an overview of the toxicological database). Significant increases in the incidences of squamous cell carcinomas of the forestomach were observed in male and female rats administered 1,2-dibromoethane by gavage at 37 mg/kg-bw per day or more for up to 61 weeks (NCI, 1978). Exposure of rats to 77 mg/m^3 or more via inhalation for 103 weeks resulted in significant increases in the incidences of adenocarcinomas and adenomas of the nasal cavity in both sexes, mammary gland fibroadenomas in females and tunica vaginalis mesotheliomas and nasal cavity adenomatous polyps in males (NTP, 1982). Dermal exposure of mice to 25 mg/day for up to 594 days (approximately equivalent to 833 mg/kg-bw per day; Health Canada, 1994) resulted in an increased incidence of papillomas of the lung in female mice (Van Duuren et al., 1979). In each of these bioassays, these significant increases were observed at the lowest exposure level tested.

1,2-Dibromoethane was genotoxic in a large number and variety of assays, including *in vivo* DNA binding, DNA damage and non-mammalian mutagenicity assays and *in vitro* mutagenicity, clastogenicity and DNA damage assays (Table 2).

The weight of evidence of mutagenicity and carcinogenicity of 1,2-dibromoethane is supported by rule-based structure–activity analysis (DEREK; LHASA Ltd., 2002).

Male reproductive effects are considered to be the critical non-neoplastic effect. In a short-term longitudinal study in male forestry workers, significantly decreased sperm velocity and semen volume were observed in subjects exposed via inhalation to 0.46 mg/m^3 or greater (occupational time-weighted average) levels of 1,2-dibromoethane in conjunction with dermal exposure (Schrader et al., 1988). Male reproductive effects were also observed in multiple species of experimental animals exposed to the lowest doses or concentrations tested. The lowest Lowest-Observed-Effect Level (LOEL) for reproductive effects for the oral route of exposure was 2 mg/kg-bw per day for 12 months (followed by further administration at 4 mg/kg-bw every second day for an additional 10–12 months) in bulls for reversible low sperm density, poor motility and altered spermatozoa morphology (Amir and Volcani, 1965). Testicular degeneration in male rats was observed at an inhalation concentration of 77 mg/m^3 in conjunction with other neo-plastic effects including toxic nephropathy in males, retinal atrophy and adrenal cortex degeneration in females and increases in hepatic necrosis in both sexes (NTP, 1982).

Owing to an extensive data set on carcinogenicity and *in vivo* and *in vitro* genotoxicity assays, there is high confidence in the health effects database upon which the conclusion that 1,2-dibromoethane is considered to be a genotoxic carcinogen is based.

On the basis of available information, it is concluded that 1,2-dibromoethane induces tumours likely by direct interaction with genetic material. It is, therefore, considered to be a substance for which there may not be a level of exposure below which there is no probability of adverse health effects.

Table 1: Upper-bounding estimates of daily intake for 1,2-dibromoethane

Route of exposure	**Estimated intake (µg/kg-bw per day) of 1,2-dibromoethane by various age groups**						
	0–6 months[1,2,3]		**0.5–4 years[4]**	**5–11 years[5]**	**12–19 years[6]**	**20–59 years[7]**	**60+ years[8]**
	formula fed	**not formula fed**					
Ambient air[9]	0.0050		0.011	0.0084	0.0048	0.0041	0.0036
Indoor air[10]	0.0044		0.0095	0.0074	0.0042	0.0036	0.0031
Drinking water[11]	0.0043	0.0016	0.0018	0.0014	8.0×10^{-4}	8.0×10^{-4}	9.0×10^{-4}
Food and beverages[12]		0.078	0.058	0.037	0.022	0.020	0.016
Soil[13]	1.6×10^{-5}		2.6×10^{-5}	8.4×10^{-6}	2.0×10^{-6}	1.7×10^{-6}	1.7×10^{-6}
Total intake	0.014	0.089	0.080	0.054	0.032	0.028	0.024

1 No data were identified on concentrations of 1,2-dibromoethane in breast milk.

2 Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (not formula fed) and to ingest 30 mg of soil per day (EHD, 1998).

3 For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of 1,2-dibromoethane in water used to reconstitute formula was based on data from City of Toronto (1990). No data on concentrations of 1,2-dibromoethane in formula were identified for Canada. Approximately 50% of non-formula-fed infants are introduced to solid foods by 4 months of age, and 90% by 6 months of age (NHW, 1990).

4 Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day (EHD, 1998).

5 Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day (EHD, 1998).

6 Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day (EHD, 1998).

7 Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day (EHD, 1998).

8 Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day (EHD, 1998).

9 Based on the highest concentration (0.143 µg/m^3) detected for 1,2-dibromoethane in 6766 of 8275 samples of ambient air collected in a national survey across Canada between 1998 and 2002 (Environment Canada, 2002). This survey was selected due to its expansiveness and its currency, which will likely reflect declining use of 1,2-dibromoethane in Canada. Canadians are assumed to spend 3 h per day outdoors (EHD, 1998). Data from which the critical data were selected included Health Canada (2003), Environment Canada (1991, 1992, 1994, 1995 and 2001b), OMEE (1994) and CMHC (1989).

10 In the absence of measured data, the detection limit (0.018 µg/m^3) for a recent indoor air study of 75 homes in Ottawa, Ontario, was used (Health Canada, 2003b). Canadians are assumed to spend 21 h indoors every day (EHD, 1998). Data from which the critical data were selected included Otson (1986), Cal. EPA (1992) and Cohen et al. (1989).

11 In the absence of measured data, the detection limit (0.04 µg/L) from 7 bottled and 27 tap water samples in Toronto, Ontario, was used (City of Toronto, 1990). Data from which the critical data were selected included OME (1988), OMEE (1993) and Golder Associates (1987).

12 In the absence of Canadian monitoring data, detection limits were used in the calculations. A single 1,2-dibromoethane measurement of 13 µg/kg in sweet cucumber pickles in 1995 (U.S. FDA, 2003) was not considered, as the use of detection limits overcompensated its contribution to the overall intake of vegetables in the calculations. In addition, older studies (Gunderson, 1988) in which 1,2-dibromoethane was detected were not used to calculate intake levels, as pesticidal use of 1,2-dibromoethane at that time likely led to levels in food that would not be representative currently.

- Dairy products
- Fats
- Fruits
- Vegetables
- Cereal products
- Meat & poultry
- Fish
- Eggs
- Foods, primarily sugar
- Mixed dishes & soups
- Nuts & seeds
- Soft drinks & alcohol

Amounts of foods consumed on a daily basis by each age group are described by Health Canada (EHD, 1998).

[13] The method detection limit (4.0 ng/g) for soil measurements in urban (59 samples) and rural (102 samples) parklands in Ontario was used to represent the maximum exposure concentration of 1,2-dibromoethane (OMEE, 1993). Data from which the critical data were selected included Golder Associates (1987).

Table 2: Summary of health effects information for 1,2-dibromoethane

Endpoint	Lowest effect levels[1]/Results
Laboratory animals and *in vitro*	
Acute toxicity	Lowest **oral LD_{50}** (rabbit) = 55 mg/kg-bw (Rowe et al., 1952) Lowest **inhalation LC_{50}** (rat) = 3080 mg/m^3 (Rowe et al., 1952) [Additional studies: Koptagel and Bulut (1998)]
Short-term repeated-dose toxicity	Lowest **oral (gavage) LOEL** (mice) = 125 mg/kg-bw per day, based on increased cholesterol levels and increased *in vitro* phagocytosis of cultured cells from dosed animals (Ratajczak et al., 1994)
Subchronic toxicity	Lowest **oral (gavage) LOEL** (mice) = 125 mg/kg-bw per day, based on alterations in *in vivo* serum and hematology parameters and *in vitro* lymphocyte response (Ratajczak et al., 1995) Lowest **inhalation LOEC** (rats) = 77 mg/m^3, based on epithelial hyperplasia of the nasal turbinates (Nitschke et al., 1981) [Additional studies: Reznik et al. (1980)]
Chronic toxicity/ carcinogenicity	**Oral (gavage) carcinogenicity bioassay in rats:** Males were exposed to a time-weighted average of 0, 38 or 41 mg/kg-bw per day (5 days per week for up to 49 weeks). Females were exposed to 0, 37 or 39 mg/kg-bw per day (5 days per week for up to 61 weeks). Both sexes initially received 0, 40 or 80 mg/kg-bw per day of 1,2-dibromoethane but due to excessive mortality the exposure levels and the overall duration of the study were reduced. In both sexes, there were significant increases in the incidence of squamous cell carcinoma of the forestomach in exposed groups (0/20 for both male and female controls, 45/50 for low-dose males, 33/50 for high-dose males, 40/50 for low-dose females, 29/50 for high-dose females). In males in the lowest dose group, there was a significant increase in the incidence of hemangiosarcomas of the circulatory system (0/20 controls, 11/50 low dose); after time-adjusted analysis in high-dose females, there was a significant increase in the incidence of hepatocellular carcinomas (0/20 controls, 5/25 high dose) (NCI, 1978). **Oral (gavage) carcinogenicity bioassay in mice:** Mice were exposed to time-weighted average doses of 0, 62 or 107 mg/kg-bw per day (5 days a week for 53 weeks). There were significant increases in the incidence of squamous cell carcinomas of the forestomach (males: vehicle control, 0/20; low dose, 45/50; high dose, 29/49; females: 0/20, 46/49, 28/50) and in alveolar/bronchiolar adenomas (males: control, 0/20; high dose, 10/47; females: control, 0/20; low dose, 11/43) (NCI, 1978). [Additional studies: Van Duuren et al. (1985) (drinking water) – evidence of carcinogencity was observed] **Inhalation carcinogenicity bioassay in rats:** Rats were exposed by inhalation to 0, 77 or 308 mg/m^3 (6 hours per day, 5 days per week, for 88–103 weeks). There were significant increases in the incidence of nasal cavity carcinomas at high doses (males:

	controls, 0/50; high dose, 21/50; females: controls, 0/50; high dose, 25/50) and adenocarcinomas at both doses (males: controls, 0/50; low dose, 20/50; high dose, 28/50; females: 0/50, 20/50, 29/50). There was a significant increase in the incidence of hemangiosarcomas of the circulatory system in the high-dose groups of both sexes (males: controls, 0/50; high dose, 15/50; females: controls, 0/50; high dose, 5/50). Female rats had a significantly increased incidence of mammary gland fibroadenomas (controls, 4/50; low dose, 29/50; high dose, 24/50), and the highest-dose females exhibited significant levels of alveolar/bronchiolar adenomas combined with carcinomas (controls, 0/50; high dose, 5/47). Male rats had a significant increase in the incidence of tunica vaginalis mesotheliomas at both doses (controls, 0/50; low dose, 7/50; high dose, 25/50) and nasal cavity adenomatous polyps at low doses (controls, 0/50; low dose, 18/50) (NTP, 1982). **Inhalation carcinogenicity bioassay in mice:** Mice were exposed by inhalation to 0, 77 or 308 mg/m^3 (6 hours per day, 5 days per week, for 78–103 weeks). There were significantly increased incidences of alveolar/bronchiolar carcinomas (males: control, 0/41; high dose, 19/46; females: control, 1/49; high dose, 37/50) and adenomas (males: controls, 0/41; high dose, 11/46; females: controls, 3/49; high dose, 13/50) in the highest-dose groups of both sexes. In dosed females, there was also a significantly increased incidence of hemangiosarcomas of the circulatory system (controls, 0/50; low dose, 11/50; high dose, 23/50), subcutaneous fibrosarcomas (controls, 0/50; low dose, 5/50; high dose, 11/50), nasal cavity carcinomas (controls, 0/50; high dose, 6/50) and mammary gland adenocarcinomas (controls, 2/50; low dose, 14/50; high dose, 8/50) (NTP, 1982). [Additional studies: Stinson et al. (1981); Wong et al. (1982) – evidence of carcinogenicity was observed in both studies] **Dermal carcinogenicity bioassay in mice:** Female mice were given 0, 25 or 50 mg/mouse in acetone, dermally, 3 times a week for 440–594 days. There was a significant increase in the incidence of benign lung papillomas at both dose levels (low dose, 24/30; high dose, 26/30) and a significant increase in the incidence of combined squamous cell papillomas and carcinomas at the highest dose level (Van Duuren et al., 1985). Lowest **non-neoplastic oral (gavage) effect level** (rats) = 38 (male) and 37 (female) mg/kg-bw per day, based on hyperkeratosis and acanthosis of the forestomach in females, degenerative changes in the liver, cortical cell degeneration of the adrenal gland and an earlier onset of testicular atrophy in males (lowest dose tested, carcinogenic dose) (NCI, 1978) [Additional studies: NCI (1978)] Lowest **non-neoplastic inhalation concentration** (rats) = 77 mg/m^3, based on toxic nephropathy in males, retinal atrophy and adrenal cortex degeneration in females and increases in hepatic necrosis in both sexes (lowest dose tested, carcinogenic dose NTP, 1982). [Additional studies: Stinson et al. (1981); NTP (1982); Wong et al. (1982)]

Reproductive toxicity	Lowest **oral (feed) LOEL** (bulls) = 2 mg/kg-bw per day for 12 months (followed by 4 mg/kg-bw every 2 days for 10–12 months), based on reversible low sperm density, poor motility and altered spermatozoa morphology (Amir and Volcani, 1965) [Additional studies: Shivanandappa et al. (1987); NCI (1978)] Lowest **inhalation LOEC** (rats) = 77 mg/m^3, based on testicular degeneration in males (NTP, 1982) [Additional studies: Short et al. (1979) for reduced reproductive capability of male rats]
Developmental toxicity	Lowest **inhalation LOEC** (rats) = 51.2 mg/m^3, based on decreased maternal body weight and improved rotorod performance and T-maze brightness discrimination acquisition in offspring (Smith and Goldman, 1983) [Additional studies: Short et al. (1978)]
Genotoxicity and related endpoints: *in vitro*	**GENE MUTATION** **Positive results:** *Salmonella typhimurium* TA98 (+/-S9), TA100 (+/-S9), TA100(GSH-) (-S9, +GSH), TA100(GSTA1-1 or GST1-1) (-S9), TA100W(Str^r, 8AG^r) (-S9), TA102 (activation not specified), TA1530 (-S9), TA1535 (+/-S9), TA1535(GST1-1) (-S9), TA2638(activation not specified) G46 (-S9) BA13 (+/-S9) [Ames and Yanofsky (1971); Von Buselmaier et al. (1972); Brem et al. (1974); McCann et al. (1975); Rosenkranz (1977); Rannug and Beije (1979); Elliott and Ashby (1980); Shiau et al. (1980); Stolzenberg and Hine (1980); van Bladeren et al. (1980, 1981); Barber et al. (1981); Principe et al. (1981); Barber and Donish (1982); Moriya et al. (1983); Buijs et al. (1984); Dunkel et al. (1985); Kerklaan et al. (1983, 1985); Guobaitis et al. (1986); Tennant et al. (1986, 1987); Hughes et al. (1987); Zoetemelk et al. (1987); Ong et al. (1989); Roldán-Arjona et al. (1991); Zeiger et al. (1992); Simula et al. (1993); Novotná and Duverger-van Bogaert (1994); Thier et al. (1996); Watanabe et al. (1998)] *Escherichia coli* WP2 (+/-S9), WP2/pKM101 (activation not specified), WP2 *uvr*A/pKM101 (activation not specified), CHY832 (-S9), 343/286 (+/-S9), K12 (+/-S9), KI201 (-S9), KI211 (-S9), *uvr*B5[Scott et al. (1978); Hemminki et al. (1980); Izutani et al. (1980); Moriya et al. (1983); Hayes et al. (1984); Mohn et al. (1984); Dunkel et al. (1985); Foster et al. (1988); Watanabe et al. (1998)] *Bacillus subtilis* TKJ5211, TKJ6321 (+S9) [Shiau et al. (1980)] *Streptomyces coelicolor* (-S9, spot test) [Principe et al. (1981)] *Aspergillus nidulans* [Scott et al. (1978); Principe et al. (1981)] *Neurospora crassa* ad-3 (forward mutation) [de Serres and Malling (1983)] *Tradescantia* clone 02, 0106, 4430 [Sparrow et al. (1974); Nauman et al. (1976); Vant'Hof and Schairer (1982)] Mouse L5178Y (+/-S9) [Clive et al. (1979); Tennant et al. (1986, 1987)] Chinese hamster CHO-K1(+/-S9) [Tan and Hsie (1981); Brimer et al. (1982)] Human cell line AHH-1, TK6 (-S9) [Crespi et al. (1985)] Human cell line EUE (-S9) [Ferreri et al. (1983)] **Negative results:** *Salmonella typhimurium* TA 98 (+/-S9), TA100(+/-S9), TA1537 (+/-S9), TA1538 (+/-S9), E503 [Brem et al. (1974); Alper and Ames (1975); Shiau et al. (1980); Principe et

al. (1981); Wildeman and Nazar (1982); Moriya et al. (1983); Dunkel et al. (1985); Tennant et al. (1986)]
Serratia marcescens a21 (-S9) [Von Buselmaier et al. (1972)]
Escherichia coli 343/113 (-S9) [Mohn et al. (1984)]
Streptomyces coelicolor (-S9, plate method) [Principe et al. (1981)]

UNSCHEDULED DNA SYNTHESIS
Positive results:
Rat hepatocytes [Williams et al. (1982); Tennant et al. (1986); Working et al. (1986)]
Rat spermatocytes [Working et al. (1986)]
Opossum lymphocytes [Meneghini (1974)]
Human lymphocytes (+/-S9) [Perocco and Prodi (1981)]
Mouse (C3Hfx101)F1 germ cells [Sega and Rene (1980)]

SISTER CHROMATID EXCHANGE
Positive results:
Fish lymphocytes (-S9) [Ellingham et al. (1986)]
Chinese hamster V79 cl-15 (-S9) [Tezuka et al. (1980)]
Chinese hamster CHO (+/-S9) [Tennant et al. (1987); Ivett et al. (1989)]
Human lymphocytes (-S9) [Tucker et al. (1984); Ong et al. (1989)]

CHROMOSOME ABERRATIONS
Positive results:
Fish lymphocytes (-S9) [Ellingham et al. (1986)]
Chinese hamster V79 cl-15 (-S9) [Tezuka et al. (1980)]
Chinese hamster CHO (+/-S9) [Tennant et al. (1987); Ivett et al. (1989)]

MICRONUCLEI INDUCTION
Positive results:
Tradescantia clone 03, 4430 [Ma et al. (1978, 1984)]
Human lymphocytes [Channarayappa et al. (1992)]

DNA DAMAGE
Positive results:
Escherichia coli polA1-/polA+(-S9) [Brem et al. (1974)]

Negative results:
Bacilis subtilis TKJ5211, TKJ6321 (+/-S9) [Shiau et al. (1980)]

SOS INDUCTION
Positive results:
Salmonella typhimurium TA1535/pSK1002 (+/-S9), NM5004 expressing GST 5-5 [Ong et al. (1987); Oda et al. (1996)]
Escherichia coli [Ohta et al. (1984); Quillardet et al. (1985)]

Negative results:
Salmonella typhimurium TA1535/pSK1002 (-S9) [Oda et al. (1996)]

MITOTIC GENE CONVERSION
Positive results:
Saccharomyces cerevisiae ade2, trp5 [Fahrig (1974)]

	SOMATIC SEGREGATION **Positive results:** *Aspergillus nidulans* diploid 35x17 (-S9) [Crebelli et al. (1984)] **CELL PROLIFERATION** **Positive results:** Human lymphocytes [Channarayappa et al. (1992)] **DNA STRAND BREAKS** **Positive results:** Rat hepatocytes [Sina et al. (1983)] Rat testicular cells [Bradley and Dysart (1985)] Rat and human testicular cells [Bjørge et al. (1996)] **DNA BINDING** **Positive results:** Calf thymus DNA [Arfellini et al. (1984); Colacci et al. (1985); Prodi et al. (1986)] Rat hepatocytes [Inskeep et al. (1986); Cmarik et al. (1990)] Human hepatocytes [Cmarik et al. (1990)] **Negative results:** *Escherichia coli* Q13 (+/-S9) and mouse Ehrlich ascites (+/-S9) [Kubinski et al. (1981)] **CELL TRANSFORMATION** **Positive results:** Balb/c 3T3 mouse cells [Perocco et al. (1991); Colacci et al. (1995)] **Negative results:** Balb/c 3T3 mouse cells (-S9) [Tennant et al. (1986)]
Genotoxicity and related endpoints: *in vivo*	**GENE MUTATION** **Positive results:** *Drosophila melanogaster* [Graf et al. (1984); Ballering et al. (1993)] *Salmonella typhimurium* G46 host-mediated [Von Buselmaier et al. (1972)] Barley [Ehrenberg et al. (1974)] **Negative results:** *Serratia marcescens* host-mediated [Von Buselmaier et al. (1972)] Silk worm [Sugiyama (1980)] **RECOMBINATION** **Positive results:** *Drosophila melanogaster* [Graf et al. (1984); Ballering et al. (1993)] **SEX-LINKED RECESSIVE LETHAL MUTATIONS** **Positive results:** *Drosophila melanogaster* [Vogel and Chandler (1974); Kale and Baum (1979a,b, 1981, 1982, 1983); Yoshida and Inagaki (1986); Ballering et al. (1993, 1994); Foureman et al. (1994); Kale and Kale (1995)]

CHROMOSOME ABERRATIONS
Positive results:
Barley root tips [Ehrenberg et al. (1974)]
Negative results:
Mouse (intraperitoneal) bone marrow [Krishna et al. (1985)] (IARC reports weakly positive)
Mouse (intraperitoneal) bone marrow [National Toxicology Program Database (1993)]

DNA STRAND BREAKS
Positive results:
Rat hepatocytes [Nachtomi and Sarma (1977); Kitchin and Brown (1994)]
Mouse hepatocytes [White (1982); Storer and Conolly (1983)]
Rat testicular cells [Bradley and Dysart (1985)]

MICRONUCLEI
Positive results:
Mouse (peripheral blood) [Witt et al. (2000)]
Various amphibians [Fernandez et al. (1993)]
Tradescantia [Ma et al. (1978)]

Negative results:
Mouse [Krishna et al. (1985); Asita et al. (1992)]

DNA BINDING
Positive results:
Mouse (liver, stomach, kidney, lung) [Arfellini et al. (1984); Prodi et al. (1986)]
Mouse hepatocyte DNA [Kim & Guenguerich (1990)]
Rat (liver, stomach, kidney, lung) [Arfellini et al. (1984); Prodi et al. (1986)]
Rat hepatocyte DNA [Inskeep et al. (1986); Kim & Guenguerich (1990)]

SPECIFIC LOCUS TEST
Negative results:
Mouse [Russell (1986); Barnett et al. (1992)]

SISTER CHROMATID EXCHANGE
Negative results:
Mouse (intraperitoneal) bone marrow [Krishna et al. (1985)]
Mouse (intraperitoneal) bone marrow [National Toxicology Program Database (1992)]

DOMINANT LETHAL
Negative results:
Rat [Short et al. (1979); Teramoto et al. (1980); Teaf et al. (1990)]
Mouse [Epstein et al. (1972); Teramoto et al. (1980); Barnett et al. (1992)]

DNA REPAIR EXCLUSIVE OF UNSCHEDULED DNA SYNTHESIS
Negative results:
Mouse hepatocytes [White et al. (1981)]

UNSCHEDULED DNA SYNTHESIS
Positive results:
Rat hepatocytes [Working et al. (1986)]

	Negative results: Rat spermatocytes [Working et al. (1986); Bentley and Working (1988)] **DNA DAMAGE** **Positive results:** Mouse (stomach, liver, kidney, bladder, lung) [Sasaki et al. (1998)]
Humans	
Acute toxicity	Estimated **oral lethal dose** (human) = 200 mg/kg-bw, based on an observation that a 60-kg woman died from ingesting 12 g of 1,2-dibromoethane (Alexeeff et al., 1990) Estimated **inhalation lethal concentration** (human) = 154 mg/m^3 for more than 30 minutes (IPCS, 1996) [Additional studies: Peoples et al. (1978); Letz et al. (1984); Jacobs (1985); Sarawat et al. (1986); Singh et al. (1993); Prakash et al. (1999); Raman and Sain (1999); Mehrotra et al. (2001)]
Chronic toxicity/ carcinogenicity	Mortality assessed in employees who were exposed to 1,2-dibromoethane in two production units (level of exposure was not provided in secondary accounts). In the first production unit, there were 2 deaths from malignant neoplasms (3.6 expected), and in the second production unit, there were 5 deaths from malignant neoplasms (2.2 expected). However, employees of the second production unit were also exposed to other chemicals, and overall there was no increase in total deaths or malignant neoplasms with increased exposure (Ott et al., 1980). [Additional studies: Ter Haar (1980)]
Reproductive and developmental toxicity	Lowest **inhalation LOEC** = 0.46 mg/m^3 (occupational time-weighted average in conjunction with dermal exposure) in male forestry workers, based on significantly decreased sperm velocity and semen volume (Schrader et al., 1988) [Additional studies: Ter Haar (1980); Wong et al. (1985); Dobbins, (1987); Ratcliffe et al. (1987); Schrader et al. (1987)]
Genotoxicity and related endpoints	**Negative results:** Chromosomal aberrations and sister chromatid exchange were not detected in workers exposed to mean concentrations ranging from 0.12 to 1.35 mg/m^3 (Steenland et al., 1986). [Additional studies: Steenland et al. (1985)]

[1] LC_{50} = median lethal concentration; LD_{50} = median lethal dose; LOEC = lowest-observed-effect concentration; LOEL = lowest-observed-effect level.

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