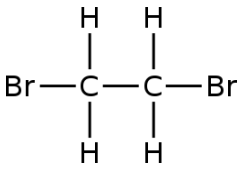
INITIAL TARGETED ASSESSMENT PROFILE

CAS No.	106-93-4
Chemical Name	Ethane, 1,2-dibromo- (1,2-Dibromoethane)
Structural Formula	

SUMMARY CONCLUSIONS OF THE TARGETED ASSESSMENT

NOTE: The present assessment is targeted to address the following human health endpoints: carcinogenicity and genotoxicity; and the following environment endpoints: photodegradation, stability in water, bioaccumulation potential, and acute and chronic toxicity to aquatic organisms. It cannot be considered as a full SIDS Initial Assessment. Summary information on exposure is also reported here. Other endpoints for human health and the environment are included in the Canadian screening assessment but have not been presented to OECD member countries, and thus are not included in this profile.

The final screening assessment has been published under the responsibility of the Government of Canada. [http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=C1B0BBD3-1].

Rationale for Targeting the Assessment

The Government of Canada "categorized" or prioritized all 23,000 chemical substances on its Domestic Substances List (DSL) from 1999 to September 2006, as required by its *Canadian Environmental Protection Act, 1999* (CEPA 1999). Using information from Canadian industry, academic research and other countries, Government of Canada scientists applied a set of rigorous tools to the 23,000 chemical substances on the DSL. They were categorized to identify those that were: **inherently toxic** to humans or to the environment and that might be **persistent** and/or **bioaccumulative**; and substances to which people might have **greatest potential for exposure**. During this priority-setting exercise, distinct approaches were taken for identifying substances of likely concern for human health and the environment, and subsequent assessment activities may have focused on either human health or ecological endpoints. Through categorization, the Government of Canada has identified approximately 4,000 of the 23,000 chemical substances on the DSL as priorities for further assessment, research and/or measures to control their use or release.

The substance 1,2-dibromoethane was identified as a priority for assessment because it was considered to meet the criteria for persistence and inherent toxicity to aquatic organisms, as well as for greatest potential for human exposure.

Under CEPA 1999, a screening assessment is conducted to determine whether a substance presents or may present a risk to the environment or to human health. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the Controlled Products Regulations, which is part of the regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use.

Physical-chemical properties

The substance, 1,2-dibromoethane, is a liquid at ambient temperature, and has a melting point of 9.9°C, boiling

point of 131.6°C and vapour pressure of 1493 Pa at 25°C (all measured values). The measured octanol-water partition coefficient (log K_{ow}) is 1.96, and the measured water solubility is 3910 mg/L at 25°C. The organic carbon-water partition coefficient (log K_{oc}) was estimated to be 1.70 (PCKOCWIN 2008).

Human Health Targeted Endpoints

The majority of the studies described here have been reviewed by the International Agency for Research on Cancer (IARC 1999).Additional data [designated in square brackets] relevant to the screening assessment were also included.

Genotoxicity: A sufficient genotoxicity database was available.

- The chemical induced gene mutations in the majority of many bacterial [including data reviewed by IARC and additional data] and ascomycetes fungi mutation assays conducted with and without metabolic activation.
- It induced gene mutations in mouse L5178Y and Chinese hamster cells with and without metabolic activation, human cell lines without activation, and the lacZ reversion assay in E. coli [additional data].
- Chromosomal aberration and induction of sister chromatid exchanges (SCEs) were positive in Chinese hamster cells with and without metabolic activation, while SCE was positive in human lymphocytes without metabolic activation.
- 1,2-Dibromoethane induced unscheduled DNA synthesis in human and opossum lymphocytes, rat hepatocytes and spermatocytes, and mouse germ cells.
- It also induced micronuclei in human lymphocytes.
- DNA damage, strand break and binding studies were mostly positive in various bacterial and mammalian cells, including human hepatoctyes and testicular and nasal mucosa cells, although negative results were observed for B. subtilis in a DNA damage study and for E. coli and mouse Ehrlich ascities in a DNA binding study.
- Indicator tests such as mitotic gene conversion was positive in yeast cells, somatic segregation was positive in ascomycetes fungi, cell proliferation was positive in human lymphocytes, SOS induction was mostly positive in bacterial cells, and cell transformation assays showed mixed results in mouse Balb/c 3T3 mouse cells.

Overall, ***in vitro*** mutagenicity, clastogenicity and DNA damage assays showed positive results.

The genotoxic effects of 1,2-dibromoethane were corroborated in a series of *in vivo* studies.

- D. melanogaster showed positive results for somatic gene mutation and recombination and sex-linked recessive lethal mutations.
- DNA damage, strand break, and binding [including DNA damage and binding data reviewed by IARC and additional studies] studies were all positive in rats and/or mice (many different organ cells tested).
- Mixed results were observed in micronuclei assays in mice (positive in peripheral blood [additional data] but negative in bone marrow and reticulocytes) and unscheduled DNA synthesis in rats (hepatocytes and spermatocytes analyzed).
- 1,2-Dibromoethane did not induce chromosomal aberrations or SCEs in the bone marrow of mice treated via intraperitoneal injection.
- DNA repair exclusive of unscheduled DNA synthesis was negative in the mouse (hepatocytes) and the dominant lethal test was negative in both rats and mice, and the specific locus test was negative in the mouse.

Based on the weight of evidence, 1,2-dibromoethane was genotoxic ***in vivo***.

Carcinogenicity potential was determined on the basis of long-term oral, inhalation and dermal studies. In each

of these bioassays, significant increases in incidence of tumours were observed at the lowest exposure level tested and higher.

Oral

In an oral carcinogenicity bioassay in rats, males were exposed by gavage to a time-weighted average of 0, 38 or 41 mg/kg-bw per day (5 days/week for up to 49 weeks), and females were exposed to 0, 37 or 39 mg/kg-bw per day (5 days/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 carcinomas 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 low-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).

In an oral carcinogenicity bioassay in mice, animals were exposed by gavage to time-weighted average doses of 0, 62 or 107 mg/kg-bw per day (5 days/week for 53 weeks) of 1,2-dibromoethane. Mortality was high in all treated groups and due to this, all males and high-dose females were sacrificed at wk 78 (25 wks after dosing ceased). Low-dose females were sacrificed at wk 90. 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: vehicle control, 0/20; low dose, 46/49; high dose, 28/50) and in alveolar/bronchiolar adenomas (males: control, 0/20; high dose, 10/47; females: control, 0/20; low dose, 11/43). The lowest non-neoplastic LOAEL for the oral carcinogenicity studies was found in the rat study: 38 (male) and 37 (female) mg/kg-bw per day based on hyperkeratosis and acanthosis of the forestomach in females, and degenerative changes in the liver, cortical cell degeneration of the adrenal gland and testicular atrophy in males (lowest dose tested, carcinogenic dose). The non-neoplastic effects in the forestomach and liver are considered as separate or precursor effects to the tumours observed in these organs.

In another oral study, mice were administered 0 or 4 mmol/L 1,2-dibromoethane (equivalent to 0 or 103-116 mg/kg bw/day) in distilled drinking-water for 450 days. Squamous-cell carcinomas of the forestomach (26/28 males and 27/29 females) and squamous-cell papilloma of the oesophagus (3/30 females) were observed compared to none in 45 male and 50 female controls.

Inhalation

In a carcinogenicity bioassay, rats were exposed by inhalation to 0, 10 or 40 ppm 1,2-dibromoethane (equivalent to 0, 77 or 308 mg/m^3) 6 h/day, 5 days/week, for 88–103 weeks. High mortality at the high concentration (90% in males, 84% in females) resulted in sacrifice of the remaining high-dose animals at wks 88 (males) or 91 (females). 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: controls, 0/50; low dose, 20/50; high dose, 29/50) and adenomas at low doses (males: control, 0/50; low dose, 11/50; females: controls, 0/50; low dose, 11/50). 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 the low dose (controls, 0/50; low dose, 18/50).

In a carcinogenicity bioassay in mice, animals were exposed by inhalation to 0, 10, or 40 ppm 1,2-dibromoethane (equivalent to 0, 77 or 308 mg/m^3) 6 h/day, 5 days/week, for 78–103 weeks). High mortality in both treated and control males resulted in sacrifice of all remaining males at wk 78. In females, high mortality was observed only at the high concentration (86%), and all remaining females at this concentration were sacrificed at wk 90. 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). The lowest non-neoplastic LOAEL for the inhalation carcinogenicity studies was found in the rat study: 77 mg/m^3, based on toxic nephropathy and testicular degeneration in males, retinal atrophy and adrenal cortex degeneration in females and increases in hepatic necrosis in both sexes (lowest dose tested, carcinogenic dose). The non-neoplastic effects in the testes are considered as separate to the tunica vaginalis tumours observed in this organ.

Additional inhalation carcinogenicity studies in rats exposed to 1,2-dibromoethane for 18 months to 0 or 20 ppm (equivalent to 0 or 154 mg/m^3) resulted in haemangiosarcomas of the spleen and subcutaneous mesenchymal tumours in both sexes and mammary tumours in females, and in mice exposed to 1,2-dibromoethane for up to 2 years to 10 or 40 ppm (equivalent to 77 or 308 mg/m^3) resulted in a dose-realted increase in hyperplastic lesions of the nasal cavity squamous epithelium of both sexes.

Dermal

In a dermal carcinogenicity bioassay, 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 skin combined squamous cell papillomas and carcinomas (3/30), as well as skin papillomas (5/30) at the high dose

Carcinogenicity Potential in Humans

There was very limited information on carcinogenicity in humans. Mortality was assessed in employees occupationally exposed to 1,2-dibromoethane in two production units while working as still and reactor operators (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.

Based on the available human and animal/in vitro data, the International Agency for Research on Cancer (IARC) 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).

1,2-Dibromoethane possesses properties indicating a hazard for the human health endpoints, carcinogenicity and genotoxicity (increases in tumour incidences in rats and mice exposed via multiple routes, clear evidence of genotoxicity).

Environment

According to the results of Level III fugacity modelling (EQC 2003), 1,2-dibromoethane is expected to distribute mainly into air (93.7%) if only released into the atmospheric compartment. If only released into water, the substance is expected to mainly reside in water (85.6%), to some extent partition to air (13.7%) and to weakly adsorb to suspended solids and sediment (<1%). If only released to soil, the substance will mostly reside in this environmental compartment (79%), and also partition to water (6.54%) and air (14.4%). When released equally to all three compartments, 1,2-dibromoethane is expected to distribute in air at 28.9%, water at 58.8%, soil at 12.1% and sediment <1%. A Henry's Law Constant of 65.9 Pa•m^3/mole at 25 ^{o}C also suggests that the substance volatilizes and may evaporate from surface of water or soil into air. The log K_{oc}, based on the log K_{ow}, was estimated as 1.70 (PCKOCWIN 2008), which indicates a low potential of the substance to accumulate in soil and sediment.

Based on its physical-chemical properties, a characteristic travel distance (CTD) has been used as an indicator for long range transport potential. The CTD has been calculated as 51 022 km for 1,2-dibromoethane (TaPL3 2000), hence the substance is considered to have a high potential for long-range transport in air (CTD > 2000 km).

1,2-Dibromoethane degrades very slowly in the atmosphere, with a measured half-life of 64 to 69 days, by reaction with photochemically-produced hydroxyl radicals. The photooxidation half-life in air has been reported between 10.7 to 107 days. From surface water, the substance volatilizes rapidly into the air (volatilization half-

lives ranging from 1 to 16 days). Otherwise, hydrolysis is the primary mode of degradation for 1,2-dibromoethane in water, occuring at a very slow rate (hydrolysis half-lives ranging from 354 days to 13.2 years). In soil, most of the substance is expected to be lost by volatilization to the atmosphere and by leaching to surface waters and groundwater. Otherwise, the substance is almost completely degraded within 1 week by soil microorganisms.

1,2-dibromoethane is not expected to bioaccumulate in organisms based on experimental bioconcentration factors (BCF) ranging from <1 to 20. An experimental log K_{ow} value of 1.96 for 1,2-dibromoethane also suggests that this chemical has low potential to bioaccumulate in biota.

Experimental data have been identified for 1,2-dibromoethane relating to acute and chronic toxicity of the substance to fish and aquatic invertebrates, as summarized below. The reported values were measured concentrations, unless otherwise indicated.

Acute

- Fish, Japanese medaka (*Oryzias latipes*), LC_{50} (96hr) = 32.1 mg/L
- Fish, fathead minnow (*Pimephales promelas*), LC_{50} (96hr) = 4.30 mg/L
- *Daphnia magna*, LC_{50} (48hr) = 6.5 mg/L
- *Ceriodaphnia dubia*, LC_{50} (48hr) = 3.61 mg/L

Chronic

- Fish, Japanese medaka (*Oryzias latipes*)
  - NOEC (12d reproduction) = 0.034 mg/L – The NOEC is based on the concentration used in the study's flow-through control group, where no toxic effect was observed.
  - LOEC (12d reproduction) = 0.133 mg/L. The LOEC is based on the lowest of three exposure concentrations found to cause a toxic effect in the study.
  - The maximum acceptable toxicant concentration (MATC) = 0.067 mg/L, The MATC was calculated as the geometric mean between the NOEC and LOEC values in the study.
- Fish, Japanese medaka (*Oryzias latipes*), carcinogenicity at 6.20 mg/L with exposure of 73 to 97 days

1,2-Dibromoethane possesses properties indicating hazard to the environment (chronic aquatic toxicity below 1 mg/L). Additionally, the substance has potential for long range transport in air and it is not expected to degrade rapidly in water. It is not expected to bioaccumulate.

Exposure Summary Information

1,2 dibromoethane is solely used in Canada (Sponsor country) as a scavenger of lead to prevent build-up of lead oxide in engines running on leaded gasoline. Presently, 99.8% of gasoline used in Canada is unleaded. Use of leaded gasoline in aircraft represented 98% of total leaded fuel in Canada in 2009, while high-performance competition vehicles represented 2%. However, leaded aviation gasoline may represent a small percentage (approximately 1.5%) of total aircraft fuel.

Globally, 1,2-dibromoethane is used principally as a chemical intermediate and industrial solvent. Uses include activation of magnesium in the preparation of Grignard reagents; use as a chemical intermediate in the production of plastic, latex, and vinyl bromide; a flame retardant used in modacrylic fibres; and use in the formulation of polyester dyes, resins and waxes. Some 1,2-dibromoethane may remain as an unintended manufacturing residue in articles. Use of 1,2-dibromoethane in consumer products has not been identified.

1,2-Dibromoethane was introduced worldwide as a soil and grain fumigant in 1946. Canada and the United States discontinued its use in pesticide products in 1984, and it was subsequently banned as an agricultural pesticide in member states of the European Union and many other countries. Today, 1,2-dibromoethane is listed under the Prior Informed Consent (PIC) procedure of the Rotterdam Convention, 1998, under the sponsorship of the United Nations Food and Agriculture Organization and the United Nations Environment Programme.

Based on the most recent survey for this compound, between 10 000 and 100 000 kg of 1,2-dibromoethane were reported to be imported into Canada in the 2000 calendar year. 1,2-Dibromoethane was also reported to be manufactured in or imported into Canada in the 2000 calendar year, in a mixture of a product at a low concentration (< 1% w/w); however the total quantity of 1,2-dibromoethane in the product at a low concentration

(<1% w/w) in 2000 was unknown.

1,2-Dibromoethane is not reportable to Canada's National Pollutant Release Inventory. According to the United States Toxics Release Inventory Program, total on-site and off-site disposal or other releases of 1,2-dibromoethane in the 2007 calendar year amounted to 1921 kg, where 1686 kg were released as fugitive air emissions, 96 kg as point source air emissions, 0.45 kg as surface water discharges and 0 kg as land treatment. This indicates that air may be the primary receiving compartment of 1,2-dibromoethane releases.

In addition, 1,2-dibromoethane appears to be formed naturally by microalgae growth and has been detected in ocean waters and air. Arctic brown, red and green macroalgae release volatile halogenated organic compounds including 1,2-dibromoethane. The extent of the contribution of these natural sources to global emissions is unknown. Baseline concentrations of 1,2-dibromoethane were found in air (20 ng/m^3) and in marine waters (0.02 ng/L) collected from open areas of the North and South Atlantic Ocean. The source of the compound could be the natural production by algae and/or the anthropogenic emissions.

General population exposure to 1,2-dibromoethane is expected mainly through indoor air. Drinking water and food and beverages are considered to be more minor sources of overall general population exposure. As no consumer products containing 1,2-dibromoethane were identified in Canada, exposure from use of consumer products is not expected.