1,2-Benzenediol
(Catechol)

Chemical Abstracts Service Registry Number
120-80-9

Synopsis

The Ministers of the Environment and of Health have conducted a screening assessment of 1,2-benzenediol, Chemical Abstracts Service Registry Number (CAS RN 120-80-9), a substance identified in the categorization of the Domestic Substances List as a high priority for action under the Ministerial Challenge. 1,2-Benzenediol was identified as a high priority as it was considered to pose an intermediate potential for exposure to individuals in Canada (IPE) and had been classified by other agencies on the basis of carcinogenicity. Since the substance did not meet the ecological categorization criteria for persistence, bioaccumulation or inherent toxicity to aquatic organisms, the focus of this assessment of 1,2-benzenediol relates to human health aspects.

Under information reported pursuant to section 71 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the total quantity of 1,2-benzenediol that was manufactured in Canada or imported into the country in 2006 ranged between 1 000 000 and 10 000 000 kg. The majority of 1,2-benzenediol manufactured in Canada is generated as a by-product of kraft pulp production, however, it is destroyed elsewhere in the process through combustion or removed during effluent treatment. 1,2-Benzenediol is used as a component in photographic developer and in various applications (e.g., laboratory reagent, antioxidant in electroplating baths) that would not result in exposure to the general population. 1,2-Benzenediol is found to occur naturally, including in various food items.

The predominant source of general population exposure to 1,2-benzenediol is expected to be as a result of its naturally occurring presence in food and beverages. Contributions to total exposure from the other media (ambient and indoor air, water and soil) are considered negligible in comparison. There may also be inhalation and dermal exposure to 1,2-benzenediol from its presence in photographic developer.

Based principally on weight of evidence based assessments by other agencies, a critical effect for the characterization of risk to human health is carcinogenicity, based on observation of tumours, including tumours in the glandular stomach in rats chronically exposed to the substance. 1,2-Benzenediol was genotoxic in several *in vitro* and *in vivo*

assays. Therefore, although the mode of induction of tumours has not been fully elucidated, it cannot be precluded that the tumours observed in experimental animals resulted from direct interaction with genetic material.

On the basis of the carcinogenicity of 1,2-benzenediol, for which there may be a probability of harm at any level of exposure, it is concluded that 1,2-benzenediol is a substance that may be entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

On the basis of ecological hazard and reported releases of 1,2-benzenediol, it is concluded that this substance is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends. Additionally, 1,2-benzendiol does not meet criteria for persistence and bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations.*

This substance will be included in the Domestic Substances List inventory update initiative, to be launched in 2009. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

Based on the information available, 1,2-benzenediol meets one or more of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999*.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or human health. Based on the results of a screening assessment, the Ministers can propose to take no further action with respect to the substance, to add the substance to the Priority Substances List (PSL) for further assessment, or to recommend that the substance be added to the List of Toxic Substances in Schedule 1 of the Act and, where applicable, the implementation of virtual elimination.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce; and/or

- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE), and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), that challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment, and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as the highest priorities.

The substance 1,2-benzenediol was identified as a high priority for assessment of human health risk because it was considered to present IPE and had been classified by other agencies on the basis of carcinogenicity. The Challenge for 1,2-benzenediol was published in the *Canada Gazette* on February 3, 2007 (Canada 2007a). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information were received.

Although 1,2-benzenediol was determined to be a high priority for assessment with respect to human health, it did not meet the criteria for potential for persistence, bioaccumulation or inherent toxicity for aquatic organisms. Therefore, this assessment focuses principally on information relevant to the evaluation of risks to human health.

Under CEPA 1999, screening assessments focus on information critical to determining whether a substance meets the criteria for defining a chemical as toxic as set out in section 64 of the Act, where

> "64. […] a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that
>
> (*a*) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;
>
> (*b*) constitute or may constitute a danger to the environment on which life depends; or
>
> (*c*) constitute or may constitute a danger in Canada to human life or health."

Screening assessments examine scientific information and develop conclusions by incorporating a weight of evidence approach and precaution.

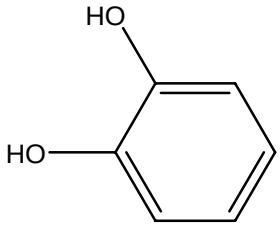
This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents, stakeholder research reports and from recent literature searches, up to October 2007. Key studies were critically evaluated; modelling results may have been used to reach conclusions. Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-

occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritization the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. This assessment has undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from Exponent and Starodub & Associates. While external comments were taken into consideration, the final content and outcome of the screening risk assessment remain the responsibility of Health Canada and Environment Canada. Additionally, the draft of this screening assessment was subject to a 60-day public comment period. The critical information and considerations upon which the assessment is based are summarized below.

Substance Identity

Table 1. Substance identity

Chemical Abstracts Service Registry Number (CAS RN)	120-80-9
DSL name	1,2-Benzenediol
National Chemical Inventory (NCI) names[1]	1,2-Benzenediol (TSCA, DSL, ENCS, AICS, ECL, SWISS, PICCS, ASIA-PAC, NZIoC); Pyrocatechol (DSL, EINECS, PICCS); Catechol (PICCS); Pyrocatechin (PICCS)
Other names	Catechol, 1,2-Benzoldiol; 1,2-Dihydroxybenzene; 2-Hydroxyphenol; C.I. 76500; C.I. Oxidation Base 26; Durafur Developer C; Fouramine PCH; Fourrine 68; NSC 1573; o-Benzenediol; o-Dihydroxybenzene; o-Dioxybenzene; o-Hydroquinone; o-Hydroxyphenol; o-Phenylenediol; Oxyphenic acid; Pelagol Grey C; Phthalhydroquinone; Phthalic alcohol; Pyrocatechine; UN 2811
Chemical group	Discrete organics
Chemical sub-group	Phenols
Chemical formula	$C_6H_6O_2$
Chemical structure	
SMILES	Oc(c(O)ccc1)c1
Molecular mass	110.11 g/mol

1 **Source**: National Chemical Inventories (NCI), 2007: AICS (Australian Inventory of Chemical Substances); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Chemical Substances); ELINCS (European List of Notified Chemical Substances), ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); TSCA (Toxic Substances Control Act Chemical Substance Inventory); ASIA-PAC (Combined Inventories from the Asia-Pacific Region); and NZIoC (New Zealand Inventory of Chemicals)

Physical and Chemical Properties

A summary of key physical and chemical properties of 1,2-benzenediol is presented in Table 2.

Table 2. Physical and chemical properties of 1,2-benzenediol

Property	Type	Value (SI units)[1]	Temperature	Reference
Boiling point (ºC)	Experimental	245		(PhysProp 2003)
Melting point (ºC)	Experimental	105		(PhysProp 2003)
Henry's Law constant ($Pa \cdot m^3/mol$)	Experimental	3.18 x 10-4 (3.14×10^{-9} $atm \cdot m^3/mol$)		(PhysProp 2003)
Dissociation constant	Experimental	9.45		(Serjeant and Dempsey 1979 [cited in PhysProp 2003])
Log K_{ow}	Experimental	0.88		(Hansch et al. 1995 [cited in PhysProp 2003])
Vapour Pressure (Pa)	Experimental	0.488 (0.00366 mm Hg)	25ºC	(Boublik et al. 1984 [cited in PhysProp 2003])
Solubility in Water (kg/m^3)	Experimental	461 (461 000 mg/L)		(Granger and Nelson 1921)
Density (kg/m^3)	Experimental	1344 ($1.344\ g/cm^3$)	20ºC	(Lide 2007)
Log K_{oc}	Modelled	2.65		(PCKOCWIN 2000)

[1] If different, values in brackets represent the original ones as reported by the authors or as estimated by the models.

Sources

1,2-Benzenediol is found to occur naturally in the tannin layer of mycorrhiza of the Douglas pine; in the leaves and branches of oak and willow; and in various food items such as apples, potatoes and refined olive oil (Marshall 2000; Brenes et al 2004; Sternitzke et al. 1992; Singh et al. 1994; McDonald et al. 2001).

Based on a survey made under section 71 of CEPA 1999, the total quantity of 1,2-benzenediol that was manufactured and/or imported into Canada in 2006 ranged between 1 000 000 and 10 000 000 kg (Canada 2007a).

Most of the 1,2-benzenediol manufactured in Canada is generated as a by-product of kraft pulp production and is present in black liquor, an internal process stream (Canada 2007a). According to the National Council for Air and Stream Improvement (NCASI 2007), 1,2-benzenediol is virtually destroyed during the recovery process (i.e., through combustion). While some 1,2-benzenediol does enter the pulp and paper mill sewers through losses of pulping liquor, these are typically removed in the wastewater treatment system (March 2008 e-mail from Forestry, Agriculture and Aquaculture Division of Environment Canada; unreferenced). 1,2-Benzenediol has been identified in cigarette smoke (Roemer et al. 2004), and wood smoke (Fine et al. 2001; Fine et al. 2002). Another source of 1,2-benzenediol in humans is from the metabolism of benzene (Medeiros and Bird 1997).

Uses

According to submissions made under section 71 of CEPA 1999, 1,2-benzenediol is used as a photographic developer, and in various applications that would not result in exposure to the general population (Canada 2007a). Based on voluntary data submitted by industry to Environment Canada, it is also used in small quantities as a laboratory reagent for raw material testing in the pharmaceutical industry (Canada 2007c), and is used as an antioxidant in electroplating baths where it is completely destroyed (oxidized) during the process (Canada 2007d).

This substance is currently listed on Health Canada's Cosmetic Ingredients Hotlist prohibiting its use in cosmetic products (Health Canada 2007). In Canada, 1,2-benzenediol is not registered as an active ingredient in pest control products, nor is it present as a formulant in pest control products (PMRA 2007a; PMRA 2007b).

Other potential or historical uses of 1,2-benzenediol include its use as a developer in fur dyes (HSDB 2005), as an intermediate for antioxidants in rubber and lubricating oils, in polymerization inhibitors and in pharmaceuticals (US EPA 2000). 1,2-Benzenediol may also be used as a reagent, in the synthesis of adhesives, in fax papers, and specialty inks (IARC 1999; Ash and Ash 2002). 1,2-Benzenediol has been used in the past as an oxidizing agent in hair colourants (Winter 2005) and as an antioxidant for perfumes and essential oils (Ash and Ash 2002).

Releases to the Environment

Information reported under section 71 of CEPA 1999 indicated that 100 to 1000 kg of 1,2-benezenediol were released into the environment in 2006; however, the report did not specify into which media the substance was released (Canada 2007).

1,2-Benzenediol is reportable under the National Pollutant Release Inventory (NPRI). Since 1994 there have been few releases of 1,2-benzenediol—on-site air emissions in 2001 as a result of a spill, and in 2003, 150 kg were sent to an off-site landfill (NPRI 2006).

Environmental Fate

The results of a Level III fugacity model, which predict the distribution of 1,2-benzenediol in the environment following release to various media, are summarized in Table 3.

As indicated in Table 2, 1,2-benzenediol has a very high solubility in water and has a moderate soil adsorption coefficient, which suggests that if released to water, this substance would remain in water, otherwise releases tend to partition to soil. If 1,2-benzenediol is released to the atmosphere, it is expected to be rapidly oxidized. 1,2-Benzenediol may also be removed from the atmosphere by wet deposition processes, considering the very high water solubility of this substance.

Table 3. Results of the Level III fugacity modelling (EPIWIN 2004) for 1,2-benzenediol

	Fraction of substance partitioning into each compartment			
Substance released to	**Air**	**Water**	**Soil**	**Sediment**
Air (100%)	0.18	22.5	77.3	0.04
Water (100%)	0.00	99.8	0.00	0.20
Soil (100%)	0.00	18.6	81.4	0.04
Air, water, soil (33.3% each)	0.06	37.1	62.8	0.07

Persistence and Bioaccumulation Potential

Persistence

According to its physical and chemical properties (Table 2) and on the weight of evidence based on the empirical and modelled degradation data below (Tables 4a and 4b), 1,2-benzenediol does not meet the persistence criteria (half-lives in air ≥ 2 days, in soil and water ≥182 days, and in sediments ≥365 days) set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Table 4a. Empirical data for persistence of 1,2-benzenediol

Medium	Fate process	Degradation value	Degradation endpoint/units	Reference
Air	Photodegradation	1.04×10^{-10}	Rate constant, cm^3/molecule · sec	(Atkinson 1989)
Air	Photodegradation	0.103	Half-life, days	(Atkinson,1989)
Water	Biodegradation	83	Biodegradation, %	(Chemicals Inspection and Testing Institute 1992)

Table 4b. Modelled data for persistence of 1,2-benzenediol

Medium	Fate process	Degradation value	Degradation endpoint/units	Reference
Air	Atm. Oxidation	0.4606	Half-life, days	(AOPWIN 2000)
Air	Ozone reaction	Non-reactive	Half-life, days	(AOPWIN 2000)
Water	Biodegradation	15	Half-life, days	(BIOWIN 2000, Ultimate survey)
Water	Biodegradation	0.691	Probability	(BIOWIN 2000, MITI Non-linear probability)
Water	Biodegradation	0.546	Probability	(BIOWIN 2000, MITI Linear probability)
Water	Biodegradation	0.998	Probability	(Topkat 2004)
Soil	Biodegradation	15	Half-life, days	(Boethling et al. 1995)[1]
Sediment	Biodegradation	60	Half-life, days	(Boethling et al. 1995)[1]

[1] Values were derived from the modelled half-life in water using Boethling et al.'s extrapolation factors:
$t_{1/2\ water} : t_{1/2\ soil} : t_{1/2\ sediment} = 1:1:4$.

Bioaccumulation

Since no experimental data on the bioaccumulation factor (BAF) and the bioconcentration factor (BCF) of 1,2-benzenediol were identified, a quantitative structure-activity relationship (QSAR)-based weight-of-evidence approach (Environment Canada 2007) was applied. The modelled data presented in Table 5 indicates that 1,2-benzenediol does not meet the bioaccumulation criteria (BCF/BAF ≥5 000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Table 5. Modelled data for bioaccumulation of 1,2-benzenediol

Test organism	Endpoint	Value (wet wt, L/kg)	Reference
Fish	BAF	1	(Arnot & Gobas 2003) Gobas BAF T2MTL
Fish	BCF	1–19	(OASIS 2004; Forecast v 1.2; Arnot & Gobas 2003; BCFWIN 2000) Modified Gobas BCF 5% T2LTL

Potential to Cause Ecological Harm

As indicated earlier, 1,2-benzenediol does not meet the persistence or bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Experimental ecotoxicological data (ECOTOX database) indicate that 1,2-benzenediol does not cause significant harm to aquatic organisms at low concentrations. For two species of fish, acute LC_{50} values vary within a narrow range of 3.5-10 mg/L. Toxicity values for aquatic plants are slightly higher (13-27.5 mg/L), while for invertebrates (shrimp), the LC_{50} exceeds 40 mg/L.

Information reported under Section 71 of CEPA 1999, indicated that 100 to 1 000 kg of 1,2-benezenediol were released to unspecified media in 2006 (Canada 2007a). The National Pollutant Release Inventory reports 0.00 tonnes were released in 2005. Given the quantity and nature of these releases, they are deemed unlikely to result in significant exposure of organisms in the environment.

Based on the information available, 1,2-benzenediol is unlikely to be causing ecological harm in Canada.

Potential to Cause Harm to Human Health

Exposure Assessment

Measured concentrations of 1,2-benzenediol in environmental media in Canada were not available. Intake values were therefore estimated based on limited data measured elsewhere for surface water (Boyd 1994) and various food items (Brenes et al. 2004; Sternitzke et al. 1992; Singh et al. 1994; McDonald et al. 2001). ChemCAN (CEMC 2003) was used to estimate concentrations of 1,2-benezenediol in air and soil, as no measured data were available. The amount of 1,2-benzenediol released was obtained from industrial data submitted through the section 71 survey. No information was available regarding the media into which the substance was released, therefore, an approximate value (percentage) was estimated for each media based on data (trends) from the 2005 U.S. Toxic Release Inventory (TRI). According to the TRI, 1,2-benzenediol is mainly released to water (TRI 2005). Appendix 1 presents upper-bounding estimates of intake for each age group in the general population of Canada, based on this limited information. The upper-bounding estimate of daily intake for the general Canadian population ranges from 0.02 µg/kg-bw (kilogram of body weight) per day for formula-fed infants (0 to 6 months old) to 847 µg/kg-bw per day for adults (20–59 years of age), with intakes from food and beverages representing the predominant source of exposure. Other than the presence of 1,2-benzenediol in meats and poultry (from smoke condensate), the sources of 1,2-benzenediol in food and beverages are considered to be naturally occurring. Contributions to total intake from other media (ambient and indoor air, water and soil) from manufacturing and industrial uses of 1,4-benzenediol were considered to be negligible in comparison to intake from food and beverages.

Based on information provided through section 71 (Canada 2007), photographic developer was the only consumer product identified that would contain 1,2-benzenediol. As illustrated in Appendix 2, the ConsExpo evaporation model (RIVM 2006), which takes into account that not all of the substance will be released from the product, was used to estimate air concentrations from use of photographic developer (0.023 mg/m^3).

The upper-bounding exposure estimate resulting from dermal exposure to photographic developer was estimated to be 0.98 µg/kg-bw/day.

Confidence in the exposure database is considered to be low for the upper-bounding estimates from the environment, as modelling was used to determine concentrations of 1,2-benzenediol in air and soil, and there was only one study available on concentrations of this substance in marine and waste waters. The studies documenting concentrations in food were very limited. However, the method used to estimate intakes from the various food groups likely results in an overestimate. There is also low confidence in the estimate of exposure from consumer products. However, since the estimates of exposure are conservative, confidence is high that actual exposure levels do not exceed these estimates.

Health Effects Assessment

Appendix 3 contains a summary of the available health effects information for 1,2-benzenediol in experimental animals. An overview of health effects reported in humans is presented in Appendix 4.

The International Agency for Research on Cancer (IARC 1999) has classified 1,2–benzenediol as "possibly carcinogenic to humans" (Group 2B) based on sufficient evidence of carcinogenicity in experimental animals. It has been reported that long-term administration of 1,2-benzenediol in the diet induces adenocarcinoma of the glandular stomach in several strains of rats (IARC 1999); however, no epidemiological data has been identified in this regard. Administration of 0.1, 0.2, 0.4 or 0.8% (33, 65, 141, or 318 mg/kg-bw/day) 1,2-benzenediol in the diet in male F344 rats for 34 weeks caused hyperplasia and adenomas of the pyloric gland (glandular hyperplasia) at the 141 or 318 mg/kg-bw/day dose levels, but little or a very weak hyperplasia was noted at the 33 or 65 mg/kg-bw/day dose levels. After a 2-year exposure, submucosal hyperplasias of the glandular stomach were found at the 33 mg/kg-bw/day and higher dose levels. Adenocarcinomas were observed in 3/25 rats at the 318 mg/kg-bw/day dose level (Hagiwara et al. 2001).

1,2-Benzenediol was genotoxic in several *in vitro* and *in vivo* assays and it caused gene mutations, chromosomal aberrations and sister chromatid exchanges in mammalian cells in culture. After administration to mice, 1,2-benzenediol was negative in one study (Gad-El karim et al. 1986) and positive in three studies of bone marrow micronucleus formation (Ciranni et al. 1988a,1988b; Marrazzini et al. 1994). 1,2-Benzenediol induced DNA strand breaks, gene mutations, chromosomal aberrations, aneuploidy and cell transformation in non-human mammalian cells with or without metabolic activation (Brandt 1986; do Ceu Silva et al. 2003). Information regarding the genotoxic effects of 1,2-benzenediol has been reviewed in detail in Brandt (1986) and IARC (1999).

Although a mode of action analysis is beyond the scope of this screening assessment, nongenotoxic mechanisms have been proposed for the carcinogenicity of

1,2-benzenediol. A potential role of regenerative cell proliferation due to toxicity has been proposed for glandular stomach tumours in mice (Hirose et al. 1993). However, a potential role of genetic damage in the development of tumours cannot be precluded.

With respect to noncancer effects, a single 8-hr inhalation (aerosol) exposure to 1500 mg/m^3 1,2-benzenediol did not cause any signs of toxicity in rats (no-observed-effect concentration, or NOEC). However, irritation of the extremities and loss of toe or tail tips were noted in some animals following exposure to 2000 or 2800 mg/m^3 1,2-benzenediol (Flickinger 1976). As noted above, the chronic toxicity study in rats indicates a dietary LOEL of 33 mg/kg-bw/day 1,2-benzenediol based on hyperplasias of the glandular stomach and benign proliferative glandular stomach lesions (Hagiwara et al. 2001).

Confidence in the toxicological database is considered low to moderate. Gaps in the health effects database include lack of repeat-dose studies by the inhalation route.

Characterization of Risk to Human Health

Based on the weight of evidence assessment by IARC, a critical effect for characterization of risk to human health is carcinogenicity, for which a mode of induction involving direct interaction with genetic material cannot be precluded.

With respect to noncancer effects, the lowest dietary LOEL in the database is 33 mg/kg-bw/day based on effects in the stomach (the apparent target organ) of rats. Given that the predominant source of exposure to the general population is through the naturally occurring presence of 1,2-benzenediol in foods and beverages, derivation of a margin of exposure between effect levels in experimental animals and upper-bounding estimates of exposure to the general population would not be meaningful. For noncancer effects, the incremental risk associated with 1,2-benzenediol in environmental media resulting from its industrial uses is considered to be negligible.

One consumer product use was identified (i.e., photographic developer). When air concentrations resulting from this use (0.023 mg/m^3) are compared to the only inhalation NOEC in the database (1500 mg/m^3), the margin of exposure is approximately 65 200. Dermal exposure may contribute to total exposure if gloves and/or tongs are not used as recommended on product labels. This margin is considered adequate to account for uncertainties in the databases on exposure and effects.

Uncertainties in Evaluation of Risk to Human Health

There is uncertainty regarding interspecies differences in sensitivity to 1,2-benzenediol. Existing literature indicates that most of the 1,2-benzenediol data comes from dietary studies conducted in rats, whereas mice appear less responsive to treatment with this substance. In addition, the carcinogenicity and genotoxicity data demonstrated species or even strain-specific effects of 1,2-benzenediol. The neoplastic changes were evident mostly in the glandular part of the rat stomach and the incidence of adenocarcinoma was

noted in 67, 73 and 77% of Wistar, Lewis, and SD rats respectively, but in only 10% of WKY rats (Tanaka et al. 1995). The scope of this screening assessment does not take into consideration an analysis of the mode of action for tumour induction from exposure to 1,2-benzenediol.

Modelling was used to derive estimates of 1,2-benzenediol in air and soil; and there was only one study available on 1,2-benzenediol concentrations in water. Based on the physical and chemical properties of this substance and the results of the section 71 survey, 1,2-benzenediol is not likely found in soil or in air. The studies available for food were not from typical food products, were not Canadian-specific and often lacked specific parameters needed to derive realistic estimates (e.g., the amount of smoke condensate used in various products). As a result of the lack of data, and taking a conservative approach, the values measured in the various food items were used to represent an entire food group. For example, the concentration measured in refined olive oil was used to represent the entire "fats" group by assuming all food items in the fats group contain the measured concentration of 1,2-benzenediol from refined olive oil. This is very likely to result in an overestimate of actual exposures from foods. Estimates of exposure from use of photographic developer containing 1,2-benzenediol were based on conservative assumptions and the current use pattern is not well known.

Conclusion

Based on the available information, it is concluded that 1,2-benzenediol is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the carcinogenicity of 1,2-benzenediol, for which there may be a probability of harm at any level of exposure, it is concluded that 1,2-benzenediol is a substance that may be entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that 1,2-benzenediol does not meet the criteria in paragraph 64a and 64b of CEPA 1999, but it does meet the criteria in paragraph 64c of CEPA 1999. Additionally, 1,2-benzenediol does not meet criteria for persistence and bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations.*

References

[ACGIH] American Conference of Governmental Industrial Hygienists 2005 [CD ROM]. Documentation of the TLV's and BEI's with other world wide occupational exposure values. Cincinnati (OH). 45240-1634. [cited in HSDB 2006].

[AOPWIN] Atmospheric Oxidation Program for Windows. 2000. Version 1.91. Washington (DC): U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm.

Arnot JA, Gobas FA. 2003. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. QSAR Comb Sci 22(3):337-345.

Ash M, Ash I, compilers. 2002. Handbook of Cosmetic and Personal Care Additives, 2 Volume Set. 2nd Ed. Endicott (NY): Synapse Information Resources. p. 1456.

Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J Phys Chem Ref Data Monograph No. 1:1-246.

[BCFWIN] BioConcentration Factor Program for Windows. 2000. Version 2.15. Washington (DC): U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm.

Bingham E, Cohrssen B, Powell CH. 2001. Patty's Toxicology Volumes 1-9, 5th Edition. New York (NY): John Wiley & Sons. p. 401.

[BIOWIN] Biodegradation Probability Program for Windows. 2000. Version 4.02. Washington (DC): U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm.

Bleehen SS, Pathak MA, Hori Y, and Fitzpatrick TB. 1968. Depigmentation of skin with 4-isopropylcatechol, mercaptoamines and other compounds. J Invest Dermatol 50:103-117.

Boethling RS, Howard PH, Beauman JA, Larosche ME. 1995. Factors for intermedia extrapolations in biodegradability assessment. Chemosphere 30(4):741–752.

Boublik T, Fried V, Hala E. 1984. The vapor pressure of pure substances: selected values of the temperature dependence of the vapor pressures of some pure substances in the normal- and low-pressure region. Vol.17. Amsterdam (NL): Elsevier.

Boyd TJ. 1994. Identification and quantification of mono-, di- and trihydroxybenzenes (phenols) at trace concentrations in seawater by aqueous acetylation and gas chromatographic-mass spectrometric analysis. J Chromatogr A 664:281-292.

Brandt K. 1986. Final report on the safety assessment of hydroquinone and pyrocatechol. J Am Coll Toxicol 5(3):123-165.

Brenes M, Romero C, Garcia A, Hidalgo FJ, Ruiz-Méndez. 2004. Phenolic compounds in olive oils intended for refining: formation of 4-Ethylphenol during olive paste storage. J Agric Food Chem 52:8177-8181.

Canada. 1999. *Canadian Environmental Protection Act, 1999 = Loi canadienne sur la protection de l'environnement, 1999*. Statutes of Canada = Statuts du Canada, Chapter 33. Act assented to September 14, 1999. Ottawa: Queen's Printer. Available at Canada Gazette (Part III) 22(3): chapter 33 http://canadagazette.gc.ca/partIII/1999/g3-02203.pdf (accessed August 3, 2007).

[Canada]. 2000. *Canadian Environmental Protection Act: Persistence and Bioaccumulation Regulations,* P.C. 2000-348, 23 March, 2000, SOR/2000-107, Canada Gazette. Part II, vol. 134, no. 7, p. 607−612. Ottawa: Queen's Printer. Available from: http://canadagazette.gc.ca/partII/2000/20000329/pdf/g2-13407.pdf

[Canada]. 2006. Dept. of the Environment, Dept. of Health. *Canadian Environmental Protection Act, 1999*: *Notice of intent to develop and implement measures to assess and manage the risks posed by certain substances to the health of Canadians and their environment*. Canada Gazette. Part I. Vol. 140, No. 49, p. 4109 – 4117. Ottawa: Queen's Printer. Available from: http://canadagazette.gc.ca/partI/2006/20061209/pdf/g1-14049.pdf

[Canada]. 2007a. *Canadian Environmental Protection Act, 1999. Notice with respect to certain substances on the Domestic Substances List (DSL).* Ottawa: Public Works and Government Services.Canada Gazette, Part I, Vol. 141, No.5. p. 165-177. Available from: http://www.ec.gc.ca/Ceparegistry/documents/notices/g1-14105_n2.pdf

[Canada]. 2007b. Department of the Environment, Department of Health. Substance profile for the challenge 1,2-benzenediol (catechol) CAS No. 120-80-9. Available from: http://www.ec.gc.ca/substances/ese/eng/challenge/batch1_120-80-9.cfm

[Canada]. 2007c. Challenge Questionnaire [voluntary data submitted by industry]. Gatineau (QC): Environment Canada, Existing Substances Division. Available upon request from: Existing Substances Division, Environment Canada, Ottawa, K1A 0H3.

[Canada]. 2007d. [Additional voluntary information on substance CAS No. 120-80-9 submitted by industry]. Gatineau (QC): Environment Canada, Existing Substances Division. Available upon request from: Existing Substances Division, Environment Canada, Ottawa, K1A 0H3.

[ChemCAN]. 2003. ChemCAN: level III. fugacity model of regional fate of chemicals. Version 6.00. Peterborough (ON): Canadian Environmental Modelling Centre, Trent University. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/CC600.html.

Chemicals Inspection and Testing Institute. 1992. Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology, Toxicology and Information Center. Report No.: ISBN 4-89074-101-1.

Ciranni R, Barale R, Ghelardini G, Loprieno N. 1988a. Benzene and the genotoxicity of its metabolites. II. The effect of the route of administration on the micronuclei and bone marrow depression in mouse bone marrow cells. Mutat Res 209(1-2):23-28.

Ciranni R, Barale R, Marrazzini A, Loprieno N. 1988b. Benzene and the genotoxicity of its metabolites. I. Transplacental activity in mouse fetuses and in their dams. Mutat Res 208(1):61-67.

Dean BJ. 1985. Recent findings on the genetic toxicology of benzene, toluene, xylenes and phenols. Mutat Res 154(3):153-181.

Deichmann WB, Keplinger ML. 1981. Phenols and Phenolic Compounds (Chapter 36). *In*: Patty's Industrial Hygiene and Toxicology. Eds. Clayton GD and Clayton FE. 3rd revised ed. Vol 2A. New York: John Wiley & Sons Inc.

[DERMWIN] Dermal Permeability Coefficient Program [Estimation Model]. 2000. Version 1.43. Washington (DC): U.S. Environmental Protection Agency. [cited 2008 May]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

do Ceu Silva M, Gaspar J, Silva ID, Leao D, Rueff J. 2003. Induction of chromosomal aberrations by phenolic compounds: possible role of reactive oxygen species. Mutat Res 540(1):29-42.

Environment Canada. 2007. Guidance for conducting ecological assessments under CEPA 1999: Technical guidance module - QSARs. science resource technical series. Gatineau (QC): Environment Canada , Existing Substances Division. Internal reviewed draft working document available on request.

[EPIWIN] Estimation Programs Interface for Microsoft Windows. 2004. Version 3.12. Washington (DC): U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm.

Fine PM, Cass GR, Simoneit BR. 2001. Chemical characterization of fine particle emissions from fireplace combustion of woods grown in the northeastern United States. Environ Sci Technol 35:2665-2675.

Fine PM, Cass GR, Simoneit BR. 2002. Chemical characterization of fine particle emissions from the fireplace combustion of woods grown in the southern United States. Environ Sci Technol 36:1442-1451.

Flickinger CW. 1976. The benzenediols: catechol, resorcinol and hydroquinone - a review of the industrial toxicology and current industrial exposure limits. Am Ind Hyg Assoc J 37(10):596-606.

Gad-El Karim MM, Sadagopa Ramanujam VM, Legator MS. 1986. Correlation between the induction of micronuclei in bone marrow by benzene exposure and the excretion of metabolites in urine of CD-1 mice. Toxicol Appl Pharmacol 85(3):464-477.

Gellin GA, Maibach HI, Misiaszek MH, Ring M. 1979. Detection of environmental depigmenting substances. Contact Dermatitis 5(4):201-213.

Glatt H, Gemperlein I, Setiabudi F, Platt KL, Oesch F. 1990. Expression of xenobiotic-metabolizing enzymes in propagatable cell cultures and induction of micronuclei by 13 compounds. Mutagenesis 5(3):241-249.

Glatt H, Padykula R, Berchtold GA, Ludewig G, Platt KL, Klein J, Oesch F. 1989. Multiple activation pathways of benzene leading to products with varying genotoxic characteristics. Environ Health Perspect 82:81-89.

Granger FS, Nelson JM. 1921. Oxidation and reduction of hydroquinone and quinine from the standpoint of electromotive force measurements. J Am Chem Soc 43(7):1401-1415.

Hagiwara A, Takesada Y, Tanaka H, Tamano S, Hirose M, Ito N, Shirai T. 2001. Dose-dependent induction of glandular stomach preneoplastic and neoplastic lesions in male F344 rats treated with catechol chronically. Toxicol Pathol 29(2):180-186.

Hansch CA, Leo A, Hoekman D. 1995. Exploring QSAR: Volume 2: Hydrophobic, electronic, and steric constants. Oxford (GB): Oxford University Press

Haworth S, Lawlor T, Mortelmans K, Speck W, Zeiger E. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ Mutagen 1(Suppl 5):1-142.

Health Canada. 2007. The Cosmetic Ingredient Hotlist. List of Prohibited and Restricted Cosmetic Ingredients. [cited 2007 October 3]. Available from http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/framework-int-cadre_e.pdf.

Health Canada. 1998. Exposure factors for assessing total daily intake of priority substances by the general population of Canada. Unpublished report. Ottawa (ON): Health Canada, Environmental Health Directorate.

Hirose M, Fukushima S, Tanaka H, Asakawa E, Takahashi S, Ito N. 1993. Carcinogenicity of catechol in F344 rats and B6C3F1 mice. Carcinogenesis 14(3):525-529.

Hirose M, Inoue T, Asamoto M, Tagawa Y, Ito N. 1986. Comparison of the effects of 13 phenolic compounds in induction of proliferative lesions of the forestomach and increase in the labelling indices of the glandular stomach and urinary bladder epithelium of Syrian golden hamsters. Carcinogenesis 7(8):1285-1289.

Hirose M, Wada S, Yamaguchi S, Masuda A, Okazaki S, Ito N. 1992. Reversibility of catechol-induced rat glandular stomach lesions. Cancer Res 52(4):787-790.

[HSDB] Hazardous Substances Databank [database on the Internet]. 2006. Catechol. Bethesda (MD): U.S Department of Health and Human Services, National Institutes of Health, National Library of Medicine, Toxicology Data Network. [cited 2006 Dec]. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

IARC. 1999. Catechol. Monographs on the evaluation of carcinogenic risk to humans. Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. IARC Monogr Eval Carcinog Risks Hum . 71(Part 2):433-451.

Kavlock RJ. 1990. Structure-activity relationships in the developmental toxicity of substituted phenols: in vivo effects 1. Teratology 41(1):43-59.

Kodak. 2007. Material safety data sheet: KODAK HC-110 Developer [Internet]. Rochester (NY): Kodak Canada Inc. [cited 2008 may 22]. Available from: http://www.kodak.com/eknec/PageQuerier.jhtml?pq-locale=en_CA&pq-path=4648

Kurata Y, Fukushima S, Hasegawa R, Hirose M, Shibata M, Shirai T, Ito N. 1990. Structure-activity relations in promotion of rat urinary bladder carcinogenesis by phenolic antioxidants. Jpn J Cancer Res 81(8):754-759.

Lee EW, Johnson JT, Garner CD. 1989. Inhibitory effect of benzene metabolites on nuclear DNA synthesis in bone marrow cells. J Toxicol Environ Health 26(3):277-291.

Lehman AJ, Fitzhugh OG, Nelson AA, Woodard G. 1951. The pharmacological evaluation of antioxidants. Adv Food Res 3:197-208.

Lide DR, editor. 2007. CRC Handbook of Chemistry and Physics. 87th Ed. Boca Raton (FL): Taylor and Francis. Boca Raton, FL.

Marrazzini A, Chelotti L, Barrai I, Loprieno N, Barfale R. 1994. In vivo genotoxic interactions among three phenolic benzene metabolites. Mutat Res 341:29-46.

Marshall MR, Jeongmok K, Cheng-I W. 2000. Enzymatic Browning in Fruits, Vegetables and Seafoods. Food and Agriculture Organization of the United Nations (FAO). [cited 2007 July 5]. Available from: http://www.fao.org/ag/ags/agsi/ENZYMEFINAL/Enzymatic%20Browning.html.

Martinez A, Urios A, Blanco M. 2000. Mutagenicity of 80 chemicals in Escherichia coli tester strains IC203, deficient in OxyR, and its oxyR(+) parent WP2 uvrA/pKM101: detection of 31 oxidative mutagens. Mutat Res 467(1):41-53.

Matsushima T, Hayashi M, Matsuoka A, Ishidate M, Miura KF, Shimizu H, Suzuki Y, Morimoto K, Ogura H, Mure K, Koshi K, Sofuni T. 1999. Validation study of the in vitro micronucleus test in a Chinese hamster lung cell line (CHL/IU). Mutagenesis 14(6):569-580.

McDonald TA, Holland NT, Skibola C, Duramad P, Smith MT. 2001. Hypothesis: phenol and hydroquinone derived mainly from diet and gastrointestinal flora activity are causal factors in leukemia. Leukemia 15:10-20.

Medeiros AM, Bird MG. 1997. Potential biomarkers of benzene exposure. J Toxicol Environ Health 51:519-539.

Morimoto K. 1983. Induction of sister chromatid exchanges and cell division delays in human lymphocytes by microsomal activation of benzene. Cancer Res 43(3):1330-1334.

Nakamura SI, Oda Y, Shimada T, Oki I, Sugimoto K. 1987. SOS-inducing activity of chemical carcinogens and mutagens in Salmonella typhimurium TA1535/pSK1002: examination with 151 chemicals. Mutat Res 192(4):239-246 [cited in IARC 1999].

Nazar MA, Rapson WH, Brook MA, May S, Tarhanen J. 1981. Mutagenic reaction products of aqueous chlorination of catechol. Mutat Res 89(1):45-55.

[NCASI] National Council for Air and Stream Improvement [Factsheet]. 2007. Draft Forest Products Industry Catechol Fact Sheet Revision 2.0 30/08/07 (unplublished).

NCI (National Chemical Inventories). 2007. Columbus (OH): Thomas Technology Solutions Inc.; American Chemical Society. Available from: http://www.cas.org/products/cd/nci/require.html

[NHW] Department of National Health and Welfare. 1990. Present patterns and trends in infant feeding in Canada. Ottawa (ON): Department of National Health and Welfare. 9 pp. Catalogue No. H39-199/1999E; ISBN 0-662-18397-5 [cited in Health Canada, 1998].

[NPRI] National Pollutant Release Inventory [database on the Internet]. 2006. Gatineau (QC): Environment Canada. Available from: http://www.ec.gc.ca/pdb/querysite/query_e.cfm.

Ohgaki H, Szentirmay Z, Take M, Sugimura T. 1989. Effects of 4-week treatment with gastric carcinogens and enhancing agents on proliferation of gastric mucosa cells in rats. Cancer Lett 46(2):117-122.

[PCKOCWIN] Organic Carbon Partition Coefficient Program for Windows. 2000. Version 1.66. Washington (DC): U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm.

Pellack-Walker P, Blumer JL. 1986. DNA damage in L5178YS cells following exposure to benzene metabolites. Mol Pharmacol 30(1):42-47.

[PhysProp] Interactive PhysProp Database [database on the Internet]. 2003. Syracuse (NY): Syracuse Research Corporation. [cited 2003 Mar] Available from: http://www.syrres.com/esc/physdemo.htm

[PMRA] Pest Management Regulatory Agency. 2007a. PMRA List of Formulants. Ottawa (ON): Health Canada, Pest Management Regulatory Agency. [cited July 10, 2007]. Available from: http://www.pmra-arla.gc.ca/english/pubs/reg-e.html.

[PMRA] Pest Management Regulatory Agency. 2007b. PMRA Product Label Database [database on the internet]. Available from: http://pr-rp.pmra-arla.gc.ca/portal/page?_pageid=34,17551&_dad=portal&_schema=PORTAL
.
[RIVM] Rijksinstituut voor Volksgezondheid en Milieu - Consumer Exposure (ConsExpo) Model version 4.1. 2006. The Netherlands: The National Institute for Public Health and the Environment (Rijksinstituut

voor Volksgezondheid en Milieu). Available from: http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp#tcm:13-42840

Roemer E, Stabbert R, Rustemeier K, Veltel DJ, Meisgen TJ, Reininghaus W, Carchman RA, Gaworski CL, Podraza KF. 2004. Chemical composition, cytotoxicity and mutagenicity of smoke from US commercial and reference cigarettes smoked under two sets of machine smoking conditions. Toxicology 195:31-52.

Serjeant EP, Dempsey B. 1979. Ionisation constants of organic acids in aqueous solution. In: IUPAC Chemical Data Series 23. New York (NY): Pergamon.

Shibata MA, Hirose M, Yamada M, Tatematsu M, Uwagawa S, Ito N. 1990a. Epithelial cell proliferation in rat forestomach and glandular stomach mucosa induced by catechol and analogous dihydroxybenzenes. Carcinogenesis 11(6):997-1000.

Shibata MA, Yamada M, Hirose M, Asakawa E, Tatematsu M, Ito N. 1990b. Early proliferative responses of forestomach and glandular stomach of rats treated with five different phenolic antioxidants. Carcinogenesis 11(3):425-429.

Singh J, Gupta K, Arora SK. 1994. Changes in the anti-nutritional factors of developing seeds and pod walls of fenugreek (*Trigonella foenum graecum* L.). Plant Foods Hum Nutr 46:77-84.

Sternitzke A, Legrum W, Netter KJ. 1992. Effects of phenolic smoke condensates and their components on hepatic drug metabolizing systems. Food Chem Toxicol 30(9):771-781.

Tanaka H, Hirose M, Hagiwara A, Imaida K, Shirai T, Ito N. 1995. Rat strain differences in catechol carcinogenicity to the stomach. Food Chem Toxicol 33(2):93-98.

[TOPKAT] Toxicity Prediction Program. 2004. Version 6.2. San Diego (CA): Accelrys Software Inc. Available from: http://www.accelrys.com/products/topkat/index.html.

[TRI] Toxic Release Inventory Program [Internet]. 2005. Washington (DC): US Environmental Protection Agency. Available from: http://www.epa.gov/tri/tridata/tri05/index.htm

Tsutsui T, Hayashi N, Maizumi H, Huff J, Barrett JC. 1997. Benzene-, catechol-, hydroquinone- and phenol-induced cell transformation, gene mutations, chromosome aberrations, aneuploidy, sister chromatid exchanges and unscheduled DNA synthesis in Syrian hamster embryo cells. Mutat Res 373(1):113-123.

[US EPA] United States Environmental Protection Agency. 2000. Catechol (Pyrocatechol) Hazard Summary. [cited 2006 October 26]. Available from: http://www.epa.gov/ttnatw01/hlthef/pyrocate.html.

Versar Inc. 1986. Standard scenarios for estimating exposure to chemical substances during use of consumer products. Volume II. Available from: United States Environmental Protection Agency (US EPA); Contract No. 68-02-3968.

Walles SA. 1992. Mechanisms of DNA damage induced in rat hepatocytes by quinones. Cancer Lett 63(1):47-52.

Winter R. 2005. A consumer's dictionary of cosmetic ingredients: complete information about the harmful and desirable ingredients found in cosmetics and cosmeceuticals. New York: Three Rivers Press. p. 433.

Yamazaki M, Moto M, Takizawa Y, Kashida Y, Imai T, Mitsumori K, Hirose M. 2005. Tumorigenic susceptibility of catechol on the gastric mucosa in rasH2 mice. J Toxicol Pathol 18:1-5.

Yoshida D, Fukuhara Y. 1983. Mutagenicity and co-mutagenicity of catechol on Salmonella. Mutat Res 120(1):7-11.

Appendix 1. Upper-bounding estimates of daily intake of 1,2-benzenediol by the general population in Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of 1,2-benzenediol 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					
Air[9]	1.4×10^{-9}		3.0×10^{-9}	2.4×10^{-9}	1.3×10^{-9}	1.2×10^{-9}	1.0×10^{-9}
Drinking water[10]	0.02	7.5×10^{-3}	8.5×10^{-3}	6.7×10^{-3}	3.8×10^{-3}	4.0×10^{-3}	4.2×10^{-3}
Food and beverages[11]		231	663	539	518	847	660
Soil[12]	7.0×10^{-11}		1.1×10^{-10}	3.7×10^{-11}	8.8×10^{-12}	7.4×10^{-12}	7.3×10^{-12}
Total intake	**0.02**	**231**	**663**	**539**	**518**	**847**	**660**

1 No data were identified on concentrations of 1,2-benzenediol 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 (Health Canada 1998).

3 For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of 1,2-benzenediol in seawater used to reconstitute formula was based on a sample collected from the Sweetwater Channel of San Diego Bay at an 11-m depth (Boyd 1994). No data on concentrations of 1,2-benzenediol in formula were identified for Canada. For non-formula-fed infants, approximately 50% 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 (Health Canada 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 (Health Canada 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 (Health Canada 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 (Health Canada 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 (Health Canada 1998).

9 Based on the 2005 release data for 1,2-benzenediol in the USA, obtained from the Toxic Release Inventory (TRI) (TRI 2005), it was assumed that 7% of the maximum estimated quantity of 1,2-benzenediol (1 000 kg) released from manufacturing facilities in Canada, was released directly into the atmosphere. Modelling using ChemCAN 6.0 (CEMC 2003), and selecting the Average for Canada region, indicated that the concentration of 1,2-benzenediol in ambient air would be approximately 5.03×10^{-9} µg/m^3. Ambient air was assumed to be representative of exposure to indoor air since there is no indication of additional sources of 1,2-benzenediol in indoor environments. No measured data were identified.

10 No Canadian-specific concentrations of 1,2-benzenediol in drinking water were identified. The maximum concentration value identified in the literature was from seawater in the Sweetwater Channel of San Diego Bay at 0.188 ± 0.030 µg/L measured at a depth of 11 m in 1992. The number of samples was not specified (Boyd 1994). Although this value was measured in seawater, which is not a potable water source, it was the only measured value identified and was greater (more conservative) than the modeled value from ChemCAN (5.26×10^{-5} µg/L).

11 Estimates of intake from food are based upon concentrations in foods that are selected to represent the twelve food groups addressed in calculating intake (Health Canada 1998):

Dairy products: detected but no values measured, no detection limit given (McDonald et al. 2001).

Fats: maximum concentration identified in refined olive oil 176.1 mg/kg of oil (Brenes et al. 2004).
Fruits and fruit products: detected but no values measured, no detection limit given (Marshall et al. 2000).
Vegetables: detected in potato but no measured values, no detection limit given (Marshall et al. 2000).
Cereal products: no data identified
Meat and poultry: use value calculated for catechol in phenolic fraction of smoke condensate in ham (50 mg total phenol/kg ham x 7.60% catechol = 3.8 mg/kg = 3800 µg/kg) (Sternitzke et al. 1992).
Fish: no data identified
Eggs: no data identified
Foods, primarily sugar: no data identified
Mixed dishes: no data identified
Nuts and seeds: maximum concentration of catechol measured in fenugreek seeds 510 mg/kg (Singh et al. 1994).
Beverages (soft drinks/alcohol/coffee/tea): Data was identified on the concentration of 1,2-benzenediol in coffee (roasted beans). The maximum concentration found in roasted coffee beans was 120 mg/kg. The number of samples and the location were not specified (McDonald et al. 2001). Used consumption of coffee (in g/day) from Health Canada (1998).

[11] Based on the 2005 release data of this substance in the USA, obtained from the Toxic Release Inventory (TRI 2005), it was assumed that 8% of the maximum estimated quantity of 1,2-benzenediol released from manufacturing facilities in Canada, was released directly into soil. Modelling using ChemCAN 6.0 (CEMC 2003), and selecting the Average for Canada region, indicated that the concentration of 1,2-benzenediol in soil would be approximately 1.74×10^{-5} ng/g solids. No measured data were identified.

Appendix 2. Upper-bounding estimates of exposure to 1,2-benzenediol from consumer products

Consumer product scenarios	Assumptions	Estimated exposure
Photographic developer[1]	**Inhalation (evaporation)** - Use ConsExpo model version 4.1, exposure to vapour, evaporation as mode of release (RIVM 2005). - Based on a reported maximum concentration of 0.66% in photographic developer (Canada 2007a). - Assume amount of product used is 700 g/event, a room volume of 9 m^3, exposure frequency of 12 events/year, exposure duration of 8 hr, and ventilation rate of 0.5 times/hr (Versar Inc. 1986). - Assume release area is 1 m^2, use Langmuir's method for mass transfer rate, molecular weight matrix of 18 g/mol. - Assume 100% uptake. - Assume adult exposed weighs 70.9 kg (Health Canada 1998).	Mean event concentration = 0.023 mg/m^3
Photographic developer[1]	**Dermal** - Assume a Kp value (permeability coefficient) of $1.7x10^{-3}$ cm/hr estimated using DERMWIN [2000] and comparable to a Kp submitted by industry (Canada 2007a). - Based on a reported maximum weight fraction of 0.66% in photographic developer (Canada 2007a) and a density of 1.24 g/cm^3 (Kodak 2007); the concentration of catechol in photo developer is $8.2x10^{-3}$ g/cm^3. - Assuming an exposed surface area of 20 cm^2. This is an estimated value based on consideration of an exposed surface area of 200 cm2 (Versar 1986) and public comment received that indicates only fingertips of one hand will likely be exposed during the development process. - Assuming a frequency of use of 12 events/yr (Versar Inc 1986). - Assuming a total exposure time of 15 minutes (0.25 hrs per session or 0.25 hrs/day). This is an estimated value based on consideration of an average darkroom session of 8 hrs (Versar Inc 1986) and public comment received indicating that actual contact time with the developer solution during the development process will be brief as the photo hobbyist would be expected to wipe his/her hands after immersion in the developer solution to reduce contamination of post-developer solutions with developer. This value would be an overestimate if the hobbyist was to follow recommended safe handling procedures for this product by wearing protective gloves and/or using tongs rather than fingertips to insert and remove the photographs from the developer solution. - Assume adult exposed weighs 70.9 kg (Health Canada 1998). - Assume one event per day Estimated dose per event = $\frac{Kp \times C \times ET \times SA}{BW}$ Estimated dose per event = $\frac{(1.7x10^{-3}\ cm/hr)(8.2x10^{-3}\ g/cm^3)(0.25\ hrs/day)(20\ cm^2)}{70.9\ kg}$ = $9.8x10^{-7}$ g/kg bw per day or 0.98 µg/kg-bw per day	Acute exposure = 0.98 µg/kg-bw per day

[1] Possible exposure to teenagers (12–19 years old), adults (20–59 years old) and seniors (60+). Scenario was completed using adults.

Appendix 3. Summary of health effects information for 1,2-benzenediol

Endpoint	Lowest effect levels[1] / Results
Acute toxicity	**Oral LD_{50}** = 300 mg/kg (rats, mice) (single dose, mortality observed in 14-day post-exposure period) (Lehman et al. 1951; Flickinger 1976). [Additional information: [Deichmann and Keplinger 1981]. **Dermal LD_{50}** = 800 mg/kg (rabbit) (Flickinger 1976) **Acute inhalation NOEL** = 1500 mg/m^3 (465 mg/kg/day) (rat - single 8-hr exposure, animals sacrificed 14 days post exposure) (Flickinger 1976)
Short-term repeated-dose toxicity 2–89 days	Dietary exposure to 0.8% (400 mg/kg/d) of 1,2-benzenediol for 4 or 8 weeks. Male and female F344 rats. Significant increase in proliferation of forestomach epithelium and increase in DNA synthesis in rat glandular stomach (both sexes) (Ohgaki et al. 1989; Shibata et al. 1990a and 1990b). Dermal application to unepilated skin of ear and wax-epilated skin of back) at 1-10% for 5 times/wk for 1 month. Black guinea pigs. 1% caused no irritation or depigmentation, 5% caused weak irritation and depigmentation, and 7–10% caused very strong irritation and depigmentation. (Bleehen et al. 1968) [cited in Brandt 1986]. [Additional information: Gellin et al. 1979].
Reproductive or developmental toxicity	Pregnant rats were given 1,2-benzenediol by oral intubation at 100, 333, 667 or 1000 mg/kg on gestation day 11. **NOEL** = 100 mg/kg. **LOEL** = 333 mg/kg (decrease in maternal weight). Higher doses, i.e., 667 or 1000 mg/kg caused maternal deaths, decreased implantation sites, decrease in litter size and teratogenic effects in offspring including abnormalities of hind limb, tail and urogenital system (Kavlock 1990).
Subchronic toxicity 90 days	1,2-Benzenediol given in drinking water as 0.1 or 4.0 g/L for 20 weeks. Mice. No adverse effects at 4 g/L (800 mg/kg/d). (Nakamura et al. 1987) [cited in Brandt (1986]. [Additional information: Hirose et al. 1986; Gellin et al. 1979].
Chronic toxicity / carcinogenicity	Dietary exposure to 1,2-benzenediol at 0.1, 0.2, 0.4, or 0.8% (33, 65, 141 or 318 mg/kg/day) for 34 or 104 weeks (2 years). Male F344/DuCrj rats (Hagiwara et al. 2001). **LOEL** = 33 mg/kg/day for 2 years. Slight hyperplasia observed in the glandular stomach in 33 mg/kg group after 34 weeks of exposure. In the 2-year study, benign proliferative glandular stomach lesions were seen in 33 or 65 mg/kg group. Submucosal hyperplasia or adenomas of glandular stomach found in 33 mg/kg and higher dose groups. Adenocarcinoma of glandular stomach found in 3/25 rats in 318 mg/kg dose group. Incidence of acinar cell adenoma (pancreas) increased significantly in rats in 318 mg/kg dose group.

	[Additional information: Yamazaki et al. 2005; Hirose et al. 1992; Hirose et al. 1993; Lehman et al. 1951].
Genotoxicity *In vivo*	Positive. Micronucleus test - Induction of micronuclei in bone marrow cells of pregnant mice which were given 1,2-benzenediol via gastric intubation (Ciranni et al. 1988a). - Induction of micronuclei in bone marrow cells of mice following oral or ip exposure. Oral exposure caused significant ($p < 0.05$) increase in micronuclei at 24 hr only with evident bone marrow depression, whereas, ip exposure caused significant ($p < 0.01$) bone marrow induction at 24 hr and bone marrow depression from 18 hr after treatment (Ciranni et al. 1988b). - Induction of micronuclei in bone marrow cells of mice (Marrazzini et al 1994). Negative. Micronucleus test - No induction of micronuclei in bone marrow cells of mice given 1,2-benzenediol via oral route (Gad-El Karim et al. 1986). No effect were seen on the DNA synthesis in the rat urinary bladder epithelium. (Kurata et al. 1990). F344 rats were given 1,2-benzenediol in diet for 36 weeks following treatment with a tumor initiator (BBN).
In vitro	Positive: Sister chromatid exchange was induced in mammalian cell cultures (Dean 1985; Morimoto 1983; Tsutsui et al. 1997). Negative (with or without metabolic activation). Ames assay *Salmonella typhimurium* (TA98, 100, 1535, 1537) (Nazar etal. 1981; Yoshida and Fukuhara 1983; Haworth et al. 1983; Brandt 1986; Glatt et al. 1990). Negative (with or without metabolic activation). *umu* test *S. typhimurium* (TA 1535/pSK1002). (Nakamura et al. 1987) [cited in IARC 1999]. Negative (with activation), positive (without activation). Reverse mutation assay (*E. coli*) (Martinez et al. 2000). Positive. Chromosomal aberration assay (V79 cells) (with or without metabolic activation) (Brandt 1986; do Ceu Silva et al. 2003). Weakly positive (with or without metabolic activation). Micronucleus test (Chinese hamster lung cells) (Matsushima et al. 1999). Positive. Induction of micronuclei and sister chromatid exchange in Chinese hamster V79 lung cells (Glatt et al. 1989). Positive. Single strand breaks in DNA. (Walles 1992). Inhibition of DNA synthesis. (Pellack-Walker and Blumer 1986). Positive/negative. DNA synthesis. (Lee et al. 1989).

Appendix 4. Overview of reported human health effects of 1,2-benzenediol

Human data is limited and confidence in the database is low. Dermal contact with 1,2-benzenediol in humans produced eczematous dermatitis and caused symptoms which resembled those induced by phenol, except that convulsions were more pronounced (Bingham et al. 2001; ACGIH 2005) [cited in HSDB 2006]. It is not clear whether these health effects were observed following acute or chronic exposure. Workers in Japan exposed to 1,2-benzenediol (2–72 ppm) and phenol for two years developed an occasional sore throat, cough and eye irritation and had a greater incidence of skin disorders than the control population. (ACGIH 2005) [cited in HSDB 2006]. In a few instances, development of acute dermatitis and allergic reaction to 1,2-benzenediol was reported in women following exposure through cosmetics and work, respectively (Bingham et al. 2001) [cited in HSDB 2006].