Screening Assessment Report

Ethylbenzene

Chemical Abstracts Service Registry Number 100-41-4

Environment and Climate Change Canada
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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act*, *1999* (CEPA), the Ministers of the Environment and Climate Change and of Health have conducted a screening assessment of benzene, ethyl- also known as ethylbenzene (Chemical Abstracts Service Registry Number 100-41-4). Ethylbenzene was identified as a priority for assessment on the basis of greatest potential for human exposure and also because it was classified by other agencies on the basis of carcinogenicity.

Ethylbenzene occurs naturally in the environment in crude oil and some natural gas streams and as a result of incomplete combustion of natural materials, making it a component of forest fire smoke. Ethylbenzene is a component of vehicle and aviation fuels as well as a component of mixed xylenes, which are used as solvents in various applications including in paints, stains, and automotive cleaners. Ethylbenzene is also synthetically produced and mainly used in the manufacture of styrene. Styrene is then used to manufacture various types of polymers such as polystyrene. Ethylbenzene is used in the oil and gas industry in a number of oilfield applications such as a non-emulsifier, as an acid additive and as a surfactant in hydraulic fracturing fluids. Minor applications of the synthetically produced ethylbenzene include use as a solvent and in the production of other chemicals such as diethylbenzene.

The most recent available information on ethylbenzene production in Canada is from 2003, during which a total of 906 000 tonnes of ethylbenzene was produced. Approximately 545 tonnes of ethylbenzene was imported into Canada in 2009, and approximately 51.6 tonnes were exported the same year. According to the results from a section 71 *Notice with Respect to Certain Substances on the Domestic Substances List (DSL)* conducted for the year 2000, approximately 1 700 000 tonnes of ethylbenzene at a concentration greater than 1% were manufactured in and imported into Canada during that year, mainly by companies in the petrochemical sector. Ethylbenzene has been internationally identified as a high production volume (HPV) chemical.

Ethylbenzene is included in the National Pollutant Release Inventory (NPRI), to which facilities manufacturing, processing, or otherwise using more than 10 tonnes per year of the substance must report their releases. In 2013, facilities across Canada reported to the NPRI on-site environmental releases totalling approximately 326 tonnes, transfers for disposal totalling 1346 tonnes, and transfers for off-site recycling totalling 3482 tonnes.

Ethylbenzene has been detected in ambient and indoor air, drinking water, surface water, groundwater, soil, and biota but not in sediment in Canada. Ethylbenzene has also been detected in various food items in the United States. Ethylbenzene has been identified in numerous consumer products such as liquid and aerosol coatings, caulking, lacquers, stains and varnishes, and building materials. Ethylbenzene has also been measured in the blood of individuals living in the United States.

Based on its physical and chemical properties and half-lives in surface water, groundwater, wastewater treatment systems, soil, and sediments, ethylbenzene is expected to degrade relatively rapidly in water, soil, and sediment under aerobic conditions, but degradation under anaerobic conditions is slower. Ethylbenzene will degrade in air with an estimated half-life of about 2 days. Ethylbenzene has a low potential to accumulate in organisms or biomagnify in trophic food chains.

Short-term effects to aquatic and terrestrial organisms range from 1.8 to 9.6 mg/L and 112 to 259 mg/kg dry weight, respectively. Predicted environmental concentrations (PECs) in air, surface water, sediment, and soil do not exceed concentrations associated with effects. While there is some uncertainty respecting the extent of risk in groundwater due to the fact that the concentration data is not recent and to the consideration of surrogate organisms, concern to the environment is not identified

Based on the information available, there is low risk of harm to organisms or the broader integrity of the environment from ethylbenzene. It is therefore concluded that ethylbenzene does not meet the criteria under paragraph 64(*a*) or (*b*) of CEPA as it 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.

The critical health effects associated with exposure to ethylbenzene are considered to be tumour induction and non-cancer systemic effects, primarily on the auditory system and on the liver, kidney and pituitary glands.

The general population of Canada is exposed to ethylbenzene from environmental media, food, and the use of consumer products. The margins between levels associated with effects in experimental animals and upper-bounding estimates of exposure from environmental media (including vehicle interior air), food, and from scenarios such as pumping gasoline or living near service stations are considered to be adequate to account for uncertainties in the health effects and exposure for both cancer and non-cancer effects. The margins between upper-bounding estimates of exposure from use of consumer products and critical effect levels are also considered adequate to account for uncertainties in the health effects and exposure databases.

Based on the information available, it is concluded that ethylbenzene does not meet the criteria under paragraph 64(*c*) of CEPA as it is not 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.

Based on the information available, it is concluded that ethylbenzene does not meet any of the criteria set out in section 64 of CEPA.

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1 Introduction

Section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999) requires the Minister of the Environment and Climate Change 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 to human health.

Ethylbenzene, CAS RN (Chemical Abstracts Service Registry Number) 100-41-4 was identified as a priority for assessment because it met the criteria for greatest potential for human exposure and had been classified by other agencies on the basis of carcinogenicity and it met the criteria for persistence, but did not meet the criteria for bioaccumulation potential or inherent toxicity to non-human organisms.

The 2006 version of the *State of the Science Report for a Screening Health Assessment* of ethylbenzene was posted on the Health Canada website on January 30th, 2006 (Health Canada 2006). The *State of the Science Report for a Screening Health Assessment* was externally reviewed by staff of Toxicology Advice and Consulting Limited and by V.C. Armstrong (consultant) for adequacy of data coverage and defensibility of the conclusions. The external comments were taken into consideration in drafting the *State of the Science Report*. The health screening assessment included here is an update of the *State of the Science Report* and supersedes that report.

Screening assessments focus on information critical to determining whether a substance presents, or may present, a risk to the environment or to human health, according to the criteria set out in section 64 of CEPA. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.[1]

This screening assessment includes consideration of information on chemical properties, hazards, uses, and exposure. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents and stakeholder research reports and from recent literature searches, up to June 2014 for ecological sections of the document and August 2014 for human health sections of the document. In addition, an industry

survey was conducted in 2001 through a *Canada Gazette* notice issued under the authority of section 71 of CEPA (Canada 2001). This survey collected data on the Canadian manufacture and import of substances selected for the *Domestic Substances List* (DSL) screening assessment pilot project (Environment Canada 2001). Key studies were critically evaluated; modelling results were used to reach conclusions. When available and relevant, information presented in hazard assessments from other jurisdictions was considered. This screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the conclusion.

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 of the substance). Decisions for risks to 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.

This screening assessment was prepared by staff in the Existing Substances programs at Health Canada and Environment and Climate Change Canada. As mentioned above, the *State of the Science Report* was also previously externally reviewed. The ecological component of this assessment has undergone external written scientific peer review/consultation and comments received were considered in the production of this report. Comments on the technical portions relevant to human health in the draft screening assessment were received from scientific experts, including Cathy Petito Boyce, Leslie Beyer and Chris Long from Gradient. Additionally, the draft of this screening assement was subject to a 60-day public comment period. Although external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

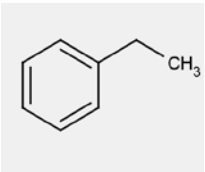
The critical information and considerations upon which this assessment is based are summarized below.

2 Substance Identity

Substance Name

Information relevant to the identity of ethylbenzene is presented in Table 2-1.

Table 2-1: Substance identity for ethylbenzene

Chemical Abstracts Service Registry Number (CAS RN)	**100-41-4**
DSL name	**Benzene, ethyl-**
National Chemical Inventories (NCI) names[a]	*Benzene, ethyl* (TSCA, AICS, SWISS, PICCS, ASIA-PAC, NZIoC) *Ethylbenzene* (EINECS, ENCS, ECL, PICCS)
Other names	*α-Methyltoluene; EB; Ethyl benzene; Ethylbenzol; NSC 406903; Phenylethane; UN 1175; UN 1175* (*DOT*) *Aethylbenzol; Ethylbenzeen; Etilbenzene; Etylobenzen*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Cyclic organic
Major chemical subclass	Monoaromatic hydrocarbon
Chemical formula	C_8H_{10}
Chemical structure	
SMILES[b]	CCc1ccccc1
Molecular mass	106.17 g/mol

[a] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia–Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); PICCS (Philippine Inventory of Chemicals and Chemical Substances); SWISS (Giftliste 1 and Inventory of Notified New Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[b] Simplified Molecular Input Line Entry System.

3 Physical and Chemical Properties

The experimental and modeled physical and chemical properties of ethylbenzene relevant to its environmental fate are summarized in Table 3-1.

Table 3-1: Physical and chemical properties of ethylbenzene

Property	Type	Value[a]	Temperature (°C)	Reference
Physical characteristics	–	colourless, flammable liquid	20	O'Neil et al. 2006
Melting point (°C)	Experimental	–94.9 to –95	–	Mabey et al. 1982; O'Neil et al. 2006; Lide and Haynes 2010
Melting point (°C)	Modelled	–46.94	–	MPBPWIN 2008
Boiling point (°C)	Experimental	136.2	–	Mabey et al. 1982; O'Neil et al. 2006; Lide and Haynes 2010
Boiling point (°C)	Modelled	148.30	–	MPBPWIN 2008
Density (kg/m^3)	Experimental	866	20	O'Neil et al. 2006;
Density (kg/m^3)	Experimental	863 (0.8626 g/mL)	25	Lide and Haynes 2010
Vapour pressure (Pa)	Experimental	930 (7 torr)	20	Mabey et al. 1982; O'Neil et al. 2006
Vapour pressure (Pa)	Experimental	1280 (9.6 mm Hg)	25	Daubert and Danner 1985
Vapour pressure (Pa)	Experimental	1270	25	ATSDR 2010
Vapour pressure (Pa)	Modelled	1010 (7.596 mm Hg)	25	MPBPWIN 2008
Henry's law constant (Pa·m^3/mol)	Experimental	675 (0.0066 atm·m^3/mol)	20	Mabey et al. 1982
Henry's law constant (Pa·m^3/mol)	Experimental	854 (0.00843 atm·m^3/mol)	25	Mackay et al. 1979
Henry's law constant	Experimental	798 (0.00788	25	Sanemesa et al. 1982

Property	Type	Value[a]	Temperature (°C)	Reference
(Pa·m^3/mol)		atm·m^3/mol)		
Henry's law constant (Pa·m^3/mol)	Modelled	800[b]	25	HENRYWIN 2008
Log K_{ow} (octanol–water partition coefficient) (dimensionless)	Experimental	3.13–3.15	25	Tewari et al. 1982; Kamlet et al. 1988
Log K_{ow} (octanol–water partition coefficient) (dimensionless)	Modelled	3.03	–	KOWWIN 2008
Log K_{oc} (organic carbon–water partition coefficient) (dimensionless)	Experimental	2.21[c] (soil OM[d])	–	Chiou et al. 1983; OECD 2005
Log K_{oc} (organic carbon–water partition coefficient) (dimensionless)	Experimental	3.04 (sediment OM)	–	Mabey et al. 1982
Log K_{oc} (organic carbon–water partition coefficient) (dimensionless)	Modelled	2.65–2.73	–	KOCWIN 2008
Water solubility (mg/L)	Experimental	140	15	Verschueren 1983
Water solubility (mg/L)	Experimental	152	20	Verschueren 1983
Water solubility (mg/L)	Experimental	111 (seawater)	25	Verschueren 1983
Water solubility (mg/L)	Experimental	169	25	Verschueren 1983
Water solubility (mg/L)	Modelled	52.19	25	WSKOWWIN 2008

[a] Values in parentheses represent the original ones as reported by the authors or as estimated by the models.

[b] Estimate was derived by means of measured vapour pressure of 1280 Pa and water solubility of 152 mg/L.

[c] Chiou et al. (1983) reported a log K_{om} of 1.98 for ethylbenzene. OECD (2005) derived a log K_{oc} from this value by dividing the K_{om} of 95 by 0.58 to obtain a K_{oc} of 163 and therefore a log K_{oc} of 2.21, citing this procedure to Howard (1989).

[d] OM = organic matter

4 Sources

Ethylbenzene is naturally present in crude oil and some natural gas streams and is a by-product of petroleum and coal refining (IPCS 1996; CAPP 2006; EURAR 2007; VCCEP 2007). It is also produced by incomplete combustion of natural materials, which makes it a component of forest fire or wood burning smoke (IPCS 1996; IARC 2000). Anthropogenic sources of ethylbenzene to the environment include releases from petrochemical plants, coal power plants, landfills, contaminated sites, and gasoline (e.g., evaporative emissions from vehicles and service stations; CONCAWE 1997). As a natural constituent of petroleum substances, ethylbenzene is often found in emissions from industrial activities related to the upstream oil and gas sector (glycol dehydrators, oil sands upgrading, and fugitive equipment leaks; Picard et al. 2002), the petroleum refining sector (manufacture, processing, use, storage, and disposal), and the combustion of vehicle and aviation fuels and coal (IPCS 1996; German Chemical Society 1997). Environmental tobacco smoke (ETS) has also been shown to be a source of ethylbenzene (Nelson et al. 1998; Daisey et al. 1994; Xie et al. 2003).

Globally, the majority of manufactured ethylbenzene is produced by alkylating benzene with ethylene in the liquid phase with an aluminum chloride catalyst or in the vapour phase with a synthetic zeolite or Lewis acid catalyst (IARC 2000; Berthiaume and Ring 2006). Other methods of producing ethylbenzene include preparation from acetophenone, benzene, chlorobenzene, ethylenebenzene, naphthenes, and xylene (VCCEP 2007; ATSDR 2010). Ethylbenzene is also produced from the mixed xylenes stream in the petroleum refining industry (Fishbein 1985; Coty et al. 1987).

According to Camford Information Services (2004), two companies were manufacturing ethylbenzene in 2003 and a total of 906 kt of ethylbenzene was produced in the same year. Camford Information Services (2004) estimated that quantities of ethylbenzene manufactured in Canada have remained stable at 985 kt/year since 1999. More recent information on the manufacturing of ethylbenzene in Canada was not identified; approximately 650 002 kg of ethylbenzene were imported into Canada in 2013, and approximately 257 880 kg were exported the same year (CIMT 2014). Import and export quantities for the years 2000-2013 (CIMT 2010, 2014) are listed in Table 4-1. Import and export quantities have been variable over the years. Ethylbenzene has been internationally identified as a high production volume (HPV) chemical (OECD 2005).

Table 4-1: Canadian import and export quantities of ethylbenzene from the years 2000 to 2013 (CIMT 2010, 2014)

Year	Import quantities (kg)	Export quantities (kg)
2013	650 002	257 880
2012	61 487	20 744 035
2011	126 358	480 517
2010	137 524	420 674
2009	545 147	90 290
2008	162 767	63 070
2007	133 315	No data
2006	116 588	No data
2005	161 656	35 474 963
2004	170 239	8 524 901
2003	130 640	18 167 873
2002	284 954	40 540
2001	164 154	30 289 662
2000	212 089	319 749

Based on information received in response to a notice issued under the authority of section 71 survey of CEPA (Canada 2001), approximately 1700 kilotonnes (kt) of ethylbenzene at a concentration higher than 1% were manufactured in or imported into Canada during the year 2000, mainly by companies in the petrochemical sector (Environment Canada 2004). In addition, several companies reported either importing or manufacturing ethylbenzene at a concentration lower than 1% and in a quantity meeting the reporting threshold of 10 000 kg (Environment Canada 2004). Both upstream petroleum producing facilities and downstream petroleum industries (refinery/petrochemical) responded as manufacturers of ethylbenzene. Because refineries are supplied by the extractors, it is possible that double counting had occurred; however, it was not possible to determine to what extent (Environment Canada 2004).

5 Uses

Globally, almost all (>99%) of the ethylbenzene commercially produced is used as an intermediate in the manufacture of styrene (IARC 2000; Berthiaume and Ring 2006). Styrene is subsequently used to produce various polymers including polystyrene, acrylonitrile–butadiene styrene, styrene–acrylonitrile, styrene–butadiene latexes, styrene–butadiene rubber, and unsaturated polyester resins (Berthiaume and Ring 2006; VCCEP 2007). These styrenic polymers are used in a variety of applications such as for food packaging, appliances, and sporting goods, in the automotive and electronic industry, and in building materials (VCCEP 2007). The remaining synthetically produced ethylbenzene is used as a solvent or occasionally in the production of diethylbenzene, acetophenone, ethyl

anthraquinone, cellulose acetate, ethylbenzene sulfonic acids, propylene oxide, and a-methylbenzyl alcohol (Berthiaume and Ring 2006; ATSDR 2010).

The ethylbenzene that is naturally occurring in crude oil is a component of automotive and aviation fuels including gasoline (VCCEP 2007; Dow 2009). Levels of ethylbenzene in gasoline range from <1 to 5.4% (IARC 2000; FLL 2008). It is also a constituent of refined products including mixed xylenes at a concentration of 15 to 20%. Mixed xylenes are used as a solvent in various applications including spray paints, primers, paint removers and thinners, wood stains, and varnishes, as well as household and automotive cleaners (IPCS 1996; VCCEP 2007; Dow 2009). Ethylbenzene may also be a component of asphalt and naphtha (VCCEP 2007).

Ethylbenzene has been reported to be used as a component in a number of hydraulic fracturing fluids used in the United States (US) for developing and unlocking natural gas supplies in shale and other unconventional oil and gas formations across the country (US House of Representatives 2011).

In Canada, the results of a notice issued under the authority of section 71 of CEPA for the year 2000 reported the use of ethylbenzene as a feedstock for petrochemicals and other organic chemicals, as a solvent in paints and coatings, and in other solvent applications (Environment Canada 2004). According to Camford Information Services (2004), the majority of ethylbenzene in Canada is manufactured for its use in the production of styrene monomer with small amounts being used as a solvent. Ethylbenzene is also used in the oil and gas industry in a number of oilfield applications such as a non-emulsifier, an acid additive and as a surfactant in hydraulic fracturing fluids (FracFocus 2013).

Ethylbenzene is not an active ingredient in pest control products registered for use in Canada but is a formulant and is currently present in approximately 130 pest control products with concentrations ranging from close to zero to 3.2% (e-mail from Pest Management and Regulatory Agency, Health Canada to Risk Management Bureau, Health Canada, 2014; unreferenced). Ethylbenzene was identified in manicure preparation products in Canada (CNS 2010). Ethylbenzene is not currently listed on Health Canada's List of Prohibited and Restricted Cosmetic Ingredients (or The Cosmetic Ingredient Hotlist), an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances, when present in a cosmetic, may contravene (a) the general prohibition found in section 16 of the *Food and Drugs Act* or (b) a provision of the *Cosmetic Regulations* (Health Canada 2011).

The use of ethylbenzene in insecticides, printing inks, glues, perfumes, and pharmaceuticals has also been reported (IARC 2000; EURAR 2007; VCCEP

2007). Reported uses in other jurisdictions fall into the categories of manufacture, solvents, fuels, and coatings (HSDB 2009; ATSDR 2010). The Danish Environmental Protection Agency (EPA) also detected ethylbenzene in candles (Eggert et al. 2002), incense (Eggert and Hansen 2004), adult toys (Nilsson et al. 2006), products made of exotic wood (Witterseh 2004), printed material (Hansen and Eggert 2003), Christmas decorations (Danish EPA 2003), and waders and dive gloves made with chloroprene (Nilsson and Pedersen 2004).

6 Releases to the Environment

Ethylbenzene is released from facilities that manufacture the substance or use it as a solvent or as an intermediate in the production of other chemicals. It is also a component of vehicle exhaust after combustion (Health Canada 2004). Recent ethylbenzene releases reported to the National Pollutant Release Inventory (NPRI) (Environment Canada 2013b) by Canadian industries are presented in Table 6-1. Most releases occur to air, with smaller releases to water and land. The NPRI database indicates the following methods are used for the disposal of ethylbenzene: incineration, underground injection, physical treatment, containment landfill, and biological treatment (Environment Canada 2009).

The number of companies reporting to the NPRI for the years 1994 to 2013 has increased from 73 in 1994 to 228 in 2013. In 2013, facilities from across Canada reported to the NPRI on-site environmental releases to air, water and land totalling approximately 326 tonnes, transfers for disposal totalling 1346 tonnes (on-site 900 and off-site 446 tonnes, respectively), and transfers for off-site recycling totalling 3482 tonnes (Table 6-1). The majority of the ethylbenzene released from upstream oil and gas (e.g glycol dehydrators) is not reported to the NPRI due to reporting thresholds for the conventional oil and gas extraction sector.

Table 6-1**: NPRI release and disposal data (tonnes) for ethylbenzene from 2004 to 2013 (Environment Canada 2013b)**

Year	On-site releases to air	On-site releases to water	On-site releases to land	Disposal on-site	Disposal off-site	Off-site recycling
2013	322	4.1	0.003	900	446	3482
2012	345	2.0	2.5	1241	434	1268
2011	328	2.4	0.011	1213	65	1215
2010	900	2.8	0.626	983	102	541
2009	838	4.1	0.125	1059	81	427
2008	940	3.8	0.069	966	121	1041

Year	On-site releases to air	On-site releases to water	On-site releases to land	Disposal on-site	Disposal off-site	Off-site recycling
2007	599	3.0	0.343	914	112	977
2006	778	4.4	0.121	879	378	1328
2005	815	4.7	0.386	26	388	1242
2004	911	2.6	0.837	15	146	1021

As a component of benzene, toluene, ethylbenzene, and xylenes (BTEX) emissions, ethylbenzene is also released from glycol dehydrators used to remove water from natural gas prior to entering the pipeline (Health Canada 2004). In 2007, the estimated population of glycol dehydrators was 5,195 units. These units emit approximately 1470 tonnes of benzene per year (CAPP 2009). In a study of BTEX wet gas out of the Western Sedimentary Basin, ethylbenzene concentrations from glycol dehydrators were found to be approximately 8.4% of the benzene values, resulting in estimated ethylbenzene emissions from glycol dehydrators of approximately 123.5 tonnes per year (Murray 2010). Based on 2007 NPRI data for Oil and Gas extraction release, of the 137 tonnes released to air, 8.5 tonnes were from conventional upstream oil and gas extraction and 128.5 tonnes originated from oil sands extraction. Therefore, a minimum of 115 tonnes of additional ethylbenzene are released from glycol dehydrators.

Ethylbenzene may be released to the aquatic compartment through industrial or household waste effluents contaminated with ethylbenzene-containing products. Releases of ethylbenzene to soil may result from landfilling of industrial or household waste (Health Canada 2004).

According to the U.S. Toxics Release Inventory, total on- and off-site disposal and industrial releases of approximately 2 kt and 1.5 kt were reported in 2008 and 2009, respectively (US EPA 2009).

Industrial and non-industrial emissions to air were estimated for ethylbenzene in the Great Lakes region of the United States and Ontario. In 2001, 42.5 kt of ethylbenzene were released according to the Inventory of Toxic Air Emissions (Great Lakes Commission 2004). These emissions were attributed as follows: 28% from light-duty gasoline vehicles, 12% from light-duty gasoline trucks (<2.7 tons [2.4 tonnes] gross vehicle weight), 12% from recreational vehicles, 8% from lawn and garden equipment, 7% from light-duty trucks (2.7–3.9 tons [2.4–3.5 tonnes] gross vehicle weight), 5% from pleasure craft, 5% from architectural surface coating, and 23% from other sources, where individual sectors contributed less than 5% of the total emissions. In 2002, the estimated ethylbenzene emissions to air were reported to be 32.4 kt (Great Lakes

Commission 2006). The Ontario-specific emissions from all sources were estimated to be 3.7 kt and 3.8 kt in 2001 and 2002, respectively (Great Lakes Commission 2004, 2006).

Ethylbenzene concentrations have also been measured in individual releases to Canadian air, surface water, and groundwater from major anthropogenic sources, including from the upstream oil and gas sector, the petroleum refining sector, coal power plants, landfills, deep injection wells, and former gasworks sites; however, no total annual release quantities have been calculated. No release data were located for soil and sediment in Canada, but contamination of these media from petroleum-related activities and disposal sites is likely.

7 Environmental Fate

Environmental fate analysis combines information on the chemical behaviour of the substance with the properties of the receiving environment. The objective of fate analysis is to determine the multimedia distribution of the substance after its release into the environment. This includes consideration of the persistence and bioaccumulation of the substance in the environment.

The results of Level III fugacity modelling (Table 7-1) (EQC 2003) show that ethylbenzene is expected to remain mostly in the medium to which it is released: if emitted only to air, 99.3% of the ethylbenzene remains in the air; if released only to water or soil, 91.2% and 92.1% remain in these media, respectively.

Table 7-1: Results of the Level III fugacity modelling (EQC 2003)

Substance released to:	Air (%)	Water (%)	Soil (%)	Sediment (%)
Air (100%)	99.3	0.3	0.4	0.0
Water (100%)	7.6	91.2	0.0	1.2
Soil (100%)	7.6	0.3	92.1	0.0

8 Persistence and Bioaccumulation Potential

8.1 Environmental Persistence

Ethylbenzene is expected to persist in air but not in water, soil, or sediment, based on degradation half-lives (Table 8-1). Ethylbenzene mobility in soil is relatively low (Swann et al. 1983). It can however leach to groundwater, based on its moderate log organic carbon–water partition coefficient (K_{oc}) of 2.21–3.04. Removal can also be by advection which is not affected by anaerobic conditions.

Degradation in groundwater may be slower than in surface water owing to anaerobic conditions (Wilson et al. 1986, 1988).

Table 8-1: Environmental half-lives and removal processes of ethylbenzene

Medium	Fate process	Degradation value	Degradation endpoint / units	Reference
Air	Photodegradation	7.0×10^{-12}	Rate coefficient / $cm^3 \cdot molecule^{-1} \cdot second^{-1}$	Calvert et al. 2002
Air	Photodegradation	0.5–2.7	Half-life / days	Singh et al. 1981; Ohta and Ohyama 1985; Atkinson 1989; Howard 1989
Surface water	Biodegradation	2	Half-life / days	Bouwer and McCarty 1984
Surface water	Volatilization	13 (winter) 20 (spring) 2.1 (summer)	Half-life / days	Wakeham et al. 1983
Groundwater	Biodegradation	4.4 (aerobic)		Aronson et al. 1999
Groundwater	Biodegradation	8–46 (anaerobic)	Half-life / days	Kappeler and Wuhrmann 1978; Aronson and Howard 1997
Wastewater treatment systems	Biodegradation	71–96	Activated sludge system, facultative lagoon and aerated lagoon, trickling filter	Hannah et al. 1986
Landfill aquifer material	Biodegradation	74	Anaerobic biodegradation / % after 40 weeks	Wilson et al. 1986, 1988
Soil	Biodegradation	3–10	Half-life / days	Howard 1991
River sediments	Mineralization	19	Half-life / days	Ludzak and Ettinger 1963

Ethylbenzene is probably subject to long-range transport, based on an intermediate characteristic travel distance of 700–2000 km, estimated by TaPL3 fugacity modelling (Beyer et al. 2000; TaPL3 2000). According to the model, up to 5% of the mass fraction of the substance can travel farther than three times this distance. This is supported by the detection of ethylbenzene in the tissues of fish in remote areas (Lockhart et al. 1989, 1992) and in Antarctic snow (Desideri et al. 1994).

8.2 Potential for Bioaccumulation

Experimental and modelled log K_{ow} values for ethylbenzene indicate that this chemical has low potential to bioaccumulate (see Table 3-1).

Ethylbenzene is not expected to bioaccumulate significantly in aquatic organisms, based on its highest reported bioaccumulation factor (log BAF) of 1.78 (BAF of 60), which is a calculated value (Park and Lee 1993), and its highest reported bioconcentration factor (log BCF) of 1.19 (BCF of 15.5), which was determined experimentally in goldfish, *Carassius auratus* (Ogata et al. 1984).

9 Potential to Cause Ecological Harm

9.1 Ecological Exposure Assessment

Ethylbenzene is expected to be found throughout Canada, given its persistence in air, its potential for long-range transport, and its numerous sources (including natural ones). Ethylbenzene concentrations measured in surface water, groundwater, soil, and biota in Canada and other relevant locations are summarized in Tables 7–10.

9.1.1 Air

The data and studies on ethylbenzene in ambient air in Canada are summarized in Appendix A. This appendix also contains data from five Canadian studies (Windsor, Regina, Halifax, Edmonton, and Ottawa) that measured ethylbenzene in outdoor air just outside of residences.

The National Air Pollution Surveillance (NAPS) program maintains an extensive database of ambient air concentrations monitored across Canada, including volatile organic compounds such as ethylbenzene. The NAPS program has been in existence since 1969 and currently has 368 monitoring sites in 255

communities located in every province and territory in Canada (Environment Canada 2009). Measured concentrations of ethylbenzene in air were compiled from 42 NAPS monitoring stations dating from 2005 to 2009 with a minimum of 90 samples per station for a total of 13 462 samples across Canada. However, only stations that measured ethylbenzene for all 5 years and therefore containing many samples were included in the compilation (31 stations). Mean 24-hour concentrations ranged from 0.103 to 1.28 µg/m^3 with corresponding 95th percentile 24-hour concentrations ranging from 0.206 to 4.40 µg/m^3. The maximum ethylbenzene concentration measured across all NAPS monitoring stations from 2005 to 2009 occurred within the Burnaby area of the Greater Vancouver Regional District, British Colombia with a value of 35.84 µg/m^3 (with a mean and 95% percentile value of 0.71 ± 3.07 and 1.06 µg/m^3, respectively, for that monitoring station between 2005 and 2009) (Environment Canada 2011a). An analysis of the NAPS data from 2010 to 2012 showed ethylbenzene concentrations fell within the same range as those reported from 2005-2009.

Published data on ethylbenzene in air are also available from a number of sites in Alberta (Alberta Environment 2005, 2010; FAP 2010). Fort Air Partnership (FAP), a multi-stakeholder group with members from industry, government, and the public, monitored eight permanent continuous ambient air quality monitoring stations in an area northeast of Edmonton in 2009. Five sites are in the immediate vicinity of petrochemical and oil and gas facilities, one is not in close proximity to an industry site, one is located in the city of Fort Saskatchewan, and one station is located in Elk Island National Park.

Ethylbenzene was measured on a semi-continuous (four samples per hour) basis at the Scotford 2 Air Quality Monitoring station which monitors local industrial emissions on air quality. Industries monitored at the station include: Shell Canada Energy Scotford Upgrader, Shell Canada Products Scotford Oil Refinery, Shell Chemicals Canada Ltd. Styrene and MEG Plant, and BA Energy Heatland Bitumen Upgrader. Ethylbenzene concentrations were measured below the limit of detection (detection limit of 0.08 µg/m^3) more than 87% of the time and a maximum value of 87.7 µg/m^3 was measured over the year.

Alberta Environment investigated odour complaints from February to May 2010 from the Three Creeks area, Alberta (Alberta Environment 2010). Air samples were collected at the sites by drawing air into 6 liter evacuated stainless steel canisters. Two types of sample collection methods were used: i) the sample was drawn in at a constant rate for a period of time or ii) the canister was used to grab instantaneous samples. The first method resulted in an integrated sample and the concentrations quantified using this method was an average for the sample time. Air was sampled for 1 hour at seven sites and a 10-minute sampling interval was used at the eighth site. A fifteen minute sampling interval was used

at the eighth site. One-hour average concentrations ranging from 0.29 to 4.03 µg/m^3 were reported.

Ethylbenzene was detected in air in a study of volatile organic compounds sampled every day for 24 hours at two sites commencing 12 September 2004 to 30 March 2006 in an area with more than 30 major industrial facilities in Fort Saskatchewan, Alberta (Mintz and McWhinney 2008). Maximum concentrations ranged from 2.14 to 6.49 µg/m^3. You et al. (2008) observed that oil and gas facilities contributed to airborne concentrations of ethylbenzene (maximum of 6.21 µg/m^3) in rural western Canada.

Atari and Luginaah (2009) monitored ethylbenzene using 37 samplers in Sarnia, Ontario, where more than 40% of Canadian chemicals are manufactured. A mean of 0.46 µg/m^3 and maximum of 1.06 µg/m^3 ethylbenzene in air was measured over 2 weeks in October 2005. Miller et al. (2009) carried out a similar study using the same sampling sites as Atari and Luginaah (2009) but focused on the spatial variability of ethylbenzene in Sarnia during October 2005. Results indicated that spatial variability is significant in Sarnia with high pollution occurring where there is a cluster of industrial and chemical facilities or in areas that are a short distance downwind of these facilities.

Ethylbenzene was monitored as part of an ambient air monitoring program at six stations over approximately 2 years (1 June 2003 to 31 March 2005) in the Clarkson Airshed (Oakville and Mississauga, Ontario) (OMOE 2006). The highest annual average concentration was 1.46 µg/m^3, and a maximum 24-hour value of 9.63 µg/m^3 was reported for the substance. Badjagbo et al. (2009) presented results for three urban locations in Canada (general mechanics garage, storm drain of an industrial waste landfill site, two-lane street in an industrial area) and found mean concentrations ranging from <8 µg/m^3 to 13 µg/m^3.

In 2007, 60% of the biggest landfills (permitted to receive 40 000 tonnes of waste per year) captured their landfill gas and 95% captured their leachate. Only 5% used no treatment, only natural attenuation, to treat their leachate (Conestoga Rovers and Associates 2009). Ethylbenzene is expected to be present in landfill gas, but assumed it will be destroyed at a 99% rate by combustion.

9.1.2 Surface Water

Canadian surface water data for ethylbenzene are limited to measurements made as part of the Municipal/Industrial Strategy for Abatement, a provincial monitoring program of the Ontario petroleum refining sector conducted from 1 December 1988 to 30 November 1989 (OMOE 1990, 1992). Concentrations of

ethylbenzene were measured in industrial process effluent streams, cooling and intake water, farmland leachate, and storm-water effluent (see Table 9-1).

The Sarnia–Lambton Environmental Association (SLEA), a voluntary environmental association co-operative of 20 industrial facilities in Lambton County, Ontario, has been monitoring air and water quality along the St. Clair River since 1988. Levels of ethylbenzene in the river have ranged from a maximum value of 285 µg/L in 1990 down to 1 µg/L in 1995 (SLEA 2007–2008). Maximum concentrations of ethylbenzene in the St. Clair River decreased in 2007 and 2008 with results of 0.15 and 0.09 µg/L, respectively.

Table 9-1: Concentrations (µg/L) of ethylbenzene in surface waters and effluents in Canada

Media	Details	Mean concentration[a] (µg/L)	Maximum concentration (µg/L)	Reference
Surface water	150 samples of intake water from an Esso Sarnia plant in Ontario	**0.71***	31.2	OMOE 1992
Surface water	St. Clair River		0.09–0.15	SLEA 2007–2008
Process effluent stream water	1095 samples of process effluent stream water at 7 refineries in Ontario	0.347	0.060–24.300	OMOE 1992
Once-through cooling water effluent stream	143 samples of once-through cooling water effluent stream at 4 refineries in Ontario	1.101	0.180–43.390	OMOE 1992
Landfarm leachate	25 samples of landfarm leachate at 2 refineries in Ontario	0.234	0.060–0.36	OMOE 1992
Storm-water effluent stream	150 samples of storm-water effluent stream at 3 refineries in Ontario	0.443	0.060–13.810	OMOE 1992

[a] Values in bold denoted with an asterisk (*) were selected as predicted environmental concentrations (PECs) for the calculation of risk quotients (RQs) later in this report.

9.1.3 Groundwater

Groundwater concentrations of ethylbenzene, often measured with other BTEX (benzene, toluene, ethylbenzene, xylenes) chemicals, are available for several contaminated sites in Ontario (Reinhard et al. 1984; Jackson et al. 1985; Cherry

1987; Barker 1988; Barker et al. 1989; Lesage et al. 1990a, 1990b, 1991, 1993, 1997; MacRitchie et al. 1994; OMOE 2005), as well as for natural background levels at other locations in Canada (Reinhard et al. 1984; Cherry 1987) (see Table 9-2).

Table 9-2: Concentrations (µg/L) of ethylbenzene in groundwater in Canada

Details	Concentration[a] (µg/L)	Reference
Background concentration, Canada	0.1	Reinhard et al. 1984
Background concentration, North Bay, Ontario	0.1	Cherry 1987
5 sites in the Niagara Falls area, Ontario	1–3	Lesage et al. 1997
From gasoline stations (on-site): Scarborough, Ontario Aurora, Ontario Flamborough County, Ontario (total of 56 groundwater samples)	 111 (median) 541 (median) 1 (median)	Lesage et al. 1997
Concentrations measured in contaminant plume in groundwater at the landfill in North Bay, Ontario	0.03–14	Cherry 1987
Westbay multilevel monitoring well (8 different depths from surface in 1988) installed close to industrial waste disposal wells that had been used for deep injection of liquid waste in order to compare these BTEX[b] concentrations with those at other sampling wells in shallow aquifers	5–133	Lesage et al. 1991
Leachate concentrations at: Landfill, Guelph, Ontario (1988 and 1989) and Landfill, Muskoka, Ontario (1989)	35–83	Lesage et al. 1993
At 5 of 6 southern Ontario landfills (Old Borden, North Bay, New Borden, Upper Ottawa Street, Woolwich, Tricil) (note: this is a summary report; values from this report are also presented below)	Maximum range 1–3320	Barker 1988
Landfill, North Bay, Ontario, measured 460 m off-site	58*****	Barker et al. 1989
Landfills: North Bay, Old Borden, New Borden, Upper Ottawa Street, Woolwich, and Tricil, Ontario	<1–3320	Barker et al. 1989; MacRitchie et al. 1994
Landfill, Elmira, Ontario (monitoring wells installed beside or into former waste disposal lagoons)	2000–120 000	Lesage et al. 1990b
Concentrations measured at different wells within the landfill in Woolwich, Ontario (1981), and the landfill in North Bay, Ontario (1981)	0.08–480	Reinhard et al. 1984

Details	Concentration[a] (µg/L)	Reference
Concentrations measured at different wells within the landfill in Gloucester, Ontario (1982)	0.6–38	Jackson et al. 1985
Landfill, Gloucester, Ontario (1988) In outwash aquifer: 3% frequency of identification of ethylbenzene in 37 samples collected	2	Lesage et al. 1990a
Detected in 1 of 5 monitoring wells	3	Lesage et al. 1990a
Various brownfield sites in Ottawa and Toronto, Ontario	1.09–1.5	OMOE 2005

[a] Values in bold denoted with an asterisk (*) were selected as predicted environmental concentrations (PECs) for the calculation of risk quotients (RQs) later in this report.
[b] BTEX = benzene, toluene, ethylbenzene, xylenes

9.1.4 Soil

No data were found for concentrations of ethylbenzene in Canadian sediment. Soil data were found for three parkland sites in Ontario (OMEE 1993), and more recent data are available for Ontario sites in the Brownfields Environmental Site Registry (OMOE 2005) (see Table 9-3). However, both of these data sources pertain to contaminated sites and do not provide details on soil sampling sites or methodology.

Table 9-3: Concentrations (µg/kg) of ethylbenzene in soil in Canada

Details	Concentration[a] (µg/kg)	Reference
Rural parkland in Ontario	**0.**46*****	OMEE 1993
Old urban parkland in Ontario	0.40	-
Various brownfield sites in Ottawa and Toronto, Ontario	40–50	OMOE 2005

[a]Values in bold denoted with an asterisk (*) were selected as predicted environmental concentrations (PECs) for the calculation of risk quotients (RQs) later in this report.

9.1.5 Biota

Data available for levels of ethylbenzene in biota are for fish and are presented in Table 9-4. Concentrations of ethylbenzene in Burbot and Whitefish muscle tissue were higher than in the Burbot liver tissue from the Northwest Territories, Canada. Mean levels ranged from 2.45 to 104 µg/kg in muscle tissue compared to 1.81 to 46.3 in Burbot liver tissue. (Lockhart et al. 1992).

Table 9-4: Concentrations (µg/kg wet weight) of ethylbenzene in biota in Canada

Details	Mean Concentration (µg/kg)	Maximum Concentration (µg/kg)	Reference
Burbot, *Lota lota*, muscle tissue from Mackenzie River, Northwest Territories	2.45–49.6	115	Lockhart et al. 1992
Burbot liver tissue from Mackenzie River, Northwest Territories	1.81–46.3	84	Lockhart et al. 1992
Whitefish, *Coregonus clupeaformis*, muscle tissue from Mackenzie River, Northwest Territories	7.46–104	273	Lockhart et al. 1992

9.2 Ecological Effects Assessment

Key toxicity studies for aquatic and soil organisms are presented in Tables 9-5 and 9-6. Acute and chronic endpoint values for fish, aquatic invertebrates, and algae fall in the range of 1–10 mg/L (Table 9-5), indicating that ethylbenzene is moderately toxic to aquatic species. Among the more sensitive species are the freshwater water flea, *Daphnia magna*, with the lowest 48-hour EC_{50} of 1.8 mg/L (Vigano 1993) and the estuarine mysid shrimp, *Mysidopsis bahia*, with a 96-hour LC_{50} of 2.6 mg/L (Masten et al. 1994). In addition, Niederlehner et al. (1998) reported a 7-day No-Observed-Effect Concentration (NOEC) and Lowest-Observed-Effect Concentration (LOEC) of 1.0 and 1.7 mg/L, respectively, for significantly reduced reproduction in the freshwater water flea, *Ceriodaphnia dubia*, while Tsai and Chen (2007) used a novel closed-system testing technique to determine a 48-hour EC_{50} of 1.34 mg/L for significantly inhibited growth in the freshwater green alga, *Pseudokirchneriella subcapitata*.

Table 9-5: Empirical data for toxicity of ethylbenzene to aquatic organisms

Classification	Test organism	Endpoint	Value (mg/L)[a]	Reference
Vertebrate	Atlantic silverside, *Menidia menidia*	96-hour LC_{50}[b] (mortality)	5.1	Masten et al. 1994
Vertebrate	Fathead minnow, *Pimephales promelas*	96-hour LC_{50} (mortality)	9.1	Brooke 1987
Vertebrate	Rainbow trout, *Oncorhynchus mykiss*[c]	96-hour LC_{50} (mortality)	4.2	Galassi et al. 1988
Vertebrate	Guppy, *Poecilia reticulata*	96-hour LC_{50} (mortality)	9.6	Galassi et al. 1988
Invertebrate	Water flea, *Ceriodaphnia dubia*	2-day LC_{50} (mortality)	3.2 (30 µM)	Niederlehner et al. 1998
Invertebrate	Water flea,	7-day LC_{50}	3.6	Niederlehner et

Classification	Test organism	Endpoint	Value (mg/L)[a]	Reference
	Ceriodaphnia dubia	(mortality)	(34 µM)	al. 1998
Invertebrate	Water flea, *Ceriodaphnia dubia*	7-day NOEC[d] (reproduction)	1.0 (9 µM)	Niederlehner et al. 1998
Invertebrate	Water flea, *Ceriodaphnia dubia*	7-day LOEC[e] (reproduction)	1.7 (16 µM)	Niederlehner et al. 1998
Invertebrate	Water flea, *Ceriodaphnia dubia*	7-day IC_{50}[f] (reproduction)	3.3 (31 µM)	Niederlehner et al. 1998
Invertebrate	Water flea, *Daphnia magna*	24-hour IC_{50} (immobilization)	2.2	Galassi et al. 1988
Invertebrate		48-hour EC_{50}[g] (immobilization)	2.9	MacLean and Doe 1989
Invertebrate	Water flea, *Daphnia magna*	48-hour EC_{50} (immobilization)	1.8–2.4	Vigano 1993
Invertebrate	Brine shrimp, *Artemia salina*	48-hour EC_{50} (immobilization)	9.2	MacLean and Doe 1989
Invertebrate	Mysid shrimp, *Mysidopsis bahia*	96-hour LC_{50} (mortality)	2.6	Masten et al. 1994
Plant	Diatom, *Skeletonema costatum*	96-hour EC_{50} (growth inhibition)	7.7	Masten et al. 1994
Plant	Green alga, *Pseudokirchneriella subcapitata*	48-hour EC_{50} (growth inhibition)	1.3	Tsai and Chen 2007
Plant	Green alga, *Selenastrum capricornutum*[h]	72-hour EC_{50} (growth inhibition)	4.6	Galassi et al. 1988
Plant	Green alga, *Selenastrum capricornutum*[h]	96-hour EC_{50} (growth inhibition)	3.6	Masten et al. 1994

[a] Values in parentheses represent the original ones as reported by the authors.
[b] LC_{50} = the concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[c] Formerly *Salmo gairdneri*.
[d] NOEC = the No-Observed-Effect Concentration is the highest concentration in a toxicity test not causing a statistically significant effect in comparison with the controls.
[e] LOEC = the Lowest-Observed-Effect Concentration is the lowest concentration in a toxicity test that caused a statistically significant effect in comparison with the controls.
[f] IC_{50} = the inhibiting concentration for a 50% effect. A point estimate of the concentration of a substance that causes a 50% reduction in a quantitative biological measurement, in this case, reproduction.
[g] EC_{50} = the concentration of a substance that is estimated to cause some effect (in this case, immobilization) to 50% of the test organisms.
[h] The name of this species was later changed to *Pseudokirchneriella subcapitata*.

Toxicity data for soil organisms are limited to two studies. One study by Neuhauser et al. (1985), which determined an LC_{50} of 47 µg/cm^2 for the earthworm, *Eisenia fetida*, used filter paper rather than actual soil as the substrate. A more recent study by ESG International, Inc. (2002), with soil concentrations recalculated by Komex International Ltd. (2002), reported acute toxicity values (14-day LC_{25}) for a soil invertebrate, the hexapod collembolan, *Onychiurus folsomi*, of 576 mg/kg dry weight (dw) for coarse sandy loam soil and

259 mg/kg dw for fine clay loam soil. ESG International, Inc. (2002) also reported a 14-day NOEC for the earthworm, *Eisenia andrei*, of 16 mg/kg dw and a 14-day LOEC of 112 mg/kg dw in coarse sandy loam soil. Komex International Ltd. (2002) recalculated the values from ESG International, Inc. (2002) and reported a NOEC of 16 mg/kg dw and a LOEC of 112 mg/kg dw for a 14-day exposure of the earthworm in fine clay loam soil (Table 9-6).

Table 9-6: Empirical data for toxicity of ethylbenzene to soil organisms

Organism	Endpoint	Concentration (mg/kg dw[a])	Reference
Collembola (springtail), *Onychiurus folsomi*	14-day LC_{25}[b] (mortality)	576 (coarse sandy loam)	ESG International, Inc. 2002
Earthworm, *Eisenia andrei*	14-day NOEC[c]	16 (coarse sandy loam, and fine clay loam)	ESG International, Inc. 2002; Komex International Ltd. 2002
Collembola (springtail), *Onychiurus folsomi*	14-day NOEC[c]	259 (fine clay loam)	Komex International Ltd. 2002
Earthworm, *Eisenia andrei*	14-day LOEC[d] (mortality)	112 (coarse sandy loam, and fine clay loam)	ESG International, Inc. 2002; Komex International Ltd. 2002
Northern wheatgrass, *Agropyron dasystachyum*	14-day IC_{25}[e] (reduction of root wet mass)	3 (coarse sandy loam)	ESG International, Inc. 2002
Northern wheatgrass, *Agropyron dasystachyum*	14-day IC_{25}[e] (reduction of root wet mass)	218 (fine clay loam)	Komex International Ltd. 2002
Alfalfa, *Medicago sativa*	14-day IC_{25} (reduction of root length)	462 (coarse sandy loam)	Komex International Ltd. 2002
Alfalfa, *Medicago sativa*	14-day IC_{25} (reduction of root length)	316 (fine clay loam)	Komex International Ltd. 2002

[a] dw = dry weight
[b] LC_{25} = the concentration of a substance that is estimated to be lethal to 25% of the test organisms.
[c] NOEC = the No-Observed-Effect Concentration is the highest concentration in a toxicity test not causing a statistically significant effect in comparison with the controls.
[d] LOEC = the Lowest-Observed-Effect Concentration is the lowest concentration in a toxicity test that caused a statistically significant effect in comparison with the controls.
[e] IC_{25} = the inhibiting concentration for a 25% effect. A point estimate of the concentration of a substance that causes a 25% reduction in a quantitative biological measurement, in this case, root growth.

In terms of soil toxicity to plants, the ESG and Komex studies reported the most sensitive endpoint for northern wheatgrass, *Agropyron dasystachyum*, to be

significantly reduced root wet mass, with 14-day IC_{25} values of 3 mg/kg dw for coarse sandy loam soil and 218 mg/kg dw for fine clay loam soil (ESG International, Inc. 2002; Komex International Ltd. 2002). The most sensitive endpoint for alfalfa, *Medicago sativa*, was a significant reduction in root length, with 14-day IC_{25} values of 462 and 316 mg/kg dw for coarse sandy loam and fine clay loam, respectively (Table 9-6).

No toxicity data were found for terrestrial wildlife; however, laboratory studies using rodents and other mammals have been conducted to evaluate the potential for impacts on human health, and relevant data from these studies are considered here in the context of terrestrial wildlife species. The results indicate that chronic inhalation exposure to ethylbenzene may be associated with organ damage, reproductive and developmental effects, and possible carcinogenicity in mammals (see Human Health Effects section). The study endpoint value considered most relevant to potential effects in terrestrial wildlife is a LOEC of 326 mg/m^3 (75 ppm) reported for increased severity of nephropathy in female rats exposed to ethylbenzene for 104 weeks (6 hours/day, 5 days/week) (NTP 1999).

9.3 Characterization of Ecological Risk

The approach taken in this ecological screening assessment is to examine various supporting information and develop conclusions based on a weight of evidence approach as required under CEPA. Particular consideration has been given to risk quotient analyses, as well as persistence, bioaccumulation, and trends in ambient concentrations.

Risk Quotient Analysis

Risk quotient (RQ) analyses, integrating known or potential exposures with known or potential adverse ecological effects, were performed for each relevant compartment. This involved first selecting a Critical Toxicity Value (CTV) based on the most sensitive species of the compartment. A Predicted No-Effect Concentration (PNEC) was then derived from the CTV by applying an assessment factor (AF) to account for the following sources of uncertainty: (1) inter- and intraspecies variations in sensitivity, (2) extrapolation of results from laboratory to field, and (3) the use of short-term studies to model long-term exposure. For each medium, a Predicted Exposure Concentration (PEC) was selected for conservative exposure scenarios based on reasonable worst-case situations. PECs, CTVs, AFs, PNECs, and resulting RQs for each medium are presented in Table 9-7. A RQ value of greater than 1 suggests the possibility of adverse effects.

Table 9-7: Values used to calculate risk quotients (RQs) for all media

Medium/ exposure scenario	Organism	Endpoint	CTV	Reference	AF	PNEC	PEC[a]	RQ
Air	Rat	104-week LOEC	326 mg/ m^3	NTP 1999	100	3.26 mg/m^3	4.40 $\mu g/m^3$	0.001
Surface water	*C. dubia*	7-d LOEC	1.7 mg/L	Niederlehner et al. 1998	10	0.17 mg/L	0.000 71 mg/L	0.004
Ground-water	*C. dubia*	7-d LOEC	1.7 mg/L	Niederlehner et al. 1998	100	0.017 mg/L	0.058 mg/L	3.4
Sediment (pore water)	*C. dubia*	7-d LOEC	1.7 mg/L	Niederlehner et al. 1998	100	0.017 mg/L	0.0058 mg/L	0.34
Soil (pore water)	*C. dubia*	7-d LOEC	1.7 mg/L	Niederlehner et al. 1998	100	0.017 mg/L	0.000 14 mg/L	0.008
Soil	Northern wheatgrass	14-day IC_{25}	3 mg/k g dw	ESG International, Inc. 2002; Komex International Ltd. 2002	100	0.03 mg/kg	0.000 46 mg/kg	0.02

[a] PEC selection is explained in the text with reference to Appendix A and Tables 7–9.

The first scenario was developed for exposure of terrestrial wildlife to ethylbenzene in air. Given the lack of toxicity data for terrestrial wildlife, data for laboratory mammals were considered in choosing the CTV. The study endpoint value considered most relevant to potential effects in terrestrial wildlife is a LOEC of 326 mg/m^3 (75 ppm) reported for increased severity of nephropathy in female rats exposed for 104 weeks (6 hours/day, 5 days/week) (NTP 1999). A conservative AF of 100 was applied to this chronic endpoint to account for species variability and the extrapolation from laboratory to field conditions. The resulting $PNEC_{air}$ is 3.26 mg/m^3.

A 95th percentile ambient air concentration of 4.40 $\mu g/m^3$ was selected as the worst-case predicted environmental concentration (PEC) (Environment Canada 2011a, Appendix A). This site is located in Montreal, Québec. Therefore, the conservative RQ for exposure of terrestrial wildlife to ethylbenzene in air is

RQ_{Air1} = PEC / PNEC = 4.40 $\mu g/m^3$ / 3260 $\mu g/m^3$ = 0.001.

For the aquatic compartment, exposure scenarios were analyzed for both surface water and groundwater. The lowest chronic effect value, a 7-day LOEC of 1.7 mg/L for significantly reduced reproduction in *Ceriodaphnia dubia* (Niederlehner

et al. 1998), was selected as the CTV for both surface water and groundwater assuming comparative sensitivity between surface water and groundwater invertebrates to ethylbenzene. Given the comparatively rich empirical database for toxicity to surface water species (Table 9-5), an AF of 10 was applied to the CTV to yield a PNEC value of 0.17 mg/L. In the absence of empirical data for groundwater organisms, a larger AF of 100 was used and the resulting PNEC for groundwater is therefore 0.017 mg/L.

For the surface water scenario, Canadian data are mostly limited to measurements made as part of a provincial monitoring program of the Ontario petroleum refining sector in 1988–1989 (OMOE 1992). The maximum ethylbenzene concentration found in intake water (which would correspond to surface water before use in any chemical process) is reported to be 31.2 µg/L for a station outside the Esso Sarnia plant. The PEC was selected as this site's average concentration (0.71 µg/L) based on 150 measurements (see Table 9-1). The RQ for surface water can be calculated as follows:

$RQ_{\text{Surface Water}}$ = PEC / PNEC = 0.000 71 mg/L / 0.17 mg/L = 0.004.

For the groundwater exposure scenario, the PEC was selected as 58 µg/L (0.058 mg/L), the highest dissolved concentration of ethylbenzene measured in groundwater near a landfill in North Bay, Ontario (Barker et al. 1989). Higher concentrations have been reported (Table 9-2), but this study was chosen for its good quality in terms of experimental design of monitoring and sampling. As opposed to other monitoring reports, Barker et al. (1989) clearly outlined the geological and hydrological situation of the site and the different wells and described the sampling site selection for measured concentrations of ethylbenzene in groundwater. The selected value, 58 µg/L, corresponds to the maximum concentration found in an off-site sampling well at a distance of approximately 460 m downstream from the landfill (Barker et al. 1989). Although higher ethylbenzene concentrations were identified closer to the landfill, Barker et al. (1989) demonstrated clearly that with increasing distance from the main source, the concentrations decrease rapidly. At a distance of 620 m downstream from the groundwater flow, ethylbenzene could not be detected at one well and was measured at 2.1 µg/L at another well. The authors assumed that this large decrease in concentrations was due to microbial degradation. According to provincial regulations (e.g., the Hazardous Waste Regulation of the British Columbia *Environmental Management Act*), a distance of 300 m between hazardous waste sites and landfill sites and the closest surface water body must be respected (Government of British Columbia 1988). Assuming that the sensitivities of groundwater invertebrates are similar to those inhabiting surface waters, the RQ for groundwater can be calculated as follows:

$RQ_{Groundwater}$ = PEC / PNEC = 0.058 mg/L / 0.017 mg/L = 3.4.

For sediment exposure (to determine a PEC for sediment pore water concentrations), a scenario was developed in which ethylbenzene in groundwater discharges into a surface water body, such as a river or creek, or into a wetland. Given its properties (moderate log K_{oc} of 2.65–3.04 and water solubility of 111–169 mg/L), ethylbenzene would not adsorb significantly to soil particles but instead would partition into the pore water of river sediments and possibly present a risk to benthic organisms. For this scenario, the concentration of ethylbenzene in sediment pore water is estimated to be comparable with an ethylbenzene concentration found in groundwater at a distance of 460 m from the main cell of the landfill in North Bay (Barker et al. 1989). At the North Bay landfill, the groundwater flow actually crosses a sandy aquifer containing springs and wetlands before discharging first into the Chippewa Creek about 800 m from the landfill site and then into other rivers downstream (Barker et al. 1989). Therefore, the $PEC_{pore\ water}$ for sediments was derived using the groundwater concentration (0.058 mg/L, Barker et al. 1989) and an application factor $(AF)^2$ of 10 to account for the uncertainty in estimating the $PEC_{pore\ water}$ based on a measured groundwater concentration.

In the absence of suitable sediment toxicity data, the CTV selected for sediments is the same as the CTV for the aquatic scenario (i.e., 7-d LOEC of 1.7 mg/L for *Ceriodaphnia dubia*), when *C. dubia* is used as a surrogate for benthic organisms. A PNEC of 0.017 mg/L is then obtained by applying an AF of 100. Thus,the RQ for sediment is

$RQ_{Sediment} = PEC_{pore\ water} / PNEC_{benthic\ invertebrate}$

$= 0.0058\ mg/L / 0.017\ mg/L = 0.34,$

where $PEC_{pore\ water} = PEC_{groundwater} / AF$.

For the soil compartment, two different scenarios were analyzed because of the limited exposure data available. The highest soil concentration published for a Canadian site other than a brownfield or other urban site (see Table 9-3) is 0.00046 mg/kg dw, from rural parkland in Ontario (OMEE 1993). No details of the sampling and analytical methods could be located. In the absence of more

reliable or more recent data for non-urban soil concentrations, for the first exposure scenario, a soil PEC was developed from this bulk soil PEC, based on the equilibrium partitioning of pore water and soil carbon (DiToro et al. 1991). More specifically, the $PEC_{pore\ water}$ for soil was calculated with the following equation, which is based on an equation originally developed for sediment (DiToro et al. 1991):

$PEC_{soil\ pore\ water}$ (mg/L) = $PEC_{bulk\ soil}$ (mg/L) / [$K_{oc\text{-}soil}$ (L/kg) × f_{oc} (no units)],

where

$PEC_{bulk\ soil}$ = 0.00046 mg/kg dw soil in rural parkland (OMEE 1993)
$K_{oc\text{-}soil}$ = partition coefficient for soil (L/kg) = 163 (Chiou et al. 1983; OECD 2005)
f_{oc} = organic carbon content (default value for soil is 2% = 0.02)

Therefore:

$PEC_{soil\ pore\ water}$ = 0.00046 mg/kg / (163 L/kg × 0.02) = 0.000 14 mg/L.

For this scenario, the CTV for aquatic invertebrates (7-d LOEC of 1.7 mg/L for *C. dubia*) was selected as representative of a CTV for soil invertebrates exposed to pore water. Dividing the CTV by an AF of 100 results in a $PNEC_{soil\ invertebrates}$ of 0.017 mg/L. The RQ is calculated as follows:

$RQ_{soil\ pore\ water}$ = $PEC_{soil\ pore\ water}$ / $PNEC_{soil\ invertebrates}$

= 0.00014 mg/L / 0.017 mg/L = 0.008.

For comparison, in a second scenario, a RQ_{soil} was derived directly from the $PEC_{bulk\ soil}$ of 0.00046 mg/kg dw from soil in rural parkland (OMEE 1993) and a CTV based on the northern wheatgrass, *Agropyron dasystachyum*, 14-day IC_{25} value of 3 mg/kg dw for coarse sandy loam soil (ESG International, Inc. 2002; Komex International Ltd. 2002). Applying an AF of 100 to the CTV results in a PNEC of 0.03 mg/kg dw.

RQ_{soil} = $PEC_{bulk\ soil}$ / $PNEC_{plant}$ = 0.00046 mg/kg / 0.03 mg/kg = 0.02.

9.3.1 Consideration of Lines of Evidence and Conclusion

The approach taken in this ecological screening assessment was to examine various supporting information and develop conclusions based on a weight-of-

evidence approach, using precaution as required under CEPA. Lines of evidence considered include results from a risk quotient analysis, as well as information on persistence, bioaccumulation, ecotoxicity, sources, and fate of the substance.

Ethylbenzene meets the *Persistence and Bioaccumulation Regulations* (Canada 2000) criteria for persistence in air but does not meet the criteria for water, sediment, and soil. Ethylbenzene does not meet the bioaccumulation criteria as specified in the *Persistence and Bioaccumulation Regulations*. The available toxicity data indicate that ethylbenzene is moderately toxic to aquatic and terrestrial species.

Ethylbenzene has many possible sources of release throughout Canada, mainly to air but also to other compartments, especially near disposal sites, and it is expected to be found in all media. Calculated RQs for air, surface water, sediment, and soil indicate that ethylbenzene concentrations in these compartments probably do not exceed concentrations associated with effects, even when conservative scenarios and assumptions are used. The RQ obtained for groundwater, however, exceeded 1 (a value of 3.4), which suggests some potential risk to organisms living in groundwater near landfills. However, there is high uncertainty relating to the lack of data for effects on groundwater organisms, which required use of an additional application factor.

The manufacture of ethylbenzene in Canada has remained relatively stable since 1999. Ethylbenzene is a high production volume (HPV) chemical. Reported industrial releases of ethylbenzene appear to have slightly increased in recent years with the number of reporting companies (mainly from the petrochemical industry). Other releases of ethylbenzene, especially as a product of fuel combustion, may be increasing as well, with increasing population and demand for energy. However, several regulations made under CEPA directly or indirectly limit hydrocarbon emissions from on-road and off-road vehicles as well as from the refuelling of on-road vehicles. These include, but are not limited to the *Gasoline and Gasoline Blend Dispensing Flow Rate Regulations, the Heavy-duty Vehicle and Engine Greenhouse Gas Emission Regulations*, the *On-Road Vehicle and Engine Emission Regulations* and the *Passenger Automobile and Light Truck Greenhouse Gas Emission Regulations*. Actual quantification of Canadian releases and exposure concentrations for this substance at this time is limited.

Based on the information available, there is low risk of harm to organisms or the broader integrity of the environment from this substance. It is therefore concluded that ethylbenzene does not meet the criteria under paragraph 64(*a*) or (*b*) of CEPA as it 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.

9.3.2 Uncertainties in Evaluation of Ecological Risk

Uncertainties associated with the ecological screening assessment of ethylbenzene are discussed below.

A range of experimental values was available for certain physical/chemical properties. Although experimental data were used as input to models, some uncertainties are introduced in the resulting model output.

There were limited data available for ethylbenzene exposure concentrations in surface water, soil, and sediments. PECs were therefore based on older or extrapolated data, usually from contaminated sites or related sites representing worst-case exposure scenarios in air, water, sediment, and soil.

Many uncertainties are associated with the PNEC determinations. Toxicity data for aquatic organisms were readily available; however, for effects on soil organisms and terrestrial plants exposed to ethylbenzene in soil, only one recent study was found to be acceptable. No acceptable data were found for sediment or groundwater organisms exposed to ethylbenzene.

10 Potential to Cause Harm to Human Health

10.1 Exposure Assessment

Exposure to ethylbenzene through various environmental media has been well documented (HSDB 1983; VCCEP 2007; ATSDR 2010). According to results from Level III fugacity modelling (Table 7-1), ethylbenzene is expected to remain mostly in the medium to which it is released. Given that air is the predominant medium of release based on results from NPRI (Table 6-1), inhalation is expected to be the predominant route of human exposure. Data pertaining to concentrations of ethylbenzene in ambient air, indoor air, drinking water, food, and consumer products, identified for Canada and elsewhere, are presented in this section. Although numerous studies were identified, only those deemed most relevant for assessing ethylbenzene exposure for the general population of Canada are summarized.

10.1.1 Ambient Air

Appendix A lists the various Canadian studies that have measured ethylbenzene in outdoor air.

The National Air Pollution Surveillance (NAPS) program referred to in the Ecological Exposure Assessment Section was used to estimate human exposures to ethylbenzene in ambient air. Measured concentrations of ethylbenzene in air are available for 14 commercial, 13 residential, 2 industrial and 2 undeveloped rural NAPS monitoring stations in Canada dating from 2005 to 2009. For this screening assessment, commercial, residential and industrial monitoring stations are considered urban areas and undeveloped rural areas are considered rural. Among the rural and urban monitoring locations, for years 2005 to 2009, the mean 24-hour concentrations of ethylbenzene ranged from 0.199 to 1.08 µg/m^3 and from 0.103 to 1.28 µg/m^3, respectively. The 95th percentile 24-hour concentrations ranged from 0.586 to 2.54 µg/m^3 for rural locations and from 0.206 to 4.40 µg/m^3 for urban locations. The maximum ethylbenzene 24-hour concentration measured across all NAPS monitoring stations from 2005 to 2009 occurred within the Burnaby area of the Greater Vancouver Regional District, British Columbia; with a value of 35.84 µg/m^3. During this same time period, the mean± standard deviation and 95th percentile values were 0.71 ± 3.07 µg/m^3 and 1.06 µg/m^3, respectively (Environment Canada 2011a). An analysis of the NAPS data from 2010 to 2012 showed ethylbenzene concentrations fell within the same range as those reported from 2005-2009.

Five Canadian studies measured ethylbenzene in outdoor air in the immediate area of residential homes (Zhu 2005; Health Canada 2010a,b; Health Canada 2012; Health Canada 2013) and the results are presented in Appendix B (Table B1). Measurements took place in Windsor, Ontario (Health Canada 2010a), Regina, Saskatchewan (Health Canada 2010b), Halifax, Nova Scotia (Health Canada 2012), Edomonton, Alberta (Health Canada 2013), and Ottawa, Ontario (Zhu 2005). The maximum concentration identified from all five studies was 146.5 µg/m^3 in Edmonton (Health Canada 2013), with mean concentrations across studies ranging from 0.13 to 1.14 µg/m^3, and 95th percentile values across studies ranging from 0.3 to 2.0 µg/m^3.

Individuals living near the vicinity of an oil and gas facility or a manufacturing facility that releases ethylbenzene into the air may be exposed to higher concentrations of ethylbenzene in outdoor air. In the Ecological Exposure Assessment Section on air, the results of several studies that measured ethylbenzene in the air near petrochemical and oil and gas facilities, and

industrial sites in Canada were described. Mean concentrations of ethylbenzene in the air near these industrial sites ranged from 0.054-13 µg/m^3 and maximum ethylbenzene concentrations ranged from 0.93 to 87.7 µg/m^3 (Badjagbo et al. 2009; FAP 2010; Alberta Environment 2010; Mintz and McWhinney 2008; You et al. 2008; Atari and Luginaah 2009; Miller et al. 2009). The maximum concentration of 87.7 µg/m^3 was measured in Alberta however 87% of the samples measured were below the limit of detection of 0.08 µg/m^3 (FAP 2010); this measurement was not considered representative of a typical high end concentration and was not used to estimate exposure. The University of British Columbia (UBC) conducted a human health impact assessment on air emissions from the Chevron North Burnaby Refinery as a result of concerns from residents living near the refinery (Kennedy et al. 2002). The maximum concentration of ethylbenzene measured in the area adjacent to the tank farm was 5.5 µg/m^3, and the mean value was 1.82 µg/m^3. This maximum concentration is lower than the maximum concentration detected in the NAPS data and is similar to the highest 95th percentile value measured in the same data set.

The highest 95th percentile value of 4.40 µg/m^3 from the NAPS 2005-2009 data is considered upper-bounding representing long-term inhalation exposure for both rural and urban populations as well as populations living near a point source; this value was used to estimate the upper-bounding daily intake of ethylbenzene by the general population from outdoor air (Appendix D, Table D1).

10.1.2 Indoor Air

Empirical data on ethylbenzene levels in indoor air were identified in the literature and are presented in this section. The presence of ethylbenzene in indoor air may be attributed to various sources including smoking, vehicle exhaust and fuel vapour intrusion from attached garages, use of building materials, and consumer products (Wallace et al. 1987; Batterman et al. 2007; Héroux et al. 2008). Although data on emissions of ethylbenzene from attached garages, smoking, building materials and electronic products are presented in this section, emissions from these uses are considered to be captured by the empirical indoor air measurements of ethylbenzene. Information on exposures while using certain consumer products is presented in the Consumer Products section.

Canadian data on concentrations of ethylbenzene in residential indoor air have been identified and reviewed. Results and technical details from the various studies are presented in Appendix B.

In a Canadian indoor air survey conducted in 1991, volatile organic compounds (VOCs) were measured in 754 randomly selected homes from across Canada

(Fellin et al. 1992). For each residence, the indoor air concentration of ethylbenzene was measured over a 24-hour period. The maximum indoor air concentration of ethylbenzene measured within a residence was 539 µg/m^3 (mean, 8.2 µg/m^3; detection limit, 0.66 µg/m^3).

A more recent Canadian indoor air survey was conducted from 2009 to 2011 as part of the second cycle of the Canadian Health Measures Survey (CHMS), an on going national survey that collects important health information from individuals aged 3 to 79 years old living in private households (Statistics Canada 2012; Wheeler et al. 2013). Eighty-four VOCs, including ethylbenzene, were measured by survey participants who deployed the samplers in their homes for 7 consecutive days. A total of 3857 valid indoor air samplers, from various dwellings including houses, apartments, mobile homes, and hotels, and including both smoking and non-smoking occupants, were analysed from 18 sites across Canada (personal communication from Environmental Health Science and Research Bureau December 2012). The mean concentration of ethylbenzene in indoor air was 4.09 µg/m^3 and the 95th percentile value was 15.07 µg/m^3 (weighted data at the person level) (Wheeler et al. 2013). The mean and 95th percentile indoor air concentrations weighted at the household level were 4.22 µg/m^3 and 13.63 µg/m^3, respectively (Zhu et al. 2013). The five Canadian surveys mentioned in the outdoor air section also monitored indoor air for ethylbenzene (Health Canada 2010a,b; Health Canada 2012; Health Canada 2013a; Zhu 2005). In the Windsor survey, 46–47 non-smoking participant homes were monitored between January 2005 and August 2006 with samples collected every 24 hours for 5 consecutive days (reported as an average of the 5 individual 24-hour samples). In the Regina survey, 146 homes, of which 34 homes had at least one smoking participant, were monitored in 2007 with samples collected over a single 24 hour period. In the Halifax study, 50 homes were monitored in both the winter and the summer of 2009 with samples collected every 24 hours for 7 consecutive days. In the Edmonton study, 50 homes were monitored in both the winter and the summer of 2010 with samples collected every 24 hours for 7 consecutive days. All four studies deployed active air samplers concurrently inside and outside the home. The Ottawa survey is an earlier study sponsored by Health Canada in which ethylbenzene was measured in 75 homes between November 2002 and March 2003. Each home was sampled once and indoor and outdoor active samplers were deployed with 10 L of air collected over 100 minutes (Zhu 2005). Health Canada also conducted an indoor air study of 96 homes in Québec City, Québec, during the winter and spring of 2005 with samples collected continuously over 7 consecutive days using passive samplers (Héroux et al. 2008).

The mean residential indoor concentrations of ethylbenzene recorded across all six studies ranged from 1.8 to 15.3 µg/m^3, and 95th percentile concentrations

ranged from 5.0 to 54.3 µg/m^3. The highest indoor air concentration of ethylbenzene reported across the Canadian studies occurred in a residence in Windsor, which had a value of 1199 µg/m^3. Several other high maximum values were noted in the various studies and are presented in Appendix B (Table B1).

A number of adult participants in the 2005 Windsor study also wore backpacks equipped with sampling apparatus, over 24-hour periods for five consecutive days, to measure personal exposure to ethylbenzene in air. Participants were asked to wear the sampling equipment during the normal course of a day. The highest concentration reported among Windsor participants wearing a personal backpack during the winter was 565 µg/m^3, while the corresponding mean and 95th percentile values were 8.3 and 9.8 µg/m^3, respectively. The maximum concentration of ethylbenzene reported during the summer sampling was 392 µg/m^3, while the corresponding mean and 95th percentile values were 10.6 and 27.3 µg/m^3, respectively (Health Canada 2010a).

10.1.2.1 Attached Garages

A study conducted in Québec City, Québec, compared housing characteristics and indoor air concentrations of VOCs including ethylbenzene. Higher indoor air concentrations of ethylbenzene were associated with homes that had attached garages (n,18; geometric mean, 5.15 µg/m^3) compared to those without (n,78; geometric mean, 2.31 µg/m^3) (p = 0.0006) (Héroux et al. 2008). Graham et al. 2004 studied the contribution of vehicle emissions from attached garages to indoor air in 16 residential homes in Ottawa, Ontario. Indoor air and garage air samples were collected for various compounds including ethylbenzene, before and during hot-soak and cold-start operation of a light-duty vehicle (the same vehicle was used in all homes). Results from the study showed that there was a positive net change in the concentration of hydrocarbons including ethylbenzene between the background sample in the houses before the tests commenced (referred to as pre-test) and samples collected while the car was operating in the garage (referred to as during-test). Cold-start and hot-soak pre-test results for ethylbenzene ranged from 1.17 to 15.2 µg/m^3 while during-test results for ethylbenzene ranged from 2.51 to 59.3 µg/m^3. Levels of ethylbenzene in the air of the garage during cold-start and hot-soak tests ranged from 31.5 to 675 µg/m^3 (Graham et al. 2004). Wheeler et al. (2013) used univariate regressions to determine that having an attached garage was one of the significant predictors of ethylbenzene in indoor air based on data from the recent CHMS indoor air survey.

Batterman et al. (2007) examined the migration of pollutants from attached garages into 15 houses in southeast Michigan in the United States. The mean

concentration of ethylbenzene in attached garages was 28.0 µg/m^3 while the corresponding mean indoor air concentration in the same homes was 2.3 µg/m^3 and the mean outdoor concentration was 0.2 µg/m^3. Dodson et al. (2008) reported similar results in a study of 55 homes in Boston, Massachusetts.

The presence of ethylbenzene and other compounds in garages are likely attributed to emissions related to vehicles, other gasoline-powered equipment and gasoline storage containers. Ethylbenzene levels measured in the Graham et al. (2004) and Batterman et al. (2007) study were higher in garages than either indoors or outdoors, suggesting that evaporative emissions from attached garages represent a source of indoor ethylbenzene.

10.1.2.2 Tobacco Smoke

Environmental tobacco smoke (ETS) has been shown to be a source of ethylbenzene (Nelson et al. 1998). Daisey et al. (1994) measured volatile organic compounds from various cigarette brands over a 4-hour period after 24- and 27-minute sessions of smoking, using a smoking machine, in a room sized (20m^3) environmental chamber. The concentrations of ethylbenzene in ETS range from 10.1 to 21.1 µg/m^3 (detection limit not stated) (mean concentrations from different cigarette brands range from 11.5 to 19.3 µg/m^3). Xie et al. (2003) reported ethylbenzene concentrations of 1.02 to 16.4 µg/m^3 (mean of 9.38 µg/m^3) from environmental tobacco smoke in a vacant office. Bi et al. (2005) conducted a similar study and reported the level of ethylbenzene in environmental tobacco smoke from 3 brands of cigarettes to range between 69.2 to 84.2 µg/cigarette. Polzin et al. (2007) measured ethylbenzene in mainstream smoke following ISO 3308:2000 standard where an automated smoking machine simulated smoking conditions (35 mL puff of 2-second duration every 60 seconds). Levels of ethylbenzene in mainstream cigarette smoke from various brands of cigarettes ranged from 0.8 to 7.8 µg/cigarette (Polzin et al. 2007). Wallace and Pellizzari (1986) measured the concentration of ethylbenzene in the breath of 198 smokers and 322 non-smokers. The ethylbenzene breath concentration in smokers (2.6 µg/m^3) was significantly higher ($P < 0.001$) than in non-smokers (0.8 µg/m^3) (Wallace and Pellizzari 1986).

Data from the air study conducted in Regina indicated that cigarette smoking in the home did not result in a large concentration increase of ethylbenzene in air when compared with homes of non-smokers (Health Canada 2010b). Indoor air concentrations of ethylbenzene ranged from 0.27 to 13.5 µg/m^3 and from 0.10 to 33.6 µg/m^3 in homes with at least one smoker and without any smokers, respectively. The mean concentrations for these homes ranged from 1.8 to 2.4 µg/m^3 and from 1.9 to 3.8 µg/m^3, respectively (see Appendix B, Table B1)

(Health Canada 2010b). This suggests that although cigarette smoke may contribute to the concentration of ethylbenzene in the home, it is unlikely a significant source. Kim et al. (2001) reported among home studies, certain VOCs including ethylbenzene were higher in the homes of non-smokers compared with homes of smokers. The authors suggest that non-cigarette sources of VOCs including infiltration of vehicle exhaust, cooking, and use of solvent-based products contribute to indoor air levels of ethylbenzene. Furthermore, in a tobacco smoking simulation experiment conducted in a vacant office, ethylbenzene concentrations in air did not correlate well with ETS markers produced during cigarette smoking. The authors propose that the concentration of ethylbenzene in indoor air is mainly attributed to non-smoking sources (Xie et al. 2003). Ethylbenzene exposure estimates for individuals who smoke cigarettes are presented in the Consumer Products section.

10.1.2.3 Building Materials

Ethylbenzene has been identified in various building materials such as flooring and furniture. National Research Council Canada has a database containing information on emissions of VOCs from various building materials created through a series of projects entitled “Consortium of Material Emissions and Indoor Air Quality Modeling”. The emission testing was conducted using a flow-through chamber system for 69 different materials including carpet, plywood and adhesive (Won et al. 2005). A list of some of the materials in which ethylbenzene was detected and the corresponding emission factors can be found in Table 10-1.

Table 10-1: Range of ethylbenzene emission factors of selected materials (µg/m2/h) at 24 hours (Won et al. 2005)

Material Type	Specific Material	Minimum	Maximum
Solid and Engineered Wood Materials	Oriented Strand Board (OSB)	0.13	1.3
Solid and Engineered Wood Materials	Plywood	0.05	0.09
Solid and Engineered Wood Materials	Solid Wood	0.03	0.28
Solid and Engineered Wood Materials	Medium Density Fibreboard (MDF)	0.94	0.94
Flooring	Carpet/Assembly	0.03	291
Flooring	Underpad	0.21	0.23
Flooring	Laminate/Assembly	0.01	0.20
Flooring	Linoleum/Vinyl Flooring	0.04	0.11
Installation Materials	Adhesive	5	5
Installation Materials	Caulking	151	4 457 281

Park et al. (1996) conducted chamber studies (chamber volume of 0.006 m^3) on the flooring, wall, and ceiling materials similar to those that would be installed in a newly constructed residence. Initial emission rates of ethylbenzene from flooring, wall, and ceiling material were 67.1 µg/m^2/h, 64.6 µg/m^2/h, and not detected (detection limit not stated), respectively (Park et al. 1996). Salthammer (1996) reported levels of ethylbenzene emitted from five wood cabinets treated with different coatings. The concentration of ethylbenzene in the air surrounding and inside the cabinet ranged from not detected (detection limit not stated) to 962 µg/m^3 after 24 hours. Concentrations of ethylbenzene in the air surrounding and inside of the cabinets were lower when measured after 400 hours (Salthammer 1996). Qin et al. (1999) conducted a study using two experimental rooms to determine the air concentration of various volatile organic compounds after installing plastic flooring, after using floor wax, and after using wall paint. Ethylbenzene concentrations in indoor air after installing plastic flooring was 557 µg/m^3 after 5 hours but dropped to 17 µg/m^3 after 9 days. Ethylbenzene concentrations in indoor air after using wall paint were 283 µg/m^3 after 2 hours but dropped to levels not detected after 10 days (Qin et al. 1999). Wallace et al. (1987) detected ethylbenzene in the air above glued carpet (6.4 µg/m^3) in a chamber study and estimated an emission rate of 77 ng/m^2 per minute. Ethylbenzene was one of the main VOCs emitted from laminate flooring in a chamber study conducted in Korea, however, only values for total VOCs were reported (An et al. 2011).

10.1.2.4 Electronic Products

Ethylbenzene is emitted from various electronic products such as television sets and video monitors. Malmgren-Hansen et al. (2003) used test chambers to measure emissions from television sets (2 µg/unit per hour at 7 hours and 3 µg/unit per hour at 9 hours or 0.23 and 0.34 µg/m^3), from monitors (33 and 14 µg/unit per hour at 7 hours and 9 hours, respectively, or 3.8 and 1.6 µg/m^3), and from voltage converters (139 and 74 µg/unit per hour at 7 hours and 9 hours, respectively, or 16.0 and 8.5 µg/m^3).

Ethylbenzene has been detected in various types of office equipment such as printers and photocopiers. Lee et al. (2001) conducted a chamber study to determine emissions from laser printers, ink-jet printers, and an all-in-one machine. Ethylbenzene was detected in both laser printers, one of two ink-jet printers, and the all-in-one machine. Average levels of ethylbenzene ranged from 1.26 to 3.00 ppb (5.5 to 13 µg/m^3) for machines in operation and from 1.2 to 2.07 ppb (5.2 to 9 µg/m^3) for the same machines not in operation (idle) (Lee et al. 2001).

Levoic et al. (1996) conducted chamber studies to estimate emission rates of various compounds from dry-process photocopiers used in office environments both in idle mode and during operation. The emission rates for ethylbenzene ranged from <10 to 180 µg/hour per copier for the photocopiers in idle mode and from <50 to 28 000 µg/hour per copier for the photocopiers in operation mode (Levoic et al. 1996). Levoic et al. (1998) conducted a similar study using various laboratories to test their method. Emission rates for ethylbenzene, while photocopiers were in operation, ranged from 23 000 to 29 000 µg/hour per copier used in an office environment. Headspace analysis of the toner used in the photocopiers was also conducted with ethylbenzene headspace concentrations in toner cartridges ranging from 260 to 620 ng/mL headspace (Levoic et al. 1998). Brown (1999) conducted a chamber study to determine various types of chemicals that are emitted from dry-process photocopiers. The average ethylbenzene air concentrations while the copier was in operation ranged from 552 to 608 µg/m^3, and the average ethylbenzene air concentration was 4.1 µg/m^3 while the copier was in idle-mode (Brown 1999).

10.1.2.5 Summary

Ethylbenzene has been identified in indoor air in Canada and may be attributed to various sources. The highest 95th percentile value of 54.3 µg/m^3 reported in the Windsor study over the summer of 2006 (Health Canada 2010a) is considered to be an upper-bounding ethylbenzene concentration representative of long-term inhalation for the general population from indoor air and accounts for daily exposures to ethylbenzene from attached garages, building materials, and electronic products.

10.1.3 Vehicle Interior Air

Ethylbenzene has been identified in new car interiors in Spain, Australia, and Taiwan (Grabbs et al. 1999; Brown and Cheng 2000; Chien 2007; Esteve-Turrillas et al. 2007). Chien (2007) measured interior air concentrations (sampling time of 45 minutes) of various VOCs, including ethylbenzene, in new domestic and imported cars (20 cars in total) in Taiwan in order to examine inter-brand, intra-brand, and intra-model variations. In total, 20 cars were included in the study ranging in age from a few weeks to 4 months after manufacture. Ethylbenzene concentrations ranged from not detected (method detection limit of 5.5 µg/m^3) to 240 µg/m^3. The concentrations of all the analyzed VOCs including ethylbenzene varied between brands and models most likely as a result of the

different types of materials used in the different cars such as upholstery, adhesives, and lubricant (Chien 2007).

According to Brown and Cheng (2000), levels of ethylbenzene in car interiors decrease over time. Various VOCs were measured in three new cars (two in Australia and one imported from Korea). Only the two cars made in Australia had detectable levels of ethylbenzene. One car had an ethylbenzene air concentration of 140 µg/m^3 after 10 weeks and only 0.9 µg/m^3 after 115 weeks. The other car had ethylbenzene levels of 880 µg/m^3 after 3 weeks, 56 µg/m^3 after 9 weeks, and 7.5 µg/m^3 after 95 weeks (Brown and Cheng 2000).

Yoshida and Matsunaga (2006) measured interior air concentrations in one car over a 3-year period in Japan. The concentration of ethylbenzene the day after delivery, approximately 2 weeks after manufacture, was 361 µg/m^3 (average over a 24-hour period). The concentration of ethylbenzene, as well as for other aromatic hydrocarbons, decreased rapidly for the first 6 months with concentrations ranging from one-hundreth to one-tenth of the original concentration (3.6 to 36 µg/m^3). During the first summer, concentrations increased slightly with the rise in outdoor temperatures; however, by the second year, little difference was noticed during the winter and summer months (Yoshida and Matsunaga 2006).

Ethylbenzene may also be present in vehicles while in transit. Novamann International (1994a,b) examined driver exposures to various substances while commuting during morning and evening rush hour in winter and summer in Toronto, Ontario. Ethylbenzene concentrations ranged from below method detection limit (BMDL) to 109.8 µg/m^3 (average of 14.1 µg/m^3) and from BMDL to 15.2 µg/m^3 (average of 3.5 µg/m^3) in winter and summer, respectively. The concentration of ethylbenzene as well as other compounds were usually higher in winter than in the summer most likely as a result of windows being closed during the winter months (Novamann International 1994a,b).

Karmen and Graham (2002) examined the concentration of various compounds in ambient air on a busy street in Ottawa, Ontario as well as in vehicles on long commuting trips. Sampling took place in January/February and July/August of the year 2000. Mean (±standard deviation) concentrations of ethylbenzene on the roadside were 2.49(2.62) µg/m^3 and 1.36(0.78) µg/m^3 in winter and summer, respectively. Mean (±standard deviation) concentrations of ethylbenzene in cars were 3.09(3.24) µg/m^3 and 2.90(1.30) µg/m^3, and in buses were 2.58(1.23) µg/m^3 and 3.57(1.77) µg/m^3 in winter and summer, respectively (Karmen and Graham 2002).

In-vehicle monitoring of ethylbenzene was also performed on public buses in northern Spain; concentrations of ethylbenzene ranged from 0.20 to 4.89 µg/m^3 (mean concentrations ranged from 1.05 to 1.30 µg/m^3) (Parra et al. 2008). Ethylbenzene was also detected on 22 public buses in Changsha, China; concentrations of ethylbenzene ranged from 19.6 to 95.9 µg/m^3. The authors reported that levels of BTEX increased when in-vehicle temperatures or relative humidity increased and levels decreased with age of the vehicle or if the travel distance increased (Chen et al. 2011). Shiohara et al. (2005) reported median in-vehicle concentrations of ethylbenzene of 36.8 µg/m^3 in cars, 25.6 µg/m^3 in microbuses, 17.8 µg/m^3 in buses, and 11.3 µg/m^3 in the metro in Mexico City during commutes along defined routes. The authors suggested that the VOCs they measured (benzene, toluene, ethylbenzene, m/p-xylenes) in vehicles were probably from gasoline vapors or exhaust fume penetration from the vehicle itself or from the surrounding vehicles (Shiohara et al. 2005). Novamann International (1994a) stated that the major sources of substances in a vehicle are: exhaust from the vehicle itself; exhaust from the surrounding vehicles; substances in ambient air while in transit; and, compounds being emitted from inside the vehicle itself.

Exposures to ethylbenzene from vehicle interior air varies greatly depending on the age and brand of the vehicle, ventilation within the vehicle, the location, and season, as well as on the frequency and duration of exposures. The maximum value of 240 µg/m^3 measured in the Chien (2007) study was chosen to represent an upper-bound inhalation exposure level from interior air in vehicles. Higher concentrations were measured in other studies; however, these had smaller sample sizes and were therefore not as representative of potential exposures.

10.1.4 Drinking Water

Canadian data relating to the concentration of ethylbenzene in drinking water has been identified and reviewed. Ethylbenzene is listed in the Guidelines for Canadian Drinking Water Quality published by Health Canada (Health Canada 2014a). A Maximum Acceptable Concentration or MAC has been established at 140 µg/L, based on health effects considerations and an Aesthetic Objective or AO has been established at 1.6 ug/L based on considerations such as taste and odour. The World Health Organization (WHO) has published guidelines for chemicals in drinking water based on human health concerns. The WHO recommends that the concentration of ethylbenzene in drinking water not exceed 300 µg/L (WHO 1996).

Ethylbenzene has been detected in drinking water in several surveys in Canada. Otson et al. (1982) tested the raw and effluent water from 29 municipalities

across Canada in which concentrations as high as 10 µg/L (detection limit, 1 µg/L) were observed in a treated sample; however, the mean concentration did not exceed 1 µg/L. In a similar survey of nine municipalities along the Great Lakes from 1982 to 1983, ethylbenzene was not identified above the detection limit (detection limit, 0.1–0.4 µg/L) in 12 of 24 raw water samples and 14 of 42 treated water samples (Otson 1987). A survey of municipal drinking water sources in the Atlantic region determined mean concentrations of ethylbenzene to be 0.2 µg/L and 0.5 µg/L (detection limits not stated) in 1987 and 1988, respectively (Environment Canada 1989). More recent data were available through the Ontario Ministry of the Environment's Drinking Water Surveillance Program (MOE 2009). During the 2007 reporting year, the concentration of ethylbenzene was measured across 120 water systems throughout Ontario. The highest reported ethylbenzene concentrations among samples of raw water, treated water, and samples from the distribution system did not exceed trace levels (0.1–0.2 µg/L; detection limit, 0.05 µg/L).

Approximately 30% of Canadians use groundwater in their homes (Environment Canada 2011b). Background levels of ethylbenzene in wells in North Bay were identified at 0.1 µg/L (Reinhard et al. 1984; Cherry 1987). Goss et al. (1998) sampled 160 wells in rural Ontario and were unable to detect ethylbenzene in any of the samples (detection limit, 1.17 µg/L). Several other studies, listed in Table 9-2 of the Ecological Exposure Assessment section showing levels of ethylbenzene in Canadian groundwater located near landfills, waste sites, leaking underground fuel tanks, or other contaminated sites, which most likely would not be used as a source of drinking water. The U.S. Geological Survey (USGS) conducted a study on 55 VOCs in groundwater from large aquifers, some of which are used for drinking water. Levels of ethylbenzene in domestic and public wells collected from 1985 to 2001 ranged from 0.003 to 5.4 µg/L with the majority of samples containing <0.03 µg/L (Zogorski et al. 2006). More recent data from a similar study conducted by the USGS identified ethylbenzene concentrations ranging from 0.013 to 0.52 µg/L from 2002 to 2005 (Carter et al. 2007).

Drinking water is not expected to be a significant route of general population exposure to ethylbenzene in Canada. In all but one study examined, ethylbenzene concentrations fell below the Health Canada Aesthetic Objective of 1.6 ug/L and all sources examined fell far below the Health Canada MAC or the WHO drinking water guideline. The maximum value found by Otson et al. (1982) does not reflect the findings found in more current available databases and was published before the availability of the Health Canada Guideline. Studies identified on the presence of ethylbenzene in Canadian municipal and well water are limited, and therefore the Canadian Drinking Water Aesthetic Objective of 1.6 µg/L will be used in derivation of the upper-bounding estimate of daily intake of

ethylbenzene from drinking water. It is recognized, however, that this is a conservative assumption since ethylbenzene concentrations at this level and above are expected to alter the taste and smell of the water and would likely result in complaints and action to reduce levels in the drinking water.

10.1.5 Food and Beverages

Data on levels of ethylbenzene in food in Canada are limited, and available measurements of ethylbenzene in food from other countries are presented in this section.

Ethylbenzene does not likely occur naturally in plants (Tang et al. 2000); however, it has been identified in various unpackaged or fresh food items. According to VCCEP (2007), ethylbenzene may accumulate in foods as a result of its presence in the atmosphere. The empirical data on levels of ethylbenzene in unpackaged food items is presented below.

Enviro-Test Laboratories (1991, 1992, 1993) conducted a study of 34 to 36 food groups in grocery stores located in Alberta, Ontario, and Québec from 1991 to 1993. Ethylbenzene was below the detection limit (50 µg/kg in solids for the Alberta study and 5 µg/kg in solids for the Ontario and Québec studies, 1 µg/kg in liquids for all studies) in all of the food groups tested. In the Northwest Territories and northern Manitoba, in 1985 and 1986, ethylbenzene was detected in the muscle tissue and liver tissue of burbot, *Lota lota*, with concentrations ranging from not detectable to 115.0 µg/kg (weighted mean of 10. 6 µg/kg, detection limit not stated) and from not detectable to 84.0 µg/kg (weighted mean of 26.7 µg/kg, detection limit not stated), respectively. Ethylbenzene was also detected in the muscle tissue of whitefish, *Coregonus clupeaformis*, with concentrations ranging from not detectable to 273 µg/kg (weighted mean: 19.8 µg/kg, detection limit not stated) (see Table 9-4) (Lockhart et al. 1992). These concentrations of ethylbenzene are in fish tissue near industrial sources in northern areas and, therefore, are not considered to be representative of typical levels to which most of the Canadian population would be exposed. Segments of the population, however, who consume fish and live in northern areas, may be exposed to these higher levels of ethylbenzene.

In 1986, ethylbenzene was detected in 43 out of 138 fish samples in Japan with concentrations ranging from 1.0 to 9.8 µg/kg wet weight (detection limit of 1 µg/kg wet weight) (Government of Japan 2004; IPCS 1996; IARC 2000). Ethylbenzene was detected in various Korean salt-fermented fish and shrimp pastes with mean concentrations of 76.6 µg/kg for anchovy, 38.3 µg/kg for hairtail, and 72.5 µg/kg for shrimp (Cha and Cadwallader 1995). Ethylbenzene

was identified in the neutral fraction of roast beef flavour isolate; however, the actual concentrations were not reported (Min et al. 1979).

Ethylbenzene has been detected in various fruits, vegetables, and legumes. It was detected in parsley at 256.7 µg/kg and in orange peel at 23.6 µg/kg (detection limit not stated) in a European study that examined the peel, pulp, and roots of 14 different vegetables and 10 different fruits (Górna-Binkul et al. 1996). Lovegren et al. (1979) reported the presence of ethylbenzene in various dry legumes including beans (concentrations ranging from 0 to 11 µg/kg), split peas (13 µg/kg), and lentils (5 µg/kg). Ethylbenzene was also detected in chickpea seed (Rembold et al. 1989). Ethylbenzene was identified in tomatoes and tomato products, apples (Golden Delicious), strawberries, and kiwis, but no concentrations were reported (Dirinck et al. 1977; Chung et al. 1983; Takeoka et al. 1986).

Ethylbenzene was detected in various forms of olive oil, including extra-virgin olive oil, virgin olive oil, olive oil, and refined olive oil, contained in different types of packaging (glass, plastic, or metal) at concentrations ranging from not detected (limit of detection of 0.25 ng/mL) to 34.3 ng/mL in a study conducted in Spain (Carrillo-Carrión et al. 2007). Vichi et al. (2007) also detected ethylbenzene in 54 samples of virgin olive oils from three different crops with concentrations ranging from 14 to 201 µg/kg (mean of 45 µg/kg, limit of detection of 0.6 µg/kg) in Spain. The presence of ethylbenzene, as well as other aromatic hydrocarbons, in olive oil is thought to arise as a result of its presence in the atmosphere from spills, combustion, and evaporation of fuel oil, vehicular and industrial emissions, and geochemical processes. The aromatic hydrocarbons are lipophilic in nature and tend to contaminate oils and fats (Vichi et al. 2007).

Ethylbenzene may also be present in foods as a result of migration from food packaging and containers made from styrenic polymers (VCCEP 2007). Polystyrene, including general purpose polystyrene (GPPS), high impact polystyrene (HIPS), and foam, is used in a variety of food packaging and food contact materials such as cutlery, drink cups, meat trays, egg cartons, dinnerware, fast-food packaging, cookie and cake trays, dairy containers, soda fountain cups, and lids (Shariq and Funada 2008). The European Union’s specific migration limit (SML) for ethylbenzene is 600 µg/kg (0.6 mg/kg) (Nerín et al. 2002).

Tang et al. (2000) reported that certain polymer food packaging materials, mainly polystyrene, may contain ethylbenzene as a residual. Ethylbenzene was reported to range from 8 to 473 ppm (median of 50 ppm) in 41 out of 44 samples of polystyrene products (Hempel and Rüdt, in Tang et al. 2000). The same study reported ethylbenzene in all 12 samples of styrene graft and copolymer products

with concentrations ranging from 61 to 202 ppm (median of 84 ppm) (Hempel and Rüdt, in Tang et al. 2000). The Polystyrene Work Group (PSWG) of the Society of the Plastics Industry's Food, Drug, and Cosmetic Packaging Materials Committee conducted a study to determine the potential dietary exposure to ethylbenzene from food-contact items made of polystyrene. An industrial survey was carried out to collect data on the residual levels of ethylbenzene present in various polystyrene food packaging and disposable food-contact items. The weighted average residual ethylbenzene concentrations collected during the survey (PSWG 1997, cited in VCCEP 2007) are shown in Table 10-2. The concentration of ethylbenzene in commercial polystyrene resins will depend on the technical process used (Durst and Laperle 1990, in Tang et al. 2000), and the eventual residual content of ethylbenzene in foods is therefore variable and difficult to predict (2010 Dec 6 conversation and e-mail from Food Packaging/Incidental Additives Section to Existing Substances Risk Assessment Bureau; unreferenced).

Table 10-2: Weighted average residual ethylbenzene concentrations for polystyrene packaging and disposable items (PSWG 1997, cited in VCCEP 2007)

Material Type	Polymer/applications*	Residual ethylbenzene (ppm)
Packaging	GPPS	18
Packaging	HIPS	29
Packaging	Polystyrene foam	66
Disposables	GPPS	42
Disposables	HIPS	108
Disposables	Polystyrene foam	37
Disposables	Expandable polystyrene foam	37

* GPPS: general purpose polystyrene
HIP: high impact polystyrene

Several studies have been identified on the presence of ethylbenzene in food as a result of its migration from packaging. Chiesa et al. (2008) reported levels of ethylbenzene in various types of cheese mainly packaged in plastic and stored at 4ºC. Concentrations in the cheese ranged from 0.52 to 76.1 µg/kg (Chiesa et al. 2008). Ethylbenzene was reported to migrate from various types of plastic containers, intended for high temperature use, into powdered whole and skimmed milk (López et al. 2008). Four types of plastic (polypropylene random, polypropylene copolymer, polycarbonate, and styrene–acrylonitirile copolymer) were heated at various temperatures (75, 100, and 121°C) and exposure times (30, 60, and 120 minutes) with the powdered milk. Ethylbenzene was detected in all samples of the powdered skimmed and whole milk with concentrations ranging from 0.03 to 0.09 µg/kg and 0.02 to 11 µg/kg, respectively. Concentrations of ethylbenzene in the powdered whole milk were greater than

those of the powdered skimmed milk most likely because of the higher fat content in the powdered whole milk (López et al. 2008). In addition, concentrations of ethylbenzene increased with increasing temperature for the powdered whole milk.

Nerín et al. (2002) detected ethylbenzene in various plastics (polycarbonate, polypropylene–copolymer, polypropylene–20% talcum, polypropylene random, and styrene–acrylonitrile) used in high-temperature food containers designed for heating food in microwave ovens. Concentrations of ethylbenzene released as vapour from the packaging containers at 100ºC ranged from 0.147 to 0.360 µg/kg resulting in potential migration of ethylbenzene to food from the vapour phase ranging from 0.0165 to 0.0273 µg/kg (Nerín et al. 2002).

Gramshaw and Vandenburg (1995) reported that the migration of ethylbenzene into pork belly, cooked at 175°C for 1.5 hours in thermoset polyesters dishes (containing between 6 and 25 mg/kg ethylbenzene), ranged from <6 to 34 µg/kg (detection limit, 6 µg/kg). Ethylbenzene was detected in low fat yoghurts and chocolate desserts packaged in polystyrene with concentrations ranging from not detected (detection limit not specified) to 4 µg/kg (Ehret-Henry et al. 1994). Tan and Okada (1978) examined the migration of styrene and ethylbenzene from polystyrene cups. Ethylbenzene was detected in the following food items: in sour milk beverage at <0.0025 to 0.006 ppm; in noodle soup at 0.015 to 0.021 ppm; in noodle curry at 0.089 to 0.153 ppm; and in instant wonton soup at 0.009 to 0.028 ppm. The concentration of ethylbenzene in the various polystyrene cups ranged from 108 to 424 ppm (Tan and Okada 1978).

In the U.S. Food and Drug Administration (US FDA) Total Diet Study (US FDA 2006), which encompasses data from 1991 to 2004, ethylbenzene was detected in approximately 80 packaged and unpackaged food items (detection limit not stated), as summarized in Appendix C, with the greatest concentrations detected in muffins (plain or fruit) at 224 µg/kg (mean concentration of 10 µg/kg, detection limit not stated) and in popcorn (microwave, butter-flavour) at 129 µg/kg (mean concentration of 0.043 µg/kg, detection limit not stated). The data from the US FDA Total Diet Study (presented in Appendix C) were considered to be the most representative of potential levels in food in Canada and were used to estimate upper-bound dietary intakes of ethylbenzene to the general population of Canada (see Appendix D, Table D1). Ethylbenzene concentrations in fish from the Lockhart et al. (1992) study were used in estimating ethylbenzene exposure of individuals living in northern parts of the country (presented in Appendix D, Table D2).

Ethylbenzene has also been detected in human breast milk. Blount et al. (2010) developed and validated a method for collecting, storing and analyzing 36 VOCs,

including ethylbenzene, in breast milk. Breast milk was collected from 12 healthy women at least 30 days post-partum, in Baltimore, Maryland. Concentrations of ethylbenzene ranged from 0.053-0.58 ng/mL with a mean value of 0.232 ng/mL and a median value of 0.149 ng/mL (Blount et al. 2010). The maximum value of 0.58 ng/mL was used to estimate upper-bound exposures to infants (see Appendix D).

10.1.6 Soil and Sediment

Limited data on levels of ethylbenzene in soil were identified. Table 9-3 in the Ecological Exposure Assessment Section on soil, shows the limited Canadian soil data available. In a study of Ontario parkland, the upper 97.5th percentile concentration of ethylbenzene in soil samples was calculated to be 0.40 ng/g (detection limit, 2.0 ng/g) while the concentration of ethylbenzene in soil in rural parkland was 0.46 ng/g (OMEE 1993). The detection limit was higher than the highest detected level, and therefore there is low confidence in these data. Data from the Ontario Brownfields Environmental Site Registry ranged from 40-50 ng/g (OMOE 2005). Both of these data sources pertain to contaminated sites and do not provide details on soil sampling sites or methodology and were therefore not used to derive human exposure estimates.

The Canadian Soil Quality Guidelines for agricultural, residential, commercial, and industrial land uses, intended to be protective of environmental and human health, have been established by the Canadian Council of Ministers of the Environment (CCME) for ethylbenzene (CCME 2004). The values for coarse and fine soil are 0.082 and 0.018 mg/kg, respectively, and are identical across all land uses. In the absence of quality Canadian data, the guidelines proposed by CCME (2004) were used as a conservative surrogate value for the calculation of the upper-bound estimate of daily intake of ethylbenzene from soil ingestion.

10.1.7 Consumer Products

The survey conducted pursuant to section 71 of CEPA reported the use of ethylbenzene in numerous consumer products in the year 2000, representing several consumer product types. Ethylbenzene was reported to be used in coating products with concentrations ranging from 0.002 to 40%, and as a component of fuels, including gasoline, with concentrations ranging from 0.42 to 8.0%. However, some survey respondants had interpreted consumer to mean customer, and products and concentrations of ethylbenzene specifically available to the general population could not be determined; therefore, alternative sources

of information on levels of ethylbenzene in consumer products were used to derive exposure estimates, as presented below.

10.1.7.1 Household Products

The presence of ethylbenzene in consumer products is primarily as a result of its presence in mixed xylenes which are used as solvents (ECHA 2008). Available data on concentrations of ethylbenzene in Canadian products was limited; therefore information was collected on the presence of ethylbenzene in products from the United States as a first step. The Household Products Database (HPD 2011) listed over 300 products containing ethylbenzene including various spray paints and paint products, automotive cleaners, arts and craft supplies, sealants, wood stains and varnish, pesticide products, and an adhesive. The concentration of ethylbenzene in these products ranged from 0.01 to 25%. Other sources consulted included the Source Ranking Database (SRD) and the public literature. A summary of the information on types of products and ethylbenzene concentrations identified from various US sources is provided in Appendix E.

Not all of the products and ethylbenzene concentrations identified from the U.S. Household Products Database and the SRD are available in Canada. Therefore, follow-up research was conducted to confirm concentrations in products in Canada including searches of Canadian retailer websites and Canadian material safety data sheets as well as contacting the Canadian industry. The types of consumer products that were reported to contain ethylbenzene included both liquid and aerosol forms of interior and exterior coatings, wood finishes, stains and varnishes. The concentration in aerosol paint-products ranged from 0.01 to 3.79% and those in liquid paint-products were usually less than 1% except for certain specialty products used outdoors which could be as high as 10-14%.

In addition, Health Canada's Product Safety Laboratory measured the concentration of ethylbenzene in over 100 consumer products including various paints, coatings, stains, finishes, cleaners, and fuel treatments (Health Canada, unpublished (compositional analyses conducted in 2013-2015). The ethylbenzene concentrations in the majority of the products tested were below 1% with a few products ranging in concentration from 1 to 4.5% (Health Canada, unpublished (compositional analyses conducted in 2013-2015). Two concrete/ stone sealer products had ethylbenzene concentrations between 16 and 18% (Health Canada 2014b); however, after communicating with the manufacturers, one of these products has been discontinued and should no longer be available to consumers and the other is available for exterior use only (2014 email(s) from Risk Management Bureau, Health Canada to Existing Substances Risk Assessment Bureau; unreferenced).

Based on this information, Table 10-3 shows the product types and corresponding ethylbenzene concentrations for which exposure estimates were derived. Only exposures to products that are likely to be used indoors or in garages were estimated since these would result in the highest exposure estimates. More details on the concentration ranges selected for each scenario are provided in Appendix F.

The ConsExpo model, version 4.1 (ConsExpo 2006), was used to estimate inhalation and dermal exposures to ethylbenzene from use of spray and liquid paints, paint remover, lacquer/stain/varnish, and joint sealant (or caulking). ConsExpo is a multi-tiered predictive model used to derive estimates of exposure to substances in consumer products. It contains exposure factors for various products and uses and it is a well-established model. The US EPA's Wall Paint Exposure Model was also used to derive estimates of exposure for the liquid paint scenario. The results from this model were similar to the outputs from ConsExpo; therefore, to be consistent across all product scenarios, and to estimate dermal exposures as well as inhalation exposures, the ConsExpo model was used in this report. As illustrated in Appendix F and Table 10-3, concentrations of ethylbenzene in consumer products may vary substantially. Accordingly, a range of concentrations of ethylbenzene in each product type were used to derive estimates of exposure (see Appendix F for details). A summary of the lower- and upper-bound estimates of inhalation and dermal exposures to ethylbenzene resulting from use of certain consumer products is provided in Table 10-3. Information on the parameters used for each scenario is detailed in Appendix F. Direct use of these products by children was not considered likely and exposure estimates were derived for adults only.

As shown in Table 10-3, exposure estimates vary as a result of differences in the concentration of ethylbenzene in the products. Mean air concentrations over the day of the event ranged from 0.006 mg/m^3 for adults using spray paint to 13 mg/m^3 for adults using liquid paint. Dermal exposure ranged from 0.002 mg/kg-body weight per event for adults using spray paint to 1.1 mg/kg-body weight (bw) per event for adults using caulking.

Table 10-3: Summary of inhalation and dermal ethylbenzene exposure from use of consumer prducts by adults, estimated using ConsExpo v. 4.1

Product	Concentration of ethylbenzene in Canadian products	Mean air concentration on day of event (mg/m^3)	Dermal exposure (mg/kg-bw per event)
Spray paint	0.01 to 5 %	0.006 to 3	0.002 to 1.1

Product	Concentration of ethylbenzene in Canadian products	Mean air concentration on day of event (mg/m^3)	Dermal exposure (mg/kg-bw per event)
Liquid paint	0.1 to 1 %	1.3 to 13	0.051 to 0.51
Paint remover	4 %	2.8	0.28
Lacquer/Stain/varnish	0.1 to 2 %	0.5 to 9.4	0.051 to 1.0
Caulking (or sealant)	0.1 to 5 %	0.1 to 5.2	0.021 to 1.1

Data on concentrations of ethylbenzene in air from use of products have been identified in the literature. In a study by Nielsen et al. (2003), five products were analyzed. Measured concentrations of ethylbenzene around a simulated user spraying the product for 60 seconds were determined to range from 0.006 to 17 mg/m^3 (concentration in the 5 products ranged from not present to 1.83%) (Nielsen et al. 2003). The mean air concentration over the day of the event could not be determined from the study. Ethylbenzene was detected in proofing sprays (2 out of 16 products; 0.027 and 0.97 mg/g) (Feilberg et al. 2008). Chang et al. (2007) evaluated inhalation and dermal exposures to solvents (including ethylbenzene) in 15 male shipyard spray painters. The personal 8-hour time-weighted average (±SD) exposure concentration of ethylbenzene outside the workers mask was 59.2 ± 10.4 ppm (257 mg/m^3) and 2.60 ± 0.49 ppm (11 mg/m^3) inside the workers mask. Dermal exposures of ethylbenzene inside and outside block units of assembled ships ranged from 281.8 to 342.4 mg/9 cm^2 tape and 42.5 to 70.7 mg/9 cm^2 tape, respectively (Chang et al. 2007). Whitehead et al. (1984) conducted a study on occupational exposures to solvents in paints and glues that are applied by spraying, which mainly takes place in spray booths. The average time-weighted averages (TWAs) for workers spraying high- and low-aromatic paint ranged from 0.4 to 13.2 ppm (1.7 to 57 mg/m^3), and the highest TWAs ranged from 3.4 to 52 ppm (15 to 226 mg/m^3). The average TWAs for workers spraying aromatic- and chlorinated-hydrocarbon-dominated glues ranged from 0.3 to 37.5 ppm (1.3 to 163 mg/m^3), and the highest TWAs ranged from 1.4 to 123 ppm (6.1 to 534 mg/m^3) (Whitehead et al. 1984). These measured concentrations do not exceed occupational standards based on eye, skin and upper-respiratory irritation set out by various agencies such as OSHA, NIOSH and ACGIH (ATSDR 2010; OSHA 2011).

Ethylbenzene was detected in 16 out of 26 air freshener products during a headspace analysis conducted by Jo et al. (2008) in Korea. The same study measured mean concentrations of ethylbenzene in the air within gasoline- and diesel-fueled cars with and without air fresheners. The cars with air fresheners had only slightly higher levels of ethylbenzene than the cars without the air fresheners indicating that the level of ethylbenzene in the vehicles was likely a result of ambient air within the transportation corridor than from the air fresheners

(Jo et al. 2008). Lim et al. (2011) analyzed for BTEX in 207 consumer products obtained from a supermarket in Korea. High concentrations of ethylbenzene were detected in shoe polish (not detected (nd) – 277,928 ppm), leather cleaner (nd – 42,223 ppm), whiteout (nd – 2770 ppm), permanent pen (nd – 345,065 ppm) and glue (nd – 792 ppm) (Lim et al. 2011 – abstract only). Ethylbenzene was detected in all 5 newly produced household furniture products tested (desk chair, bedside table, dining table, sofa and cabinet) in a 5 m^3 chamber over 14 days in Korea. Mean concentrations of ethylbenzene ranged from 1.16 µg/m^3 (for desk chair) to 563 µg/m^3 (dining table) (Ho et al. 2011).

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, ethylbenzene is used in certain cosmetic products in Canada such as a few manicure preparation products (2013 email(s) from the Consumer Product Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada; unreferenced). Exposure from use of manicure products that may contain small quantities of ethylbenzene was estimated to be low compared with exposure from use of other household products.

10.1.7.2 Products Intended for use by Children

The Danish EPA has identified ethylbenzene in several children's products. Glensvig and Ports (2006) conducted emission tests (collection on solid adsorbents and analysis by GC/MS) of various children's toys and identified ethylbenzene in two out of seven children's toys that contain perfume; a rubber figurine emitting ethylbenzene at a concentration of 1100 µg/m^3 (equivalent to 1.9 µg/m^3 of ethylbenzene in a room), and a soft cube emitting 540 µg/m^3 (equivalent to 0.94 µg/m^3 of ethybenzene in a room). Hansen et al. (2004) reported the presence of xylenes/ethylbenzene in all six of the children's tents and tunnels that were sampled with levels of xylenes/ethylbenzene ranging from 2 to 40 µg/m^3. Svendson et al. (2005) measured ethylbenzene in all 14 slimy-type toys that were analyzed. Migration analyses that used artificial sweat and saliva were conducted by the Danish EPA to determine the potential release of certain substances when in contact with skin (via sweating) or saliva. The migration of ethylbenzene from slimy-type toys was determined to be <0.05 to 0.56 µg/g into artificial sweat (i.e., potential dermal exposure) and <0.05 to 0.64 µg/g into artificial saliva (i.e., potential oral exposure) (Svendson et al. 2005). Ethylbenzene was also detected in children's marker pens (no concentration given) (Hansen et al. 2008).

The Danish EPA has also identified ethylbenzene in various hobby products that can be used by adults and children. Mikkelsen et al. (2005) detected ethylbenzene in glass, window, or porcelain colourants (3 out of 10 products; not

detected to 82 mg/kg). Egmose and Pors (2005) measured ethylbenzene in textile colourants such as fabric dyes (4 out of 15 products; not detected to 19 mg/kg). Ethylbenzene has also been detected in ironing beads (4 out of 6 products; 11 to 950 µg/kg) (Pors and Fuhlendorff 2002).

Styrene-containing polymers such as polystyrene and acrylonitrile–butadiene–styrene, are used to make a variety of consumer products including children's toys (Ormonde and Yokose 2008; Shariq and Funada 2008). There is a potential for young children to mouth toys made of styrenic polymers, which most likely contain residual levels of ethylbenzene. VCCEP (2007) estimated exposure to ethylbenzene by young children mouthing toys using conservative assumptions and by predicting the daily migration rate of ethylbenzene drawing on information from the PWSG (1997) study on ethylbenzene residuals in food-contact materials (PWSG 1997, cited in VCCEP 2007). VCCEP (2007) made use of the residual concentrations of ethylbenzene in polystyrene food packaging and disposable food-contact items shown in Table 10-2 as well as some assumptions on ethylbenzene's structural similarity to styrene to estimate the potential daily migration rate of ethylbenzene from children's toys. Using the weighted-average residual concentration of ethylbenzene in non-disposable HIPS (29 ppm or 29 mg/kg), the estimated daily migration rate was determined to be 0.0002 µg/cm^2-day, which was used to predict oral intakes for young children (aged 2 to 36 months old) mouthing toys. These predicted oral intakes ranged from 6.8×10^{-10} to 1.4×10^{-7} mg/kg-bw per day, and it was concluded that this potential source of ethylbenzene exposure was unlikely to be significant (VCCEP 2007).

To characterize potential oral exposures from other types of toys identified by the Danish EPA, the predicted oral intakes determined with the VCCEP method were re-calculated with the highest weighted-average residual concentration of ethylbenzene of 108 ppm (108 mg/kg) for disposable HIPS (higher concentration than those identified by the Danish EPA). This resulted in an estimated daily migration rate of 0.00075 µg/cm^2-day. The predicted oral intakes ranged from 2.5×10^{-9} to 5.2×10^{-7} mg/kg-bw per day for children aged from 2 to 36 months old (presented in more detail in Appendix F).

10.1.7.3 Gasoline

Ethylbenzene is naturally present in crude oil and is therefore present in gasoline. Levels of ethylbenzene in gasoline range from <1 to 5.4% (IARC 2000; FLL 2008). In Ontario, typical ethylbenzene concentrations were reported to be 1.4% in regular unleaded gasoline and 1.7% in premium unleaded gasoline (CCME 2004). Evaporative losses of gasoline and therefore ethylbenzene may occur during refuelling and from gasoline storage tanks.

A national survey was conducted by the Petroleum Association for Conservation of the Canadian Environment (PACE 1987, 1989) in 1985 on the ambient concentration of ethylbenzene around gas stations in Halifax, Montreal, Toronto, Calgary, and Vancouver during summer and winter. Eight-hour air samples were collected near the gas stations; 160 samples were taken during the summer study and 156 samples during the winter for a total of 316 samples. Mean concentrations of ethylbenzene in 8-hour air samples ranged from 30 to 46 µg/m^3, with 95th percentile concentrations ranging from 83 to 184 µg/m^3 (maximum concentrations ranged from 816 to 1163 µg/m^3). A total of 233 (114 during the summer and 119 during the winter) 10- to 15-minute samples measured during fill-ups at full-serve stations (representing three to five fill-ups) were taken with a battery-operated portable pump attached close to the breathing zone of volunteers (pump operators). Mean concentrations of ethylbenzene from all gas types (regular leaded, regular unleaded, and super unleaded) in the breathing zone ranged from 142 to 389 µg/m^3, with 95th percentile concentrations ranging from 263 to 1461 µg/m^3 (maximum concentrations ranged from 733 to 2275 µg/m^3). More recent Canadian data were not available; however, Esteve-Turrillas et al. (2007) reported levels of ethylbenzene in the air near gas stations in Spain to range from 46 to 99 µg/m^3 (three samples) and from 32 to 2280 µg/m^3 (six samples) near the breathing zone of individuals refueling their vehicles. Backer et al. (1997) measured air in the personal breathing zone of 30 individuals pumping gasoline during winter in 1995. The average concentrations of ethylbenzene from the high- and low-volume sampling pumps did not exceed 200 ppb (880 µg/m^3).

The highest 95th percentile concentration (1461 µg/m^3) identified in the PACE studies was used to estimate upper-bound inhalation exposures to ethylbenzene while refuelling a vehicle. Dermal exposures to ethylbenzene while refuelling a vehicle at a service station may occur periodically and were estimated with a range of ethylbenzene concentrations (1 to 5.4%). The resulting dermal doses that used the thin-film approach and assumed 100% dermal absorption ranged from 0.01 to 0.07 mg/kg-bw per event for adults (see Appendix G). Canadians may also be exposed to gasoline when using it at home to operate lawn mowers, emergency power generators, motor chain saws, and similar equipment. No data are currently available to estimate these types of exposures.

The highest 95th percentile concentration for an 8-hour air sample (184 µg/m^3) was used to estimate upper-bound inhalation exposures to ethylbenzene for individuals living near service stations that could be exposed to higher concentrations of ethylbenzene compared with those who do not live near a service station.

10.1.8 Confidence in Exposure Database

Confidence in the database on exposure to ethylbenzene through environmental media is considered moderate to high, as representative Canadian data were available for ambient and indoor air, the most relevant sources of exposure via the environment. Confidence is moderate for exposures to ethylbenzene while inside a vehicle. Some Canadian data was available on levels while in traffic but no data on levels in new vehicles in Canada were available. Some Canadian data were available on levels of ethylbenzene in drinking water, but were limited for soil. Confidence in the exposure to ethylbenzene from food is considered moderate as levels in various food items were identified in the United States, but no recent data were available on levels in Canada. Confidence in the exposure estimates from use of consumer products is considered to be moderate as there was some Canadian-specific information available from in-house product testing, information submitted by industry stakeholders and from a more in-depth review of Canadian retailers and material safety data sheets on the types of products found in the country but there was limited information on some of the parameters used in the model including the amount of ethylbenzene dermally absorbed; however, confidence is high that the estimated exposures to ethylbenzene from all pathways are conservative.

10.2 Health Effects Assessment

An assessment by the International Agency for Research on Cancer (IARC 2000) concluded that ethylbenzene was possibly carcinogenic to humans (Group 2B), based on sufficient evidence in experimental animals and inadequate evidence in humans. Although, the US EPA has classified ethylbenzene as a Group D substance, not classifiable as to its human carcinogenicity (US EPA 1991), this assessment was conducted before completion of a 2-year inhalation carcinogenicity bioassay conducted by the US National Toxicology Program (NTP) in 1999. The available health effects information for ethylbenzene is summarized in Appendix H.

10.2.1 Carcinogenicity and Genotoxicity

The carcinogenicity of ethylbenzene was evidenced in experimental animals via inhalation and oral exposure routes. In the NTP inhalation carcinogenicity bioassay, male and female B6C3F1 mice and F344/N rats were exposed to 0, 75, 250, or 750 ppm (0, 326, 1090, or 3260 mg/m^3) ethylbenzene vapour for 103 and 104 weeks, respectively (Chan et al. 1998; NTP 1999). A significant and

concentration-related increase in incidence of both alveolar/bronchiolar adenomas and combined alveolar/bronchiolar adenomas and carcinomas of the lung, as well as a significant increase in alveolar epithelium metaplasia, were observed in male mice at 3260 mg/m^3 (750 ppm) compared with concurrent controls, but were within the NTP historical control ranges (10-42%) at this dose. In the exposed female mice, there were concentration-related increases in the incidence of both hepatocellular adenomas and combined adenomas and carcinomas, which were significant at 3260 mg/m^3 compared with concurrent controls, but remained in the NTP historical control ranges (3-54%). The incidence of eosinophilic foci in the liver was significantly greater in the female mice at 3260 mg/m^3 and was considered a precursor to hepatocellular neoplasia. In the exposed rats, a concentration-dependent increase in incidence of combined renal tubular adenomas and carcinomas, significant at 3260 mg/m^3, was observed in the males. Significant increases in incidence of renal tubular adenomas in the females and testicular adenomas in the males were also observed at 3260 mg/m^3. It should be noted that testicular adenomas are present in nearly all aged rats of this strain and were found in 80-88% of the males at 3260 mg/m^3 which is within the NTP historical control range (54–83%). In both sexes, there was a significant increase in the incidence of focal renal tubular hyperplasia at 3260 mg/m^3, which was considered to be a precursor stage of adenoma development by the study's authors. Dose-dependent increases in the severity of chronic progressive nephropathy were observed in females at all exposure levels and in males at the highest concentration (Chan et al. 1998; NTP 1999). In an oral carcinogenicity bioassay, significantly increased incidences in total malignant tumours were observed in Sprague-Dawley rats exposed to 500 mg/kg-bw per day via gavage for 104 weeks (Maltoni et al. 1985). Increased incidences in nasal cavity tumours, neuroesthesioepitheliomas, and oral cavity tumours (statistical analysis was not provided) were also observed in rats exposed to 800 mg/kg-bw per day ethylbenzene by gavage for 2 years (Miltonic et al. 1997).

Ethylbenzene has not demonstrated mutagenic or clastogenic activity in *in vivo* assays, and negative results have been shown for chromosome aberrations in rat bone marrow (ethylbenzene was administered in a mixture with xylene, Donner et al. 1980) and mouse micronuclei assays (Mohtashamipur et al. 1985; NTP 1992, 1999). Results were also negative in gene mutation assays *in vitro* in bacteria, with and without metabolic activation, and yeasts, and in insects (Nestmann and Lee 1983; Dean et al. 1985; NTP 1992, 1999). However, there were some positive results from *in vitro* assays in mammalian cells, including cell transformation after prolonged exposure periods (7 days) and micronuclei in Syrian hamster embryo cells at all dose levels tested (25 to 200 µg/mol). In addition, there was a positive response at the highest non-lethal dose (80 µg/mol; the reported lethal dose was 100 µg/mol) in the mouse lymphoma assay in the

presence of cytoxicity. Exposure to ethylbenzene at concentrations of 100–200 µM (10–20 µg/mL) also induced single DNA strand breaks in human blood lymphocytes, whereas exposure to 50 µM ethylbenzene did not elicit this effect (Chen et al. 2008). At a very high dose level (10 mM), ethylbenzene was able to induce marginal sister chromatid exchange in human lymphocytes (Norppa and Vainio 1983). Furthermore, sunlight-irradiated ethylbenzene and ethylbenzene metabolites, ethylhydroquinone and 4-ethylcatechol, in the presence of Cu(II) were able to induce oxidative DNA damage and DNA adduct formation in a dose-dependent manner (Toda et al. 2003; Midorikawa et al. 2004). Overall, the weight of evidence suggests that ethylbenzene is not likely to be directly genotoxic.

10.2.1.1 Mode of Action for Carcinogenicity

The mode of action for ethylbenzene carcinogenicity has not been fully elucidated. Midorikawa et al. (2004) reported that the ethylbenzene metabolites ethylhydroquinone and 4-ethylcatechol have the ability to induce oxidative DNA damage *in vitro*. It should be noted the study used calf thymus DNA and oxidative damage was only observed in the presence of copper catalyst. The level of copper used may be higher than physiological level. The Agency for Toxic Substances and Disease Registry (ATSDR) toxicological profile for ethylbenzene concluded that the carcinogenic activity of ethylbenzene may be, at least in part, attributed to the parent compound and/or reactive oxidative metabolites (ATSDR 2010). The California EPA, Office of Environmental Health Hazard Assessment (OEHHA 2007) also stated that although cytotoxicity or exacerbation of existing degenerative processes may be involved in tumourigenicity of ethylbenzene, which might be considered as a non-genotoxic mode of action, the current data do not conclusively establish any particular mode of action for ethylbenzene carcinogenesis.

In contrast, the Voluntary Children's Chemical Evaluation Program (VCCEP 2007), an industry led initiative, examined genotoxicity and non-genotoxicity mediated modes of action for ethylbenzene carcinogenicity based on Hill's criteria (VCCEP 2007). The VCCEP (2007) review, which was subjected to a peer-review (TERA 2007), concluded that all *in vivo* studies have been negative for genotoxicity and the *in vitro* studies have been predominantly negative for genotoxicity, and direct genotoxicity does not seem to be a relevant mode of action for ethylbenzene induced species-, sex- , and tissue-specific (kidney, liver, Leydig cell, or lung) tumours. Notably, unpublished genotoxicity test results that were included in the VCCEP data set (Seidel et al. 2006) repeated the gene mutation assay in mouse lymphoma cells and did not find mutagenic response with concentrations up to 120 mg/L. A genotoxicity review article of ethylbenzene

similarly concluded a non-genotoxic mechanism based on available data from the standard battery of genotoxicity assays (Henderson et al. 2007).

The VCCEP assessment proposed various non-genotoxic modes of action for ethylbenzene carcinogenicity including a mode of action for kidney tumours (secondary to chronic progressive nephropathy [CPN] caused by a primary ethylbenzene metabolite, 1-phenylethanol, may involve α2u-globulin accumulation), a mode of action for lung tumours (chronic cell proliferation, secondary to metabolism of ethylbenzene to cytotoxic metabolites by CYP2F2, which is expressed at relatively higher levels in mouse lung (Cruzan et al. 2009; Saghir et al. 2009, 2010a); however, it is not clear whether reactive metabolites formed in the liver could also distribute through blood to the lungs (Huff et al. 2010; Saghir et al. 2010b), a mode of action for liver tumours (secondary to a phenobarbital-like enzyme induction and cell proliferation), and a mode of action for Leydig cell tumours (Leydig cell hyperplasia, secondary to ethylbenzene-induced hepatic expression of different cytochrome P450 isozymes, resulting increased hydroxylation and clearance of testosterone). The CPN-mediated renal tubule tumours, the phenobarbital-type liver responses, and the perturbation of serum testosterone-induced Leydig cell tumours were considered qualitatively irrelevant to humans by VCCEP (2007). Even though work by Seely et al. (2002) showed that the association between CPN and renal tubule cell neoplasm is marginal (but statistically significant), more recent analyses have concluded that chemically-induced exacerbation of CPN in rats should not be acknowledged as an indicator of hazard in humans and furthermore, the renal tumours described in this case are CPN-related and their increased incidence should not be considered relevant to humans (Hard 2002; Lock and Hard 2004; Hard and Seely 2005; Hard et al. 2009, 2012, 2013). Others have argued that advanced CPN observed after ethylbenzene exposure was not sufficient to account for the increased kidney tumours in rats (Melnick et al. 2012, 2013). .

Although data for ethylbenzene in rodents indicate that it is carcinogenic at high doses, available information on the potential modes of action by which ethylbenzene induces different organ tumours (lung, Leydig cell, liver and kidney) indicates there is a threshold below which tumour formation would not be expected.

10.2.2 Reproductive / Developmental Effects

There were no indications of reproductive toxicity in either sex in rats exposed to ethylbenzene vapour up to 500 ppm (2174 mg/m^3) over two generations. No significant exposure-related changes were observed with respect to oestrous cycle length, pre-coital intervals, male and female mating and fertility indices,

gestation length, spermatogenic endpoints, reproductive organ weights, ovarian follicle counts, or F_1 and F_2 litter parameters, including pup sex ratios, live litter sizes, number of dead pups, viability indices, pup body weights, and the general physical condition of the pups. The oestrous cycle length was significantly reduced in the F_0 but not in the F_1 generation, and the authors considered it was not an ethylbenzene exposure-related effect. A no-observed-adverse-effect concentration (NOAEC) for reproductive toxicity was considered by the investigators to be 2174 mg/m^3 (Stump 2004a; Faber et al. 2006). In addition, no significant concentration-related adverse effects on female fertility were observed in Wistar rats that inhaled ethylbenzene vapour at concentrations up to 4348 mg/m^3 (1000 ppm) for 3 weeks before breeding in a developmental toxicity study (Hardin et al. 1981; NIOSH 1981). A similar absence of adverse effects on reproductive organs was observed in rats, mice, and rabbits exposed to ethylbenzene vapour up to 3400 mg/m^3 (rodents, 782 ppm) or 7000 mg/m^3 (rabbits, 1610 ppm) for 4 weeks (Cragg et al. 1989). No treatment-related effects were observed on sperm counts or motility, testicular morphology, length of oestrous cycle, or caudal or epididymal weights in rats or mice exposed to ethylbenzene vapour up to 4348 mg/m^3 (1000 ppm) for 13 weeks (NTP 1992). However, decreased peripheral hormone levels during the dioestrus stage were observed in rats that were orally administered ethylbenzene at dose levels of 500 mg/kg and above (Ungváry 1986).

Minor developmental effects were observed in the offspring of rodents and rabbits exposed to ethylbenzene during gestation. A significant increase in the incidence of foetuses with extra ribs was observed in rats exposed to ethylbenzene at 435 mg/m^3 (100 ppm, the lowest inhalation lowest-observed-effect concentration [LOEC] for developmental effects) during gestation (Hardin et al. 1981; NIOSH 1981). In the same study where rats were exposed during pregestation and gestation, increase in the incidences of fetuses with extra ribs was only observed at a higher dose level of 4350 mg/m^3 (1000 ppm), but not in rats that were exposed to a lower concentration. Hence, the authors considered the dose-response relationship for this effect at 435 mg/mg^3 was not consistent. Maternal toxicity, such as significantly increased relative and absolute liver, kidney, and spleen weights, was observed at 4350 mg/m^3 (1000 ppm) in rats in this study. Other studies have also noted minor developmental effects following *in utero* exposure to ethylbenzene during gestation, including increased number of foetuses with skeletal retardation in rats exposed to 600 mg/m^3 (138 ppm), increased incidence of foetal uropoietic apparatus malformation in mice, and reduced mean foetal body weights in rabbits observed at exposure concentrations of 500 mg/m^3 (115 ppm) (Ungváry and Tatrai 1985). Mice were treated for only one dose level of 500 mg/mg^3 (115 ppm) and anomalies of the uropoietic apparatus was not observed in other recent developmental studies (Faber et al. 2006, 2007; Saillenfait et al. 2003, 2006, 2007). Moderate and dose-

dependent maternal toxicity was observed in rats in the latter study (no further details were provided) and spontaneous abortion was observed in rabbits at 1000 mg/m^3. ATSDR (2010) noted that the Ungváry and Tatrai (1985) study did not include sufficient details regarding the adverse effects, dictating caution in the interpretation of the study findings. In the two-generation study in rats, as described in the reproductive effects section, no adverse developmental or neurodevelopmental effects or maternal effects were observed in F_1 and F_2 rats exposed to ethylbenzene up to 2174 mg/m^3 (500 ppm) (Faber et al. 2007). In more recent development toxicity studies, significant increases in the incidence of foetal skeletal variations per litter were observed in the offspring of rats exposed to 8696 mg/m^3 (2000 ppm) and significant reductions in foetal body weights were observed in the offspring of rats exposed to ≥ 4348 mg/m^3 (1000 ppm) ethylbenzene during gestation in the presence of maternal toxicity (Saillenfait et al. 2003, 2006, 2007).

In 4-week and 13-week repeated-dose toxicity studies where rats were orally administrated ethylbenzene for up to 750 mg/kg-bw/day, there were no pathological changes or weight changes to reproductive organs in male and female rats (Mellert et al. 2007).

10.2.3 Ototoxicity and Central Nervous System Effects

Ototoxicity (i.e., hearing loss featured by increased auditory thresholds and the outer hair cell losses) was consistently observed in experimental rats following repeated inhalation and oral exposure to ethylbenzene when the auditory threshold changes were measured by electrocochleography. A short-term inhalation no-observed-adverse-effect concentration (NOAEC) was identified at 1305 mg/m^3 (300 ppm) based on ototoxicity (increased auditory thresholds and outer hair cell loss) observed at 1740 mg/m^3 (400 ppm) (Cappaert et al. 2000). A subchronic inhalation lowest-observed-adverse-effect concentration (LOAEC) of 870 mg/m^3 (200 ppm) was identified based on outer hair cell loss (no NOAEC were identified in the study, Gagnaire et al. 2007), and an oral lowest-observed-adverse-effect level (LOAEL) of 900 mg/kg-bw per day (Gagnaire and Langlais 2005) was identified, also based on ototoxicity. Such auditory system effects were not detected when tested by acoustic startle in offsprings of rats (postnatal days (PND) 20 and 60) that were exposed to ethylbenzene by inhalation to doses as high as 2174 mg/m^3 (500 ppm) in a two generation study (Faber et al. 2007) and in rats administered doses of ethylbenzene up to 500 mg/kg-bw per day for 90 days via the oral route (Li et al. 2010). In addition, guinea pigs were not susceptible to ethylbenzene-induced ototoxicity after exposure to 10 879 mg/m^3 (2500 ppm) ethylbenzene for 5 days (Cappaert et al. 2002).

In an effort to develop a weight of evidence approach to determining ototoxicity from exposure to industrial chemicals, Vyskosil et al. (2011) created a structured database examining the potential ototoxicity of industrial chemicals alone or in combination with noise exposure. According to this exercise, given the current evidence from animal studies, ethylbenzene appeared to affect auditory function mainly in the cochlear mid-frequency range and could be considered a possible ototoxic agent.

Other nervous system effects induced by ethylbenzene were observed. Depletion of striatal and tubero-infundibular dopamine was observed in rabbits at a concentration of 3261 mg/m^3 (750 ppm) and above (Romanelli et al. 1986; Mutti et al. 1988) and ethylbenzene-induced moderate activation in motor behaviour was observed in rats following an acute 4 hour inhalation exposure, with a LOAEC of 1740 mg/m^3 (400 ppm; the lowest dose tested) (Molnar et al. 1986), and following subchronic oral exposure, with a NOAEL of 75 mg/kg-bw per day (Mellert et al. 2007). Acute exposure to ethylbenzene also caused non-specific depression of the central nervous system in humans and animals at higher concentrations (Yant et al. 1930; Bardodej and Bardodejova 1970).

No developmental neurotoxicity effects were observed in rats (Faber et al. 2007; Li et al. 2010), which was also described in Section 10.2.2.

There were a number of epidemiological investigations or human reports on health effects, such as altered neuronal behaviour and short-term memory capacity, and ototoxicity, associated with occupational exposure to hydrocarbon mixtures (e.g., paints and gasoline) that contain ethylbenzene. In these studies, there is uncertainty with respect to the relative contribution of ethylbenzene exposure in the case of workers who experienced ototoxicity.

A cross-sectional study was conducted from workers in petrochemical plants (Zhang et al. 2013). The workers had relatively specific exposures to ethylbenzene, since the levels of other volatile aromatic hydrocarbons (styrene, bezene, toluene and xylene) were below the limit of detection. The prevalence of hearing loss for the ethylbenzene-exposed workers was higher when compared to two reference groups (unexposed office personel in these plants and workers in a power station exposed to similar noise level), with age, cigarette smoking and alcohol drinking adjusted. Neurobehavioural function alternation was observed in these exposed workers.

10.2.4 Other Systemic Effects

Species-specific kidney and liver toxicity was consistently observed in rodents following repeated inhalation and oral exposure to ethylbenzene. Liver and/or

kidney weight changes were observed in several studies (Wolf et al. 1956; Elovaara et al. 1985; Cragg et al. 1989; NTP 1992; Stump 2004b; Mellert et al. 2007; Li et al. 2010), and clear pathological changes in the mouse liver and rat kidneys were observed at higher concentrations following chronic inhalation exposure (Chan et al. 1998; NTP 1999). The NTP 2-year chronic inhalation study examined effects in both rats and mice. Increased severity of chronic progressive nephropathy (CPN) was observed in female rats at the lowest dose tested (326 mg/m^3) and in male rats at the highest dose tested (Chan et al. 1998; NTP 1999). CPN is a spontaneously occurring disease in laboratory rats that occurs with age and its progression and severity is dependant on the strain of rat used and the diet consumed during the study (Hard et al. 2009). In some strains, like the strain described above (Fisher 344), CPN starts to develop at a relatively young age and has been observed to occur in 100% of animals with first detectable histological lesions at 4-5 months of age in control males regardless of diet used. This disease does develop in females, but is less severe (Hard et al. 2009). On the basis of differences in physiology and pathology, Hard et al. (2009) concluded that there is no clear human counterpart for CPN and recommended that chemically-induced exacerbation of CPN alone should not be used as a reliable indicator of hazard for humans. This was supported by the observation that CPN was not seen in mice exposed to ethylbenzene at similar or higher dose levels and therefore is considered a species-specific effect. The LOAEC for exposed mice in this study was set at 1090 mg/m^3 (250 ppm), based on significantly increased incidences of hyperplasia of the pituitary gland pars distalis in exposed female mice and significantly increased incidences of syncytial alteration of hepatocytes in exposed males (Chan et al. 1998; NTP 1999). The NOAEC for this study was established at 326 mg/m^3 (75 ppm).

The highest oral repeat dose NOAEL was identified to be 75 mg/kg-bw per day, based on significantly increased liver and kidney weights with corresponding liver enzyme changes, cellular effects in the kidney, and haematological parameters in subchronically (13 weeks) exposed rats at the next higher dose of 250 mg/kg-bw per day (Mellert et al. 2007). Other systemic effects, such as pathological changes in lung, thyroid, prostate gland, bone marrow, and testes in rats, were also observed in the repeated inhalation studies at higher dose levels and after prolonged exposure (Chan et al. 1998; NTP 1999).

Haematological effects (significantly increased platelets in male rats and increased leukocyte counts in female rats) were observed in a 4-week inhalation study at 3401 mg/m^3 (782 ppm, Cragg et al. 1989); however, these adverse effects were not observed in a 13-week inhalation study with rats exposed to doses up to 4350 mg/m^3 (1000 ppm, NTP 1992). Some haematological effects (increased mean corpuscular volume in both sexes of rats and decreased platelets in female rats) were also observed following subchronic oral exposure

(Mellert et al. 2007). Rats exposed to up to 2174 mg/m^3 (500 ppm) ethylbenzene for 28 days did not exhibit alterations in their immune response (Stump 2004b; Li et al. 2010).

In addition, ethylbenzene is irritating to the mucous membranes (eye and respiratory tract); such effects were observed both in humans and animals (Yant et al. 1930; Wolf et al. 1956; Smyth et al. 1962; Gerarde 1963; Bardodej and Bardodejova 1970; Moscato et al. 1987; Lewis 1992; Cometto-Muñiz and Cain 1995).

There were a number of epidemiological investigations or human reports on other health effects not previously mentioned, such as changed blood cell counts, reduced semen counts, and genotoxicity, associated with occupational exposure to hydrocarbon mixtures (e.g., paints and gasoline) that contain ethylbenzene. There was no evidence that exposure to ethylbenzene was associated with increased cancer risk in these workers. These data were not used to assess ethylbenzene effects in humans due to the co-exposure to other chemicals, such as benzene, xylene, or toluene (Nicholson et al. 1978; Angerer and Wulf 1985; Bardoděj and Círek 1988; Triebig et al. 1988; Lu and Zhen 1989; Holz et al. 1995; De Celis et al. 2000; Sliwinska-Kowalska et al. 2001; Sram et al. 2004; Chang et al. 2011).

VOCs have been associated with effects on the respiratory system (e.g., asthma, reduced lung function, rhinitis), but no epidemiological study has determined these effects were directly linked to ethylbenzene alone (Rumchev et al. 2004; Arif and Shah 2007; Hulin et al 2010; Billionnet et al. 2011; Hwang et al. 2011; Martins et al. 2012).

10.2.5 Toxicokinetics

There were a considerable number of studies that investigated the absorption, distribution, metabolism, and excretion of ethylbenzene in humans and animals (VCCEP 2007; ATSDR 2010). Ethylbenzene is well absorbed from the skin (ethylbenzene liquid, but not ethylbenzene vapour), lungs, and gastrointestinal tract and is rapidly distributed throughout the body. Data pertaining to oral absorption of ethylbenzene from rabbits and rats following exposure to single oral doses of ethylbenzene suggests rapid and effective absorption by this route with 72 and 92% of the administered dose recovered in rabbits and 84% in rats, respectively (Climie et al. 1983; El Masry et al. 1956). More recently, Faber et al. (2006) reported that ethylbenzene was detected at 0.49, 3.51, and 18.28 mg/L in maternal blood of pregnant rats 1 hour after the last administration of 0, 8.67, 30, and 114 mg/kg ethylbenzene by gavage for 4 days, respectively. Further,

ethylbenzene was not detected in blood of weanlings from the same dams. When applied dermally, Morgan et al. (1991) reported that the peak blood level of ethylbenzene (5.6 µg/ml) was reached within 2 hours of topical application of neat ethylbenzene to approximately 1% of the body surface in rats and slowly declined after 24-hrs. The total amount absorbed was reduced when ethylbenzene was administered in aqueous solutions.

Ethylbenzene can be rapidly metabolized and then eliminated from the body, primarily as urinary metabolites and conjugates. The half-life of ethylbenzene in blood was measured in the range of 3.3 minutes at 326 mg/m^3 (75ppm) to 63 minutes at 4348 mg/m^3 (1000 ppm) in mice following a 4-hour exposure (Charest-Tardif et al. 2006). In addition, saturation kinetics of ethylbenzene was observed in this study at exposure concentrations above 2174 mg/m^3 (500 ppm), while it was linear at lower concentrations.

The metabolism of ethylbenzene is mediated by cytochrome P_{450} enzymes (e.g., CYP2E1, 1A2, and 2B6 in human liver; CYP2B1, 1E1, 2E1, and 1A1 in rat liver; CYP 1A1, 1E1, and 2B1 in mouse liver), with the ethyl moiety (side-chain) oxidation as the major metabolic pathway and the ring oxidation as a minor one, followed by conjugation reactions. The metabolism of ethylbenzene, in terms of major metabolites and the percentages of the metabolites, varies with species, sex, and nutrition status. No significant qualitative metabolic differences between oral and inhalation routes were reported (ATSDR 2010). However, metabolic differences between inhalation and dermal exposure routes were observed in humans. The major metabolites of ethylbenzene in humans after inhalation exposure are mandelic acid (64–71%), phenylglyoxylic acid (19–25%), and 1-phenylethanol (5%), whereas excretion of mandelic acid was only 4.6% of a dermally absorbed dose. In rats, after exposure to ethylbenzene orally or via inhalation, the major metabolites were identified as hippuric and benzoic acids (38%), 1-phenylethanol (25%), mandelic acid (15–23%), phenylglyoxylic acid (10%), and more recently measured mercapturic acids (0.3%; Cossec et al. 2010). In rabbits, the most important metabolite is hippuric acid, which is probably formed by oxidative decarboxylation of phenylglyoxylic acid. Ring oxidation products include para- and meta-hydroxyacetophenone, 2-ethylphenol, and 4-ethylphenol. Metabolism of ethylbenzene has not been studied in children or immature animals. However, some enzymes (e.g., uridine 5'-diphospho-glucuronosyltransferase and sulfotransferases) involved in conjugation of phase I ethylbenzene metabolites are known to be developmentally regulated (VCCEP 2007; ATSDR 2010). Species and organ differences in the metoblism of ethylbenzene were also observed in *in vitro* assays (Saghir et al. 2009, 2010a). Overall, the rate of ethylbenzene metabolism by mouse liver microsomes was higher than that in rats and humans, while the latter two were similar. Both rat and mouse lung microsomes were more active in metabolizing ethylbenzene

than were liver microsomes, while human lung microsomes did not metabolize ethylbenzene to any metabolites above the detection limit. Both CYP 2E1 and 2F2 were involved in the ring-oxylation of ethylbenzene to generate reactive metabolites, while CYP 2F2 activity in mouse lung was higher than that in rat lung and much higher than that in human lung.

Several physiologically based pharmacokinetic (PBPK) models have been developed that simulate the kinetics of inhaled ethylbenzene in animals and humans (Tardif et al. 1997; Dennison et al. 2003; Nong et al. 2007). A model of dermal absorption of ethylbenzene in humans has also been reported predicting that, based on its lipophilicity, exposure to ethylbenzene via the dermal route would be almost an order of magnitude greater than that of VOCs with lower Kow values (Shatkin and Brown 1991).

The confidence in the toxicological database is high as data on acute toxicity, carcinogenicity, repeated-dose toxicity, genotoxicity, reproductive and developmental toxicity, neurotoxicity, immunotoxicity, and toxicological kinetics and dynamics are available, although data on health effects associated with dermal exposure are limited.

10.3 Characterization of Risk to Human Health

On the basis of the available health effects information, mainly obtained from the studies in experimental animals and the assessments conducted by other international agencies, the critical health effects associated with exposure to ethylbenzene are considered to be tumour induction and non-cancer systemic effects, primarily on the auditory system and on the liver, kidney and pituitary glands. Minor developmental effects, haematological effects, effects on the endocrine glands (thyroid hyperplasia), and on the central nervous system were also observed at high dose levels and following prolonged exposure periods.

Ethylbenzene is not mutagenic or clastogenic *in vivo*. It did not induce gene mutations in bacteria and yeasts and only induced gene mutations in mouse lymphoma cells at high dose levels in the presence of cytotoxicity. Although ethylbenzene elicited weak clastogenicity and DNA damage in some *in vitro* assays, overall the available information indicates that ethylbenzene is not likely to be directly genotoxic. In addition, saturated toxicokinetics of ethylbenzene was observed in mice at dose levels below the concentration where increased tumour incidence became significant, indicating the existence of a threshold exposure level for ethylbenzene-induced tumourigenesis. A summary of the critical endpoints selected for risk characterization for both cancer and non-cancer effects from exposure to ethylbenzene is presented below in Table 10-4.

Table 10-4: Summary of the endpoints selected for risk characterization of ethylbenzene

Duration and route	Critical effect	Critical effect level
Acute and short term inhalation	Inhalation NOAEC based on significant hearing loss in rats exposed to ethylbenzene for 5 days (Cappaert et al 2000).	1305 mg/ m^3 (300 ppm)
Subchronic inhalation	Inhalation LOAEC based on hearing loss in rats in a 90-day study, a NOAEC was not identified from the study (Gagnaire et al. 2007).	870 mg/m^3 (200 ppm)
Chronic inhalation	Inhalation NOAEC based on increased incidences of pituitary gland hyperplasia in female mice and syncytial alterations in livers of male mice at the next dose of 1090 mg/m^3 (250 ppm) in a chronic study (NTP 1999) (increased severity of CPN in exposed female rats was observed at 326 mg/m^3, however, this effect is not considered to be relevant to humans). Further, this level is protective of effects shown in subchronic inhalation studies, including ototoxicity at 870 mg/m^3. Significant increase in tumour incidences in various organs in both rodent species were observed in this study at 3260 mg/m^3 (750 ppm) (NTP 1999).	326 mg/m^3 (75 ppm)
Chronic oral	Oral NOAEL based on increased kidney and liver weights with corresponding liver enzyme changes, cellular effects in the kidney, and haematological parameters in rats in a 13-week study (Mellert et al 2007; Li et al. 2010).	75 mg/kg-bw per day

The general population of Canada can be exposed to ethylbenzene through environmental media (i.e., ambient air, indoor air, drinking water, and soil), food, and during the intermittent use of consumer products containing the substance. Critical health effects observed in experimental animals were used to characterize the potential human health risk associated with ethylbenzene exposure.

The chronic inhalation NOAEC of 326 mg/m^3 observed in a 2-year chronic study in mice (NTP 1999) was used to characterize the human health risk associated with inhalation exposure from environmental media. Comparing this effect concentration with the highest 95th percentile concentrations measured in indoor air (54 $\mu g/m^3$), or with the highest 95^{th} percentile concentration measured in personal air (27.3 $\mu g/m^3$), results in a margins of exposure (MOE) of 6000 and 12 000, respectively. Significantly increased tumour incidences were observed in a 2-year study at 3260 mg/m^3, and thus MOEs of 60 000 and 120 000, based on indoor and personal air respectively, were derived for tumour occurrence. These MOEs are considered adequate to account for uncertainties in the health effects

and exposure databases for cancer and non-cancer effects for inhalation exposures from environmental media.

The presence of ethylbenzene in vehicle interior air is also a source of inhalation exposure. The available data indicate that the peak concentrations of ethylbenzene in the interior air of new vehicles decreased rapidly over a few months and then reached levels that were comparable to the highest 95th percentile of indoor air concentration (i.e., 54 µg/m^3). The upper-bound value of 240 µg/m^3 identified in interior air of new vehicles (Chien 2007) is considered to represent a conservative exposure from this source. Comparing this value with the lowest subchronic LO(A)EC of 870 mg/m^3(200 ppm), based on outer hair cell loss (hearing loss) in rats exposed to ethylbenzene for 90 days (Gagnaire et al. 2007), results in an MOE of approximately 3600. This MOE is considered adequate to account for uncertainties in the health effects and exposure databases.

Oral intake from environmental media (i.e., water and soil) and food represents a chronic oral exposure scenario. However, the available oral chronic toxicity studies (Maltoni et al. 1985, 1997) did not provide sufficient information on non-cancer effects in the exposed rats and tested high doses only. The highest subchronic oral NOAEL of 75 mg/kg-bw per day, based on a significant increase in liver and kidney weights with corresponding liver enzyme changes, cellular effects in the kidney, and haematological parameters in rats exposed to ethylbenzene for 13 weeks (Mellert et al. 2007), was used to characterize the human health risk of non-cancer effects from potential chronic oral exposure. Comparing this effect level with the highest oral exposure from food, water, and soil (3 µg/kg-bw per day estimated in infants aged 0–6 months, not formula fed) results in an MOE of 25 000. Following a 2-year oral dosing, a significant increase in tumour incidences was reported in rats at 500 mg/kg-bw per day and above (Maltoni et al. 1985, 1997), which is seven times the subchronic oral NOAEL. Thus, MOEs are considered adequate to account for uncertainties in the health effects and exposure databases for cancer and non-cancer effects for oral exposure from environmental media. The highest oral exposure from food, water, and soil for individuals living in northern parts of the country that may consume fish with higher concentrations of ethylbenzene (3.3 µg/kg-bw per day estimated in individuals from 6 months to 4 years old) was not dissimilar from estimates for the general population of Canada and, therefore, results in similar MOEs.

Ethylbenzene has been reported to be present in several types of consumer products that may be used indoors or in a garage. These consumer products would be used on an intermittent and sporadic basis and are likely to result in both inhalation and dermal exposure of the user. Some of the products, such as caulking, or spray paints, are only used occasionally, a few times a year or less,

and the applications are normally completed within a day. Other consumer products might be used on consecutive days, such as paint remover, liquid paint, or stain. In both cases, ethylbenzene could be released into indoor air over several days, e.g., during application as well as after paint is applied. Therefore, potential inhalation exposure of the general population from use of products such as paint or wood stains is considered to be short term rather than acute in duration.

The lowest short-term NOAEC available in the database is 1305 mg/m^3 (300 ppm) based on significant hearing loss in rats exposed to ethylbenzene for 5 days (Cappaert et al. 2000). MOEs were derived by comparing the NOAEC with the estimated mean concentrations on the day of the event derived from ConsExpo, and are shown in Table 10-5. Resulting margins of exposure are considered adequate to account for uncertainties in the health effects and exposure databases at the concentrations listed in Table 10-5.

Table 10-5: Margins of exposure from use of consumer products containing ethylbenzene for acute and short-term durations - Inhalation

Type of products	Concentrations of ethylbenzene in Canadian products	Mean concentration on day of event (mg/m^3)	Margins of exposure*
Spray paint	0.01 to 5%	0.006 to 3	217 500–435
Liquid paint	0.1 to 1%	1.3 to 13	1003-100
Paint remover	4%	2.8	466
Lacquer/stain/ varnish	0.1 to 2%	0.5 to 9.4	2610-139
Caulking (sealant)	0.1 to 5%	0.1 to 5.2	13 050-251

*****Based on a NOAEC of 1305 mg/m^3, based on significant hearing loss at the next dose in rats exposed to ethylbenzene for 5 days (Cappaert et al. 2000).

Use of these products is expected to be associated with dermal exposure to ethylbenzene. The toxicological database was inadequate to derive a critical effect level via the dermal route. Although dermal exposure would be expected to contribute to the overall exposure during use of consumer products, the primary route is considered to be inhalation. Part of the ethylbenzene deposited on skin will be volatilized, and only a portion on the non-volatilized substance will be systemically absorbed. Accordingly, the increase in exposure resulting from dermal contact is not considered to be significant enough to result in inadequate

margins of exposure for those scenarios for which margins of exposure from the inhalation route are considered adequate.

Consumers are also potentially exposed to ethylbenzene while refuelling personal vehicles. A comparison of the lowest short-term NOAEC of 1305 mg/m^3 (300 ppm), based on significant hearing loss in rats exposed to ethylbenzene for 5 days (Cappaert et al. 2000), with the 95th percentile concentration of ethylbenzene measured while pumping gasoline (1461 µg/m^3) results in a MOE of 893. This MOE is considered adequate to account for uncertainties in the health effects and exposure databases. The increase in overall exposure from dermal contact with ethylbenzene while refuelling personal vehicles is not considered to result in potentially inadequate margins of exposure.

Individuals living near service stations may be exposed to higher levels of ethylbenzene every day; the highest 95th percentile 8-hour air concentration of 184 µg/m^3 measured near gas stations was compared with the lowest inhalation NOAEC of 326 mg/m^3, based on liver and pituitary gland effects in mice at the higher dose level of 1090 mg/m^3 following chronic exposure (NTP 1999), resulting in an MOE of 1770. This MOE is considered adequately protective of non-neoplastic effects. This exposure was also compared with the effect level associated with increased tumour incidences (3260 mg/m^3), resulting in a MOE of 17 700, which is considered adequately protective of neoplastic effects.

Mainstream cigarette smoke is a source of exposure for ethylbenzene and would contribute to exposures of ethylbenzene.

Although ethylbenzene was also detected in some young children's toys that may be mouthed, the conservative oral exposure estimates from use of these products (i.e., 2.5×10^{-9} to 5.2×10^{-7} mg/kg-bw per day) indicate that the contribution of this source of exposure is minimal.

10.3.1 Biomonitoring Data

No Canadian biomonitoring data were identified; however, concentrations of ethylbenzene in blood for the general population of the United States are available. The National Health and Nutrition Examination Survey (NHANES) conducted by the U.S. Center for Disease Control and Prevention (CDC) is a series of surveys that collect data on levels of chemicals found in blood, serum, and urine, as well as other information related to the health and nutritional status of the U.S. population (CDC 2009, 2014). The report provides data on levels of ethylbenzene in the blood of adults aged 20 to 59 years old for the years 2001 to 2006, for adults 60 years and older and for adolescents aged 12 to 19 years old

for the year 2005-2006 (CDC 2014). The geometric mean blood concentrations for adults were 0.034 ng/mL, 0.035 ng/mL and 0.040 ng/mL for the years 2001–2002, 2003–2004, and 2005-2006 respectively. The 95th percentile values were 0.140 ng/mL, 0.110 ng/mL, and 0.150 ng/mL for the years 2001–2002, 2003–2004 and 2005-2006, respectively (CDC 2014). Similar ethylbenzene levels in blood have also been measured through the NHANES surveys in 1988–1994 and in 1999–2000 (CDC 2009). For adults 60 years and older, the geometric mean blood concentration was 0.037 ng/mL with a 95th percentile blood concentration of 0.130 ng/mL (CDC 2014). For adolescents aged 12 to 19 years old, the geometric mean blood concentration was 0.032 ng/mL with a 95th percentile blood concentration of 0.096 ng/mL (CDC 2014). U.S. data on the concentration of ethylbenzene in the blood of children were also identified. In a study conducted in the years 2000 and 2001, a stratified random sample of 152 children aged 6–10 years was selected across two elementary schools in Minneapolis, Minnesota (Sexton et al. 2005). The mean concentration of ethylbenzene measured in the blood of 134 children was 0.04 ng/mL and the 95th percentile value was reported to be 0.07 ng/mL. According to CDC (2009), the presence of ethylbenzene in blood indicates recent exposure.

Aylward et al. (2010) derived equations to convert external exposure concentrations of ethylbenzene into human steady-state venous blood concentrations, using metabolic parameters provided by a human PBPK model (Haddad et al. 2001; Alyward et al. 2010). Conversion of the chronic oral NOAEL (75 mg/kg-bw per day, Mellert et al. 2007) and inhalation NOAEC (326 mg/m^3, NTP 1999), identified as critical effects for risk characterization of ethylbenzene, results in steady-state venous blood concentrations that are two orders of magnitude above the highest blood concentrations identified from the NHANES surveys (0.150 ng/mL). These results are consistent with the risk characterization conclusion that margins of exposure between chronic exposure to ethylbenzene and critical effect levels are adequate taking into consideration uncertainties in the exposure and health effects databases.

Based on the available health effects and exposure information, it is concluded that ethylbenzene does not meet the criteria under paragraph 64(*c*) of CEPA as it is not 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.

10.4 Uncertainties in Evaluation of Risk to Human Health

Although a wide range of toxicological studies are available, adequate epidemiological data for characterizing the human health risks associated with ethylbenzene exposure were not identified.

In light of the species differences in ethylbenzene toxicokinetics and dynamics, there might be some quantitative and qualitative differences between human responses to ethylbenzene exposure and those observed in experimental animals. There have been efforts made to reduce the uncertainty in interspecies extrapolation using PBPK models (Tardif et al. 1997; Dennison et al. 2003; Nong et al. 2007). Nevertheless, as a conservative approach in the absence of reliable human health effects data, effects observed in experimental animals and the exposure levels associated with those effects were used to characterize the human health risks.

For characterizing the risks associated with chronic inhalation exposure from environmental media and from pumping gasoline, the critical health effects chosen for risk characterization were non-neoplastic liver and pituitary gland effects in 2-year inhalation-exposed mice. Although the human relevance of ethylbenzene-induced tumours from both the rat and mouse chronic inhalation studies is uncertain, risk characterization for both non-neoplastic and neoplastic effects from chronic exposure was conducted and the resulting MOEs were adequate to address uncertainties in the health effects and exposure databases. This approach is considered conservative.

The available health effects data were inadequate to identify a chronic oral endpoint and a subchronic LO(A)EL based on increased liver and kidney weights observed in rats exposed for 13 weeks was used for characterizing the risk associated with chronic oral intake from food, water, and soil. There is uncertainty in using a subchronic LOAEL since effects might occur at exposure levels higher than in a chronic study. However, margins of exposure were considered large enough to address this uncertainty.

Ototoxicity (hearing loss) was observed in experimental animals and in workers occupationally exposed to solvents including ethylbenzene. There is some uncertainty with respect to the relative contribution of ethylbenzene exposure of workers observed to suffer from ototoxicity.

In addition, no dermal effect level was identified in the data set to be suitable for risk characterization.

There is some uncertainty in how much ethylbenzene is present in vehicles (new and old) and while they are in traffic as only a few studies on this topic were identified. More information on characterizing the sources of ethylbenzene concentration in indoor air would be useful. There is some uncertainty related to the estimation of daily intakes from food and beverages, as Canada-specific data were limited; however, confidence is high that the estimated exposures are

conservative and most likely overestimate potential exposures to ethylbenzene from foods. There is some uncertainty in the estimation of exposure to individuals living in northern areas that may consume fish with higher concentrations of ethylbenzene. Only one document was available that measured concentrations of ethylbenzene in fish in Canada. The maximum concentration of ethylbenzene in fish was used as a conservative approach to estimating exposures to these populations. There is also uncertainty in the estimated intakes of ethylbenzene from soil as no relevant Canadian studies were available.

Exposure estimates could not be derived for all potential consumer products identified to contain ethylbenzene, such as automotive and arts and craft products, owing to a lack of data specific to each of these products; however, the upper-bounding estimates of exposure from use of paint, caulking and other coating products derived with the ConsExpo model are considered to account for these other scenarios. There is some uncertainty in the estimates of exposure to ethylbenzene from use of certain consumer products because of the lack of information on specific parameters used in the model (e.g., amount of product used for certain scenarios). There is also some uncertainty associated with exposures from use of consumer products to other age groups such as infants, toddlers, and teenagers. The use of upper-bound Canadian-specific ethylbenzene concentrations for each product scenario and the ConsExpo model which contains conservative assumptions ensures that upper-bound exposures are estimated.

There is also some uncertainty related to the estimates of both inhalation and dermal exposures to ethylbenzene while refueling a vehicle and for those living near service stations as measured concentrations may not be representative of current levels of ethylbenzene in gasoline. However, conservative assumptions were used to estimate these exposures to ethylbenzene such as the length of time spent at a gas station, and the use of the highest 95th percentile concentrations measured both at the pump and near the gas stations. There is also uncertainty regarding exposures to gasoline when refuelling motor-operated equipment used at home, such as lawn mowers; however, exposures associated with these uses are considered limited and intermittent and are considered to be covered by the automobile refuelling scenario.

11 Conclusion

On the basis of the information presented in this screening assessment, it is concluded that ethylbenzene does not meet the criteria under paragraph 64(*a*) or (*b*) of CEPA as it 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.

Based on the information presented in this screening assessment, it is concluded that ethylbenzene does not meet the criteria under paragraph 64(*c*) of CEPA as it is not 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 concluded that ethylbenzene does not meet any of the criteria set out in section 64 of CEPA.

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Appendix A. Summary of Canadian Outdoor Air Studies

Table A1: Concentrations of Ethylbenzene in Ambient (Outdoor) Air in Canada

Details	Mean concentration (µg/m^3)	Maximum concentration [a] (µg/m^3)	Reference
42 locations, suburban and urban across all provinces (2005–2009)	0.103–1.28	35.84 **(4.40* 95th percentile)**	Environment Canada 2011a
Northeast Edmonton, Alberta. Eight continuous ambient air locations	N/A	87.7	FAP 2010
Three Creeks area, Alberta. Community and industrial source sites	0.29–4.03 (1-hour average)	0.93 (maximum 1-hour average)	Alberta Environment 2010
Champlain Heights, New Brunswick, 2007	1.0 (annual average)	3.65 (maximum 24-hour average)	New Brunswick Department of Environment 2009
Edmonton East, Alberta, 1993–2003	0.97 (24-hour average)	21.82	Alberta Environment 2005
Industrialized zone in Fort Saskatchewan, Alberta, September 2004–March 2006	0.33–0.36	2.14–6.49	Mintz and McWhinney 2008
Alberta, northeastern British Columbia, and central and southern Saskatchewan, April 2001–December 2002	0.054	6.21	You et al. 2008
37 locations in Sarnia, Ontario	0.46 (for 2-week average)	1.06	Atari and Luginaah 2009
37 locations in Sarnia, Ontario	0.48	N/A	Miller et al. 2009
Three urban locations: mechanics garage, storm drain of industrial waste landfill, two-lane street in industrial area	10–13	N/A	Badjagbo et al. 2009
Clarkson Airshed: Oakville and Mississauga, Ontario	0.40–1.46 (annual average)	9.63	OMOE 2006
Residential homes in Windsor, Ontario Winter 2005, Non-smokers, 201 samples (~47 homes)	0.43 (average of five 24-hr samples)	2.4 (0.90 95th percentile)	Health Canada 2010a
Residential homes in Windsor, Ontario Summer 2005, Non- smokers, 216 samples (~47 homes)	0.75 (average of five 24-hr samples)	10.9 (1.7 95th percentile)	Health Canada 2010a
46-47 Residential homes in	0.37	4.8	Health Canada 2010a

Details	Mean concentration ($\mu g/m^3$)	Maximum concentration [a] ($\mu g/m^3$)	Reference
Windsor, Ontario Winter 2006, Non-smokers, 214 samples (~47 homes)	(average of five 24-hr samples)	(0.81 95th percentile)	
Residential homes in Windsor, Ontario Summer 2006, Non-smokers, 214 samples (~47 homes)	0.74 (average of five 24-hr samples)	13.8 (1.7 95th percentile)	Health Canada 2010a
Residential homes in Regina, Saskatchewan Winter 2007 Smokers, 17 samples (34 homes)	0.17 (single 24-hr sample)	0.38 (0.38 95th percentile)	Health Canada 2010b
Residential homes in Regina, Saskatchewan Winter 2007 Non-smokers, 77 samples (~112 homes)	0.28 (single 24-hr sample)	1.2 (0.97 95th percentile)	Health Canada 2010b
Residential homes in Regina, Saskatchewan Summer 2007 Smokers, 12 samples (34 homes)	0.17 (single 24-hr sample)	0.47 (0.47 95th percentile)	Health Canada 2010b
Residential homes in Regina, Saskatchewan Summer 2007 Non-smokers, 95 samples (~34 homes)	0.36 (single 24-hr sample)	16.6 (0.46 95th percentile)	Health Canada 2010b
Residential homes in Halifax, Nova Scotia Winter 2009, Non-smokers, 287 samples (50 homes)	0.13 (24-hr sample collected for 7 days)	1.4 (0.31 95th percentile)	Health Canada 2012
Residential homes in Halifax, Nova Scotia Summer 2009, Non-smokers, 287 samples (50 homes)	0.28 (24-hr sample collected for 7 days)	8.3 (0.53 95th percentile)	Health Canada 2012
Residential homes in Edmonton, Alberta Winter 2010, Non-smokers, 332 samples (50 homes)	1.139 (24-hr sample collected for 7 days)	146.51 (1.998 95th percentile)	Health Canada 2013
Residential homes in Edmonton, Alberta Summer 2010, Non-smokers, 324 samples (50 homes)	0.407 (24-hr sample collected for 7 days)	14.99 (0.724 95th percentile)	Health Canada 2013
Residential homes in Ottawa, Ontario Winter 2003, Smokers and Non-smokers, 74 samples (74 homes)	0.58 (24-hr sample 10L every 100 minutes)	9.4	Zhu et al. 2005

Abbreviations: N/A, not available;

[a] Values in bold denoted with an asterisk (*) were selected as predicted environmental concentrations (PECs) for the calculation of risk quotients (RQs) later in this report.

Appendix B. Summary of Canadian Indoor Air Studies

Table B1: Indoor air concentrations of ethylbenzene in Canada

City, Season and Participant Type	Location and Type of Sample	Number of Samples	Minimum (µg/m^3)	Maximum (µg/m^3)	Mean (µg/m^3)	95th Percentile (µg/m^3)
Windsor[a] 2005 Winter Non-smoking	Personal backpack (avg of five 24 hr samples)	225	0.33	565	8.3	9.8
Windsor[a] 2005 Winter Non-smoking	Indoor stationary (avg of five 24 hr samples)	232	0.22	610	7.7	11.3
Windsor[a] 2005 Summer Non-smoking	Personal backpack (avg of five 24 hr samples)	207	0.55	392	10.6	27.3
Windsor[a] 2005 Summer Non-smoking	Indoor stationary (avg of five 24 hr samples)	217	0.41	913	15.3	39.7
Windsor[a] 2006 Winter Non-smoking	Indoor stationary (avg of five 24 hr samples)	224	0.27	1199	10.7	10.2
Windsor[a] 2006 Summers Non-smoking	Indoor stationary (avg of five 24 hr samples)	211	0.29	308	10.3	54.3
Regina[b] 2007 Winter Smoking	Indoor stationary 24 hour	21	0.27	13.5	1.8	5.0
Regina[b] 2007 Winter Non-smoking	Indoor stationary 24 hour	84	0.23	14.3	1.9	5.8
Regina[b] 2007 Summer Smoking	Indoor stationary 24 hour	13	0.36	11.4	2.4	11.4
Regina[b] 2007 Summer Non-smoking	Indoor stationary 24 hour	91	0.10	33.6	3.8	15.6
Halifax[c] 2009 Winter Non-smoking	Indoor stationary (24 hour)	312	0.14	107	4.2	11.0
Halifax[c] 2009 Summer Non-smoking	Indoor stationary (24 hour)	331	0.068	210	6.9	23.1
Edmonton[d] 2010 Winter	Indoor stationary (avg of 7 24-hr	337	0.18	551.9	10.5	17.4

Non-smoking	samples)					
Edmonton[d] 2010 Summer Non-smoking	Indoor stationary (avg of 7 24-hr samples)	328	0.10	25.8	2.0	7.9
Ottawa[e] 2003 Winter Smoking / non-smoking	Indoor stationary	75	0.005	201	4.7	No data
Quebec City[f] 2005 Winter and early Spring	Indoor stationary	96	0.40	19.50	2.69	No data
Various locations across Canada[g] 1991	Indoor stationary	754	No data	539.31	8.2	No data

a Health Canada 2010a
b Health Canada 2010b
c Health Canada 2012
d Health Canada 2013
e Zhu et al. 2005
f Héroux et al. 2008
g Fellin et al. 1992

Table B2. Sampling details for Canadian indoor air studies

Location / Reference and Measured Parameter	Sampling Period	Sampling Duration	Sampling Equipment	Total Number of Samples	Method Detection Limit (MDL) in µg/m^3	% of samples > MDL
Windsor, ON / Health Canada 2010a Indoor, outdoor and personal air	Winter and Summer 2005	1-week (5 consecutive 24 hour samples) in each season	SUMMA canisters (active sampling)	1298	0.046	100
Windsor, ON / Health Canada 2010a Indoor and outdoor air	Winter and Summer 2006	Five consecutive 24 hour samples in each season	SUMMA canisters (active sampling)	863	0.038	99.5 to 100
Regina, SK / Health Canada 2010b Indoor and outdoor air (smoking and non-smoking homes)	Winter and Summer 2007	24 hour sample and a 5-day sample in each season	SUMMA canisters (active sampling)	699 (Full-set) (smoking homes: 587) (non-smoking	0.029	98.9 to 100

				homes: 109)		
Halifax, NS / Health Canada 2011b Indoor and outdoor air	Winter and Summer 2009	24 hour samples collected for 7 consecutive days	SUMMA canisters (active sampling)	1254	0.002	99.7 to 100
Edmonton, AB / Health Canada 2013 Indoor and outdoor air	Winter and Summer 2010	24 hour samples collected for 7 consecutive days	SUMMA canisters (active sampling)	1321	0.015 (Winter) 0.035 (Summer)	99.1 to 100
Ottawa, ON / Zhu et al. 2005 Indoor and outdoor air	November 2002 to March 2003	24 hour sample10 L over 100 min	Adsorbent tubes (active sampler)	75	0.1	73 to 83
Québec City, QC / Héroux et al. 2008 Indoor air	January to April 2005	7-day continuous sampling	Passive monitors	96	0.2	100
Canadian National Study (ON, AB, QC, NFLD, BC, NB, SK, MB, NS) / Fellin et al. 1992 Indoor air	1991	24 hour sample	Passive samplers (organic vapour monitors)	754	0.66	Not specified

Appendix C. Ethylbenzene in Various Food Items

Table C1. Summary of Ethylbenzene Concentrations in Various Food Items (US FDA 2006)

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
Dairy products Cheese, American, processed	0.64	2	12	44	1	6
Dairy products Cheese, cheddar, natural (sharp/mild)	0.73	2	12	44	1	4
Dairy products Ice cream, light, vanilla	0.16	2	3	44	0	3
Dairy products Cheese, Swiss, natural	0.23	2	4	44	0	4
Dairy products Ice cream, regular, vanilla	0.09	2	2	44	0	2
Dairy products Sour cream	0.05	2	2	44	0	1
Fats Margarine, regular (salted)	2.39	2	20	44	4	13
Fats Butter, regular (salted)	4.45	2	16	44	11	11
Fats Olive/safflower oil	1	2	23	40	1	5
Fats Salad dressing, creamy/buttermilk type, low-calorie	1.75	7	7	4	0	1
Fats Olive oil	11.5	4	18	4	3	1
Fruits and fruit products Apple (red), raw (with peel)	1.23	5	25	44	2	2
Fruits and fruit products Banana, raw	0.05	2	2	44	0	1
Fruits and fruit products Strawberries, raw/frozen	0.51	4	18	43	1	1
Fruits and fruit products Avocado, raw	0.2	2	4	44	0	3
Fruits and fruit products Orange juice, frozen concentrate,	0.55	3	11	44	1	3

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
reconstituted						
Fruits and fruit products Sherbet, fruit-flavored	0.11	2	3	44	0	2
Fruits and fruit products Cranberry juice cocktail, canned/bottled	1.5	6	6	4	0	1
Vegetables Corn, cream style, canned	0.05	2	2	40	0	1
Vegetables Tomato, raw	0.91	2	29	44	1	3
Vegetables Potato chips	2.27	2	26	44	5	7
Vegetables BF[a], carrots	0.05	2	2	44	0	1
Vegetables Potato, french-fried, fast-food	2.3	2	22	44	3	13
Vegetables Potato salad, mayonnaise-type, from grocery/deli	1.5	2	4	4	0	2
Vegetables Coleslaw, mayonnaise-type, from grocery/deli	3.5	3	8	4	0	3
Vegetables Popcorn, popped in oil	0.35	2	4	40	0	5
Vegetables Popcorn, microwave, butter-flavored	42.75	5	129	4	2	1
Cereal products Bread, white, enriched	1.25	2	28	44	2	3
Cereal products Muffin, fruit or plain	10	2	224	44	6	9
Cereal products Corn/tortilla chips	0.32	2	4	44	0	5
Cereal products Fruit-flavoured cereal, presweetened	0.43	2	7	44	0	5
Cereal products Macaroni and cheese, prepared from box mix	0.34	15	15	44	1	0
Cereal products Cake, chocolate with	1.98	2	13	44	1	16

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
icing						
Cereal products Sweet roll/Danish pastry	1.36	2	12	44	1	12
Cereal products Chocolate chip cookies	1.7	2	33	44	2	9
Cereal products Sandwich cookies with crème filling	0.48	2	8	44	0	6
Cereal products Apple pie, fresh/frozen	1.86	2	14	44	3	12
Cereal products Pumpkin pie, fresh/frozen	0.66	29	29	44	1	0
Cereal products Crackers, graham	1.39	2	23	44	1	9
Cereal products Crackers, butter-type	0.8	3	8	44	0	6
Cereal products Cheese pizza, regular crust, from pizza carry-out	1.38	2	22	40	2	5
Cereal products Pizza, cheese and pepperoni, regular crust, from pizza carry-out	0.98	2	7	44	0	12
Cereal products Doughnut, cake-type, any flavour	2.02	2	16	44	3	10
Cereal products Brownie	1.86	2	14	44	4	10
Cereal products Sugar cookies	1.68	2	19	44	2	11
Cereal products Breakfast tart/toaster pastry	1.25	5	5	4	0	1
Cereal products Macaroni salad, from grocery/deli	5.25	3	12	4	1	2
Meat and poultry Beef, ground, regular, pan-cooked	0.36	2	4	44	0	6
Meat and poultry Beef roast, chuck, oven-roasted	0.48	2	14	44	1	3
Meat and poultry Pork bacon, oven-	1.16	2	16	44	2	7

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
cooked						
Meat and poultry Liver (beef/calf), pan-cooked with oil	0.48	21	21	44	1	0
Meat and poultry Frankfurter (beef/pork), boiled	0.91	2	9	44	0	10
Meat and poultry Bologna (beef/pork)	1.27	2	20	44	1	10
Meat and poultry Salami, luncheon-meat type (not hard)	0.68	2	8	44	0	9
Meat and poultry Quarter-pound hamburger on bun, fast food	2.43	2	38	44	2	11
Meat and poultry Meatloaf, beef, homemade	0.43	2	9	44	0	5
Meat and poultry BF, beef and broth/gravy	0.09	4	4	44	0	1
Meat and poultry Chicken nuggets, fast-food	2.82	2	23	44	4	14
Meat and poultry Chicken, fried (breast, leg, and thigh), fast-food	1.25	2	22	40	2	6
Meat and poultry Quarter-pound cheeseburger on bun, fast food	0.77	2	11	44	1	9
Meat and poultry BF, veal and broth/gravy	1.5	2	4	4	0	2
Meat and poultry BF, turkey and broth/gravy	0.5	2	2	4	0	1
Meat and poultry Chicken breast, fried, fast-food (with skin)	5.75	2	15	4	1	2
Meat and poultry Chicken leg, fried, fast-food (with skin)	1.5	6	6	4	0	1
Meat and poultry Chicken filet (broiled) sandwich on bun, fast-food	2.5	3	7	4	0	2

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
Fish Tuna, canned in oil, drained	0.18	2	3	40	0	3
Fish Fish sticks or patty, frozen, oven-cooked	3.34	2	19	44	7	12
Fish Fish sandwich on bun, fast-food	0.23	10	10	44	1	0
Fish Catfish, pan-cooked with oil	12.5	6	22	4	2	2
Fish Tuna, canned in water, drained	1.25	2	3	4	0	2
Eggs Eggs, scrambled with oil	0.39	2	5	44	0	6
Food primarily sugar Candy bar, milk chocolate, plain	2.3	2	15	44	3	14
Food primarily sugar Candy, caramels	0.15	2	4	40	0	2
Food primarily sugar Candy bar, chocolate, nougat, and nuts	4.5	6	12	4	1	1
Mixed dishes and soups Taco/tostada with beef and cheese, from Mexican carry-out	1.84	2	28	44	1	13
Mixed dishes and soups Burrito with beef, beans and cheese, from Mexican carry-out	2.5	4	6	4	0	2
Nuts and seeds Peanut butter, creamy	2.61	2	14	44	5	13
Nuts and seeds Mixed nuts, no peanuts, dry roasted	4.75	3	38	40	7	11
Nuts and seeds Sunflower seeds (shelled), roasted, salted	14	14	21	4	3	0
Soft drinks and alcohol Carbonated beverage, cola, regular	0.27	5	7	44	0	2
Soft drinks and alcohol Coffee, from ground	0.39	17	17	44	1	0

Food item	Mean (µg/kg)	Minimum (µg/kg)	Maximum (µg/kg)	Number of analyses	Number of results ≥ LOQ[a,b]	Number of trace results[c]
Soft drinks and alcohol Bottled drinking water (mineral/spring), not carbonated or flavored	0.5	2	2	4	0	1

[a] Abbreviations: LOQ: limit of quantification; BF: baby food .
[b] These data represent samples of approximately 285 foods collected and analysed in 44 market baskets between 1991 and 2003.
[c] Trace: number of results that were greater than or equal to the limit of detection but less than the LOQ.

Appendix D. Estimates of Daily Intake of Ethylbenzene by Canadians

Table D1. Upper-bound estimates of daily intake of ethylbenzene by the general population in Canada

Route of exposure	0–6 months[a,b,c] Breast fed (µg/kg-bw per day)	0–6 months[a,b,c] Formula fed (µg/kg-bw per day)	0–6 months[a,b,c] Not formula fed (µg/kg-bw per day)	6 months–4 years[d] (µg/kg-bw per day)	5–11 years[e] (µg/kg-bw per day)	12–19 years[f] (µg/kg-bw per day)	20–59 years[g] (µg/kg-bw per day)	60+ years[h] (µg/kg-bw per day)
Ambient air[i]	0.15	0.15	0.15	0.33	0.26	0.15	0.13	0.11
Indoor air[j]	13	13	13	28	22	13	11	9
Total intake via inhalation	**13.2**	**13.2**	**13.2**	**28.3**	**22.3**	**13.1**	**11.1**	**9.1**
Drinking water[k]	N/A	0.17	0.06	0.07	0.06	0.03	0.03	0.03
Food and beverages[l]	0.057	NI	2.8	2.4	1.6	0.97	0.88	0.72
Soil[m]	3.0×10^{-4}	3.0×10^{-4}	3.0×10^{-4}	5.0×10^{-4}	2.0×10^{-4}	4.0×10^{-5}	3.0×10^{-5}	3.0×10^{-5}
Total intake via ingestion	**0.057**	**0.17**	**2.9**	**2.5**	**1.7**	**1.0**	**0.91**	**0.75**

Abbreviations: N/A, not applicable; NI, data not identified in the literature

[a] Human breast milk data was available from one study conducted in Baltimore, Maryland. The maximum ethylbenzene concentration reported in the study was 0.58 µg/L with a mean concentration of 0.232 µg/L. Assumed that infants consume 0.742 L/day of breast milk (Health Canada 1998).

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

[c] For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of ethylbenzene in water used to reconstitute formula was based on the Canadian Drinking Water Aesthetic Objective of 1.6 µg/L (Health Canada 2014a). Data on concentrations of ethylbenzene in formula were not identified. Approximately 50% of not-formula-fed infants are introduced to solid foods by 4 months of age and 90% by 6 months of age (NHW 1990).

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

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

[f] Assumed to weigh 59.4 kg, breathe 15.8 m^3 of air per day, drink 1.2 L of water per day, and ingest 30 mg

of soil per day (Health Canada 1998).

[g] Assumed to weigh 70.9 kg, breathe 16.2 m^3 of air per day, drink 1.5 L of water per day, and ingest 30 mg of soil per day (Health Canada1998).

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

[i] Outdoor air quality measurements are available nationwide through The National Air Pollution Surveillance Inventory (NAPS). The upper-bound intake estimation was based on the highest 95th percentile measured 24-hour concentration recorded across all monitoring stations with a value of 4.40 µg/m^3. The maximum 24-hour concentration occurred in the Burnaby area of British Colombia with a value of 35.84 µg/m^3 (Environment Canada 2011a). Measured values below the detection limit (0.009 ug/m^3) were replaced with half the detection limit (0.0045 ug/m^3). Canadians are assumed to spend 3 hours outdoors each day (Health Canada 1998).

[j] Six recent Canadian residential studies were identified that measured the indoor air concentrations of various chemicals (Zhu 2005; Health Canada 2010a,b; Health Canada 2012; Health Canada 2013a; Héroux et al. 2008). The highest 95th percentile value reported among the six studies was deemed appropriate to estimate the chronic upper-bounding estimate for exposure. The highest 95th percentile value (54 µg/m^3) was reported during the 2006 survey of 46 Windsor homes. Canadians are assumed to spend 21 hours indoors each day (Health Canada 1998).

[k] The concentration of ethylbenzene in water used to estimate the upper-bound exposure was based on the Canadian Drinking Water Aesthetic Objective of 1.6 µg/L (Health Canada 2014a). Concentrations of ethylbenzene above this level would result in taste and odour problems that would probably be addressed before continuing to consume.

[l] Estimates of intake from food are based upon concentrations in foods that are selected to represent the 12 food groups addressed in calculating intake (Health Canada 1998). Lockhart et al. (1992) analyzed fish samples from northern Manitoba and the Northwest Territories, observing a maximum concentration of 273 µg/kg in whitefish muscle. This value was not used to estimate the "fish" component for the food intake calculation as the source of ethylbenzene may have been industrial and therefore not representative of exposures to the general population of Canada. Estimates of intake from food are based upon concentrations of ethylbenzene identified in the total diet study conducted in the United States from 1991 to 1993 and from 2003 to 2004 and are shown in Appendix C (US FDA 2006). The maximum concentrations identified for each food category were selected except for the vegetable and cereal categories. The maximum concentrations in these food categories (popcorn for vegetable category and muffins for cereal products category) were quite a bit higher than the other items in the category and did not represent a typical maximum daily value for the category. More typical maximum values listed below were selected for the vegetable and cereal product categories.

- Dairy products: maximum concentration value of 12 µg/kg of ethylbenzene identified in cheddar cheese.
- Fats: maximum concentration value of 23 µg/kg of ethylbenzene identified in olive/safflower oil.
- Fruits and fruit products: maximum concentration value of 25 µg/kg of ethylbenzene identified in apples.
- Vegetables: maximum concentration value of 29 µg/kg of ethylbenzene in vegetables identified in tomatoes.
- Cereal products: maximum concentration value of 33 µg/kg of ethylbenzene identified in chocolate chip cookies (similar to concentration identified in white bread).
- Meat and poultry: maximum concentration value of 38 µg/kg of ethylbenzene identified in a fast-food quarter-pound hamburger.
- Fish: maximum concentration value of 22 µg/kg of ethylbenzene identified in pan-cooked catfish.
- Eggs: maximum concentration value of 5 µg/kg of ethylbenzene identified in eggs.
- Foods, primarily sugar: maximum concentration value of 15 µg/kg of ethylbenzene in a plain, milk chocolate bar.
- Mixed dishes: maximum concentration value of 28 µg/kg of ethylbenzene in a take-out taco with beef and cheese.
- Nuts and seeds: maximum concentration value of 38 µg/kg of ethylbenzene in mixed nuts (dry roasted).
- Beverages (soft drinks/alcohol/coffee/tea): maximum concentration value of 17 µg/L of ethylbenzene in coffee.

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

[m] The highest concentration of ethylbenzene found in 122 soil samples collected from typical urban, residential, and parkland locations in Ontario was below the study detection limit (2 ng/g). The Canadian Council of Ministers of the Environment (CCME) published Canadian Soil Quality Guidelines for ethylbenzene. The limits for coarse and fine soil are 0.082 and 0.018 mg/kg, respectively, and are identical across all land uses. The upper-bound intake calculation was based on the guidance value of 0.082 mg/kg.

Table D2. Upper-bound estimates of daily intake of ethylbenzene by individuals living in northern Canada that may consume fish with high concentrations of ethylbenzene

Route of exposure	0–6 months[a,b,c] Breast fed (µg/kg-bw per day)	0–6 months[a,b,c] Formula fed (µg/kg-bw per day)	0–6 months[a,b,c] Not formula fed (µg/kg-bw per day)	6 months–4 years[d] (µg/kg-bw per day)	5–11 years[e] (µg/kg-bw per day)	12–19 years[f] (µg/kg-bw per day)	20–59 years[g] (µg/kg-bw per day)	60+ years[h] (µg/kg-bw per day)
Drinking water[k]	N/A	0.17	0.06	0.07	0.06	0.03	0.03	0.03
Food and beverages[l]	0.057	NI	2.8	3.3	2.3	1.4	1.3	1.0
Soil[m]	3.0×10^{-4}	3.0×10^{-4}	3.0×10^{-4}	5.0×10^{-4}	2.0×10^{-4}	4.0×10^{-5}	3.0×10^{-5}	3.0×10^{-5}
Total intake via ingestion	**0.057**	**0.17**	**2.9**	**3.4**	**2.4**	**1.4**	**1.3**	**1.0**

Abbreviations: N/A, not applicable; NI, data not identified in the literature

[a,b,c,d,e,f,j,h,,k] See description of footnotes in Table D1

[l] Estimates of intake from fish are based upon the maximum concentration of ethylbenzene identified in fish samples from northern Manitoba and the Northwest Territories. The maximum concentration was 273 µg/kg measured in whitefish muscle (Lockhart et al. 1992).

Appendix E. Consumer Product Information

Table E1. Information on Consumer Products in the United States and Denmark

Product category	Type of product	Number of products	Concentration (%)
Arts and crafts[a]	Spray paint	73	0.01 to 15
Arts and crafts[a]	Thinner (liquid)	1	15 to 25
Arts and crafts[a]	Rubber coating (aerosol)	7	4
Arts and crafts[a]	Cleaner (aerosol)	1	<1
Arts and crafts[a]	Glue (aerosol)	1	<1
Automotive products[a]	Spray Paint	14	0.01 to 20
Automotive products[a]	Cleaner (aerosol and liquid)	8	<1 to 25
Automotive products[a]	Liquid paint	10	0.6 to 6.87
Automotive products[a]	Oil (liquid)	1	0.005 to 0.006
Automotive products[a]	Fuel related products	10	<0.1 to 5
Home maintenance[a]	Spray paint	77	0.01 to 10
Home maintenance	Liquid paint	39	<0.1 to 3 (wood paint up to 20)
Home maintenance[a]	Sealant (paste or liquid)	14	0.1 to <5
Home maintenance[a]	Stain (liquid or aerosol)	8	0.118 to 1
Home maintenance[a]	Cleaner (liquid)	3	<1 to 20
Home maintenance[a]	Varnish (liquid)	2	0.6 to 3
Home maintenance[a]	Stain stripper (aerosol)	1	<12
Home maintenance[a]	Thinner (liquid)	1	5 to 15
Home maintenance[a]	Adhesive (paste)	5	0.1 to <3
Other inside home products[a]	Spray coatings	65	0.1 to 15
Other inside home products[a]	Art spray	1	1 to 3
Other inside home products[a]	Stain (aerosol)	2	<5
Other inside home products[a]	Snow spray	1	<1
Consumer products[b]	paint (aerosol and liquid), paint remover, stains, furniture polish and cleaners, and insecticides	200	<0.1 to 23% (two products were reported to contain approximately 70% ethylbenzene; however, the details of these two products were not given as the information was classified as confidential)
Automotive[c]	Not specified	157/658	7.2%

Household cleaners and polishes[c]	Not specified	157/658	0.1%
Paint[c]	Not specified	157/658	2.4%
Fabric and leather[c]	Not specified	157/658	1%
Spray paints[d]	Not specified	5	"not present" to 1.83%

[a] US Household Products Database (HPD, 2011), United States
[b] US EPA's Source Ranking Database (SRD, 2004), United States
[c] Sack et al. (1992), United States
[d] Nielsen et al. (2003), Denmark

Appendix F. Estimates of Exposure to Ethylbenzene

Table F1. Estimates of exposure to Ethylbenzene from Consumer Products by Canadians[a,b]

Consumer product type	Assumptions	Estimated concentrations and daily intakes
Mouthing plastic	Based on the results from VCCEP (2007) report for young children mouthing plastic toys • Assume all non-pacifying objects mouthed by young children are made of styrene-containing polymers, and • Migration rate of ethylbenzene from toys does not decrease over age interval for which exposure is estimated. • Assume mouthable toy contains 108 ppm (µg/g) ethylbenzene (concentration from disposable HIPS food-contact materials) (PWSG 1997 cited in VCCEP 2007), and assume a density of 1 g/cm^3 to give an initial residual ethylbenzene in the polymer of 108 µg/cm^3 (C_{p0}) • Assume that general diffusion of ethylbenzene is expected to be similar to that of styrene, based on their structural similarities, at body temperature, therefore, the estimated diffusion coefficient of ethylbenzene is 1.08×10^{-13} cm^2/s (D_p) • Assume the toy is 2 months old at time of purchase • Based on these assumptions, daily migration rate (DMR) of ethylbenzene is 0.00075 µg/cm^2-day using following equations: DMR = M_t (2 months + 1 day) – M_t (2 months) $M_t = 2 \times C_{p0} \times [(Dp \times t)/\pi]^{1/2}$ • Assume for 2- to 12-month olds: average mouthing time (ET) of 35 min/day (maximum of 350 min/day), mean body weight (BW) of 8.5 kg, oral surface area (SA_{oral}) of 24.4 cm^2. • Assume for 13- to 24-month olds: average mouthing time of 35 min/day (maximum of 350 min/day), mean body weight of 12.2 kg, oral surface area of 31.0 cm^2. • Assume for 25- to 36-month olds: average mouthing time of 2 min/day (maximum of 220 min/day), mean body weight of 34.1 kg, oral surface area of 34.1 cm^2. Ethylbenzene intake = $\frac{DMR \times ET \times SA_{oral} \times \text{conversion factor}}{1440 \text{ min/day} \times BW}$	**2 to 12 months of age:** 5.2×10^{-8} to 5.2×10^{-7} mg/kg-bw per day **13 to 24 months of age:** 4.6×10^{-8} to 4.6×10^{-7} mg/kg-bw per day **25 to 36 months of age:** 2.5×10^{-9} to 2.8×10^{-7} mg/kg-bw per day 2.5×10^{-9} to 5.2×10^{-7} mg/kg-bw per day Range covers calculations using average and maximum mouthing times.

Consumer product type	Assumptions	Estimated concentrations and daily intakes
	Refer to VCCEP 2007 for more details	
Aerosol spray paint[c] (ConsExpo model – using spray paint scenario but evaporation model since EB is volatile) Assume use entire can or approximately 300 g)	**Reported weight fractions ranging from 0.01 to 5% were used (HPD 2011, Home Hardware 2013, Rust-Oleum 2013a, Health Canada 2013b, 2014b).** **Frequency of 2 times/year (RIVM 2007a).** **Inhalation: evaporation from an increasing area** Exposure duration of 20 min, application duration of 15 min, applied amount of 300 g, room volume of 34 m^3, ventilation rate of 1.5/hour (well ventilated), release area of 2 m^2, use Langmuir method for mass transfer rate, molecular weight matrix of 300 g/mol since compound of interest is not the main solvent (RIVM 2007a). **Dermal: contact rate** Contact rate of 100 mg/min, release duration of 15 min (RIVM 2007a)	**Inhalation –** Mean concentration on day of event = 0.006 to 3 mg/m^3 **Dermal –** Acute applied dose = 0.002 to 1.1 mg/kg-bw per event
Liquid paint (high solid paint – painting wood lathed wall)	**Reported weight fractions ranging from 0.1 to 1% were used (HPD 2011, Rust-Oleum 2013b, ICI Paints 2010, Health Canada 2013b, 2014b). The maximum concentration of 20% was not used as it was for a specialized product that no longer appears to be available.** **Frequency of 1 time/year (RIVM 2007a).** **Inhalation: evaporation from an increasing area** Exposure duration of 132 min, application duration of 120 min, room volume of 20 m^3, ventilation rate of 1.5/hour (well ventilated), applied amount of 1300 g, release area of 10 m^2, molecular weight matrix of 550 g/mol (compound of interest is not the main solvent), use Langmuir method for mass transfer rate (RIVM 2007a). **Dermal: constant rate** Contact rate of 30 mg/min, release duration of 120 min (RIVM 2007a)	**Inhalation –** Mean concentration on day of event = 1.3 to 13 mg/m^3 **Dermal –** Acute applied dose = 0.051 to 0.51 mg/kg-bw per event
Paint remover (liquid spot remover)	**Assume a weight fraction of 4%, (IPCS 1996; SRD 2004; WM Barr 2012, Health Canada 2013b, 2014b)** **Frequency of 1 time/year (RIVM 2007b).** **Inhalation: evaporation from an increasing area** Exposure duration of 60 min, application duration of 60	**Inhalation –** Mean concentration on day of event = 2.8 mg/m^3

Consumer product type	Assumptions	Estimated concentrations and daily intakes
	min, room volume of 20 m^3, ventilation rate of 1.5/hour (well ventilated), release area of 2 m^2, molecular weight matrix of 300 g/mol (compound of interest is not the main solvent), use Langmuir method for mass transfer rate (RIVM 2007b), applied amount of 106 g (assuming use entire bottle (133 mL) of spot remover in one application (use density from msds (0.797 g/mL) and volume of product (133 mL) = 106 g) (WM Barr 2012), **Dermal: instant application** Exposed surface area of 430 cm^2 (palms of both hands), applied amount of 0.5 g (RIVM 2007b).	**Dermal –** Acute applied dose = 0.28 mg/kg-bw per event
Lacquer/Stain /varnish (use solvent-rich paint scenario)	**Reported weight fractions ranging from 0.1 to 2% were used (HPD 2011; Rust-Oleum 2011, Performance Coatings 2013, Sherwin-Williams 2010, Health Canada 2013b, 2014b)** **Frequency of 4 times/year, based on mean frequency (US EPA 1997).** **Inhalation: evaporation from an increasing area** Exposure duration of 132 min, application duration of 120 min, room volume of 20 m^3, ventilation rate of 1.5/hour (well ventilated), release area of 10 m^2, molecular weight matrix of 300 g/mol (compound of interest is not the main solvent), use Langmuir method for mass transfer rate (RIVM 2007a), applied amount of 460 g, based on mean amount of product used (US EPA 2009) **Dermal: constant rate** Contact rate of 30 mg/min, release duration of 120 min (RIVM 2007a)	**Inhalation –** Mean concentration on day of event = 0.5 to 9.4 mg/m^3 **Dermal –** Acute applied dose = 0.051 to 1.0 mg/kg-bw per event
Caulking/Sealant	**Reported weight fractions of 0.1 to 5% were used (Henkel 2008, 2009; Sherwin-Williams 2008; HPD 2011, Health Canada 2013b, 2014b)** **Frequency of 3 times/year (RIVM 2007b).** **Inhalation: evaporation from an increasing area (use weight fractions 0.1 to 1% (products used indoors) as 5% was reported in a product meant for exterior use only)** Exposure duration of 45 min, application duration of 30 min, room volume of 10 m^3, ventilation rate of 1.5/hour, applied amount of 75 g, release area of 30 m^2, molecular weight matrix of 300 g/mol (compound of interest is not main solvent), use Langmuir method for mass transfer	**Inhalation –** Mean concentration on day of event = 0.09 to 5.2 mg/m^3 **Dermal –** Acute applied dose = 0.021 to 1.1 mg/kg-bw per event

Consumer product type	Assumptions	Estimated concentrations and daily intakes
	rate (RIVM 2007b). **Dermal: constant rate (use weight fractions of 0.1 to 5%)** Contact rate of 50 mg/min, release duration of 30 min, exposed surface area of 2 cm^2 (RIVM 2007b)	

[a] Since these products are used primarily by adults (20–59 years old), estimated exposures have been derived for this age group only unless otherwise stated.
[b] Assume 100% absorption across the lungs.
[c] Exposure to an aerosol spray paint was considered representative of exposures to aerosol paint removers as well.

Appendix G. Estimates of Potential Exposure to Ethylbenzene from Gasoline

Table G1. Estimates of Potential Exposure to Ethylbenzene from Gasoline

Consumer product type	Assumptions	Estimated concentrations and daily intakes
Gasoline[a]	**Dermal exposure while refuelling a vehicle** Reported weight fractions range from 1.0 to 5.4% were used (CONCAWE 1997) • Use thin-film thickness to derive mass of gasoline on the skin, and assume that the thin-film on skin measures 0.002 cm (value for mineral oil, immersion with partial wipe scenario) (US EPA 2011) • Assume gasoline has a density of 0.79 g/cm^3 (CONCAWE 1992) • Assume that gasoline gets onto one-eighth of one hand (57 cm^2) (Health Canada 1995). Mass of gasoline on skin = 0.002 cm × 0.79 g/cm^3 × 57 cm^2 = 0.09 g Dose = $\frac{0.09\ g \times 0.054}{70.9\ kg}$ = 6.85 × 10^{-5} g/kg-bw = 0.0685 mg/kg-bw	Estimated short-term dermal dose = 0.01 to 0.07 mg/kg-bw per event

[a] The highest 95th percentile concentration of 1461 µg/m^3 identified in the PACE studies (1987, 1989) was used to estimate inhalation exposures to ethylbenzene while refuelling a vehicle.

Appendix H. Summary of Health Effects

Table H1. Information for Ethylbenzene in laboratory animals and *in vitro*

Endpoint	Lowest effect levels[a]/Results
Acute toxicity	**Lowest oral LD_{50}** = 3500 mg/kg-bw in rats (Wolf et al. 1956). [Additional studies: Smyth et al. 1962; NTP 1986]. **Lowest dermal LD_{50}** = 15 354 mg/kg-bw in rabbits (Smyth et al. 1962). [Additional studies: Harton and Rawl 1976]. **Lowest inhalation LC_{50}** = 17 200 mg/m^3 in rats (4 hours) (Smyth et al. 1962). [Additional studies: Ivanov 1962]. **Lowest inhalation LOEC** (rats) ≥ 1740 mg/m^3 (400 ppm), based on arbitrary assessment of the authors that a moderate activation in motor behaviour was observed in male CFY rats (8 per group) exposed to ethylbenzene vapour at concentrations between 1740 to 6514 mg/m^3(400 and 1500 ppm) for 4 hours, compared with other solvent-exposed rats. The minimum narcotic concentration for ethylbenzene was 9466 mg/m^3 (2180 ppm) (Molnar et al. 1986). [Additional studies: Yant et al. 1930; Gerarde 1960; Ivanov 1962; Tegeris and Baltser 1994].
Short-term repeated-dose toxicity	**Lowest inhalation LOEC** (mice) = 326 mg/m^3 (75 ppm), based on significant reductions in liver pentoxyresorufin *O*-dealkylase (PROD) and ethoxyfluorocoumarin-*O*-dealkylase activities and concentration-related, although not significant, reductions in lung ethoxyresorufin *O*-dealkylase and PROD activities in male and female mice exposed to 326 mg/m^3 ethylbenzene for 1 week. In this study, six mice per group were exposed to ethylbenzene at 326 mg/m^3 for 1 week or at 3260 mg/m^3 (750 ppm) for 1 or 4 weeks (6 hours/day, 5 days/week). At higher concentration (3260 mg/m^3)significantly increased relative liver weights, hepatic S-phase DNA synthesis and mitotic figures, hepatoenzyme activities, and hepatocellular hypertrophy were observed in both sexes of mice exposed to ethylbenzene for 1 week or 4 weeks. Significantly increased lung S-phase DNA syntheses were observed after exposure to ethylbenzene for 1 week in both sexes but decreased after 4 weeks exposure in males, while in females, no significant difference between exposed and control mice was observed after 4 weeks exposure. In addition, several mixed function oxygenases in mice lung altered after 1 or 4 week exposure (Stott et al. 2003). **Lowest inhalation LOAEC** (rats) = 1740 mg/m^3 (400 ppm), based on ototoxicity.with a NOAEC identified at 1305 mg/m^3 (300 ppm) (Cappaert et al. 2000). See Neurotoxicity/ototoxicity section below. [Additional studies: Andersson et al. 1981; Toftgård and Nilsen 1982; Elovaara et al. 1985; EPA 1986 a, 1986b; Romanelli et al. 1986; Mutti et al. 1988; Cragg et al. 1989; Cappaert et al. 1999, 2001, 2002; Stott et al. 2003 (rats); Saillenfait et al. 2006; Li et al. 2010].

Endpoint	Lowest effect levels[a]/Results
	Lowest oral (gavage) LO(A)EL (rats) **=** 250 mg/kg per day, based on significantly increased absolute and relative liver weights, with centrilobular hepatocyte hypertrophy, relative kidney weights, and significantly increased numbers of granular and epithelial cell casts in the urine of exposed male rats. Increased incidence and severity of hyaline droplet nephropathy were also observed in the exposed male rats at this dose level. Although the authors speculate the nephropathy was α2u-globulin-associated, no further test has been conducted to confirm the α2u-globulin deposition in the animals. The NOAEL = 75 mg/kg-bw per day as defined by the authors. In this study, 5 rats/sex per group were administered 0, 75, 250, or 750 mg/kg per day ethylbenzene by gavage for 4 weeks. At highest dose level (750 mg/kg-bw per day), significantly increased absolute and relative liver weights and significantly increased serum alanine aminotransferase, serum urea, and cholesterol concentrations were observed in both sexes. In addition, significantly increased total bilirubin in females and the number of transitional epithelial cells in urinary sediment in males were observed. Histological results showed centrilobular hepatocyte hypertrophy in mid (males only) and high dose groups (male and females) and an increase incidence and severity of hyaline droplet nephropathy in mid and high dose males (Mellert et al. 2007). [Additional study: Gagnaire and Langlais 2005].
Subchronic toxicity	**Lowest inhalation LOEC** (rat) = 435 mg/m^3 (100 ppm), based on significantly decreased serum alkaline phosphatase levels in female rats exposed to ethylbenzene, 6 hours/day, 5 days/week for 13 weeks. In this study, 10 of each sex of F344 rats per group were exposed to ethylbenzene at 0, 435, 1087, 2175, 3263, or 4350 mg/m^3(0, 100, 250, 500, 750, or 1000 ppm). Ten additional rats of each sex were included at each exposure level to provide blood samples for clinical pathology. Clinical chemistry data were collected on day 5, 23, and after 13 weeks. Toxicity data were analysed at 13 weeks. At higher concentrations (≥1087 mg/m^3), significantly decreased alkaline phosphatase levels were observed in both sexes of rats. In addition, significantly increased absolute kidney weights in both sexes and increased relative kidney weights in males were observed at ≥2175 mg/m^3; significantly increased absolute liver weights in both sexes and increased relative liver weights in males were observed at ≥1087 mg/m^3; significantly increased absolute lung weights were observed in females at ≥1087 mg/m^3. No effects on sperm, testicular morphology or the length of the oestrous cycle were observed. No histopathological changes were observed in an association with the liver or kidney weights changes. Lymphoid hyperplasia in the bronchial and mediastinal lymph nodes and inflammatory cell infiltrates around vessels with foci of inflammatory cells in septae and lumen of alveoli in lung were observed in rats exposed to ethylbenzene at ≥1087 mg/m^3; however, the severity of these lesions were not dose related and the characteristics of the lesions were more of a response to an infectious agent. The authors thus stated that the inflammatory lung lesions were probably unrelated to ethylbenzene exposure (NTP 1992). [Additional studies: Wolf et al. 1956; Elovaara et al. 1985; NTP (mice) 1992; Gagnaire et al. 2007, described in the “neurotoxicity” section of this table; Zhang et al. 2010].

Endpoint	Lowest effect levels[a]/Results
	Lowest oral LO(A)EL (rats) = 250 mg/kg-bw per day, based on significantly increased absolute and relative liver weights and relative kidney weights in both sexes, and significantly increased absolute kidney weights in males, significantly increased alanine aminotransferase and gamma glutamyltransferase levels, significantly increased total bilirubin, number of transitional epithelial cells and granular and epithelial cell casts in urinary sediments, serum potassium and calcium concentrations in males, and significantly increased cholesterol and reduced prothrombin time in both sexes of rats. NOAEL = 75 mg/kg-bw per day as defined by the authors. In this study, 10 of each sex of Wistar rats were exposed to 0, 75, 250, or 750 mg/kg-bw per day ethylbenzene by gavage for 13 weeks (daily dosage was divided into two doses administered to each rat at approximately 8-hour intervals). In the high dose groups, significantly increased mean corpuscular volume, alanine aminotransferase and serum magnesium concentrations in both sexes, and significantly increased total serum protein and reduced platelet counts in females were observed. In addition, landing foot-splay was significantly decreased in high dose males and motor activity was significantly increased in high dose females. Histological results revealed significantly increased incidence of centrilobular hypertrophy of hepatocytes in both sexes of mid- and high-dose treated groups. A treatment-related increase in hyaline droplet storage in the male renal tubular epithelium was observed; however, no treatment-related effects were seen in the incidence of initial signs of chronic progressive neuropathy. Thymus weights were reduced in mid- and high-dose females without any histomorphological changes (Mellert et al. 2007). Significantly increased relative liver and kidney weights in male rats were also observed at 250 and 500 mg/kg-bw per day dose levels in another subchronic (13 weeks) study with Crl:CD(SD) rats (10–11/sex per dose. Rats were administered 0, 50, 250, or 500 mg/kg-bw per day ethylbenzene by gavage; daily dosage was divided into two doses administered to each rat at approximately 3-hour intervals). Significantly increased relative liver weights were observed at the 500 mg/kg-bw per day dose level in female rats. No treatment related histopathological changes were observed in livers or kidneys of rats in the 500 mg/kg-bw per day dosage group (Li et al. 2010). [Additional study: Wolf et al. 1956; Barnett 2006].
Chronic toxicity/ carcinogenicity	**Carcinogenicity bioassay via inhalation in rats and mice:** F344 rats and B6C3F1 mice were exposed to 0, 326, 1090, or 3260 mg/m^3 (0, 75, 250, or 750 ppm) ethylbenzene, 6 hours/day, 5 days/week, for 104 and 103 weeks, respectively. In the rat study, at the highest concentration, significantly increased incidences of renal tubular neoplasms (3 out of 50 [3/50], 5/50, 8/50, 21/50; historical control ranged 0–4%), interstitial cell adenomas in the testis (36/50, 33/50, 40/50, 44/50; historical control ranged 54–83%), and bilateral testicular adenoma (27/50, 23/50, 32/50, 40/50) were observed in males, and significantly increased renal tubular neoplasms (0/50, 0/50, 1/50, 8/50) were observed in females. In the mouse study, at the highest concentration, significantly increased incidences of alveolar/bronchiolar neoplasms were observed in males (7/50, 10/50, 15/50, 19/50; historical control ranged 10–42%) and significantly increased hepatocellular neoplasms were observed in females (13/50, 12/50, 15/50, 25/50; historical control ranged 3–54%) (Chan et al. 1998; NTP 1999). **Carcinogenicity bioassay via oral exposure in rats**

Endpoint	Lowest effect levels[a]/Results
	SD rats, 40 of each sex per group were exposed to 500 mg/kg-bw per day ethylbenzene in olive oil by stomach tube, 4–5 days/week for 104 weeks. Animals were examined after week 141. Total malignant tumours were increased in exposed rats (14/40 and 17/37 in exposed males and females, respectively, and 12/45 and 11/49 in control males and females, respectively). No further information was provided in the report (Maltoni et al. 1985). Additional information was published later (Maltoni et al. 1997) in which SD rats were also exposed to 800 mg/kg-bw ethylbenzene. Increased incidences in nasal cavity tumours, type not specified (2% in exposed females versus 0% in controls), neuroesthesioepitheliomas (2% in exposed females versus 0% in controls; 6% in exposed males versus 0% in controls), and oral cavity tumours (6% in exposed females versus 2% in controls; 2% in exposed males versus 0% in controls) were observed at 800 mg/kg-bw. Statistical analysis was not provided. **Non-cancer endpoints:** **Lowest inhalation LOAEC** (rats) = 326 mg/m^3 (75 ppm), based on significantly increased severity of nephropathy in female rats (104-week study). Nephropathy was characterized by a spectrum of changes, including dilation of renal tubules with hyaline or cellular casts, interstitial fibrosis and mononuclear inflammatory cell infiltration, foci of tubular regeneration, and transitional epithelial hyperplasia of the renal papilla. Details of the study were described above. The severities of nephropathy were significantly increased in all exposed female rats and in 3260 mg/m^3 (750 ppm) male rats. At 3260 mg/m^3, significantly increased incidences of renal tubule hyperplasia in exposed both male and female rats and significantly decreased survival of male rats were observed. Other pathological lesions, such as bone marrow and parathyroid gland hyperplasia, prostate gland inflammation, cystic degeneration of the liver, oedema, congestion and haemorrhage in the lungs, haemorrhage in mesenteric and slightly increased renal lymph nodes, were also observed in exposed male rats; the authors considered that the biological significance of these effects was unclear and their relationship to ethylbenzene exposure was uncertain. **LOAEC** (mice) = 1090 mg/m^3(250 ppm), based on significantly increased incidences of hyperplasia of the pituitary gland pars distalis in exposed female mice and significantly increased incidences of synctyial alteration of hepatocytes in exposed males. **NOAEC** (mice) = 326 mg/m^3 (75 ppm). At 3260 mg/m^3, significantly increased incidences of synctyial alteration of hepatocytes, hepatocellular hypertrophy and hepatocyte necrosis in males and significantly increased incidences of eosinophilic foci of the liver and pituitary gland pars distalis hyperplasia in females were observed. Significantly increased thyroid gland follicular cell hyperplasia and alveolar epithelial metaplasia in both males and females were observed at 3260 mg/m^3 (Chan et al. 1998; NTP 1999).
Genotoxicity and related endpoints: *in vivo*	**Chromosomal aberrations** *Negative results:* Rat bone marrow cells collected from rats exposed to a dose equivalent to 239 mg/m^3 of xylene containing 18.3% ethylbenzene (300 ppm), 6 hours/day, 5 days/week, for 9, 14, and 18 weeks (no further details available) (Donner et al. 1980). **Micronuclei test** *Negative results:* Mouse peripheral lymphocytes collected from male and female B6C3F1 mice

Endpoint	Lowest effect levels[a]/Results
	exposed to ethylbenzene vapour for 13 weeks (details of this study were described above in the subchronic data set) (NTP 1992, 1999). Mouse bone marrow cells collected from male NMRI mice exposed to ethylbeneze by intraperitoneal injection of two similar doses, 2 mL/kg-bw (equivalent to 1.74 mg/kg-bw), 24 hours apart. Mice were sacrificed 30 hours after the first injection (Mohtashamipur et al. 1985). [Additional study: negative results were observed in mouse bone marrow cells with 1-phenylethanol, the major phase I metabolite of ethylbenzene, in NMRI male mice, five per group, administered a single gavage dose of 187.50, 375, or 750 mg/kg of 1-phenylethanol. Animals were sacrificed 24 or 48 hours post-treatment and bone marrow was sampled (Engelhardt 2006)]. **Unscheduled DNA synthesis** *Negative results:* Mouse liver cells collected from B6C3F1 males exposed to 2175 or 4350 mg/m^3 (500 or 1000 ppm) and females exposed 1631 or 3263 mg/m^3 (375 or 750 ppm) of ethylbenzene vapour for 6 hours (Clay 2001). **Non-mammalian sex-linked recessive lethal assay** *Negative results:* *Drosophila* (Donner et al. 1980).
Genotoxicity and related endpoints: *in vitro*	*Positive results:* Gene mutation assay in mouse lymphoma cells without metabolic activation, only at higher dose level (80 µg/mL) that elicited cytotoxicity (McGregor et al. 1988; NTP 1992, 1999). *Negative results:* Ames assays in *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535 with and without metabolic activation (NTP 1992, 1999; Zeiger et al. 1992); *Salmonella typhimurium* strains TA98, TA100, TA1535, TA 1537, and TA 1538, *Escherichia coli* WP2, Wp2uvrA, and *Saccharomyces cerevisiae* JD1 with and without metabolic activation (Dean et al. 1985); *Saccharomyces cerevisiae* D7 and XV185-14C without metabolic activation (Nestmann and Lee 1983). A mouse lymphoma forward mutation assay was performed accoding to OECD, USEPA and EC guidelines. The result of the study was negative. Excessive toxicity was observed at concentrations levels from 54 µg/mL in the absence of S9 and from 80 µg/mL in the presence of S9 (Seidel et al. 2006). **Chromosomal aberrations** *Negative results:* Chinese hamster ovary with and without metabolic activation (NTP 1992, 1999); rat liver (RL4) epithelial type cells, with and without metabolic activation (Dean et al. 1985).

Endpoint	Lowest effect levels[a]/Results
	Micronuclei test *Positive results:* Syrian hamster embryo cells without metabolic activation (Gibson et al. 1997). **Sister chromatid exchange** *Positive results:* Marginal effects in human lymphocytes without metabolic activation, at the highest dose (10 mM) that elicited cytotoxicity (Norppa and Vainio 1983). *Negative results:* Chinese hamster ovary cells with and without metabolic activation (NTP 1992. 1999). **Cell transformation assay** *Positive results:* Syrian hamster embryo (SHE) cells after exposure to ethylbenzene for 7 days (the results were negative after the cells were exposed to ethylbenzene for 24 hours) (Kerckaert et al. 1996) *Negative results:* Syrian hamster embryo (SA7/SHE) cells after exposure to ethylbenzene for 24 hours and the transformed foci were scored after 6 weeks (Casto and Hatch 1977). **DNA damage (Comet assay)** *Positive results:* Single DNA strand breaks in human peripheral blood lymphocytes (Chen et al. 2008). [Additional studies: Oxidative DNA damage in human *p*53 tumour suppressor gene fragments (*in vitro* test) and DNA adducts, 8-oxo-7,8-dihydro-2′dexyguanosine, formation in calf thymus DNA (*in vitro* test) after exposure to sunlight-irradiated ethylbenzene and in the presence of Cu^{2+} (Toda et al. 2003) or after exposure to ethylbenzene metabolites, including ethylhydroquinone and 4-ethylcatechol, in the presence of Cu^{2+} in a dose-dependent manner (Midorikawa et al. 2004)]. **Gene conversion** *Negative results:* *Pseudomonas putida* (Leddy et al. 1995)
Developmental toxicity	**Lowest inhalation LOEC** = 435 mg/m^3 (100 ppm), based on significantly increased incidence of extra ribs in rats that were exposed to ethylbenzene during gestation period. In this study, female Wistar rats (29–33 per group) were exposed to 435 mg/m^3 or 4350 mg/m^3 (1000 ppm) ethylbenzene via inhalation for 7 hours/day, 5 days/week for 3 weeks. The control group rats were exposed to air. The rats were then mated and exposed daily through 19 days of gestation. The rats that were exposed to air during pregestation period were divided into three groups during gestation exposure period: control (air), 435 mg/m^3, and

Endpoint	Lowest effect levels[a]/Results
	4350 mg/m^3 groups. The rats that were exposed to a low or high concentration of ethylbenzene during pregestation were divided into two groups, respectively, during the gestation exposure period: control (no further exposure during gestation) and exposure group (at the same exposure level as they had before gestation). Maternal toxicity was observed at 4350 mg/m^3 in rats, including significantly increased relative and absolute liver, kidney, and spleen weights without pathological changes. A possible reduction in fertility, indicated by the reduction in the percent of sperm-positive rats that were pregnant following pregestational exposure to either concentration, was observed in rats at both exposure levels; however, there was no significant difference in response at 435 and 4350 mg/m^3. The significantly increased incidence of extra ribs were also observed in rats that were exposed to a high concentration of ethylbenzene during both pregestation and gestation periods, or during the gestation period only, but not in the rats that were exposed to a low concentration of ethylbenzene during both pregestation and gestation periods. Therefore, the authors considered that the dose–repsonse relationship for this effect at 435 mg/m^3 was not consistent. In addition, the authors considered the increased incidence of extra ribs is not a teratogenic response, but rather an indication for teratogenesis at higher exposure levels (Hardin et al. 1981; NIOSH 1981). [Additional studies: Ungvary and Tatrai 1985; NIOSH 1981; Saillenfait et al. 2003, 2006, 2007; Faber et al. 2007].
Reproductive toxicity	**Inhalation NOAEC** for reproductive toxicity (rats) > 2174 mg/m^3 (500 ppm, the highest concentration tested), based on no significant exposure-related reproductive effects, were observed in this study. In this two-generation study, Crl:CD(SD) IGS BR rats (F_0 generation, 30/sex per group; F_1 generation, 25/sex per group) were exposed to 0, 109, 435, and 2174 mg/m^3 (0, 25, 100, or 500 ppm) ethylbenzene 6 hours/day, 7 days/week, started at least 70 consecutive days before mating. F_0 and F_1 females continued inhalation exposure throughout mating and gestation day 20. On lactation days 1–4, F_0 and F_1 females were given either corn oil or ethylbenzene via gavage at doses of 0, 26, 90, and 342 mg/kg per day. Inhalation exposure of these rats was continued on lactation days 5 to 21 (euthanasia time). For F_1 animals, inhalation exposure was initiated on postnatal day 22. The F_2 generation was not directly exposed. No significant changes in oestrous cycle length, pre-coital intervals, male and female mating and fertility indices, gestation length, spermatogenic endpoints, and reproductive organ weights were observed in exposed rats. The ovarian follicle counts for the F_1 females in the 2174 mg/m^3 group were similar to the control values. There were no exposure-related deaths or clinical observations in any test group in either generation of animals. The authors defined a NOEC of 435 mg/m^3 (100 ppm)and a NOAEC of 2174 mg/m^3 for parental systemic toxicity, based on transiently decreased body weight gain in F_0 and F_1 males at 2174 mg/m^{3}and in F_0, but not F_1, females at 435 and 2174 mg/m^3, significantly increased relative liver weights in both F_0 and F_1 males and females at 2174 mg/m^3, and significantly increased relative kidney weights in both F_0 and F_1 males at 2174 mg/m^3, without pathological changes. In addition, significantly increased absolute and relative thyroid weights in F_0, but not F_1, males, were observed at 435 and 2174 mg/m^3, and significantly increased absolute lung and prostate weights in F_0, but not F_1, males were observed at 2174 mg/m^3, without pathological findings. Although there were significant decreases in oestrous cycle length in F_0 females at 2174 mg/m^3, the results were not significant in F_1 females and the oestrous cycle

Endpoint	Lowest effect levels[a]/Results
	length in F_0 rats was similar to those historical controls. The authors considered that these effects were not ethylbenzene exposure related. Neurobehavioral development of one F2 offspring was assessed in a functional observational battery (FOB) (PND 4, 11, 22, 45, and 60), motor activity sessions (PND 13, 17, 21, and 61), acoustic startle testing (PND 20 and 60), a Biel water maze learning and memory task (initiated on PND 26 or 62), and in evaluations of whole-brain measurements and brain morphometric and histologic assessments (PND 21 and 72). There were no alterations in FOB parameters, motor activity counts, acoustic startle endpoints, or Biel water maze performance in offspring attributed to parental ethylbenzene exposure at the highest exposure level tested (Stump 2004a; Faber et al. 2006, 2007). [Additional studies: Hardin et al. 1981; NIOSH 1981; Cragg et al. 1989; NTP 1992]. **Oral LOEL** = 500 mg/kg-bw, based on significantly decreased luteinizing hormone and 17 ß-estradiol levels accompanied by uterine changes such as increased stromal tissue with dense collagen bundles and reduced lumen. In this study, CFY rats were given 500 or 1000 mg/kg ethylbenzene orally in the morning of oestrus, two dioestruses, and pro-oestrus. (The study report is very limited. The test dosage was not clearly stated as the ratio of test material weight versus body weight or versus food weight, but was assumed to be the test maternal weight versus body weight.) The author concluded that ethylbenzene exposure blocked the ovarian cycle and this blocking occurs during dioestrus, based on the vaginal smears and the structure of the uterine wall (Ungváry 1986).
Immunotoxicity	**Inhalation NOAEC** for immunotoxicity (rats) = 2174 mg/m^3 (500 ppm, the highest concentration tested), based on no treatment-related effects on functional ability of the hormonal component of the immune system in rats as measured by splenic IgM antibody-forming cell response to the T-dependent antigen, sheep erythrocytes. In this study, SD rats were exposed to doses equivalent to 0, 109, 435, or 2174 mg/m^3(0, 25, 100, 500 ppm) ethylbenzene vapour for 6 hours/day for 28 consecutive days. The rats then received a single intravenous immunization injection of sheep red blood cells approximately 4 days prior to the scheduled necropsy. No treatment-related effects on survival, clinical signs, body weight, feed consumption, haematology parameters, or IgM antibody-forming cell response were observed. Relative liver and kidney weights were increased in the 2174 mg/m^3 group (Stump 2004b; Li et al. 2010).
Neurotoxicity/ototoxicity	**Lowest acute inhalation LOEC** for neurotoxicity (rats) ≥ 1740 mg/m^3(400 ppm), based on a moderate activation in motor behaviour in male CFY rats (8 per group) exposed to ethylbenzene vapour at concentrations between 1740 to 6514 mg/m^3(400 and 1500 ppm) for 4 hours. The minimum narcotic concentration for ethylbenzene was 9466 mg/m^3 (2180 ppm) (Molnar et al. 1986). [Additional studies: Yant et al. 1930; Gerarde 1960; Ivanov 1962; Tegeris and Baltser 1994]. **Lowest short-term inhalation LOAEC** for ototoxicity (rats) = 1740 mg/m^3(400 ppm), based on ototoxic effects, defined as increased auditory thresholds and outer hair cell loss after exposure to ethylbenzene 8 hours/day for 5 days. In this study, rats were exposed to ethylbenzene at 0, 1305, 1740, 2393 mg/m^3 (0, 300,

Endpoint	Lowest effect levels[a]/Results
	400, and 550 ppm) for 8 hours/day for 5 consecutive days. Three to six weeks after the exposure, auditory function was tested by measuring compound action potentials (CAP) in the frequency range of 1–24 kHz and 2*f*1–*f*2 distortion product otoacoustic emissions (DPOAEs) in the frequency range of 4–22.6 kHz. At 1740 mg/m^3, auditory thresholds were increased by 15 and 16 dB at 12 and 16 kHz, respectively, and at 2393 mg/m^3 by 24, 31, and 22 dB at 8, 12, and 16 kHz, respectively. DPOAE amplitude growth with stimulus level was affected only after exposure to 2393 mg/m^3 at 5.6, 8, and 11.3 kHz. Outer hair cell (OHC) loss was found in two of the five examined locations in the cochlea. At 1740 mg/m^3, 25% OHC loss was found at the 11- and 21-kHz region. The highest concentration evoked 40 and 75% OHC loss at the 11- and 21-kHz location, respectively. **NOAEC** for ototoxicity = 1305 mg/m^3 (300 ppm) (Cappaert et al. 2000). In addition, ethylbenzene exposure induced significant depletion of striatal and tubero-infundibular dopamine levels in rabbits at concentration of 3260 mg/m^3 (750 ppm) and above (Romanelli et al. 1986; Mutti et al. 1988). [Additional studies: Andersson et al. 1981; Frantik et al. 1994; Cappaert et al. 1999, 2001, 2002]. **Lowest short-term oral LOAEL** for ototoxicity (rats, 2 weeks, gavage) = 900 mg/kg-bw per day, based on irreversible hearing loss measured by behavioural or electrophysiological methods and associated with damage to outer hair cells in cochlea (Gagnaire and Langlais 2005). **Lowest subchronic inhalation LO(A)EC** for ototoxicity (rats) = 870 mg/m^3(200 ppm, the lowest concentration tested), based on dose-dependent outer hair cell losses (hearing loss) during the recovery period. In this study, SD rats were exposed to 0, 870, 1739, 2609, or 3478 mg/m^3 (0, 200, 400, 600, or 800 ppm) ethylbenzene vapour for 6 hours/day, 6 days/week for 90 days with an 8-week post-exposure recovery period. Outer hair cell losses with increasing severity (4% to nearly 100%, respectively) in the rats that received 870 to 3478 mg/m^3 ethylbenzene were observed. Concentrations of 1739 mg/m^3 and greater produced significantly higher audiometric thresholds that did not recover 8 weeks after exposure ceased (Gagnaire et al. 2007). [Additional study: Faber et al. 2007, details included in the above Reproductive toxicity session]. **Lowest subchronic oral LOEL** for neurotoxicity (rats) = 750 mg/kg-bw per day, based on significantly decreased landing foot-splay in males and significantly increased motor activity in females (Mellert et al. 2007). Subchronic oral **NOEL** for neurotoxicity = 500 mg/kg per day, based on no treatment-related adverse neurotoxicological effects observed in SD rats administered 0, 50, 250, and 500 mg/kg-bw per day ethylbenzene by gavage daily for 90 days (Barnett 2006). Similarly, neurobehavioural changes, as measured by FOB, including acoustic reaction, and motor activity evaluations, were not observed in rats exposed to ethylbenzene up to 500 mg/kg-bw per day for 90 days (Li et al. 2010).
Irritation	Ethylbenzene is a mucous membrane irritant. Guinea pigs exposed to 0.2% ethylbenzene vapour for 1 minute experienced moderate eye and nasal irritation, while exposure to 0.1% ethylbenzene vapour caused slight basal irritation that ceased after 30 minutes (Lewis 1992). Instillation of undiluted ethylbenzene in

Endpoint	Lowest effect levels[a]/Results
	rabbit eyes caused conjunctival irritation (Wolf et al. 1956; Smyth et al. 1962) and moderate corneal injury (Smyth et al. 1962). Ethylbenzene is a moderate skin irritant. Uncovered application of undiluted ethylbenzene induced moderate irritation and necrosis in rabbit skin (Wolf et al. 1956; Smyth et al. 1962).

[a] Definitions: LC_{50} = median lethal concentration; LD_{50} = median lethal dose; LOAEC = lowest-observed-adverse-effect concentration; NOAEC = no-observed-adverse-effect concentration; LOEC = lowest-observed-effect concentration; NOEC = no-observed-effect concentration; LO(A)EL = lowest-observed-(adverse)-effect level; NOEL = no-observed-effect level.

Table H2. Information for Ethylbenzene in humans

Endpoint	Lowest effect levels[a]/Results
Irritation	Human volunteers exposed to ethylbenzene vapour reported severe eye irritation at 4348 mg/m^3 (1000 ppm) and above (Yant et al. 1930; Cometto-Muñiz and Cain 1995) and nasal and throat irritation at 8696 mg/m^3 (2000 ppm) and above (Yant et al. 1930). No eye irritation or other effects were observed at 870 mg/m^3 (200 ppm) and below (Gerarde 1963; Bardodej and Bardodejova 1970; Moscato et al. 1987).
Sensitization	No skin sensitization reaction occurred after dermal application of 10% ethylbenzene in 25 human volunteers (Kligman 1974)
Acute toxicity	Humans incidentally exposed to ethylbenzene above the occupational limit value (100 ppm, equivalenet to 435 mg/m^3) reported central nervous system depression, such as fatigue, sleepiness, and headache, in addition to eye and respiratory tract irritation (Bardodej and Bardodejova 1970). Dizziness was also reported in human subjects exposed to 8696 mg/m^3 (2000 ppm) ethylbenzene for 6 minutes (Yant et al. 1930).
Repeated exposure toxicity	A historical cohort was conducted in the United States among 560 styrene-production and polymerization workers who had been employed for at least 5 years on May 1, 1960. The workplace exposure included styrene, benzene, ethylbenzene, and other chemicals. Mortality was monitored from May 1, 1960 or the 10th anniversary in the plant through the end of 1975. Overall, 83 deaths were observed versus 106.41 expected from the general population; 17 died from cancer versus 21.01 expected, including nine from lung cancer (6.99 expected), one from leukaemia (0.79 expected), and one from lymphoma (1.25 expected) (Nicholson et al. 1978). A cross-sectional study investigated the blood and urine samples of 35 spraymen at six workplaces in two plants in Germany. The workers were varnishing and priming vehicles and special metal pieces, and had been exposed to solvent mixtures, mainly containing o-, m-, p-xylene, ethylbenzene, and toluene, for 2 to 24 years. Altered blood cell counts were observed in the spraymen. On average, increased lymphocytes and decreased erythrocytes and haemoglobin levels were observed in 31 exposed workers compared with matched pairs (controls) (Angerer and Wulf 1985). A biomonitoring study was conducted among 200 ethylbenzene production workers in Czechoslovakia for 20 years. The exposure levels were measured by the mandelic acid concentrations in urine samples, which never exceeded 3.25 mMol/L (500 mg/L). The biological limit for medanilic acid was established at 6.5 mMol/L (1000 mg/L). No altered haematological parameters or serum enzymes as

Endpoint	Lowest effect levels[a]/Results
	an indication of liver function were detected in the workers. No case of malignancy has been recored over the last 10 years in this facility (Bardoděj and Círek 1988). A cross-section study was conducted among 105 German house painters employed for at least 10 years who were exposed to solvent mixtures in paints and lacquers, including ethylacetate (C_{Max}, 50 ppm), toluol (C_{Max}, 15 ppm), butylacetate (C_{Max}, 11 ppm), methylisobutylketone (C_{Max}, 11 ppm), xylene (C_{Max}, 7 ppm), and ethylbenzene (C_{Max}, 3 ppm, equivalent to 13.05 mg/m^3). The control group comprised 53 non-painters, who were matched with age, training, and socio-economic status. The neurophysiologic examinations (electroencephalography and nerve conduction velocity) did not reveal any significant differences between the painters and the control group. As well, no changes in certain brain structures (ventricular diameter, cellar media index) or cerebral atrophy were observed in the painters. In the neurobehavioural tests, significant differences in the "change of personality" and "short term memory capacity" were observed in the painters with repeated prenarcotic symptoms at the workplace (Triebig et al. 1988). A study reported nerve conduction effects in ethylbenzene workers. Minor changes in evoked potential and nerve conduction velocity were found in 22 workers exposed to ethlybenzene concentrations ranging from 0.43 to 17.2 mg/m^3 (0.1 to 4 ppm) for 4 to 20 years. These workers also received exposure to styrene (about 1.5 ppm) (Lu and Zhen 1989). A historical cohort study was conducted in a rubber factory in Mexico among 48 workers who were exposed to hydrocarbons for 2–24 years; 42 unexposed workers served as controls. The hydrocarbons included ethylbenzene (220.7–234 mg/m^3), benzene (31.9 –47.8 mg/m^3), toluene (189.7–212.5 mg/m^3), and xylene (47–56.4 mg/m^3). Significantly increased abnormalities in the semen of exposed workers, including increased normozoospermia, altered sperm viscosity, decreased sperm liquefaction, increased nonspecific sperm aggregation, decreased sperm counts, and motile sperms and normal sperm percentages were observed (De Celis et al. 2000). A historical cohort study was conducted among 303 workers from four Polish paint and lacquer enterprises who were exposed to solvents for at least 6 months. The control group contained 214 unexposed workers. The exposed workers were further divided into two groups: solvent exposure only (207 workers) and solvent plus noise exposure (96 workers). The solvents contain xylene (1.0–110.0 mg/m^3), ethyl acetate (0.0–120.0 mg/m^3), white spirit (0.0–563.0 mg/m^3), toluene (0.0–92.5 mg/m^3), butyl acetate (0.0–285.5 mg/m^3), and ethylbenzene (0.0–65.6 mg/m^3). The relative risks (RR) of hearing loss in both exposed groups were significantly increased (RR 2.8, 95% CI 1.8–4.3 and RR 2.8, 95% CI 1.6–4.9, respectively) in a wide range of frequencies (2–8 kHz). No additional risk in the solvent plus noise exposure group was found. Hearing thresholds were also significantly increased in both exposed groups (Sliwinska-Kowalska et al. 2001). A cross-sectional study was conducted from workers in two different petrochemical plants in China. From these two plants, 246 and 307 male workers were classified into two ethylbenzened-exposed groups: petrochemical group 1 and group 2. Two reference groups were used for comparison: a power station

Endpoint	Lowest effect levels[a]/Results
	group (290 male workers from a power station exposed to noise level similar to petrochemical workers) and a control group (327 office personnel in these petrochemical plants). Air ethylbenzene concentrations were 122.83±22.86 mg/m^3 and 134.64±31.97 mg/m^3 in petrochemical group 1 and 2, respectively. The levels of other volatile aromatic hydrocarbons (styrene, bezene, toluene and xylene) were below the limit of detection. The prevalence of hearing loss 25 dB or more was higher in petrochemical group 1 (78.4%) and group 2 (80.1%) than that in the power station (56.9%) and control (5.2%) groups, with age, cigarette smoking and alcohol drinking adjusted. Based on neurobehavioural core test battery, descending neurobehavoural function involving adverse alteration of short-term memory, quick hand movement and hand-eye coordination were observed in exposed workers compared to controls and these changes started in the third year of working age. Acetylcholinesterase activity in blood was signficiantly decreased compared to the control group (Zhang et al. 2013).
Genotoxicity	DNA adduct formation, DNA single strand breaks, and sister chromatid exchange were not detected in 25 workers occupationally exposed to a mixture of styrene, benzene, ethylbenzene, xylenes, and toluene in a styrene production plant in the former German Democratic Republic. However, the kinetochore-positive micronuclei (suggestive of aneuploidy induction) in peripheral lymphocytes were significantly increased in exposed workers compared with the controls (25 age- and sex-matched unexposed healthy workers in the same company). The ethylbenzene levels in all areas of the factory ranged from 365 to 2340 µg/m^3 (0.08–0.53 ppm). Biomonitoring data measured by the metabolites of these aromatic hydrocarbons in the urine samples of the exposed workers indicated that the workers were exposed mainly to xylene and ethylbenzene (Holz et al. 1995). Significantly increased chromosomal aberrations were detected in 39 male workers occupationally exposed to ethylbenzene and benzene in a petrochemical plant. The concentrations of ethylbenzene and benzene in the workplaces ranged from 0.2 to 13.1 and from 0.4 to 15.1 mg/m^3, respectively. The control group consisted of 55 matched subjects (Sram et al. 2004). Levels of 8-hydroxydeoxyguanosine (8-OHdG) in urine were measured among 64 male workers (15 spray painters exposed to paint, two non-exposed groups: 19 sandblasting workers and 30 office staff). Urinary 8-OHdG was used as biomarker of oxidative DNA damage. Personal exposure to xylene and ethylbenzene (measured by urine levels of mandelic acid) in air were also collected using diffusive samplers. Urinary 8-OHdG levels displayed greater DNA damage in spray painters compared to other unexposed groups and their holiday leave samples. A significant correlation was found between urinary 8-OHdG and the exposure to ethylbenzene. Authors did acknowledge that ethylbenzene exposure could not explain all urinary 8-OHdG measured and that other components of paint could be involved in the increased levels (Chang et al 2011).

[a] See description of footnotes in Table H1