Canadian Environmental Protection Act, 1999

PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

FOLLOW-UP TO THE STATE OF SCIENCE REPORT, 2000

Ethylene Glycol

Environment Canada
Health Canada

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LIST OF ACRONYMS AND ABBREVIATIONS

ADAF	aircraft deicing and anti-icing fluids
ATAC	Air Transport Association of Canada
ACC	American Chemistry Council
BMD_{05}	benchmark $dose_{05}$
CAS	Chemical Abstracts Service
CCME	Canadian Council of Ministers of the Environment
CCSPA	Canadian Consumer Speciality Products Association
CEPA	*Canadian Environmental Protection Act*
CEPA 1999	*Canadian Environmental Protection Act*, *1999*
COM	calcium oxalate monohydrate
CTV	critical toxicity value
DO	dissolved oxygen
EEV	estimated environmental value
ENEV	estimated no-effect value
F-344	Fischer 344 rats
GA	glycolic acid
GMP	glycol mitigation plan
GOMP	glycol operational management plan
HPT	human proximal tubule
kg-bw	kilogram-body weight
95% LCL	lower 95% confidence limit
LOAEL	lowest-observed-adverse-effect level
LOEL	lowest-observed-effect level
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
OX	oxalic acid
PT	proximal tubule
PTSs	proximal tubular segments
PSL2	second Priority Substances List
PBPK	physiologically based pharmacokinetic model
SoS Report	State of the Science Report; short for "*Canadian Environmental Protection Act, 1999*: Priority Substances List State of the Science Report for Ethylene Glycol"
TC	tolerable concentration
TI	tolerable intake
US EPA	United States Environmental Protection Agency

SYNOPSIS

Ethylene glycol was included on the Priority Substances List (PSL) under the *Canadian Environmental Protection Act* (CEPA) to assess the potential environmental and human health risks posed by exposure to ethylene glycol in consumer products and the environment.

In December 2000, the Priority Substances List (PSL) assessment of ethylene glycol was formally suspended due to limitations in the available data for assessing health effects. At the same time, a state of the science report (Environment Canada and Health Canada 2000) on ethylene glycol was released, providing an in-depth review of the toxicity and exposure information related to human health and the environment. The essential information needed to complete the assessment was identified and acquired during the subsequent seven years.

During the suspension period, more data were obtained. This led to the proposed conclusion, published in 2007, that the substance met one or more of the criteria under section 64 of CEPA 1999. During the comment period that followed that publication, additional data were received on levels of ethylene glycol in latex paints as well as ethylene glycol-specific model parameters which supported a refinement of exposure estimates from use of latex paints. The revised exposure estimates were not considered to be of concern and resulted in the final conclusion that the substance does not meet any of the criteria under section 64 of CEPA 1999.

Ethylene glycol is primarily used as a component of deicer and anti-icer/anti-freeze fluid used in aircraft deicing and anti-icing operations, and as an anti-freeze component in motor vehicles. It is also used in manufacturing polyester products. Ethylene glycol is present as a slow-evaporating solvent and/or freeze-thaw stabilizer in latex paints. Ethylene glycol can also be used in a variety of other products such as floor and wall adhesives, brake fluid, automotive wax/polish and floor wax/polish. In 2006, approximately 1540 kilotonnes (kt) of ethylene glycol were manufactured in Canada by three companies in Alberta. Most Canadian glycol production is destined for export.

With regard to the environment, the highest reported releases of ethylene glycol to the environment are to land resulting from aircraft deicing/anti-icing operations, with subsequent release to the aquatic environment. However, in recent years, management practices at Canada's major airports have improved with the installation of new ethylene glycol application and mitigation facilities or improvements to existing ones.

The direct comparison of exposure concentrations measured in the aquatic environment with the estimated no-effect values (ENEVs) suggests that adverse effects are unlikely when consideration is given to the seasonal nature of releases, ambient temperatures, metabolic rates and duration of exposure. Furthermore, examination of potential indirect effects through oxygen depletion caused by biodegradation of ethylene glycol suggests a low potential for concentrations of dissolved oxygen (DO) to drop to levels of concern.

As such, it is proposed that ethylene glycol 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 constitutes or may constitute a danger to the environment on which life depends.

With regard to human health, upper-bounding estimates of daily intake of ethylene glycol by the general population of Canada, and by a highly exposed population in the immediate vicinity of an industrial point source, are well below tolerable intake (TI), derived based on a Benchmark Dose calculated for non-neoplastic renal effects in animals and an uncertainty factor. "Tolerable intake" is the level of intake to which it is believed a person may be exposed daily over a lifetime without deleterious effect. Estimates of short-term indoor air concentrations from use of consumer products containing this substance, such as latex paint, are not considered to be of concern based on a comparison of upper-bounding exposure estimates and the no-observed-adverse–effect level in an inhalation study conducted with humans. Ethylene glycol is, therefore, not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health.

This substance will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

Based on the information available for human health and the environment, it is thus concluded that ethylene glycol does not meet any of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

1.0 INTRODUCTION

Ethylene glycol was added in 1995 to the Priority Substances List (PSL) under the *Canadian Environmental Protection Act* (CEPA) to assess the potential environmental and human health risk posed by exposure to ethylene glycol in the environment and consumer products.

The PSL assessment of ethylene glycol was formally suspended in December 2000 due to the uncertainties associated with the human effect and exposure data set. At the same time, a state of the science report (SoS report) (Environment Canada and Health Canada 2000) on ethylene glycol was released, providing an in-depth review of the available toxicity and exposure information related to human health and the environment. A large number of uncertainties were identified in the SoS Report and Health Canada was unable to determine whether ethylene glycol was toxic or capable of becoming toxic to the general population in Canada. The SoS Report stated that information on concentrations of ethylene glycol present in consumer products in Canada, dose-response results for renal effects of ethylene glycol based on a chronic animal study, and information on the intake of ethylene glycol by individuals living in the vicinity of industrial point sources were essential for the completion of the human health assessment.

Furthermore, the SoS Report concluded that harmful environmental effects were unlikely to result from exposure to ethylene glycol in Canada. However, effects related to the depletion of dissolved oxygen (DO), resulting from the biodegradation of ethylene glycol in receiving waters were possible near some Canadian airports a very small percentage of the time under conditions of maximum loading. It was therefore recommended that efforts to reduce releases of ethylene glycol during aircraft deicing/anti-icing operations continue to be strengthened with the aim of reducing further the instances when ethylene glycol concentrations in stormwaters exceed the CEPA Part IV guideline of 100 mg total glycol/L.

The essential information needed to complete the PSL human health assessment was identified and acquired during the ensuing seven years, and is included in this report.

This assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The ecological and human health portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were coordinated by Toxicology Excellence in Risk Assessment (TERA) in 2007 and 2009. Dr. Douglas C. Wolf, U.S. Environmental Protection Agency, provided expert advice on endpoint selection for key dietary toxicity studies. Mike Walker, Health Canada, provided biostatistical expertise. Additionally, the draft of this assessment was subject to a 60-day public comment period. Although external comments were taken into consideration, the final content and outcome of the risk assessment remain the responsibility of Health Canada and Environment Canada.

2.0 SUMMARY OF INFORMATION CRITICAL TO THE RISK ASSESSMENT UNDER CEPA 1999

2.1 IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Ethylene glycol (CAS No. 107-21-1) belongs to the simplest group of organic chemicals of the chemical family of glycols, which are characterized by two hydroxyl (OH) groups at adjacent positions in a hydrocarbon chain (see Figure 1).

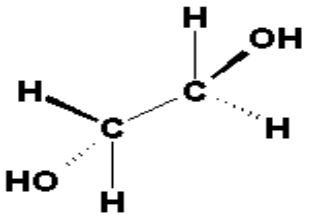

Figure 1. Chemical structure of ethylene glycol

The physical and chemical properties of ethylene glycol, also known as monoethylene glycol and 1,2-ethanediol, are presented in Table 1. Ethylene glycol is a clear, colourless, odourless, relatively non-volatile, viscous liquid (Nielsen *et al*. 1993). It has a sweet taste and imparts a warming sensation to the tongue when swallowed (Beasley and Buck 1980). Ethylene glycol has a relatively low vapour pressure (7–12 Pa at 20°C) (Verschueren 1983; Howard 1990) and a low Henry's Law constant of 5.8×10^{-6} to 6.0×10^{-3} Pa·m^3/mol (Hine and Mookerjee 1975; Howard 1990). It is completely miscible in water (Canada 1985; Budavari *et al*. 1989). It is very hygroscopic and will absorb up to 200% of its weight in water at 100% relative humidity (Budavari *et al*. 1989). The octanol/water partition coefficient of ethylene glycol is very low (i.e., log K_{ow} = –1.36) (Verschueren 1983; Budavari *et al*. 1989; Howard 1990).

2.2 ENTRY CHARACTERIZATION

2.2.1 Production, importation and use

The worldwide production capacity of ethylene glycol in 2006 was approximately 19 500 kilotonnes (kt), where the majority went into the production of polyethylene terephthalate (81.5%) (Chinn 2007).

In 2006, there were three companies (in four locations, all in Alberta) manufacturing ethylene glycol in Canada: Alberta & Orient Glycol (in Prentiss), MEGlobal Limited (in Fort Saskatchewan and Prentiss) and Shell Chemicals (in Scotford) (Chinn 2007). The total annual capacity in 2006 from these three companies was 1540 kt: 370 kt for Alberta

& Orient Glycol, 720 kt for the two MEGlobal Limited plants combined and 450 kt for Shell Chemicals (Chinn 2007).

Canada produced 1410 kt and imported 3 kt of ethylene glycol from the United States in 2006. In total, 1200 kt of ethylene glycol were exported in the same year, mainly to China (Chinn 2007).

In Canada in 2006, ethylene glycol was mainly used for anti-freeze mixtures and deicing fluids, and in the production of polyethylene terephthalate (PET) (Chinn 2007). The ethylene glycol used for anti-freeze mixtures and deicing fluids accounted for 70 kt (33% of the domestic demand) (Chinn 2007). This amount has slowly decreased since 2000 with a slight increase from 2005 (Chinn 2007). The amount of ethylene glycol used for the production of PET has increased since 2000 and was 69 kt (31% of the domestic demand) in 2006 (Chinn 2007). PET is manufactured into resins, fibres and films that are subsequently converted into numerous products such as bottles, packaging, and textiles (Chinn 2007). The amount of ethylene glycol used in other applications such as for oil and gas processing and in miscellaneous industrial applications, including its use as a solvent, totalled 70 kt in 2006 (Chinn 2007; CIS 2003).

1. Ethylene glycol is present in various surface coatings, including latex paint, as a slow-evaporating solvent and/or freeze-thaw stabilizer, as well as to provide coalescence and wet-edge control (Chinn 2007; US EPA 1986; NLM 2009). It is noteworthy that information indicates a trend in Canada towards substitution of ethylene glycol in paint formulations with other solvents/stabilizers (ICI Canada 2007). Ethylene glycol is used as a formulant in pesticide products in Canada (e-mail from Pest Management Regulatory Agency [PMRA] to Healthy Environments and Consumer Safety [HECS] September 2009, unreferenced). This substance can also be used in a variety of other products such as in automotive anti-freeze/coolant and wax/polish; brake fluid; as a solvent in adhesives; in floor wax/polish; in caulks and grout, spackling compound, concrete sealers, and shoe polish (NLM 2009; Chinn 2007; US EPA 1986). In addition, ethylene glycol may be used in asphalt emulsion paints; as a coolant and heat transfer fluid; in low-pressure laminates; in glycol diacetate production; in low-freezing dynamite; as a solvent mixture for cellulose esters and ether (a softening agent in cellophane in particular), printing inks, stamp pad inks, ballpoint pen inks, and wood stains; in lacquers; in alkyd resins; in leather dyeing; in textile processing; in humectants; and as a foam stabilizer (ATSDR 2007; Lewis 2007; O'Neil *et al.* 2006). The quantities used in Canada for most of these products are unknown.

   Ethylene glycol may also be present in pharmaceutical products as a residual solvent. It is classified by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) as a Class 2 solvent or a solvent that is to be limited in pharmaceutical products (ICH 1997). The concentration limit of 620 ppm of ethylene glycol in pharmaceutical products has been set by both the ICH and the United States Pharmacopoeia (ICH 1997; USPC 2007).

2.2.2 Sources and releases

Table 2 presents data from the National Pollutant Release Inventory (NPRI) on total industrial annual volumes of releases, disposal and recycling of ethylene glycol from all reporting sources from 1994 to 2005. There are year-to-year fluctuations, but the total of releases, disposal and transfers for recycling (together taken as an indirect measure of usage) generally increased while untreated releases dropped. Thus, untreated releases have declined in this period, both numerically and proportionally.

Annual volumes of untreated releases from all reporting sources of ethylene glycol to air, water and land for the period 1994 to 2005 are shown in Table 3. Since peaking in 1997 at 4698 tonnes, total untreated releases have trended downwards, reaching 2263 tonnes in 2005. While both air and land releases continue to show a downward trend, reported releases to water have increased fivefold since 2000.

Releases to air

The amount of untreated ethylene glycol released to air has gone down since 1995 (Table 3). While petrochemical manufacture is still the biggest contributor (144 tonnes, or 49%), significant amounts are also released by conventional oil and gas extraction (85 tonnes, or 29%), as well as from the paint and coating industry (20 tonnes, or 7%), resin and synthetic rubber manufacturing (11 tonnes, or 4%), and petroleum refineries (10 tonnes, or 3.5%) (NPRI 2005).

Other contributing industrial activity includes motor vehicle brake and motor manufacturing, printing, and iron ore mining. Together these account for approximately 7% of the total releases to air (NPRI 2005). Use of consumer products containing ethylene glycol may also contribute to releases to air.

Releases to water

Releases (untreated) to water have gone up significantly since 1994. Releases then were reported at 91 tonnes, mostly from the paper products and the primary steel industry sectors. A sharp increase in releases occurred in 2003 and continued increases were reported up to 2005. Total 2005 releases to water were reported as 572 tonnes, with oil and gas accounting for 446 tonnes (78%). The paper products sector, including pulp mills, reported a significant drop. While this sector was previously reported as the biggest contributor of releases to water, it accounted for only 8 tonnes (1.4%) in 2005. Iron and steel mills accounted for 44 tonnes (8%).

As indicated in the SoS Report, ethylene glycol is used in large volumes for aircraft deicing/anti-icing practices and these volumes are reportedly released to land (see below); however, airport collection facilities and drainage systems may divert substantial quantities to the aquatic environment. This point is presented further in Appendix D.

Releases to land

NPRI data show that land releases are the biggest component of total untreated releases in 2005. For that year, scheduled air transportation and support activities for air transport account for 95% of untreated releases to land. Other sources of untreated releases to land include chemical pulp mills, diamond mines and cement manufacturing.

Since 2000, several major federal airports have built and/or improved their glycol handling facilities. These include the following locations:

- Ottawa Macdonald-Cartier International: A new biological treatment facility was opened in 2003.
- Toronto Pearson International: The Central Deicing Facility (CDF), built in 1998, was expanded in 1999–2000. Three additional deicing pads were built in 2004. An on-site glycol recycling facility was commissioned in 2005 (GTAA 2005).
- Winnipeg James Armstrong Richardson International: A central deicing facility was opened in 2005. Aeration to Truro Creek, one of two receiving water bodies for airport runoff, was started in 2001.
- Edmonton International: A subsurface-flow (SSF) wetland facility was commissioned in 2000–2001 to treat ethylene glycol-containing aircraft deicing/anti-icing fluids (ADAFs) on-site.
- Vancouver International: work began on a new deicing pad in 2005 and the pad was operational in 2006.
- Montréal-Trudeau: extensive improvements have been made since 2000, including a new enlarged deicing pad.

Releases, disposal and recycling of ethylene glycol from airport operations for the years 1998 to 2005 are shown in Table 4. As can be seen, there is an increase in the total for these three categories from 4577 tonnes in 1998 to 6745 tonnes in 2005. This was due to an increase in the amount of ethylene glycol that was either recycled or disposed of. The term “disposal” indicates that the glycol received some form of treatment before being either released or sent to a municipal wastewater treatment system.

For the same 1998 to 2005 period, untreated releases of ethylene glycol dropped from 2450 tonnes to 1232 tonnes. This represents a decrease of 50%. For the same period, the fraction of ethylene glycol that was released with no treatment compared with the total amount (including recycling and disposal) declined steadily from 53% in 1998 to 18% in 2005.

Releases underground

Table 3 shows that compared with 1994, when underground injections (mostly on-site) amounted to 77 tonnes, some 93 tonnes were disposed of in this manner in the 2005 reporting year. There was a peak of 422 tonnes injected underground in the 2000 reporting year. The natural gas industry in western Canada is the biggest user of this type of disposal method (NPRI 2005).

2.3 ENVIRONMENTAL FATE

The SoS Report presents a detailed discussion of fate in the environment. Once released into the environment, ethylene glycol partitions mainly into surface water or groundwater. It does not bioaccumulate or persist in the environment, primarily due to biodegradation. Half-lives are estimated to typically range from 0.35 to 3.5 days in air, 2 to 12 days in water, 4 to 24 days in groundwater and 2 to 12 days in soil, but may exceed these ranges, depending on environmental conditions. Ethylene glycol has been found to biodegrade rapidly in the aquatic environment and therefore has the potential to induce depletion of the dissolved oxygen (DO) in receiving waters.

3.0 RISK ASSESSMENT UNDER CEPA 1999

3.1 CEPA 1999 64(a) and *(b): ENVIRONMENT*

3.1.1 Environmental exposure

Given that releases from airports (releases to land, with subsequent movement to receiving waters) are by far the largest releases of ethylene glycol in Canada and that those releases occur over a limited part of the year (as opposed to industrial releases that occur over the whole year), the highest environmental exposures are expected in the winter and spring in receiving waters adjacent to airports. The ecological assessment therefore focuses on potential exposure resulting from releases from airports.

Figure 2 illustrates the distribution of 3254 individual measurements of ethylene glycol sampled in stormwater at airports across Canada over the combined 2003–2004 and 2004–2005 deicing seasons. Key percentiles in this distribution and the breakdown by season are summarized in Table 5**.** Generally, mean glycol concentrations measured over these two years were very similar to the 1997 to 1999 data (as reported in the 2000 SoS Report).

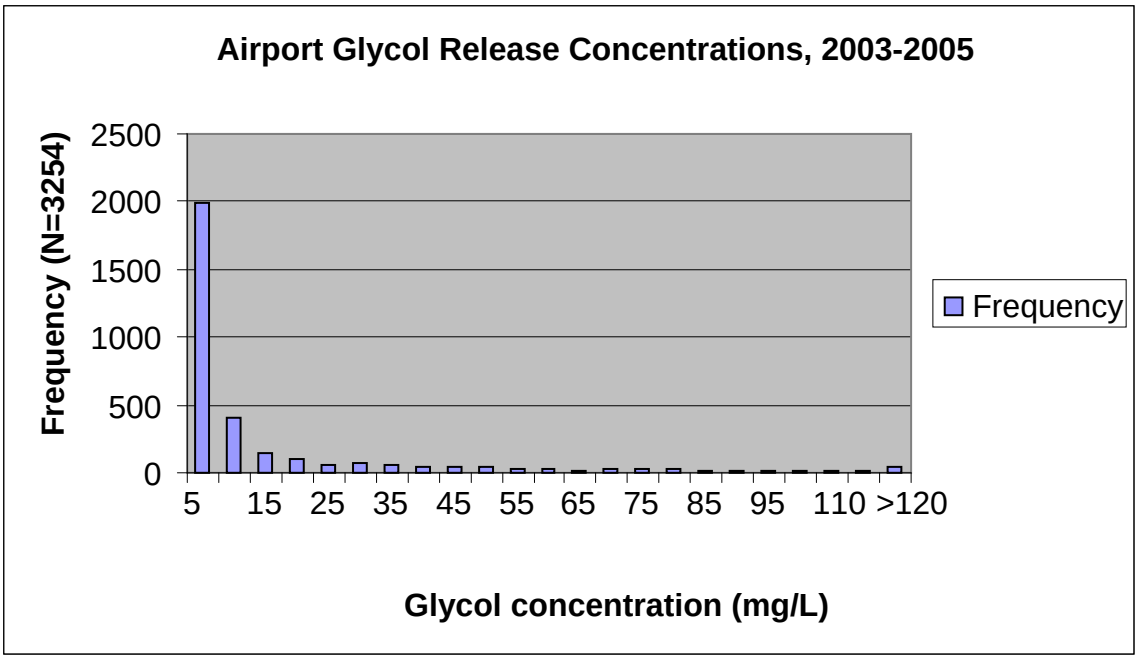

Figure 2. Frequency distribution of glycol concentrations in airport stormwater

3.1.2 Environmental effects

The critical toxicity values presented in the SoS Report (Environment Canada and Health Canada 2000), namely the IC_{25} of 3268 mg/L for the green alga *Selenastrum capricornutum* and the subchronic toxicity value of 4732 mg/L for the amphibian *Xenopus laevis*, still represent the most sensitive measurements of toxicity of ethylene glycol to aquatic organisms. Using IC_{25} of 3268 mg/L from the most conservative algae test results as the critical toxicity value (CTV) and applying an application factor of 5 to account for interspecies variability and laboratory to field extrapolation, the estimated no-effect value (ENEV) (or predicted no-effect concentration [PNEC])of 654 mg/L is obtained. As well, using 4732 mg/L as a CTV and applying an application factor of 10 to account for the fact that the amphibian study used a non-native species and for uncertainty in laboratory to field extrapolation, the subchronic ENEV becomes 473 mg/L.

3.1.3 Risk quotient calculations

Aquatic biota – direct effects

Based on the most recent available data from all airports for the 2004–2005 season, the levels of ethylene glycol in effluent streams are below 136 mg/L 99% of the time and below 200 mg/L 99.5% of the time from the over 1728 measurements taken (Table 5), with the reported maximum of 2560 mg/L measured in the spring of 2005. The

concentrations of ethylene glycol in effluent streams, measured from all the airports, for the most recent 2004–2005 season, were below 100 mg/L 97.6% of the time.

Natural dilution of effluents occurs in the receiving waters and must be considered in calculating the risk to aquatic organisms. The level of dilution varies with each location; therefore, a generic and conservative dilution factor of 10 is applied. The effluent concentrations are assumed to be reduced by one order of magnitude—that is, the isolated maximum effluent concentration of 2560 mg/L referred to above becomes 256 mg/L in the receiving waters.

It is assumed that, under worst-case conditions, high levels of ethylene glycol will be found in the effluent for a period of several days.

Conservative risk quotients for the most recent 2004–2005 season presented in Table 6 and Table 7 are all less than 1; however, the conservative risk quotients using the highest reported concentration for the 1997–1998 and 1998–1999 seasons were about 1 (0.99) for amphibians and 0.71 for algae.

Risk quotients at the 95th and 99th percentile values for the two comparison periods are quite comparable in the case of both algae and amphibians. At the maximum recorded values, the risk quotient is of course lower, again for both algae and amphibians.

Aquatic biota – indirect effects

One of the potential indirect effects of ethylene glycol is the depletion of dissolved oxygen levels in receiving waters resulting from microbiological degradation. For characterization of risk from indirect effects, the input parameters applied to the Streeter-Phelps oxygen sag model (Streeter and Phelps 1925) include the assumption of complete ice cover and therefore no re-aeration, a dilution factor of 10, an initial DO concentration of 12.4 mg/L and concentrations of ethylene glycol in stormwater (maximums and percentiles) released from 32 airports during the 1997–1998 and 1998–1999 seasons. Oxygen deficit quotients are provided in Table 8. This table has been updated to include comparative data from the latest available Transport Canada Airport Glycol Monitoring Report for the 2003–2004 and 2004–2005 seasons.

From the quotients presented in Table 8, depletion of oxygen below the Canadian Council of Ministers of the Environment (CCME) guideline of 9.5 mg/L is not expected to occur, based on the 99th percentile of effluent releases. However, the potential for oxygen depletion appears to exist when the analysis assumes the worst-case maximum levels for both pre- and post-2000 Transport Canada data. The worst-case risk quotient for the 1997–1999 season was 16.1, whereas for the 2003–2005 period it was lower at 9.1.

Results of a separate probabilistic modeling study that used maximum loadings from individual airport facilities during the 1997–1998 or 1998–99 season and assumed

complete ice cover, predicted that DO levels below the CCME DO guideline would occur about 17% of the time under worst-case conditions (Parker 1999). In a more recent study, using actual geophysical and precipitation data from several major Canadian airports, it was shown that ethylene glycol could reduce oxygen levels below the CCME guideline in the airports' receiving watercourses, even under some conditions of no ice cover, especially at higher concentrations (> 500 mg/L) (Chaulk 2003). It should be pointed out that concentrations of 500 mg/L or higher represent less than 0.5% of recently recorded values at these airports, thus indicating a very low probability for this scenario.

Terrestrial wildlife – direct effects

The SoS Report (Environment Canada and Health Canada 2000) reported the following toxicity information, which is pertinent to the potential effects of ethylene glycol on terrestrial wildlife. Ethylene glycol poisoning is common among domestic animals and has been reported in cats, pigs, poultry, wildlife and calves (Kersting and Nielsen 1965; Riddell *et al.* 1967; Black 1983; Amstrup *et al.* 1989). Ethylene glycol is a slow-acting poison. Even after a massive dose, an animal will be unaffected for 0.5–2 hours post-exposure (Penumarthy and Oehme 1975; Oehme 1983; Beasley 1985; Grauer and Thrall 1986). The oral toxicity of ethylene glycol varies among species. Cats were reported to be the most susceptible to poisoning (Osweiler *et al.* 1985). The reported lethal dose for cats is only 1.5 mL/kg-bw (1650 mg/kg-bw) (Black 1983), whereas for dogs it is 4.2–6.6 mL/kg-bw (4620–6600 mg/kg-bw) (Beasley and Buck 1980; Oehme 1983; Grauer and Thrall 1986). Osweiler *et al.* (1985) reported a lethal dose of 2–4 mL/kg-bw (2200–4400 mg/kg-bw) in cats, 4–5 mL/kg-bw (4400–5500 mg/kg-bw) in dogs and 7–8 mL/kg-bw (7700–8800 mg/kg-bw) in poultry. Mallard ducks (*Anas platyrhynchos*) exposed orally to ethylene glycol demonstrated adverse toxic effects (lowest-observed-effect dose, or LOED) at 2.3 mL/kg-bw (2530 mg/kg-bw) (Stowe *et al.* 1981). A no-observed-effect level (NOEL) for orally dosed ducks at 1221 mg/kg-bw and lethal doses for poultry at approximately 8000 mg/kg-bw were reported in CA/ICCA (2000).

For the assessment of very short-term exposure to ethylene glycol, applying an assessment factor of 10 to the LD50 for cats of 1650 mg/kg-bw, to account for interspecies and intraspecies variability in sensitivity, gives an ENEV of 165 mg/kg-bw. The 99th-percentile concentration in stormwater runoff from airports from all data from the 1997–1999 seasons is 200 mg/L. Therefore, an animal would have to drink its own weight of stormwater runoff in a short period of time in order to attain the ENEV dose of 165 mg/kg-bw. Assuming a dilution factor of 10, an animal would have to drink about 10 times its own weight of water from a receiving stream in order to attain the ENEV dose.

Elevated concentrations of ethylene glycol in receiving waters may persist for several days. In a 16-week study with rats, the lowest-observed-effect level, based on increased incidence of calcium oxalate crystals, was 150 mg/kg-bw/day (Cruzan *et al*. 2004). Dividing this value by an assessment factor of 10, to account for interspecies and intraspecies variability in sensitivity, gives an ENEV of 15 mg/kg-bw/day. A 1-kg animal would have to drink about 75 mL/day of airport stormwater runoff containing 200 mg ethylene glycol/L, or 7.5% of its body weight per day, to attain this ENEV. Assuming a

dilution factor of 10, an animal would have to drink about 75% of its own weight of water per day from a receiving stream in order to attain the ENEV dose.

Given that a 70-kg human drinks about 3 kg of water per day, or about 4% of his or her body weight and extrapolating this to other species and considering that high levels of ethylene glycol occur for only a few days at a time, it is unlikely that terrestrial wildlife would be harmed by drinking water from receiving waters in the vicinity of airports for a period of time ranging from a few days to several weeks.

3.1.4 Characterization of ecological risk

Ethylene glycol is not persistent in air, water or soil and does not accumulate in organisms. The substance has a low inherent toxicity; that is, it causes adverse effects in organisms only at relatively high doses or concentrations.

With respect to releases of ethylene glycol from all sources, as reported to the National Pollutant Release Inventory (NPRI), there is a general downward trend both in total amounts of untreated releases and in the fraction of untreated releases relative to total releases (including disposed of or recycled releases). Based on data from Table 3, the following graph shows the downward trend in total untreated releases from all sources.

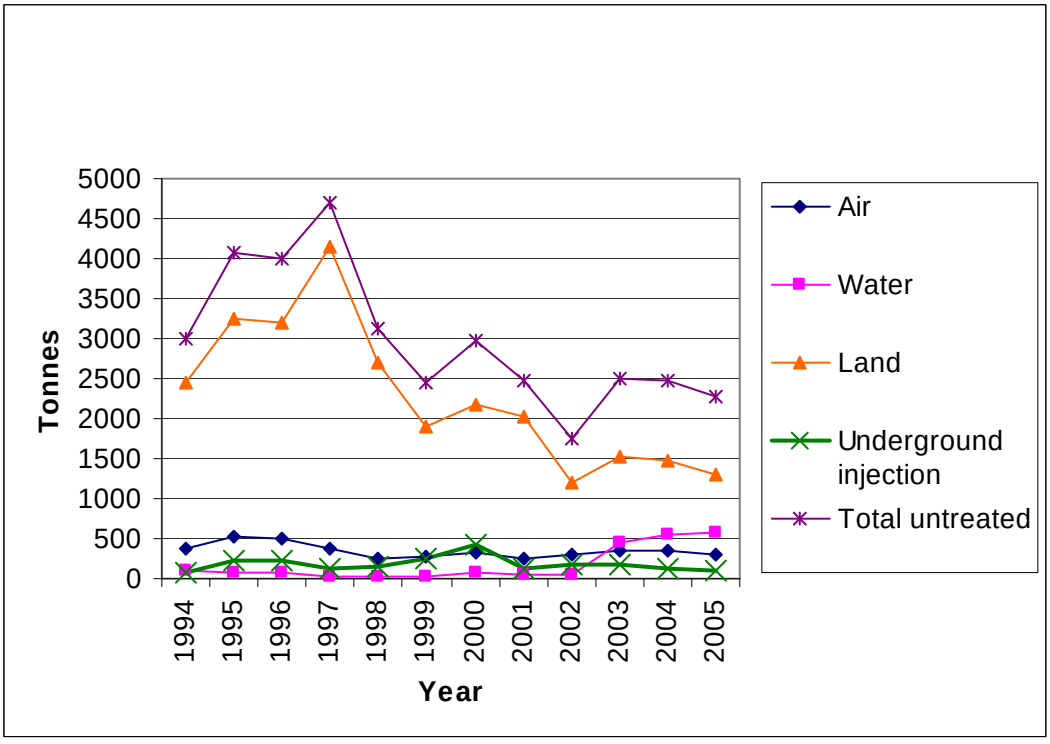

Figure 3. Untreated glycol releases – all sources

In Figure 3 above, "Total Untreated" is the sum of all ethylene glycol released untreated to air, water, land, and underground injection. The largest portion of untreated releases of ethylene glycol is to land, with 95% of those releases originating from airports. Much of the ethylene glycol released subsequently moves to watercourses, such that airports are ultimately the greatest source to water as well. For airports, improved management practices have led to increases in the amounts of ethylene glycol that are treated or disposed of, such that the proportion of untreated glycol to total glycol releases has steadily declined from 53% in 1998 to 18% in the 2005 reporting year.

Based on extensive monitoring data from airports, the risk quotients for effects in freshwater ecosystems indicate that ethylene glycol concentrations likely do not exceed concentrations associated with effects, based on the 99th percentile glycol concentration measured at airports for both direct and indirect effects. Examination of potential indirect effects through oxygen depletion suggests a low potential for dissolved oxygen (DO) levels to drop below the Canadian water quality guideline value (9.5 mg/L DO) under very infrequent maximal loading conditions. It is thus expected that direct or indirect effects are unlikely, especially when consideration is given to the seasonal and transient nature of the releases, the short duration of exposure, and the low ambient temperatures and metabolic rates at the periods of maximum release.

3.1.5 Uncertainties in evaluation of ecological risk

As reported in the SoS Report (Environment Canada and Health Canada 2000), there is a lack of measurement data for ethylene glycol in the ambient environment. However, a large data set of measurements of ethylene glycol in effluents from Canadian airports provides a very good indication of the concentrations being released. Because the conditions of the receiving waters can be highly variable across Canada, some conservative assumptions, including the use of a dilution factor of 10, have been applied in estimating concentrations in waterways. It is expected that an adequate estimate of the concentrations of ethylene glycol in the receiving waters has been obtained.

The use of deicing and anti-icing fluids at airports across Canada will vary from year to year and from region to region, depending on climatic factors. Through control programs by Transport Canada, the Air Transport Association of Canada and local airports and airlines, including the implementation of glycol mitigation plans and glycol operational management plans at the major airports in Canada, the amounts of untreated ethylene glycol being released to the ambient environment have been declining over the past years, and in particular since 2000 with improvements in glycol application and control methods.

While this assessment addressed the potential ecological impacts of ethylene glycol, it is recognized that, while ethylene glycol is the principal ingredient in airplane deicing and anti-icing formulations in Canada, other constituents can be present and can increase the toxicity of the formulation. For example, some deicing formulations can be three to ten times more toxic to certain organisms than ethylene glycol alone (Pillard 1995).

Based on the present analyses, harmful ecological effects are unlikely to result from exposure to ethylene glycol in Canada. Similarly, effects related to reductions in concentrations of dissolved oxygen are unlikely. However, concentrations could reach levels of concern near some Canadian airports a very small percentage of the time under conditions of maximum loading. Continued monitoring of stormwater effluents and receiving waters at airports would permit an ongoing determination of the occurrence or frequency of such occasional high releases.

3.2 CEPA 1999 64(c): HUMAN HEALTH

3.2.1 Population exposure

The following presentation is limited to identifying recent data considered critical to the quantitative estimation of the exposure to ethylene glycol for various age groups in the general population of Canada and, hence, to a risk assessment under paragraph 64(*c*) of the *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999).

The Environmental Monitoring and Reporting Branch of the Ontario Ministry of Environment (formerly the Ontario Ministry of Environment and Energy) used Trace Atmospheric Gas Analyzer (TAGA) 6000 units to carry out several mobile air-monitoring surveys in Windsor, Ontario, in 1991 and 1992 (OMEE 1994). The surveys were performed in order to determine the concentrations of certain substances in air that are not usually measured in routine monitoring programs (OMEE 1994). Ethylene glycol was measured during the 1992 survey that focused on determining concentrations of industrial chemicals found in areas where the general population could be exposed, such as in city parks and near schools (OMEE 1994). Levels of ethylene glycol ranged from < 1 $\mu g/m^3$ to 75 $\mu g/m^3$ (detection limit of 1 $\mu g/m^3$) (OMEE 1994). Based on the maximum value, the upper-bounding estimates of intake for ambient air range from 1.9 to 5.6 µg/kg-bw/day and are shown in Table 9.

Zhu *et al*. (2004) developed an analytical method for measuring ethylene glycol and propylene glycol in indoor air. This Canadian study involved sampling 9 residential homes (2 apartments and 7 single detached houses), 1 attached residential garage, 1 office and 2 laboratories. The samples were collected from an area that had no industrial point source releases nearby. Ethylene glycol was detected in all locations with levels from the residences (including the attached garage) ranging from 2.0 to 223 $\mu g/m^3$ and levels from the office and laboratories, ranging from 1.9 to 4.4 $\mu g/m^3$ (method detection limit of 0.07 $\mu g/m^3$). Hodgson *et al*. (2000) sampled indoor air in 11 newly built houses (4 manufactured and 7 site-built houses) in the eastern and southeastern United States. Levels of ethylene glycol were measured at least one month after the completion of the house and ranged from < 23.4–1247 $\mu g/m^3$. Latex paint was indicated as a source of ethylene glycol emissions. It is noteworthy that in a study of ethylene glycol emission

rates from carpets (possibly from an adhesive), the emission rate decreased from 949 μg/m^2/h to less than 50 μg/m^2/h (detection limit) in 28 days (Wilke *et al*. 2002).

Based on the maximum value found in residences from the Canadian study (Zhu *et al*. 2004), the upper-bounding estimates of daily intake from indoor air range from 39 to 117 μg/kg-bw/day and are shown in Table 9.

As no new data on levels of ethylene glycol in food or food packaging were identified, it is assumed that the level of ethylene glycol intake through food has not changed since the publication of the 2000 SoS Report. This source of intake is summarized in Table 9 and Table 10.

Upper-bounding estimates of total daily intake of ethylene glycol for the general Canadian population range from 53 μg/kg-bw/day in adults (60+ years) to 157 μg/kg-bw/day in children (0.5–4 years), as shown in Table 9. For each age group, indoor air is the primary source of exposure.

Sciences International, Inc. was commissioned by the Ethylene Glycol Panel of the American Chemistry Council to characterize potential exposures of the general population to ethylene glycol near an ethylene-glycol manufacturing plant located in Red Deer, Alberta (Sciences International, Inc. 2003). The purpose of this study was in part to respond to the need for more research on exposure to humans located near point source releases, which was an uncertainty identified in the SoS Report.

Sciences International, Inc. used ISC PRIME (Industrial Source Complex Plume Rise Model Enhancements), a site-specific air dispersion model, to estimate potential human exposure to ethylene glycol. The model incorporated ethylene glycol emission data acquired from the facility, as well as five years of meteorological data (Sciences International, Inc. 2003). The predicted maximum 24-hr concentration at nearby residences was 154 μg/m^3 (60 ppb). Based on this output, the upper-bounding estimates of daily intake from ambient air ranges from 3.82 in adults (60+ years) to11.55 μg/kg-bw/day (0.5 – 4 years) for individuals living near point sources (Table 10).

The intake values from exposure to soils located near a point source remain the same as those reported in the SoS Report.

Upper-bounding estimates of daily intake of ethylene glycol for a highly exposed population in the immediate vicinity of an industrial point source range from 57 μg/kg-bw/day in adults (60+ years) to 191 μg/kg-bw/day in children (0.5–4 years), as shown in Table 10. For most age groups, the present estimation is approximately two to three times higher than the estimate presented in the SoS Report. Indoor air is the primary source of exposure for all age groups living in the vicinity of a point source.

In the SoS Report, the highest exposure to the general population was considered to be from dermal exposure to ethylene glycol from use of tub and tile cleaners. Dermal exposure estimates were also derived for latex paints, floor polish/wax and auto

polish/wax. According to the Canadian Consumer Specialty Products Association (CCSPA) (2002), tub and tile cleaners found in the Canadian market do not contain ethylene glycol. CCSPA (2007) has also confirmed that floor polish/wax products containing ethylene glycol are for use in commercial and institutional settings and are not for consumer use. Therefore, the daily intake of ethylene glycol through dermal exposure is considered to be mainly from auto polish/wax and latex paints. The estimates of exposure to adults from dermal contact to these consumer products were 0.56 and 1.9 mg/kg-bw/day, respectively (Table 11). These estimates would be lower if dermal absorption is taken into account.

Information on levels of ethylene glycol in latex paint in Canada as well as on types of paint sold (primer versus topcoat) was submitted by the Canadian Paint and Coatings Association (CPCA) (2008). CPCA surveyed ten architectural paint manufacturers in Canada asking them to report the maximum content of ethylene glycol in their interior paint products, and to provide more detailed information on the average ethylene glycol content found in all paint products, including primers, as well as the ratio of sales within various concentration ranges. The results of this survey indicated that the average ethylene glycol content in consumer paints sold in Canada is 1.9%; that approximately 85% of paints contain less than 3% ethylene glycol; and 99.6% of latex paints contain less than 5% ethylene glycol (i.e., less than 0.4% of consumer paints sold in Canada exceed 5% ethylene glycol content). The ethylene glycol levels in primer were considered to be lower than 5%, with an estimated average ethylene glycol content of 1.57%. The survey also showed that based on paint sold in Canada in 2007, 1.2 gallons (4.5 L) of interior primer were sold for every 8.8 gallons (33.3 L) of interior topcoat, indicating that primers are not used as often as topcoats (ratio of approximately 1:9). Based on the information submitted by CPCA, the following concentration values were used to estimate exposures to latex paint: 1.9% (average), 3% and 5% (maximum).

Inhalation exposure to consumer products was not estimated in the SoS Report; however, based on the levels identified in indoor air from Zhu *et al*., (2004) and Hodgson *et al*. (2000), it was determined that this route of exposure should be investigated.

Table 11 shows estimated air concentrations from use of latex paint using the US EPA's Wall Paint Exposure Model (WPEM), information from CPCA on ethylene glycol content in paint and primers, as well as ethylene glycol-specific default values for mass recovery rate (Chang *et al.* 1997; Chang 2001) and emission decay rate constant for desorption (k_1) (US EPA 2001). The highest 8-hr average concentration for a do-it-yourself painter painting a room with two coats of latex paint was 2.5 mg/m^3 for paint containing 1.9% ethylene glycol; 4.0 mg/m^3 for paint containing 3% ethylene glycol; and 6.7 mg/m^3 for paint containing 5% ethylene glycol. The highest 8-hr average concentration for child occupants of the home being painted was 0.7 mg/m^3 for paint containing 1.9% ethylene glycol; 1.1 mg/m^3 for paint containing 3% ethylene glycol; and 1.8 mg/m^3 for paint containing 5% ethylene glycol (Table 11). It should be noted that all Canadian paint products are sold with the following label warning: "Use only under well-ventilated conditions" (CPCA 2008) and the model used to estimate indoor air concentrations assumed a low ventilation rate of 0.45 air changes per hour.

Although CCSPA (2007) has confirmed that floor polish/wax products containing ethylene glycol are restricted to commercial and institutional settings, inhalation exposure to occupants of these facilities is possible and was therefore investigated using the ConsExpo model developed by The National Institute for Public Health and the Environment (RIVM 2006). The mean event concentration while applying floor polish in a residential setting was 2.1 mg/m^3 (see Table 11) and is considered an upper-bounding estimate of the concentrations that occupants may be exposed to. It was considered that auto polish/wax is used primarily outdoors and inhalation exposure would be negligible (US EPA 1986).

In the SoS Report, exposure estimates from use of consumer products were derived through amortization of daily exposures over a one-year period, taking event frequency into account. However, to characterize risk from short-term exposures, daily exposure estimates during product use may be a more appropriate basis for comparison. As such, daily exposure estimates are considered the most appropriate exposure metric for the current assessment.

3.2.2 Hazard characterization

In the period following the release of the 2000 SoS Report, a number of studies have been reported on ethylene glycol toxicity, including those conducted specifically to address uncertainties identified in the report. Key recent mammalian *in vitro* and *in vivo* toxicity studies and human studies are presented below for the hazard characterization of ethylene glycol.

In human acute toxicokinetic studies, when four male volunteers were exposed to 31 mg/m^3 vaporized labelled ethylene glycol through inhalation for four hours (16 times at 15-minute intervals), 71% to 85% uptake (equivalent to 0.92–1.46 mg/kg-bw) and complete bioavailability were reported. The half-lives of labelled ethylene glycol and glycolic acid were 1.6–2.6 and 1.8–2.9 h, respectively, and urine excretion rates for ethylene glycol, glycolic acid and oxalic acid were 5.5%, 0.77% and 0.10% of inhaled ethylene glycol, respectively (Carstens *et al*. 2002, 2003; Upadhyay *et al.* 2008). The half-lives described in those studies are shorter than those derived from cases of ethylene glycol intoxication (3.0–8.6 h) and Upadhyay *et al*. 2008 propose that this is because ethylene glycol metabolism is not saturated at the lower level exposures. No adverse effect related to exposure was reported by the volunteers.

Dermal absorption was examined *in vitro* using split-thickness human skin exposed to various aqueous formulations of labelled ethylene glycol for 24 hours. The percent dose absorbed was 0.84%, 1.04% and 0.94% of the applied dose for 100% (undiluted), 50% and 10% ethylene glycol, respectively, and the skin permeability coefficient at all three concentrations was estimated to range from $1.5x10^{-4}$ to $2.6x10^{-4}$ cm/h. The average, steady-state flux of ethylene glycol through the skin was essentially linear with concentration at 217, 129 and 15 µg equivalents/cm^2xh for the 100%, 50% and 10%

aqueous formulations, respectively (Jovanovic 2008 unpublished). Dermal uptake of ethylene glycol was also determined in three male volunteers. Dermal exposure (skin area 66 cm^2) to labelled liquid ethylene glycol (undiluted) for up to six hours resulted in a maximum ethylene glycol plasma concentration of 1.1–2.0 μmol/l, and 8.1% and 0.4% of the dose was excreted in urine as ethylene glycol and glycolic acid, respectively. In addition, the skin permeability constant of liquid ethylene glycol was determined to be 2.7×10^{-5} cm/h (Upadhyay *et al.* 2008). No exposure-related adverse effect was reported.

In short-term toxicity studies, when Wistar and Sprague-Dawley rats were exposed to 1050 mg/kg-bw/day of ethylene glycol through drinking water for 42 and 28 days, respectively, both strains showed increased urinary oxalate and renal calculi (Huang *et al*. 2000, 2002, 2003; Green *et al*. 2005). Khan *et al*. (2002) conducted a similar study using Sprague-Dawley rats exposed to the same dose of ethylene glycol in their drinking water for eight weeks. Calcium oxalate crystal deposition in the kidneys was present in all treated animals. In another study, when mice were orally administered 2200 mg/kg-bw ethylene glycol for seven days, decreased body weight was reported (Mohanasundari *et al*. 2005).

A recent 16-week subchronic (Cruzan *et al*. 2004) and a 12-month chronic (ACC 2005, Corley *et al*. 2008) dietary study on rats allowed for a more in-depth characterization of the repeat dose toxicity of ethylene glycol to mammals. The subchronic toxicity study (Cruzan *et al*. 2004) was conducted using both Wistar and Fischer 344 (F-344) rats to further investigate strain differences in toxicity. When rats were exposed to 0, 50, 150, 500 and 1000 mg/kg-bw/day ethylene glycol for 16 weeks under identical dietary exposure conditions, the no-observed-adverse-effect level (NOAEL) and the lowest-observed-adverse-effect level (LOAEL) for both strains were reported as 150 and 500 mg/kg-bw/day, respectively. At the LOAEL, increased incidence of calcium oxalate crystals was found in both strains.

Wistar rats were more sensitive to ethylene glycol at higher doses than were F-344 rats; their sensitivity to ethylene glycol at 500 mg/kg-bw/day was comparable to that of F-344 rats at 1000 mg/kg-bw/day. Toxicokinetic studies showed significant strain difference in oxalic acid levels in the kidney at an ethylene glycol dosage level of 500 mg/kg-bw/day and above. At the end of a 16-week exposure period, the oxalic acid levels in kidney tissues of F-344 rats at 500 and 1000 mg/kg-bw/day were 0.033 and 20.6 mg/g, respectively, whereas in Wistar rats these levels were 33.1 and 100.8 mg/g, respectively (Cruzan *et al*. 2004). There was a clear strain difference in elimination of oxalic acid in urine. Wistar rats exposed to 500 and 1000 mg/kg-bw/day had 21 and 14 times less elimination in urine, respectively, compared to F-344 rats.

A chronic toxicity study (ACC 2005: Corley *et al*. 2008) with male Wistar rats, the most sensitive strain, is considered a key study for the human health risk assessment of ethylene glycol for chronic exposures. When rats were exposed to 0, 50, 150, 300 and 400 mg/kg-bw/day in their diet for 12 months, the NOAEL was 150 mg/kg-bw/day, and the LOAEL was 300 mg/kg-bw/day based on renal toxicity (e.g., crystal nephropathy) as well as a significant increase in plasma glycolic acid. The highest dose exceeded the

maximum tolerable dose (MTD), as all the surviving rats had to be euthanized before the scheduled termination due to excessive weight loss.

Analysis of blood, urine and kidney samples for ethylene glycol metabolites showed a rapid and non-linear increase in oxalic acid levels in the kidneys. At 0, 50, 150, 300 and 400 mg/kg-bw/day, the oxalic acid levels were 5.31, 16.07, 8.72, 6561 and 18 789 µg/g, respectively. While elimination of ethylene glycol followed a linear dose-response relationship, elimination of glycolic acid (GA) was linear up to 150 mg/kg-bw/day. However, it increased non-linearly at 300 mg/kg-bw/day and urinary elimination of oxalic acid was similar to control animals across all the doses.

In the same study, the renal clearance of oxalic acid in Wistar rats was compared with F-344 rats. A significantly higher renal clearance was present in young F-344 rats (6.06 mL/min/kg-bw) compared to young Wistar rats (3.8 mL/min/kg-bw). There was no age difference in renal clearance of oxalic acid among Wistar rats.

Poldelski *et al*. (2001) exposed isolated mouse proximal tubular segments (PTSs) to ethylene glycol or its main metabolites (glycolate, glycoaldehyde, glyoxylate or oxalate) for 15 or 60 minutes and cell injury was measured by the percentage of lactate dehydrogenase (LDH) release, LDH destruction, adenosine triphosphate (ATP) depletion or membrane phospholipid degradation. Only glyoxalate and glycoaldehyde resulted in significant ATP depletion and LDH release causing cytotoxicity. Ethylene glycol, glycolate and oxalate were not injurious to PTSs. The authors concluded that glyoxalate and glycoaldehyde are the principle metabolites responsible for ethylene-glycol-induced nephrotoxicity.

Similarly, glyoxylate-treated C57BL/6 mice showed decreased superoxide dismutase and increased malondialdehyde expression, markers for oxidative stress and renal epithelial cell injury, respectively, in renal epithelial cells. Mitochondria structure in renal tubular cells was also severely disrupted in regions with calcium oxalate crystals. These particular changes or crystal formation were not observed in ethylene glycol or glycolic acid-treated mice despite induction of hyperoxaluria in the former (Hirose *et al.* 2008). The lack of oxalate crystal formation in these mice differs from what has been observed in rats and in cases of acute poisoning in humans. Hirose *et al.* (2008) propose that this may be due to quantitative differences in the metabolic pathway for oxalate precursors and the presence of a defense mechanism against cell injury in mice.

Guo *et al*. (2005, 2007) conducted *in vitro* studies with human proximal tubule (HPT) cells and showed that calcium oxalate monohydrate (COM) dose-dependently increased the LDH release while glycolic acid, glyoxylic acid or glycoaldehyde did not increase LDH release at any of the pH levels tested (pH 6, 6.5, 7 or 7.4). The results of these studies suggest that COM, not the other metabolites of ethylene glycol, is toxic to HPT cells at the relevant concentrations.

In another *in vitro* study (Guo and McMartin 2005), the toxicity of oxalate and calcium oxalate monohydrate (COM) to rat proximal tubular (PT) cells and human proximal

tubular (HPT) cells was investigated. COM, not oxalate ion, caused the cytotoxicity in HPT cells, assessed by the release of LDH and percentage of cell death. Similar results were observed in Wistar and F-344 rat PT cells. This study also showed that HPT cells are less sensitive than rat PT cells to COM-induced cytotoxicity. This difference in sensitivity may be due to the ability of rat PT cells to bind to and internalize five times more COM crystals compared to HPT cells (McMartin and Guo 2007). Furthermore, McMartin and Wallace (2005) found that inhibition of mitochondrial respiratory function in PT cells by COM crystals is an important factor for the renal toxicity of ethylene glycol. These *in vitro* findings of COM toxicity are in agreement with the findings of Cruzan *et al*. (2004).

As reported in the SoS Report, slight reproductive effects and developmental toxicity, including teratogenicity, have been observed in rodents exposed to ethylene glycol by the oral route at doses greater than those associated with renal effects. For example, developmental toxicity was observed in mice when 11 090 mg/kg-bw/day ethylene glycol was administered orally during gestational day (GD) 7–14 (Schuler *et al*. 1984). Similar observations were made from other developmental toxicity studies.

Maternal toxicity and fetal malformations were detected when pregnant rats were exposed to ethylene glycol through a subcutaneous (≥1000 mg/kg-bw/day) bolus injection during GD 7–15, but not when the same doses were administered at a slower rate via a subcutaneous implanted infusion pump (Carney *et al*. 2001, 2002, as cited in the OECD 2009). This difference in toxicity is considered to be due to the saturation of an intermediary step in ethylene glycol metabolism, resulting in the accumulation of glycolic acid in the bolus exposure. Previous investigations have shown that ethylene glycol-induced developmental toxicity is caused by the intermediate metabolite glycolic acid (Carney *et al*. 1999, 2001).

Wistar rat whole embryo (on GD 9.5–11.5) cultures were exposed to ethylene glycol and its metabolites (glycoaldehyde, glycolic acid, glyoxale, glyoxylic acid and oxalic acid), and the LOAELs for developmental toxicity were reported as 200 mM for ethylene glycol and 3 mM for glycolic acid. Decreased growth parameters (protein content and crown-rump length) were reported at the LOAEL (Klug *et al*. 2001).

In a toxicokinetic study, when ethylene glycol was administered orally to pregnant and non-pregnant Sprague-Dawley rats, the pregnancy status did not have any impact on the pharmacokinetic parameters of ethylene glycol and its metabolites. The LOAEL for developmental toxicity was 1000 mg/kg-bw/day based on abnormal embryos and a peak blood glycolic acid level of 363 µg/g or 4.8 mM (Pottenger *et al.* 2001).

No evidence of developmental or reproductive effects was observed in rabbits in the only such study for this species, as reported in the SoS Report. This species difference has been recently addressed and was attributed to toxicokinetics. Glycolic acid levels in rabbit maternal blood and embryo were only 46% and 10% of the respective values in rats. This is possibly due to a slower rate of maternal metabolism and to fundamental differences in disposition of glycolic acid to the embryo (Carney *et al.* 2008).

In a metabolism study, Booth *et al*. (2004) exposed rat, rabbit and human liver slices to ethylene glycol. Liver glycolic acid levels in rats were approximately 10 times higher than in rabbits and were not detected in humans. Human liver tissues were also more efficient in further metabolizing glycolic acid to glyoxylic acid. There is therefore less chance for glycolic acid accumulation in humans compared to rats and rabbits, clearly suggesting that, of the three species, humans may be less sensitive because of this difference in hepatic metabolism.

There are no human developmental or reproductive toxicity data available on ethylene glycol. However, physiologically based pharmacokinetic (PBPK) models have been developed for ethylene glycol and its metabolite, glycolic acid, in rats and humans (Corley *et al*. 2005a, 2005b; Corley and McMartin 2005). They were developed to integrate partition coefficients and metabolic rate constants for ethylene glycol and glycolic acid determined in rat and human tissues *in vitro* as well as the estimated clearance of each metabolite in urine from applicable *in vivo* studies. These PBPK models have predicted that it is unlikely to achieve levels of human blood glycolic acid concentrations that could lead to developmental toxicity. Humans would only achieve the threshold for developmental effects determined in rats of 2 mM if they consumed bolus oral doses greater than 350 mg/kg (> 20 g ethylene glycol for a 58 kg female) during the critical window of susceptibility based on simulations of peak maximum blood concentrations of glycolic acid. In addition, the low volatility of ethylene glycol and its potential irritancy limits the possibility of achieving such high blood levels in humans following inhalation exposure (Corley *et al*. 2005a).

Similar conclusions were drawn in by the U.S. National Toxicology Programme's Center for the Evaluation of Risks to Human Reproduction. In 2004, they released an Expert Panel Report on the reproductive and developmental toxicity of ethylene glycol (NTP 2004). In this report, by considering all the available data from animal studies and *in vitro* metabolism studies, the panel concluded that "there is negligible concern of adverse developmental toxicity in humans from ethylene glycol at exposure levels below 125 mg/kg-bw/day." The Expert Panel also concluded that the concerns for reproductive toxicity in humans are negligible due to lack of evidence for reproductive toxicity in experimental animals.

Available data suggest that there are qualitative similarities in toxicokinetic parameters and mode of action of nephrotoxicity among experimental animals and humans (Cruzan *et al.* 2004: Corley *et al*. 2005b and 2008). Furthermore, there is evidence that humans are more efficient in metabolizing ethylene glycol into less toxic metabolites (Hess *et al.* 2004) and are more effective in eliminating oxalate metabolites than experimental animals (Corley *et al*. 2008). Although the mode of action of developmental toxicity is not fully understood, the qualitative similarity in toxicokinetics of ethylene glycol and glycolic acid in humans and experimental animals has been well characterized. Hence, this information could be of value in refining the toxicokinetic uncertainty factor in risk assessment.

There is an extensive database on accidental or intentional ingestion of large quantities of ethylene glycol, in the form of anti-freeze, among humans. These case studies (Leth and Gregersen 2005; Krenova and Pelclova 2005; Huttner *et al*. 2005; Caravati *et al*. 2005; Morfin and Chin 2005) have reported severe metabolic acidosis, elevated serum anion and osmolar gap and calcium oxalate crystalalluria in individuals acutely exposed to large quantities of ethylene glycol. A more thorough overview of systemic toxicity associated with ingestion of ethylene glycol is described in the SoS Report. While the ingested mixture prevents us from concluding that the effects are solely due to ethylene glycol, the observed toxicity is consistent with those observed in animal studies. The pathological examination of renal tissues showed widespread necrosis of the tubular epithelium and deposition of oxalate crystals in the proximal and distal tubules and collecting ducts. Renal function usually returns to normal in survivors, but permanent renal damage has occurred in some cases (Rumack 2003).

Chronic exposure to lower levels of ethylene glycol, however, is more relevant to this assessment. Renal toxicity has not been observed at relatively low exposure levels related to potential occupational or environmental exposure. For example, no kidney damage was reported in 19 adult male volunteers exposed to 3 to 67 mg/m^3 ethylene glycol for 30 days, 20–22 h daily (Wills *et al.* 1974), in 33 adult male Canadian aircraft deicing workers (Gerin *et al.* 1997) or in 10 male Finnish auto mechanics (Laitien *et al.* 1995).

3.2.3 Exposure response analysis

Chronic exposure

Table 12 presents the benchmark dose$_{05}$ (BMD$_{05}$) (i.e., the dose estimated to cause a 5% increase in incidence over the background response rate) and the corresponding 95% lower confidence limit (BMDL$_{05}$) for key toxicity studies presented in the SoS Report (Environment Canada and Health Canada 2000) and the current follow-up report.

The following polynomial model, which describes the probability of the occurrence of the given health effect, was used to derive the BMD$_{05}$ from the dose-response data:

$$P(d) = q_0 + (1 - q_0) \cdot \left[1 - e^{-q_1 d - \ldots - q_k d^k} \right],$$

where d is dose, k is the number of dose groups in the study, $P(d)$ is the probability of the animal developing the effect at dose d and $q_i > 0$, $i = 1,...,k$ and d_0 are parameters to be estimated.

The models were fit to the data using THRESH (Howe 1995) and the BMD$_{05}$s were calculated as the dose D which satisfies

$$\frac{P(D)-P(0)}{1-P(0)}=0.05$$

A chi-square lack of fit test was performed for each of the model fits. The degrees of freedom for this test are equal to *k* minus the number of q_is whose estimates are non-zero. A p-value of less than 0.05 indicates a significant lack of fit. The $BMDL_{05}$ is defined as the lower 95% confidence limit on the BMD_{05}.

The BMD_{05} of 120 mg/kg/day, based on incidence of crystal nephropathy in male Wistar rats exposed to ethylene glycol for 12 months through diet (ACC 2005: Corley *et al.* 2008), was considered the most appropriate for use in establishing the tolerable intake (TI). The primary reason for selecting the 12-month study over the 16-week study (Cruzan *et al.* 2004) is to reduce the uncertainty associated with less-than-chronic exposure. Furthermore, the results of the chronic study indicate that the kidney lesions are not progressing over long-term exposure. The $BMDL_{05}$ value for this end point was less than twofold lower than the central estimate of the BMD_{05}; the latter, therefore, was used in the calculation of TI.

In the chronic study (ACC 2005; Corley *et al.* 2008), renal changes were reported in terms of crystal nephropathy only. In contrast, the provisional tolerable intake reported in the SoS Report was established based on the BMD_{05} for incidence of total tubular damage (i.e., oxalate crystals in kidney, dilated tubules, protein casts) in a subchronic study (Gaunt *et al*. 1974). Incidence of crystal nephropathy is a more compound-specific histopathological effect, which is considered adverse. For comparison purposes, the BMD_{05} for incidence of exclusive oxalate crystal formation in the kidney (as opposed to total tubular damage) from Gaunt *et al*. (1974) is 173.4 mg/kg/day (95% LCL 67.3 mg/kg-bw/day). Similarly, the BMD_{05} from the 16-week study (Cruzan *et al*. 2004) is 161 mg/kg-bw/day based on incidence of crystal nephropathy (95% LCL of 72 mg/kg/day).

Based on the BMD_{05} of 120 mg/kg-bw/day, the tolerable intake (TI) has been derived as follows:

$$\text{TI} = \frac{\text{120 mg/kg-bw/day}}{100}$$

$$= \text{1.2 mg/kg-bw/day (1200 µg/kg-bw/day)}$$

where

120 mg/kg-bw/day is the BMD_{05} for the incidence of compound-induced crystal nephropathy in male Wistar rats after dietary exposure to ethylene glycol for 12 months (ACC 2005) and

100 is the default uncertainty factor (x 10 for interspecies variation, x 10 for intraspecies variation). Regarding the factors for interspecies and intraspecies variation, the toxicokinetic and toxicodynamic aspects of these uncertainty factors

based on available data were not further refined. However, the additional uncertainty factor of 10x, which was applied to account for less-than-chronic exposure in the SoS Report, is no longer warranted given the availability of a chronic study in the sensitive rat strain.

3.2.4 Risk characterization

The above estimated tolerance intake (TI) for chronic exposure remains protective for potential developmental effects. In the SoS Report, TIs for this end point were derived based on i) the NOAEL for developmental effects in mice (i.e., 500 mg/kg bw/day) divided by an uncertainty factor of 100; and ii) the NOEL of 150 mg/kg-bw/day in the same mice study divided by an uncertainty factor of 100. These values exceed the TI, based on renal effects, of 1.2 mg/kg-bw per day. Furthermore, NTP (2004) has concluded that there is negligible evidence of adverse developmental toxicity in humans from ethylene glycol at exposure levels below 125 mg/kg-bw/day. This is further supported by PBPK model predictions that human blood glycolic acid concentrations are unlikely to reach levels that could lead to developmental toxicity (Corley *et al*. 2005a).

Based on the information available, upper-bounding estimates of daily intake of ethylene glycol for the general population of Canada, up to 157 µg/kg-bw per day (Table 9), and for a highly exposed population in the immediate vicinity of an industrial point source, up to 191 µg/kg-bw per day (Table 10), are well below the TI of 1200 µg/kg-bw per day.

The SoS Report did not estimate inhalation exposure to consumer products. However, based on the levels identified in indoor air, this route of exposure has been investigated. The predicted highest 8-hr average air concentrations from the use of latex paint ranged from 2.5−6.7 mg/m^3 for adult do-it-yourself painters and from 0.7−1.8 mg/m^3 for child occupants. Indoor air concentrations would be lower if a higher ventilation rate was used in the model, which might be likely since paint labels instruct users to paint in well-ventilated areas. In contrast, these concentrations could be higher if levels in paint exceed 5% (however, less than 0.4% of consumer paints sold in Canada exceed this value) or if primer containing similar levels of ethylene glycol is used. These predicted highest air concentration ranges are tenfold or greater below the NOAEL for irritation of 67 mg/m^3 identified in a human study (Wills *et al.* 1974), and are therefore considered protective. Use of this NOAEL as a basis for risk characterization is also considered to be protective of developmental effects as NTP (2004) has concluded that there is negligible concern for adverse developmental toxicity in humans from ethylene glycol at exposure levels below 125 mg/kg-bw/day, and the calculated oral equivalent doses for the ranges of predicted air concentrations would be approximately two orders of magnitude below this level. Confidence in the use of the NOAEL of 67 mg/m^3 is further strengthened by PBPK model predictions that human blood glycolic acid concentrations are unlikely to reach levels that could lead to developmental toxicity (Corley *et al*. 2005a). Results from an inhalation study conducted in CD-1 mice (Tyl *et al*. 1995), summarized in the SOS Report, were not considered appropriate for use in characterizing risk from inhalation exposure, due to significant study limitations. These limitations included the confounding

effects caused by exposure through ingestion and the stress induced by use of a restraint for a nose-only exposure.

According to CCSPA (2007), floor polish/wax products containing ethylene glycol are only used in commercial and institutional settings and are not for consumer use. However, it is possible that the general population may be exposed to ethylene glycol via inhalation in institutional settings. The upper bounding estimate used to represent this route of exposure (2.1 mg/m^3) is well below the NOAEL of 67 mg/m^3 (Wills *et al.* 1974) and is not, therefore, of concern. It was considered that auto polish/wax is used primarily outdoors and inhalation exposure would therefore be negligible. (Note: As the dermal exposure estimate from use of auto polish/wax is below the TI, this consumer product scenario is not of concern.)

3.2.5 Uncertainties and degree of confidence in human health risk characterization

In the SoS Report, limitations of the available data precluded development of upper-bounding estimates of daily intake of ethylene glycol by the general population. In the current assessment, additional data permitted derivation of upper-bounding estimates of daily intake of ethylene glycol. However, the intakes from ambient air and from indoor air are each based on a single Canadian study with insufficient samples to ensure representativeness of the Canadian population. No monitoring data for drinking water and soils were identified. No new data on levels of ethylene glycol from food or food packaging were identified either and this remains an area of uncertainty. Thus, estimated total daily intake values for the general population, based on the limited data presented above, could change in cases where drinking water contributes any significant levels of ethylene glycol.

There is moderate confidence in the estimated intake in the vicinity of point sources. The computer air dispersion model (ISC PRIME) is considered to provide a reliable indication of ambient air concentrations of ethylene glycol at the dwelling and property boundary in the vicinity of industrial point sources. With respect to indoor air, it is possible that the indoor air intake value for those residents living near the vicinity of a point source is underestimated, as these values were measured in dwellings not located near industrial point sources. There is a high degree of certainty that the estimates of intake from ingestion of soil by a population exposed due to its proximity to a source of discharge to the atmosphere are upper-bounding.

Overall, there is low to moderate confidence in the estimates of exposure to ethylene glycol from use of consumer products. Based on the information provided by CCSPA (2002), there is high confidence that tub and tile cleaners do not contain ethylene glycol and that floor polish/waxes containing ethylene glycol are targeted to commercial and institutional uses (CCSPA 2002, 2007). However, there is uncertainty about occupant exposures following commercial and institutional uses. There is also some uncertainty regarding the appropriateness of using the ConsExpo residential floor polish scenario to

represent potential inhalation exposures to ethylene glycol to occupants of institutional settings. Additionally, data on Canadian-specific ranges and distributions of concentrations in the various products were not available. Information on dermal absorption, reported above, indicates that the assumption of 100% dermal absorption is very conservative and that actual dermal absorption is likely more than an order of magnitude lower than this. As noted in the SoS Report, estimated daily intakes of ethylene glycol by the dermal route from use of consumer products would be several orders of magnitude less than the values presented in Table 11 if skin permeability were taken into account (Environment Canada and Health Canada 2000). There is moderate confidence in the exposure estimates via the inhalation route from latex paint using the US EPA's Wall Paint Exposure Model and ethylene glycol-specific model parameter inputs. The model is relatively robust and has incorporated results of chamber tests involving ethylene glycol (US EPA 2001). This model was designed specifically to model indoor air concentrations and exposures from painting applications (US EPA 2001). As this model predicts that the highest air concentrations could occur approximately 1.5 days after painting has commenced, other occupant scenarios (e.g., child sleeping or playing in a freshly painted room) could result in higher exposures than the one presented. However, taking into consideration the conservative nature of inputs to the exposure assessment, exposure to ethylene glycol from consumer products is not considered to be of concern.

The degree of confidence in the database on toxicity that serves as the basis for development of the TI for ethylene glycol has increased from the database presented in the SoS Report, but remains in the moderate range. Confidence that the TI developed on the basis of renal effects is protective of other adverse effects of ethylene glycol, such as developmental effects, also remains moderate. The lack of data on progression of renal lesions following chronic exposure in the most sensitive animal model was an area of considerable uncertainty identified in the SoS Report. This has been addressed through conduct of a 12-month study in Wistar rats. It is considered that the chronic study used to derive BMD_{05} has comprehensively covered the renal histopathology, as renal tissues are the primary target sites for ethylene glycol toxicity. Furthermore, the study was conducted on Wistar rats, the strain of rats most sensitive to ethylene glycol.

3.3 CONCLUSION

Based on the information presented in this report, ethylene glycol 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 constitutes or may constitute a danger to the environment on which life depends.

Based on the information presented in this report, ethylene glycol is not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health.

Therefore, ethylene glycol does not meet any of the criteria under section 64 of CEPA 1999.

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APPENDIX A: TABLES 1 TO 13

Table 1: Chemical and physical properties of ethylene glycol

Property	Parameter	Reference	Fugacity Model Input Parameters (Mackay *et al*. 1995)
Molecular formula	$C_2H_6O_2$		
Molecular weight (g/mol)	62.07		62.07
CAS registry number	107-21-1		
Common synonyms	glycol, glycol alcohol, ethylene alcohol, ethylene dihydrate, monoethylene glycol, 1,2-dihydroxyethane, 1,2-ethanediol		
Physical state (25°C)	colourless liquid		
Melting point (°C)	–13 –11.5	Budavari *et al*. 1989 Howard 1990 Weast 1982–1983 IPCS 1993 HSDB 1999	–13
Boiling point (°C)	197.6	Budavari *et al*. 1989 Howard 1990 IPCS 1993 HSDB 1999	
Density (g/mL) at 20 ° C	1.1135 1.1 1.1088 1.1130	Budavari *et al*. 1989 IPCS 1993 HSDB 1999 Verschueren 1983	
Vapour pressure (Pa)	6.7 (20°C) 7 (20°C) 12.27 (5 °C) 11.7 (25°C)	Verschueren 1983 IPCS 1993 Howard 1990 HSDB 1999	12
Henry's Law constant ($Pa \cdot m^3/mol$)	6.08×10^{-3} 5.81×10^{-6} (calculated) 2.37×10^{-5} (calculated) 6.0×10^{-3} (experimental)	Howard 1990 Hine and Mookerjee 1975 Hine and Mookerjee 1975 Hine and Mookerjee 1975	7.5×10^{-3} (calculated based on fictitious water solubility of $1.0 \times 10_5$)
Log K_{ow}	–1.36 –1.93 –2.02	Howard 1990 Verschueren 1983 Iwase *et al*. 1985	–1.36
Solubility in water	miscible	Budavari *et al*. 1989 IPCS 1993	1.0×10^{11} mg/L
Conversion factor	multiply x 1.11 g/mL to convert µL/L to mg/L		
Half-life – air	0.35–3.5 days 0.24–2.4 hours	Howard *et al*. 1991 Darnall *et al*. 1976	55 hours
Half-life – water	2–12 days (aerobic) 8–48 days (anaerobic)	Howard *et al*. 1991 Howard *et al*. 1991	55 hours
Half-life – groundwater	4–24 days	Howard *et al*. 1991	

Half-life – soil	2–12 days	Howard *et al*. 1991	55 hours
Half-life – sediment	–	–	170 hours

Table 2: Ethylene glycol releases from all reporting sources (NPRI 1994–2005)

Report Year	Number of Reporting Facilities	Total Disposal	Total Recycled	Untreated Releases	Total of Releases, Disposal and Recycling
1994	237	2073	821	2931	5825
1995	237	3523	359	3857	7739
1996	275	3775	353	3765	7893
1997	289	3997	913	4569	9479
1998	294	2874	2748	2986	8608
1999	327	3198	1632	2207	7037
2000	333	4390	7230	2570	14 190
2001	337	5597	3358	2346	11 301
2002	358	5985	2202	1571	9759
2003	345	5215	2953	2331	10 500
2004	345	4573	2702	2358	9633
2005	353	5270	2675	2175	10 119

Notes: All releases are in tonnes. "Untreated Releases" do not include underground injection.

Table 3: Untreated ethylene glycol releases by compartment, all sources (NPRI 1994–2005)

Year	Reporting Facilities	Compartment				Total Releases
		Air	Water	Land	Underground Injection	
1994	178	377	91	2453	77	2998
1995	165	533	72	3247	220	4072
1996	188	504	69	3188	233	3994
1997	192	378	26	4161	133	4698
1998	175	256	33	2691	139	3119
1999	203	284	28	1890	245	2447
2000	190	317	68	2179	422	2986
2001	223	247	58	2037	123	2465
2002	188	312	51	1206	173	1742
2003	185	352	444	1532	173	2501
2004	184	343	545	1465	126	2479

Table 4: Ethylene glycol releases from airports

Reporting Year	Untreated Releases	Disposal	Recycling	Total
1998	2450	1418	709	4577
1999	1797	1874	466	4137
2000	2163	3090	346	5599
2001	2019	4322	347	6688
2002	1165	4364	654	6183
2003	1445	4030	844	6319
2004	1405	3536	988	5929
2005	1232	4236	1277	6745

Source: NPRI 2005. All releases are in tonnes.

Table 5: Summary statistics of concentrations of ethylene glycol in stormwater released from Canadian airports in selected years

Deicing Season	Number of Samples	Summary statistics and percentiles of distribution of measured concentrations (mg/L)						
		Mean	Median	75th	90th	95th	99th	Maximum
1997–1998	1606	22	4	10	38	80	256	3700
1998–1999	1676	23	5	12	45	65	180	4700
1997–1999 combined	3282	23	5	10	42	72	200	4700
2003–2004	1508	27	5	12	46	82	478	1860
2004–2005	1728	19	4	11	51	76	136	2560
2003–2005 combined	3236	23	5	12	49	78	224	2560

Table 6: Direct toxicity risk quotients for exposure of algae to ethylene glycol

Effluent Concentration (mg/L)	Descriptor	EEV in Receiving Water (mg/L)	Quotient[1]
4700	Highest maximum, **1997–1999** seasons	470	0.719
200	99th percentile, **1997–1999** seasons	20	0.031
72	95th percentile, **1997–1999** seasons	7	0.012
2560	Highest maximum, **2003–2005** seasons	256	0.391
224	99th percentile, **2003–2005** seasons	22	0.034
78	95th percentile, **2003–2005** seasons	8	0.012
1 Quotient is derived by dividing the EEV by the ENEV (654 mg/L).			

Table 7: Direct toxicity risk quotients for exposure of amphibians to ethylene glycol

Effluent Concentration (mg/L)	Descriptor	EEV in Receiving Water (mg/L)	Quotient[1]
4700	Highest maximum, **1997–1999** seasons	470	0.993
200	99th percentile, **1997–1999** seasons	20	0.042
72	95th percentile, **1997–1999** seasons	7	0.015
2560	Highest maximum, **2003–2005** seasons	256	0.541
224	99th percentile, **2003–2005** seasons	22	0.047
78	95th percentile, **2003–2005** seasons	8	0.017
1 Quotient is derived by dividing the EEV by the ENEV (473 mg/L).			

Table 8: Indirect toxicity risk quotients for exposure of aquatic biota to ethylene glycol

Effluent Concentration (mg/L)	Descriptor	EEV in Receiving Water (mg/L)	Oxygen Deficit[1] (mg/L)	Quotient[2]
4700	Highest maximum, **1997–1999** seasons	470	57.9	16.1
200	99th percentile, **1997–1999** seasons	20	3.1	0.86
72	95th percentile, **1997–1999** seasons	7	1.3	0.37
2560	Highest maximum, **2003–2005** seasons	256	32.9	9.13
224	99th percentile, **2003–2005** seasons	22	3.4	0.95
78	95th percentile, **2003–2005** seasons	8	1.6	0.44

Notes: 1. "Oxygen deficit" is the application of the Streeter and Phelps (1925) oxygen sag model to provide the number of mg O_2/L below the saturation point of 13.1 mg O_2/L and resulting from the assumed EEV in the receiving water.
2. The quotient represents the ratio between the calculated oxygen deficit and the minimal oxygen deficit of 3.6 mg/L needed to meet the cold-water CCME freshwater guideline of 9.5 mg/L, assuming a water temperature of 4°C.

Table 9: Upper-bounding estimates of daily intake of ethylene glycol by the general population of Canada

Route of Exposure	Estimated Intake (µg/kg-bw per day) of Ethylene Glycol by Various Age Groups in the General Population						
	0–6 Months[1]		0.5–4 Years[2]	5–11 Years[3]	12–19 Years[4]	20–59 Years[5]	60+ Years[6]
	Formula Fed	Not Formula Fed					
Ambient air[7]	2.6	2.6	5.6	4.4	2.5	2.1	1.9
Indoor air[8]	54.6	54.6	117.1	91.3	51.9	44.6	38.8
Food and beverages[9]	2.4	2.4	34.4	41.1	31.9	16.8	12.2
Drinking water[10]	-	-	-	-	-	-	-
Soil[11]	-	-	-	-	-	-	-
Total intake	60	60	157	137	86	64	53

1 Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

2 Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

3 Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

4 Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

5 Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

6 Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day (EHD 1998) and to consume food items at average daily rates indicated in EHD (1998).

7 The Ontario Ministry of Environment (formerly the Ontario Ministry of Environment and Energy) measured levels of ethylene glycol at 12 different public areas located in Windsor, Ontario in 1992 (OMEE 1994b). The maximum concentration (75 µg/m^3) was used to calculate the upper-bounding estimate of exposure for ambient air. Canadians are assumed to spend 3 hours outdoors each day (EHD 1998).

8 Zhu *et al*. (2004) measured levels of ethylene glycol in nine residential homes (two apartments and seven single detached houses), one attached residential garage, one office and two laboratories. The maximum concentration observed in a residential home (223 µg/m^3) was used to calculate the upper-bounding estimate of exposure. Canadians are assumed to spend 21 hours indoors each day (EHD 1998).

9 Refer to the State of the Science Report for Ethylene Glycol (Environment Canada and Health Canada 2000) for more details on the values of ethylene glycol that may be found in food and beverages.

10 Concentrations of ethylene glycol in Canadian drinking water or elsewhere were not identified.

11 Background concentrations of ethylene glycol in Canadian soils or elsewhere were not identified.

Table 10: Upper-bounding estimates of daily intake of ethylene glycol by a highly exposed population in the immediate vicinity of an industrial point source

Route of Exposure	Estimated intake (µg/kg-bw per day) of ethylene glycol by various age groups in a highly exposed population						
	0–6 Months [1]		0.5–4 Years[2]	5–11 Years[3]	12–19 Years[4]	20–59 Years[5]	60+ Years[6]
	Formula Fed	Not Formula Fed					
Ambient air[7]	5.39	5.39	11.55	9.01	5.12	4.40	3.82
Indoor air[8]	54.6	54.6	117.1	91.3	51.9	44.6	38.8
Food and beverages[9]	2.4	2.4	34.4	41.1	31.9	16.8	12.2
Soil[10]	17	17	28	9	2	2	2
Total intake	79	79	191	150	91	68	57

[1] Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 30 mg of soil per day (EHD 1998).

[2] Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 100 mg of soil per day (EHD 1998).

[3] Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 65 mg of soil per day (EHD 1998).

[4] Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 30 mg of soil per day (EHD 1998).

[5] Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 30 mg of soil per day (EHD 1998).

[6] Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to consume food items at average daily rates indicated in EHD (1998), and to ingest 30 mg of soil per day (EHD 1998).

[7] Based on the maximum 24-hr average concentration (154 $\mu g/m^3$) predicted in ambient air in nearby residences located outside of outer property boundary of an ethylene glycol manufacturing facility in Red Deer, Alberta, Canada (Sciences International, 2003). Canadians are assumed to spend 3 hours outdoors each day (EHD 1998). These values are likely underestimated as they do not take into account the higher levels of ethylene glycol expected to be found in indoor air of residences located near the vicinity of an industrial point source.

[8] Zhu *et al*. (2004) measured levels of ethylene glycol in nine residential homes (two apartments and seven single detached houses), one attached residential garage, one office and two laboratories. The maximum concentration observed in a residential home (223 $\mu g/m^3$) was used to calculate the upper-bounding estimate of exposure. Canadians are assumed to spend 21 hours indoors each day (EHD 1998).

[9] Refer to the State of the Science Report for Ethylene Glycol from 2000 for more details on the values of ethylene glycol that may be found in food and beverages.

[10] Based on the maximum reported concentration (4290 mg/kg) in soil near an industrial point source of discharge (AEP 1996).

Table 11: Upper-bounding estimates of exposure to ethylene glycol from use of consumer products.

Consumer Product Type	Assumptions	Estimated Concentrations and Intakes
Latex wall paint	**Inhalation (do-it-yourself painter)** - Use Wall Paint Exposure Assessment Model (WPEM), version 3.2 2001 (US EPA 2001) and its default values (unless otherwise stated) for a do-it-yourself adult painter (RESDIY) in a painted area. - Assume adult paints one bedroom with 2 coats of paint in one day. - Select ethylene glycol as the chemical of interest. - Assume the percent ethylene glycol in the paint to range from 1.9% (average) to 5.0% (CPCA 2008). - Adjust paint chemical mass by using a recovery rate of 9% (Chang *et al.* 1997) and the emission decay rate constant k_1 to 3.0 (US EPA 2001) A worst-case scenario would be if an adult paints one bedroom with one coat of primer and one coat of paint at a maximum ethylene glycol concentration of 5% in both primer and the paint (NLM 2007; ICI 2007) in one day – 7.74 mg/m^3 Concentrations would be higher for paints that contain more than 5% ethylene glycol (0.4% of paints sold in Canada)	Highest 8-hr concentration = 2.5 mg/m^3 (1.9% EG) 4.0 mg/m^3 (3% EG) 6.7 mg/m^3 (5% EG) Highest instantaneous concentration = 3.6 mg/m^3 (1.9% EG) 5.7 mg/m^3 (3% EG) 9.6 mg/m^3 (5% EG)
	Inhalation adult/child occupant - Use Wall Paint Exposure Assessment Model (WPEM), version 3.2 2001 (US EPA 2001) and its default values (unless otherwise stated) for a child residing in house being painted (RESCHILD) located in the building but not in the painted area. - Assume one bedroom is painted with 2 coats of paint. - Select ethylene glycol as the chemical of interest. - Adjust paint chemical mass by using a recovery rate of 9% (Chang *et al.* 1997) and the emission decay rate constant k_1 to 3.0 (US EPA 2001). - Assume the average percent ethylene glycol in the paint to range from 1.9% (average) to 5.0% (CPCA 2008). A worst-case scenario would be if a child occupant is present when one bedroom is being painted using one coat of primer and one coat of paint at a maximum ethylene glycol concentration of 5% in both primer and the paint (NLM 2007; ICI 2007) in one day – 3.20 mg/m3 Concentrations would be higher for paints that contain more than 5% ethylene glycol (0.4% of paints sold in Canada)	Highest 8-hr concentration = 0.7 mg/m^3 (1.9% EG) 1.1 mg/m^3 (3% EG) 1.8 mg/m^3 (5% EG) Highest instantaneous concentration = 1.7mg/m^3 (1.9% EG) 2.7 mg/m^3 (3% EG) 4.6 mg/m^3 (5% EG)
	Dermal (do-it-yourself painter) - Assume a paint density of 1.24 g/cm^3, surface area exposed to be 220 cm^2 (10% of the surface area of the face, hands and forearms), a film thickness of 0.0098 cm (US EPA 1986). - Assume the maximum percent ethylene glycol in both the primer and the paint to be 5.0% (NLM 2007; ICI, 2007) - Assume 100% absorption through skin. - Assume adult body weight of 70.9 kg (EHD 1998).	Intake = 1.9 mg/kg-bw per day

	Intake = $\frac{(\%\text{ in product})(\text{surface area})(\text{density of product})(\text{film thickness})}{(\text{body weight})}$ Intake = $\frac{(0.05)(220\ cm^2)(1.24\ g/cm^3)(0.0098\ cm)}{70.9\ kg}$ = 0.001885 g/kg-bw per day OR 1.89 mg/kg-bw per day	
Floor Polish/Wax	**Inhalation (adult/child occupant)** - Use ConsExpo, version 4.1 (RIVM, 2006) and its default values (unless otherwise stated) for adult applying floor polish to living room floor ($22m^2$) using a cloth and manually rubbing floor, twice/ yr, undiluted product, leave the room after polishing. - Assume the maximum percent ethylene glycol in floor polish to be 3.5 based on value referenced in SoS Report (2000). Note: CCSPA (2007) indicated a typical range of 1-3%.	Mean event concentration = 2.1 mg/m^3
Auto wax/paste[1]	**Dermal contact by applicator** - Assume a maximum concentration of 3.0%, an exposed surface area equal to 400 cm^2 (palm and fingers of average adult), product density of 1.022 g/cm^3, a film thickness of 0.00325 cm (US EPA 1986). - Assume adult body weight of 70.9 kg (EHD 1998). Intake = $\frac{(\%\text{ in product})(\text{surface area})(\text{density of product})(\text{film thickness})}{(\text{body weight})}$ Intake = $\frac{(0.030)(400\ cm^2)(1.022\ g/cm^3)(0.00325\ cm)}{70.9\ kg}$ = 0.000562 g/kg-bw per day OR 0.56 mg/kg-bw per day	Intake = 0.56 mg/kg-bw/day

[1] Assume this activity would be done outdoors and therefore inhalation exposure to ethylene glycol would be negligible (US EPA 1986).

Table 12: Benchmark dose (BMD) values for key toxicity studies: Gaunt *et al.* (1974), Depass *et al.* (1976), Neeper-Bradley *et al.* (1995), Cruzan *et al.* (2004) and ACC (2005)

End Point	BMD_{05} (mg/kg/day)	$BMDL_{05}$ (mg/kg/day)	Lack of Fit (P-Value)
Gaunt *et al.* (1974)*			
Kidney tubule damage	39.3	18.6	0.87
Individual nephrons with dethylene glycoleneration	83.8	45.1	0.86
Individual nephrons with dethylene glycoleneration and occasional oxalate	217.6	75.4	0.75
Several nephrons with dethylene glycoleneration and frequent crystals	553.9	180.1	1.00
Nephrons with dethylene glycoleneration and oxalate crystals	173.4	67.3	0.90
Generalized tubular damage with heavy	456.5	158.1	1.00

crystals			
Depass *et al*. (1986)			
Tubular dilation	726.5	476.1	0.70
Hydronephrosis	367.0	230.0	0.11
Oxalate nephrosis	313.2	272.5	0.41
Calcium oxalate crystalluria	704.0	521.6	0.93
Neeper-Bradley *et al*. (1995)			
Extra 14^{th} rib per litter	141.3	23.1	0.91
Extra 14^{th} rib per fetus	103.6	87.9	0.01
Cruzan *et al*. (2004)			
Wistar rats, crystal nephropathy severity >=1 vs. severity 0	160.7	71.5	0.92
Wistar rats, crystal nephropathy, severity >=2 vs. severity <=1	194.7	73.0	0.98
Wistar rats, crystal nephropathy, severity >=3 vs. severity <=2	158.2	52.9	0.68
Wistar rats, crystal nephropathy, severity >=4 vs. severity <=3	326.4	95.1	0.98
Wistar rats, crystal nephropathy, severity 5 vs. severity <=4	398.5	106.6	0.96
F-344 rats, crystal nephropathy, severity >=1 vs. severity 0	348.0	164.3	0.82
F-344 rats, crystal nephropathy, severity >=2 vs. severity <=1	367.1	214.8	0.46
F-344 rats, crystal nephropathy, severity >=3 vs. severity <=2	437.8	226.7	0.79
F-344 rats, crystal nephropathy, severity >=4 vs. severity <=3	704.3	241.6	0.99
F-344 rats, crystal nephropathy, severity >=5 vs. severity <=4	704.3	241.6	0.99
ACC (2005)			
Compound-induced nephropathy incidence	120.1	82.0	0.49
Compound-induced nephropathy severity	165.4	151.1	0.38
Birefringement crystals incidence	142.5	93.6	0.70
Birefringement crystals severity	172.7	156.2	0.25

***** These data were originally modeled in 1999 using a multi-stage model with a threshold term (d_0), which was standard practice at the time. The current practice is to omit the threshold term since the resulting BMDs are more conservative.

Table 13: Maternal and developmental effects in CD-1 mice from nose-only exposure to ethylene glycol during gestation days 6–15 (Tyl *et al.*, 1995)

Target Concentration (mg/m^3)	Average Measured Concentration (mg/m^3)	Maternal Effects Observed	Developmental Effects Observed
0	0	No effects	No effects
500	360	No significant effects observed	No significant effects observed
1000	779	Increased absolute kidney weight	No significant effects observed
2500	2505	Increased absolute and relative (~7%; $p<0.05$) kidney weights	Reduced fetal body weights per litter, increase incidence of skeletal variations and fused ribs

APPENDIX B: LITERATURE SEARCH STRATEGY — NEW INFORMATION FOR THE HUMAN HEALTH ASSESSMENT

The critical information for the hazard characterization was obtained from the rat dietary studies conducted by the Ethylene Glycol Research Task Force of the American Chemistry Council; this information was submitted under Section 71(1)(*c*) of CEPA 1999. The critical information related to exposure assessment among the general population in Canada was obtained from a letter issued by the Canadian Consumer Speciality Product Association (CCSPA). Additional information was obtained from a study report prepared for the American Chemistry Council; the report consisted of an assessment of estimated human exposure to ethylene glycol in the vicinity of an ethylene glycol manufacturing facility and was used to quantify the level of ethylene glycol to which the people living close to manufacturing facilities were exposed.

A comprehensive literature search was conducted of monitoring data in Canada and/or elsewhere (from January 2000 to January 2009) and toxicological studies in animals and humans (from January 2000 to January 2009) to identify critical new data for the assessment of the human health risk. A search was conducted by chemical name or CAS registry number in the following databases: HSDB (Hazardous Substances Data Bank), TOXLINE, Pubmed, Current Contents (SilverPlatter database), ChemIDplus, IRIS (Integrated Risk Information System), TERA (Toxicology Excellence for Risk Assessment), CCRIS (Chemical Carcinogenesis Research Information System), GENE-TOX, DART/ETIC (Developmental and Reproductive Toxicology / Environmental Teratology Information Centre), IARC (International Agency for Research on Cancer), IUCLID, US EPA (United States Environmental Protection Agency), WHO (World Health Organization) database, Patty's Toxicology database, BIBRA International, OECD (Organisation for Economic Co-operation and Development) database, NPRI 2005 (National Pollutant Release Inventory), Syracuse Research Corporation's Environmental Fate Database, NAPS (National Air Pollutant Surveillance) database, Dow Chemical website, Shell Chemicals website, MEGlobal website, Camford Information Services Product Profiles (2003), and the Pest Management Regulatory Agency (Health Canada) website. A general search was also conducted using the Google search engine.

APPENDIX C: LITERATURE SEARCH STRATEGY — NEW INFORMATION FOR THE ECOLOGICAL ASSESSMENT

Updates since January 2000 were obtained through a search of the SciFinder and Cyberus databases. In addition, on-line searches were done through Google Scholar and Google. Updated information on ethylene glycol releases were obtained from the NPRI (National Pollutant Release Inventory). The latest available data at the time of writing was for the 2004–2005 winter season. Airport glycol release information was obtained from Transport Canada's annual Airport Glycol Monitoring Program reports, up to and including 2004–2005.

APPENDIX D: MANAGEMENT OF ETHYLENE GLYCOL AT CANADIAN AIRPORTS

Management of ethylene glycol at Canadian airports was discussed at some length in the State of the Science Report (Environment Canada and Health Canada, 2000). Some recent improvements in the handling and release of ethylene glycol have been mentioned in the present report.

Data on groundwater concentrations of ethylene glycol are very limited, but some pre-2000 measurements were taken at Calgary International, Charlottetown, Montréal International (Dorval and Mirabel) and Ottawa Macdonald-Cartier International airports. These data are summarized in Table 14 below, along with data obtained from the Edmonton International Airport.

Table 15 presents concentrations of total glycol at selected monitoring stations at Canadian airports for the 2004–2005 deicing season.

Table 14: Concentrations of ethylene glycol in groundwater sampled at Canadian airports[1]

Airport	Sampling Dates	Number of Samples	Detection Limit (mg/L)	Median (mg/L)	Mean (mg/L)	Maximum (mg/L)	Reference
Calgary International	4 Oct.1996–28 Jul. 1999	17	5	<DL	4	38	CAA 1999
Montréal-Trudeau	13 Nov. 1997–25 May 1998	20	0.5	1.3	8	32	Aéroports de Montréal 1998
Montréal-Mirabel	28 Nov. 1997–6 Jul. 1999	5	6	<DL	<DL	49	Aéroports de Montréal 1999
Ottawa MacDonald-Cartier International	Dec. 1985–Dec.1986	?	5	<DL	<DL	415	Transport Canada 1987
Edmonton International	Mar.–Sept. 2002	8	5	<5	<5	<5	Transport Canada 2003

[1] For many airports, "total glycol" values have been reported; however, none of the airports listed used other glycols. All samples taken in the immediate vicinity of deicing operations and at shallow depth were excluded. The “detection limit” (DL) is equivalent to minimum values in all cases.

Table 15: Concentrations of total glycol sampled at selected monitoring stations of Canadian airports for the 2004–2005 deicing season

Airport	Sampling Dates within Deicing Season	Site	Number of Samples	Detection Limit (mg/L)	Mean (mg/L)	Median (mg/L)	Maximum (mg/L)	Number of Samples > 100 mg/L
Moncton	4 Nov. 2004–24 Mar. 2005	4	19		4	0	80	0
		6	19		13	0	>120	2
		8	19		9	0	120	2
Charlottetown	1 Oct. 2004–15 May 2005		7		0	0	0	0
Charlottetown	14 Dec. 2004 – 5 Apr. 2005	Not indicated	6	No numerical data				
Saint John	27 Oct. 2004–7 Apr. 2005	Not indicated	14		Na	na	>100	1
Montréal-Trudeau	2 Nov. 2004–26 Apr. 2005	Centre de dégivrage (PE-2)	203	10	49	53	97.5	0
		Aviation générale (R: ethylene glycolegard Whitewind)	11	10	<10	<10	20	0
		Aviation générale (R: ethylene glycolegard Skyservice)	16	10	22	11	146	1
		Aviation générale (R: ethylene glycolegard Exécaire)	17	10	17	<10	124	1
		Exutoir Bouchard (DP-1)	19	10	51	42	136	3
Montréal-Mirabel	2 Nov. 2004–26 Apr. 2005		82	10	40	<10	590	5
		Centre de dégivrage						
		Zone cargo	2	10	<10	<10	<10	0
		Site Cyr	2	10	<10	<10	<10	0
Québec-Jean-Lesage	1 Mar. 2005–31 Mar. 2005	Station CA	4		78	67	130	1
		Station 24	8		77	66	198	3
London	9 Nov. 2004–15 Apr. 2005		8	4	<4	<4	<4	0

Airport	Sampling Dates within Deicing Season	Site	Number of Samples	Detection Limit (mg/L)	Mean (mg/L)	Median (mg/L)	Maximum (mg/L)	Number of Samples > 100 mg/L
Ottawa	11 Nov. 2004–2 Jun. 2005	S3	13		0	N/D	N/D	0
		G1	16		0	N/D	N/D	0
		S4	109		2	N/D	162	1
		G11	1		0	N/D	N/D	0
		S9	110		5	N/D	172	2
Toronto	1 Oct. 2004–30 Apr. 2005	Carlingview Stormwater Facility	178	4	4	<4	32	0
		Etobicoke Creek Stormwater Facility	60	4	16	<4	129	2
		Moore's Creek Stormwater Facility	155	4	4	<4	105	6
		Water Monitoring Station WM4A	177	4	10	<4	287	3
Edmonton	2 Jan. 2004–15 Oct. 2004	Subsurface Wetlands Inlet	16	5	7	8	11	0
		Subsurface Wetlands Outlet	5	5	13	8	33	0