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Trichloroethylene (TCE) Contamination in the Bishop Street Community, Cambridge, Ontario

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Glossary

(TCE) Trichloroethylene – A nonflammable, colorless liquid, used primarily in industry as a degreaser; has been used in consumer products such as adhesives, rug cleaning fluids, paint and spot removers, and typewriter correction fluid

(ILCR) Incremental lifetime cancer risk – the extra potential risk of a cancer due to a specific exposure, in this case to TCE in residential indoor air; integrates information from the exposure (from inhalation of TCE in indoor air) and toxicity (the potency of TCE; see TRV below) to derive a quantitative estimate of human health risk

(HRV) – Heat recovery ventilation – type of indoor air mitigation technique where two separate air-handling systems collect and exhaust stale indoor air and the other draws in outdoor air and distributes it throughout the home; allows maintenance of high indoor air quality without excessive additional energy costs

(PCO) – photo-catalytic oxidation - type of indoor air mitigation technique that uses a UV lamp along with a substance called a catalyst, that reacts with the light; destroys gaseous pollutants by converting them into harmless products, but are not designed to remove particulate pollutants

(SVE) – soil vapour extraction – type of soil remediation which uses vacuum pressure to remove volatile contaminants (such as VOCs and TCE) from the soil

(VITL) – vapour intrusion target limit - has been used as a target level for indoor air concentration in homes in the Bishop Street community; are not indoor air standards, and may be exceeded in some homes where there is no source of groundwater contamination

(TRV) – toxicological reference value - concentrations at which specific non-cancer adverse effects would not be expected for a defined period of exposure; are based on the threshold determined from toxicity experiments and usually incorporates an uncertainty factor (or safety factor) to account for uncertainties in the estimate

(LOAEL) – lowest observed adverse effect level - the lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group

(NOAEL) – No observed adverse effect level - the highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects

(TCA) - Trichloroacetic acid – metabolite in urine formed from the metabolism of TCE

(TCOH) – trichloroethanol - metabolite in urine formed from the metabolism of TCE

(DCA) - dichloroacetic acid- metabolite in urine formed from the metabolism of TCE

Executive Summary

The Environmental and Occupational Health unit of the Ontario Agency for Health Protection and Promotion (OAHPP) received a request to assess the risk of adverse health effects from exposure to trichloroethylene (TCE) vapours from subsurface vapour intrusion into homes in a community surrounding an industrial complex in the Bishop Street neighbourhood in Cambridge, Ontario. The investigation included a narrative review of the available scientific literature on specific health-related questions posed by the community, including thymus cancer, reproductive toxicity, and neurological toxicity. Other cancer and non-cancer end points were also investigated.

The International Agency for Research on Cancer (IARC) has classified TCE as group 2A, *probably carcinogenic* to humans.

From the air sampling data collected in 2005-2006 (prior to any remediation or mitigation of groundwater or indoor air contamination), the highest levels of TCE in indoor air were observed, with an average of 52.3 $\mu g/m^3$ (<0.2- 2100 $\mu g/m^3$ range). These levels are not sufficiently high to cause effects from acute exposure. However, given the potential for elevated multi-decade exposures, there are concerns regarding the risk of cancer and other diseases. The most sensitive potential non-cancer effects of exposure to TCE are renal, developmental, and immunological effects. Based on an average indoor air concentration of 52.3 $\mu g/m^3$, and the estimate of cancer potency used in the risk management strategy for the Bishop Street community, the estimated incremental lifetime risk of developing cancer, assuming continuous exposure for forty years (1965-2005) is 1 to 2 in 10,000. If 10,000 people were exposed to this level of risk approximately 1 to 2 cancers may be attributable to TCE. In a population the size of the Bishop Street community (estimated at around 1500), less than 1 case would be expected. It would not be possible to detect any excess cases of cancer or other diseases in a community health study of the Bishop Street neighbourhood. Furthermore, there would not be any unique or distinguishing features for cancers attributable to TCE versus cancers attributable to other causes.

1.0 Introduction

The Ontario Agency for Health Protection and Promotion (OAHPP) received a request to assess the risk of adverse health effects from inhalation exposure to TCE in indoor air in a community surrounding an industrial area in Cambridge, Ontario. The plant was built in 1959, and the part of the business that used TCE as a degreaser is believed to have opened in 1964. During that time period, it was common to discharge waste into the ground. A photograph from the early 1970s showed staining on the surface of the soil adjacent to the plant. A monitoring well was drilled at this site and shows one of the highest concentrations of TCE in groundwater in this area (81,000 µg/L in 2005).

It is unknown how often TCE waste was discharged onto the ground and in what quantities. All TCE discharges should have ceased around 1986-1987, when new waste management regulations defined TCE as a "hazardous waste" requiring a certificate of approval came into effect (Ontario Ministry of the Environment 1985). However, it is possible that discharges onto the ground may have ceased even earlier, with regulations that governed transfers of liquid industrial waste.

In 2004, an environmental site assessment conducted by AMEC discovered TCE contamination from the Northstar Aerospace facility. Air concentrations of TCE in the basements of homes in the community were subsequently measured in 2005. Indoor air concentrations measured in 2005-2006, prior to any mitigation in groundwater or indoor air, ranged from <0.2 to 2100 µg/m^3. The average TCE indoor air concentration in the community was 52.3 µg/m^3. Data on indoor air concentrations prior to 2005 are not available.

Water supplied to this community is primarily sourced from Well P6 (raw water), which has no detectable levels of TCE. As a result, efforts to remediate or mitigate the contamination have focused on reducing exposure by reducing TCE vapour intrusion into the homes of community residents. The focus of this investigation was limited to the potential effect of the TCE on the health of residents from their exposure via inhalation of vapours.

Detecting TCE in indoor air is not uncommon; it has even been detected in indoor air of a rural agricultural community far from any industry. In addition to its industrial uses, TCE has been used in consumer products including adhesives, rug cleaning fluids, paint and spot removers, and typewriter correction fluid. Processed foods may also contain a few parts per billion of TCE. Over 30 years ago, when less information on TCE toxicity was available, TCE was used as an obstetrical anesthetic and a solvent for extracting caffeine from coffee.

Levels of TCE in Bishop Street homes are lower than levels where acute toxicity has been reported. However, given the potential for chronic exposures there are concerns regarding the risk of cancer and other diseases. Concentrations of TCE in Bishop Street homes were higher than other communities in Canada. However, the concentrations in indoor air were significantly lower than levels measured in occupational settings, where only weak associations (pooled relative risks ranging from 1.23-1.57 for cancers of different sites; See Section 5 for details) between TCE exposure and disease have been observed (See Tables 1, 2, and Figure 2).

Epidemiological studies have investigated whether exposure to TCE is associated with particular diseases. Much of the literature on the human health effects from TCE exposure is based on occupational exposures to TCE from degreasing operations. While workplace studies can provide useful

information, they have some limitations with respect to accurately estimating risks in community settings. Exposure groups in occupational studies are often not differentiated by air concentrations, but by job descriptions, or by concentrations of TCE metabolites in urine. In addition, the air concentrations that are typically observed in an occupational setting are often orders of magnitude higher than have been observed in communities such as the Bishop Street neighbourhood. In some workplaces, as in some communities, there may be simultaneous exposure to multiple pollutants which can complicate interpretation. To help address this challenge, both epidemiological and toxicological data were reviewed in investigating the potential impact of TCE exposure in the Bishop Street community.

An incremental lifetime cancer risk (ILCR) for the Bishop Street community was calculated based on assumptions that exposure was forty years in duration and included childhood. At an average inhaled air concentration of 52.3 $\mu g/m^3$ in 2005 and 2006 (52.3 $\mu g/m^3$ is the average indoor air concentration per dwelling prior to any efforts to remediate the contamination or mitigate subsurface vapour intrusion, when the highest levels of TCE in indoor air were measured), the risk of developing TCE-related cancer is 1 in 10,000. Based on 2009 statistics, about 40% of men and 45% of women are expected to develop any type of cancer over the course of their lifetime (Canadian Cancer Society 2010). With the average TCE exposure level in the Bishop Street community (population estimated at around 1500), less than 1 cancer case (0.15) attributable to TCE exposure would occur. This is in addition to the roughly 600-675 cancers that would be expected in this community as a result of the background risk in the Canadian population. A TCE related cancer would not have any unique features that would distinguish it from other cancers.

Diseases such as cancer are multi-factorial, and to date there is no medical test available to determine whether a particular disease or outcome may be partly or largely attributable to exposure to TCE, versus other causes such as genetic predisposition, diet, etc. Urine tests and blood tests are available for TCE and its metabolites, however these tests only indicate whether or not a person was exposed. They cannot predict future disease or be used in the medical management of patients diagnosed with particular diseases.

Subchronic or chronic exposures to TCE may contribute to the risk of certain types of cancer, including renal cancer and lymphoma, as well as some non-cancer effects. The most sensitive non-cancer effects may be immunological, developmental, and renal (US EPA 2009). In most instances, the concentrations which have been observed to elicit non-cancer effects in animal studies are above the concentrations observed in the Bishop Street neighbourhood in 2005-2006. Evidence regarding effects which were inquired about by members of the Bishop Street community, such as infertility and neurotoxicity, is discussed in Section 5.2.

The use of genetic signatures in cancer risk assessment has garnered much research, with particular attention to mutations in the von Hippel-Lindau (VHL) tumour suppressor gene. Biomarkers of exposure and effect will be discussed further in Sections 6 and 7.

2.0 Sources of exposure to TCE

TCE is released into the environment during manufacture, use and disposal (Wu and Schaum 2000). Releases of TCE result from use in both industrial and domestic settings where consumer products containing TCE may be found. TCE is commonly detected in the environment; it has been measured in air, water, and soil, resulting in human exposures through ingestion of water or food, inhalation of ambient or indoor air, and through dermal absorption when immersed in contaminated water (*e.g.*, while showering) (Wu and Schaum 2000). Inhalation is the only route of exposure that has been identified in the Bishop Street neighbourhood.

The major use of TCE is for metal degreasing (CEPA 1993). Trichloroethylene is volatile and primarily present in air as a gas (as opposed to being associated with particles). A 1998 survey of TCE in outdoor air in 14 US states reported air concentrations ranging from 0.01 to 3.9 µg/m^3, with a median concentration of 0.32 µg/m^3 (Wu and Schaum 2000). TCE discharged to soil may travel to ground water and form a subsurface plume. Average concentrations detected in various food products in the United States were 0.9 (0-2.7) µg/kg in grain-based foods, 1.8 (0-12) µg/kg in 'table-ready' foods, 73.6 (1.6-980)
µg/kg in butter and margarine, 3.8 (0-9.5) µg/kg in cheese products, 0.5 (0-1.7) µg/kg in peanut butter, 3.0 (0-9.2) µg/kg in ready-to-eat cereal products and 1.3 (0-4) µg/kg in highly processed foods (Heikes 1987).

A number of studies have measured exposures to volatile organic compounds such as TCE. Indoor air concentrations of TCE in recent studies in Canada have means ranging from 0.06-0.44 µg/m^3, which is approximately two orders of magnitude lower than the mean indoor air concentration measured in Cambridge (52 µg/m^3) prior to remediation and mitigation, and one order of magnitude lower than the current average indoor air concentration in Cambridge (3.2 µg/m^3). Table 1 summarizes data from available Canadian studies as well as select American studies:

Table 1 Background Exposure to TCE in the US and Canada

Location	Statistic*	Type of Air Sample	AirConcentration** (µg/m^3)	Reference
Regina, Saskatchewan	arithmetic mean	indoor air (summer)	0.17	Health Canada (2010a)
	arithmetic mean	indoor air (winter)	0.09	
Windsor, Ontario	arithmetic mean	indoor air (summer)	0.44	Health Canada (2010b)
	arithmetic mean	indoor air (winter)	0.27	
Québec City, Québec	geometric mean	indoor air	0.37	Héroux *et al*. (2008)
Ottawa, Ontario	arithmetic mean	indoor air	0.06	Zhu et al. (2005)
Minnesota – exposure of a probability sample of	mean	personal	0.8	Adgate *et al*. (2004)

Location	Statistic*	Type of Air Sample	AirConcentration** (µg/m^3)	Reference
children				
EPA Region 5, 6 states in the Great Lakes Region	median	indoor air	0.56	Clayton *et al*. (1999)
Toronto, Ontario	arithmetic mean	indoor air (domestic)	5.7	Bell *et al*. (1991)
Unspecified city, Canada	average	indoor air (Nov/Dec)	0.5	Chan *et al*. (1990)
		indoor air (Feb/Mar)	1.6	
New Jersey area with industrial/ manufacturing point sources, Fall	median	personal (incl. 12 hr overnight sample)	2.4	Wallace *et al*. (1987)
New Jersey area with industrial/manufacturing point sources, Summer	median	personal (incl. 12 hr overnight sample)	2.8	
New Jersey area with industrial/manufacturing point sources, Winter	median	personal (incl. 12 hr overnight sample)	1.6	
North Carolina area with small industries but NO chemical manufacturing/petroleum	median	personal (incl. 12 hr overnight sample)	1.5	
North Dakota – small, rural agricultural town far from any industry	median	personal (incl. 12 hr overnight sample)	0.5	

* Medians reported where means were not representative of population exposure due to a few extremely high measurements. Arithmetic mean reported over geometric mean, where available.

** Average TCE concentration in indoor air calculated for US data reported in the table is 1 µg/m^3. Average TCE concentration in indoor air for Canadian data published after 2004 is 0.2 µg/m^3.

3.0 Occupational exposure

Data from the US in the 1980s, primarily from degreasing operations (as seen in table 2 below), found workplace air concentrations which ranged from 540 to 2,000,000 µg/m^3, with most mean concentrations exceeding 10,000 µg/m^3 (with the average concentration being 157,400 µg/m^3). Not surprisingly, concentrations in industrial workplaces are higher than concentrations in dwellings of the Bishop Street neighbourhood prior to remediation and mitigation (range of <0.2 to 2100 µg/m3, average of 52.3 µg/m^3).

Table 2 Workplace TCE concentrations in the US in the 1980s

Number of Plants	Job, Task or Industry	Number of Samples	Air Concentration (µg/m^3)	Air Concentration (µg/m^3)	Reference
			Mean	Range	
1	Tank relining	8 P	1300	ND-5400	Burroughs (1980)
1	Degreasing sheet	2 P	11000	10000-12000	Johnson (1980)

Number of Plants	Job, Task or Industry	Number of Samples	Air Concentration ($\mu g/m^3$)	Air Concentration ($\mu g/m^3$)	Reference
	metal				
1	Degreasing sheet metal	2A	11000	4000-18 000	Johnson (1980)
1	Degreasing, custom finishing	23 P	8300	1000-38 000	Ruhe and Donohue (1980)
1	Degreasing, custom finishing	2 A	6000	4000-8000	Ruhe and Donohue (1980)
1	Vapour degreasing	14 P	333000	26900-1670000	Burgess (1981)
1	Degreasing, bus maintenance	3 A	3000	ND-8900	Love and Kern (1981)
1	Degreasing	24 STEL	742000	56 000-2 000 000	Ruhe *et al*. (1981)
1	Degreasing	9 TWA	145000	37 000-357 000	Ruhe *et al.* (1981)
1	Degreasing, plastics	2 P	4800	2700-7000	Burroughs and Moody (1982)
1	Degreasing, electronics	79 P	10200	ND-209000	Lee and Parkinson (1982)
1	Degreasing, medical	5 P	5400	1000-16 000	Ruhe (1982)
1	Degreasing, medical	2 A	6500	4000-9000	Ruhe (1982)
1	Degreasing, energy conservation products	2 P	36500	22000-51 000	Almaguer *et al*. (1984)
1	Degreasing, energy conservation products	10 A	1100	540-3200	Almaguer *et al*. (1984)
1	Degreasing	9 P	716000	39 000-2 288 000	Belanger and Coye (1984)
1	Degreasing	2 A	184000	540-367 000	Belanger and Coye (1984)
1	Silk screening	5 P	23600	1600-81 100	Belanger and Coye (1984)
1	Degreasing aircraft	29 TWA, P	30700	ND-208 000	Gorman *et al*. (1984)
1	Degreasing aircraft	11 TWA, A	28500	2000-121 000	Gorman *et al*. (1984)
1	Degreasing	22 STEL	320000	ND-1 256 000	Gorman *et al*. (1984)

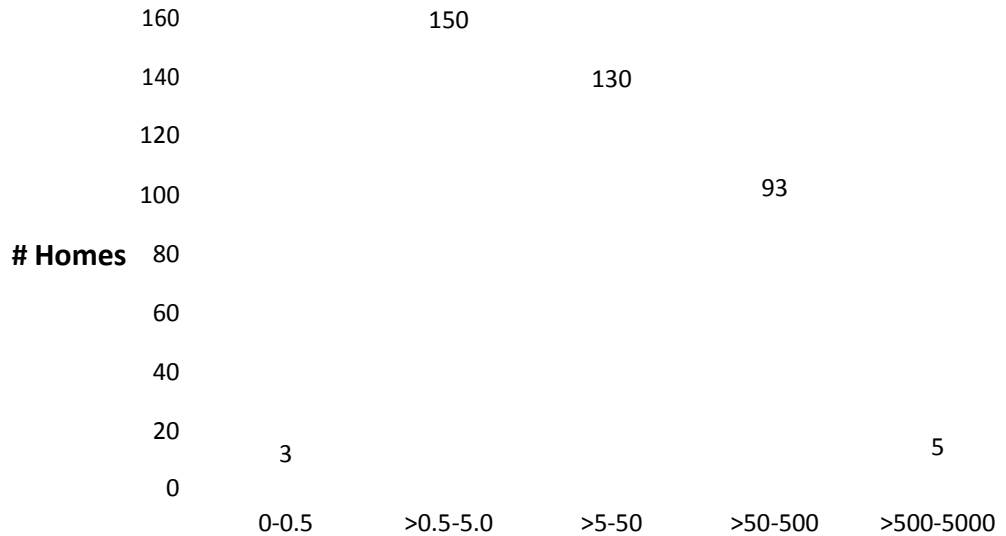
Number of Plants	Job, Task or Industry	Number of Samples	Air Concentration ($\mu g/m^3$)	Air Concentration ($\mu g/m^3$)	Reference
	aircraft				
1	Degreasing aircraft	29 TWA, P	30700	ND-208 000	Gorman *et al*. (1984)
1	Degreasing aircraft	11 TWA, A	28500	2000-121 000	Gorman *et al*. (1984)
1	Degreasing aircraft	22 STEL	320000	ND-1 256 000	Gorman *et al*. (1984)
1	Taxidermy	2 A	8900	1100-16 600	Kronoveter& Boiano (1984)
1	Taxidermy	2 P	8900	1700-16 000	Kronoveter & Boiano (1984)
1	Degreasing	TWA	205000	117000-357 000	Landrigan et al. (1987)
1	Degreasing	STEL	1084000	413 000-2 000 000	Landrigan et al. (1987)

The average occupational concentration obtained from the mean concentrations in the table above is 157 400

$\mu g/m^3$. P – Personal sample
A – Area sample
TWA – 8-hour time weighted average STEL – 15 minute average

4.0 Bishop Street community TCE contamination exposure

Prior to any groundwater remediation or mitigation of indoor air contamination, the majority of homes in the Bishop Street community had indoor air concentrations below 500 $\mu g/m^3$, with an average of 52.3 $\mu g/m^3$. While these levels were higher than indoor air concentrations in surveys done by Health Canada in different Canadian cities (see Table 1) it is still far lower than the concentrations encountered in occupational settings (see Table 2). Figure 1 summarizes concentrations of TCE in buildings prior to remediation/mitigation.



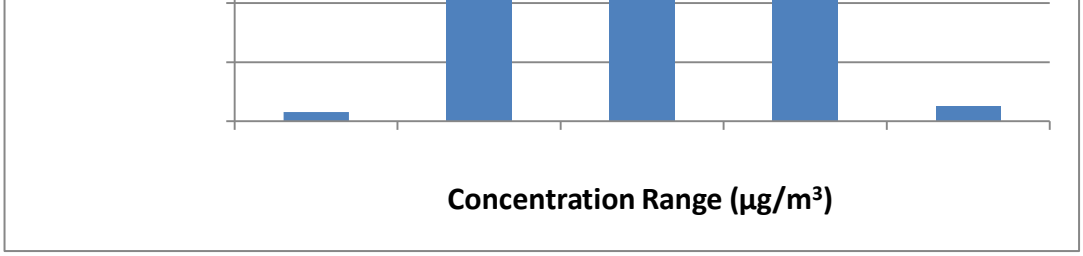


Fig. 1 Indoor Air Concentrations in Bishop Street Community Prior to Any Remediation or Mitigation, 2005-2006

Efforts to reduce TCE concentrations in the indoor air of homes commenced in 2006, and as data from the years 2005 to 2010 demonstrate, indoor air concentrations in the Bishop Street community have declined steadily since that point, even in homes where no form of remediation or mitigation has taken place (see Figures 2 and 3 below).

The average TCE indoor air concentration in the homes in the Bishop Street Community (3.17 µg/m^3, based on all available indoor air samples taken between August 1, 2009 to August 31, 2010) is higher than in other Canadian cities (0.2 µg/m^3 based on data for Windsor, Regina, Ottawa and Quebec City published between 2005-2010) and the US (1 µg/m^3). However, it is much lower than concentrations in studies of occupational cohorts and animal experiments where toxicity following acute exposure was observed. Based on data from 2009-2010, the majority of homes have indoor TCE concentrations between 0.5-50 µg/m^3.

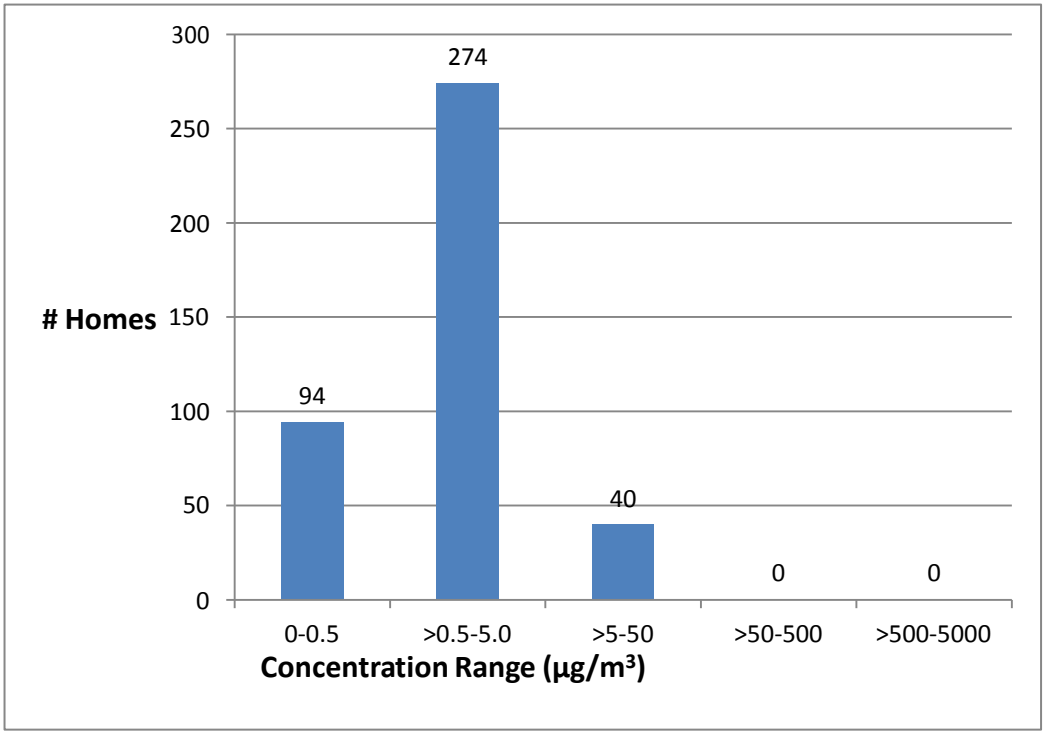


Fig. 2 **Indoor Air Concentrations in the Bishop Street Community, Based on Samples Collected Between August 1, 2009 to August 31 2010**

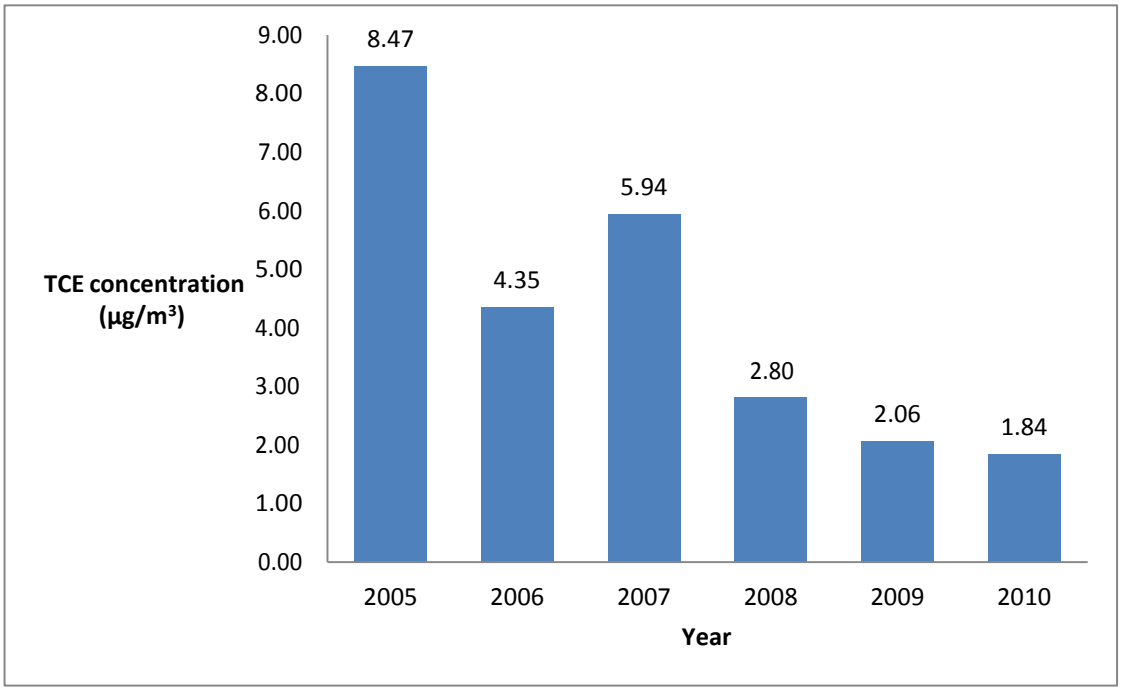


Fig.3 **Yearly Average TCE Indoor Air Concentration in Homes That Did Not Receive Remediation or Mitigation (µg/m^3)**

The current Ministry of the Environment (MOE) vapour intrusion target limit (VITL) of 0.5 µg/m^3 has been used as a target level for indoor air concentration in homes in the Bishop Street community. It is worth noting that VITLs are not indoor air standards, and may be exceeded in some homes where there is no source of groundwater contamination. It is difficult to distinguish between TCE that comes from subsurface vapour intrusion and TCE that comes from sources within the home. The VITL is a target indoor air concentration may not always be achievable due to other sources of TCE in the home.

Homes with measured TCE indoor air concentrations exceeding an intervention level of 5 µg/m^3 undergo remediation or mitigation. Based on historical summary statistics compiled by Northstar Aerospace, the highest detected TCE indoor air concentration was 2100 µg/m^3 in October 2005. Beginning December 2005, a number of measures were taken to remediate this home, including a partial basement seal in December 2005, installation of a HRV and PCO in February 2006, and the installation of a SVE device in March 2006. The indoor air concentration in this home has been reduced to 0.56 µg/m^3 as of February 2010. Efforts to remediate or mitigate have been successful at reducing the TCE indoor air concentrations, however, achieving the target concentration of below the VITL has not occurred in all homes.

Table 3 shows the air sample results taken following the installation of the remediation and mitigation measures in the home discussed:

Table 3 Remediation and Mitigation for a home with initial TCE Concentration of 2100 µg/m^3 and Average Per Cent Reduction

Type of Remediation or Mitigation	Installation Date	Date and Location of Follow-up Air Sample	Air Concentration (µg/m^3)	Average (µg/m^3)	Average % reduction
Partial basement seal and empty sump seal	2005-12-21	2006-01-31 Basement (near sump)	1707.91	1892.55	10.6%
		2006-01-31 Basement (Cellar)	1981.46		
		2006-01-31 Basement (Cellar), replicate	1988.28		
HRV/PCO	2006-02-06	2006-02-14 Sump	169.08	155.47	91.8%
		2006-02-14 Sump, replicate	169.8		
		2006-02-14 2nd fl living room	127.55		
SVE	2006-03-31	2006-04-10, sump	6.15	6.15	96%

Efforts to reduce the indoor air concentrations include groundwater remediation and installation of appropriate mitigation technology in homes with indoor air concentrations above the intervention level of 5 µg/m^3. Groundwater monitoring data show that the TCE plume is shrinking. Figures 1 and 2 show that the TCE in indoor air has been reduced, with 94 homes currently having indoor air concentrations below 0.5 µg/m^3, compared with only 3 homes in 2006.

5.0 What potential health effects are associated with TCE?

Numerous potential health effects from exposure to TCE have been described, though the strength of evidence for each potential health effect varies. Reviews of the toxicology and epidemiology of TCE are available from the National Research Council (NRC) (2006), the Agency for Toxic Substances Disease Registry (ATSDR) (1997), the International Agency for Research on Cancer (IARC) (1997), and the California Environmental Protection Agency (Cal EPA) (2009a). A draft review and toxicological profile is also available from the United States Environmental Protection Agency (US EPA) (2009). The summary below draws on these reviews as well as select papers, and places emphasis on those potential health effects for which there is the greatest evidence. As TCE is well absorbed by both inhalation and ingestion, systemic effects observed following ingestion exposure are also relevant to inhalation exposure. For this reason, toxicological studies for both routes of exposure were consulted in preparing this report.

5.1 Cancer Endpoints

The International Agency for Research on Cancer (IARC 1997) has classified TCE as group 2A, *probably carcinogenic* to humans. This classification is based on limited evidence in humans and sufficient evidence in animals. US EPA has proposed to identify TCE as a carcinogen based on the results of the recent toxicological and epidemiological review (2009). At this time, however, the US EPA proposal is still undergoing review.

Numerous epidemiological studies have investigated potential associations between TCE exposure and different types of cancer including primary liver cancer, malignant lymphoma, Hodgkin's disease, renal cell carcinoma, colon cancer, brain tumours and childhood leukemia (IARC 1997). In general, epidemiological studies of TCE and cancer are limited by a lack of information regarding exposure to other solvents and other confounding variables such as smoking and alcohol consumption, which may have also contributed to observed cancers.

Epidemiological studies of exposures in both occupational and non-occupational settings have been conducted. Non-occupational studies have primarily examined exposure to TCE through drinking water, with some exceptions (e.g., Lehmann *et al*. 2002). In occupational epidemiologic studies, exposure is typically characterized by urinary biomarker data or job exposure matrices, rather than measurements of air concentrations. Concentrations of metabolites of TCE in urine do not reflect long-term exposure to TCE (NRC 2006) and may contribute to misclassification unless exposures are stable over time. Non-differential exposure misclassification generally attenuates exposure-response relationships. Job exposure matrices are also imprecise and may contribute to misclassification.

Workers are generally exposed to higher concentrations than the general population (contrast Tables 1 and 2). In a review of 14 epidemiological studies on TCE and cancer, many of which were occupational, very little information was available regarding indoor air concentrations for exposed groups. However, Wartenburg *et al*. (2000) referred to an epidemiological study where the majority of exposures were less than 100 000 $\mu g/m^3$ as a study documenting 'low' exposures to TCE, which provides some context.

Studies of workers have generally found little evidence for excess *overall* risk for total mortality and cancer mortality (Wartenburg *et al*. 2000, Alexander *et al*. 2007). However, the epidemiological literature provides some support for an association between exposure to TCE and a slightly increased risk of *specific* types of cancer, chiefly, kidney cancer, lymphoma, and liver cancer and cancer of the bile duct (Wartenburg *et al*. 2000, Chiu and Scott 2006, US EPA 2009).

A slightly elevated incidence of kidney cancer has been consistently observed across studies of different designs done in different populations and industries, and is supported by animal studies (US EPA 2009, Wartenburg *et al*. 2000). In the case of kidney cancer, the draft meta-analysis conducted by US EPA (2009) of fourteen epidemiological studies found a pooled relative risk of 1.25 (95% confidence interval, 1.11 to 1.41) for overall TCE exposure, and 1.53 (95% confidence interval, 1.23 to 1.91) for the highest TCE exposure groups. This means that all workers who were exposed to TCE were 1.25 times more likely to develop kidney cancer, and that workers who had the greatest exposures were 1.53 times more likely to develop kidney cancer.

Lymphoma and hepatic cancer have also been linked to TCE exposure in multiple epidemiological studies (see reviews by Chiu and Scott 2006, Wartenburg *et al*. 2000) and in animal studies (see for example, Maltoni *et al*. 1986 with respect to hepatic cancer). The draft meta-analysis released by US EPA (2009), reports an increased pooled relative risk estimate for lymphoma of 1.23 (95% CI, 1.04 to 1.44) and 1.57 for the highest exposure groups (95% CI, 1.27 to 1.94), but concluded there was some study heterogeneity, potential publication bias, and weaker exposure-response results.

For hepatic cancer, US EPA (2009) commented that only cohort studies are available with small numbers of cases which limits the ability to detect an effect not due to chance. Excess relative risks are reported in several high quality studies, but with wide confidence intervals, which limits the precision of the risk estimate (US EPA 2009). The relative risks computed in the meta-analysis were heavily influenced by one study and the pooled relative risk was higher than the relative risk for more highly exposed groups.

Residents of the Bishop Street community have expressed concerns regarding other forms of cancer, including thymus cancer. The thymus gland is an organ of the immune system primarily responsible for the production of T-cell lymphocytes or simply T-cells. Tumours that originate from the thymus can be grouped into two primary forms: thymomas and lymphomas (non-Hodgkin's). Thymomas are tumours that originate from the epithelial cells of the thymus. They are fairly rare, and represent about 0.2% to 1.5% of all malignancies (NIH 2010). The cause of thymomas is not known.

Non-Hodgkin's lymphoma (NHL) refers to a group of disorders involving malignant monoclonal proliferation of lymphoid cells in lymphoreticular sites, including lymph nodes, bone marrow, the spleen, the liver, and the gastrointestinal (GI) tract (Merck 2008). These lymphomas originate from T-cells (derived from the thymus gland) or B-cells (derived from bone marrow cells).

The cause of NHL is largely unknown, but there is some evidence to implicate factors such as viruses and genetic mutations. There is evidence that T-lineage acute lymphoblastic leukemia/lymphoma (T-ALL) is caused by chromosomal aberrations that lead to abnormal expression of T-cell receptor (TCR) genes (breakpoints in TCR genes are present in about 30% to 35% of T-ALL cases) (Raimondi 2007). Viruses that have been implicated in the development of NHL include human T-cell leukemia-lymphoma virus, Epstein-Barr virus, hepatitis C virus, and human immunodeficiency virus (HIV) (Raimondi 2007).

In a review conducted by Wartenberg and his colleagues (2000) of the epidemiologic evidence from over 80 published papers and letters, the thymus gland was not included as a site where any evidence was found of an association between TCE exposure (primarily from higher level occupational exposure) and cancer. However, elevated risks for NHL were detected in the review, with the average relative risk being 1.5. An average relative risk of 1.5 means that the exposed cohorts from these studies were 1.5 times more likely to develop NHL than an unexposed reference group. This review does not differentiate between lymphomas that arise from T-cells or B-cells. Many previous studies did not use the current classification of NHL and did not make distinctions between different cell types (Scott and Chiu 2006). Generally, most lymphomas are of B-cell origin and T-cell lymphomas are rare (BC Cancer Agency 2000).

As previously discussed, there is evidence to suggest that TCE may contribute to the development of lymphomas, but not to cancers of the thymus specifically. However, lymphomas and other cancers where TCE exposure may have contributed in the initiation or progression of cancer development would not have any unique features that would distinguish them from cancers attributable to other exposures or risk factors.

Quantifying the Potential Carcinogenicity of TCE

The potency of a chemical carcinogen may be expressed as an inhalation unit risk (IUR), which is the excess lifetime risk of cancer per unit of air concentration (ppm, mg/m^3, or $\mu g/m^3$). For example, a unit risk of 2×10^{-6} $(ug/m^3)^{-1}$ means that for every 1 $\mu g/m^3$ of average lifetime exposure, two additional cancers might occur in a population of a million people. IURs for TCE have been derived by different agencies and used to guide site assessments and risk management strategies, including that currently being implemented in the Bishop Street community. Table 4 below provides some of the IURs derived for TCE. IURs differ based on the dose-response data selected by the agency for derivation, which may be affected by the period in which the IUR was derived (e.g., a more recent IUR may take into account more recent data), the specific method(s) of dose-response analysis used, as well as other factors. The inhalation unit risk used by the California Environmental Protection Agency is the one in current use by the Ontario MOE, and is used in Section 8 of this report to quantify potential incremental lifetime cancer risks for the population at different levels of potential exposure. An inhalation unit risk can be converted into a risk-specific concentration, which is an inhaled air (exposure) concentration that corresponds to a specified level of incremental lifetime cancer risk. As risk-specific concentrations are in more intuitive units (*i.e.*, $\mu g/m^3$), they are also provided in Table 4 below.

Table 4 Risk-Specific Concentrations Based on Inhalation Unit Risks from Different Agencies

Agency	Inhalation Unit Risk, $(ug/m^3)^{-1}$	1×10^{-6} Risk-Specific Concentration*, $\mu g/m^3$	Basis	Year First Published
California Environmental Protection Agency (Cal EPA)	2×10^{-6}	0.5	- geometric mean of IURs computed for hepatic and lung cancer and lymphoma in rodents	1990 (as cited in Cal EPA 2009b)
World Health Organisation (WHO)	4.3×10^{-7}	2.3	- Leydig cell testicular tumours in Sprague-Dawley rats	2000
Health Canada	6.1×10^{-7}	1.6	- Leydig cell tumours in rats	1996 (as cited in Health Canada 2004a)
US EPA *draft, subject to change*	*4×10^{-6}*	*0.25*	- based on human kidney cancer risks reported by Charbotel *et al*. (2006) and adjusted, using human epidemiologic data, for potential risk for tumours at multiple sites	2009

* the risk-specific concentrations above correspond to an incremental lifetime cancer risk of 1 in one million

5.2 Non-Cancer Endpoints

This section describes neurological, developmental, renal, immunological and hepatic effects which have been elicited by TCE, or associated with exposure to TCE, in animal and human studies of subchronic or chronic exposure. The likelihood of non-cancer effects occurring at different exposure concentrations is not typically estimated quantitatively in terms of risk or probability. A tolerable intake is derived from defined points of a dose-response curve by applying uncertainty factors intended to account for variation within and across species as well as other factors. With the inclusion of additional assumptions related to exposure, tolerable intakes can be converted to concentrations in air. Exceeding a TRV does not mean that adverse effects will occur; rather, it is typically taken to indicate a need for further investigation.

Non-Cancer Toxicological Reference Values

Table 5 provides inhalation TRVs for TCE for either subchronic or chronic exposure. The TRVs which exist are based on varying toxicological endpoints, duration of exposure, and regime of uncertainty factors. The older TRVs may not reflect some of the data reported in toxicological and epidemiological studies which have been published in the past fifteen years. A proposed TRV from US EPA (2009) is subject to change. The TRVs presented below should be interpreted with reference to their toxicological basis.

Table 5 Subchronic or Chronic Non-Cancer Inhalation Toxicological Reference Values (TRVs) for TCE

Agency	Type	TRV ($\mu g/m^3$)	Basis	Total Uncertainty Factor	Year Published	Comment
RIVM, *provisional*	chronic	200	LOAEL of 200 mg/m^3 for hepatotoxicity and CNS depression	1000	2001	LOAELs for neurological effects are close in value for differing duration of exposure (acute to chronic)
ATSDR	subchronic (>14 days to one year)	540	LOAEL of 300 000 $\mu g/m^3$ for neurological effects in rodents	300	1997	
Cal EPA	chronic	600	LOAEL of 170 000 $\mu g/m^3$ for neurological effects in humans (drowsiness, fatigue, headache) and eye irritation	100	2000	
US EPA, *draft, subject to change*	chronic	*5*	heart malformations (rats), immunotoxicity (mice), toxic nephropathy (rats, mice), and increased kidney weight (rats)	between 2 and 60, depending on specific toxicological endpoint	2009	

Indoor air concentrations may also be directly compared to concentrations which have elicited toxic effects in animal studies, which are referred to as Lowest Observable Adverse Effect Levels (LOAELs) or to concentrations that have been administered in animal studies but which have not elicited toxic effects (No Observable Adverse Effect Levels or NOAELs). It should be noted that the NOAELs and LOAELs for non-cancer effects of TCE are typically orders of magnitude greater than exposure levels experienced in the Bishop Street community. However, when comparing community indoor air concentrations to NOAELs or LOAELs it is important to understand that NOAELs and LOAELs are discrete points from a continuum of dose-response and do not represent thresholds of toxicity and that concentrations below either NOAELs or LOAELs do not represent 'zero-risk' concentrations (Leisenring and Ryan 1994, Castorina and Woodruff 2003, US EPA, Gaylor and Aylward 2004).

Kidney effects

In rodent studies examining non-cancer kidney toxicity, oral doses are typically greater than 100 mg/kg_{bw}, or near 1000 mg/kg_{bw} for some effects, and inhalation doses greater than 100 000 $\mu g/m^3$. In rodent studies, TCE causes kidney toxicity in the form of cytomegaly and karyomegaly of the renal tubules (US EPA 2009) and increased kidney weight. The damage to tubules appears to be progressive and to occur at lower doses as the duration of exposure increases (US EPA 2009). In humans, exposure to TCE is associated with proteinuria, a non-specific marker of effect on the kidney. Most research on the kidney toxicity of TCE has focused on kidney cancer.

Immunologic effects

Both animal and human studies have provided evidence that TCE may contribute to autoimmune disease in people. Some case-control studies have found an association between such autoimmune diseases as scleroderma and rheumatoid arthritis and exposure to solvents including TCE (NRC 2006; US EPA 2009). There are also numerous reports of severe, sometimes fatal, hypersensitivity skin disorders and autoimmune hepatitis following occupational exposure to TCE (see, for example, Xu *et al*. 2009, where workers were exposed to air concentrations of between 20 000 and 700 000 $\mu g/m^3$). Exposure concentrations associated with these effects ranged between <50 000 $\mu g/m^3$ to 4 000 000 $\mu g/m^3$ (Kamijima *et al*. 2007, as cited in US EPA 2009). TCE elicits a lupus-like disease in genetically susceptible mice, but not in other strains of mice (Keil *et al*. 2009). Small increases in production of autoantibodies have been observed in other studies in rodents (US EPA 2009).

Some human studies have also found immunologic changes in people exposed to solvents via contaminated drinking water (Byers *et al*. 1988), infants exposed to volatile organic compounds such as TCE in indoor air (Lehmann *et al*. 2002), and in workers exposed to TCE (NRC 2006).

Developmental effects

Cardiac valve malformations, developmental immunotoxicity, resorptions, decreased fetal weight and delayed skeletal ossification have been observed in animal studies of rodents, birds, and amphibians. A clear dose-response for the cardiac valve malformations in rodents has not been demonstrated. In birds LOAELs for this effect were 5 µmol in air space of eggs (Loeber *et al*. 1988 as cited in US EPA 2009) and or 8 ppb per egg (Drake *et al*. 2006), and in amphibians, 40 mg/L and higher (McDaniel *et al*. 2004 as cited in US EPA 2009). There is some epidemiological evidence in humans for cardiac valve malformations in case-control studies of exposure to TCE via drinking water, and for developmental immunologic perturbations from an observational study of infants exposed to multiple volatile organic chemicals, including TCE, in indoor air (total concentration of aromatic VOCs 0-154 $\mu g/m^3$, median TCE concentration 0.6 $\mu g/m^3$) (Lehmann *et al*. 2002).

Reproductive effects

Male reproductive toxicity of TCE has been studied more than female toxicity (US EPA 2009). In human studies, TCE exposure has been associated with increased sperm density and decreased sperm quality, altered sexual drive or function, and altered serum endocrine levels (US EPA 2009). The clinical significance of these measures is uncertain. Animal studies have reported effects on sperm, serum hormone levels and copulatory behavior, as well as lesions in testes and epididymes (US EPA 2009, NRC

2006). Inhalation LOAELs in animal studies for these effects are mainly in excess of 2 000 000 µg/m^3 (US EPA 2009 and references therein) and ingestion LOAELs are in excess of 100 mg/kg_{bw}/d (US EPA 2009 and references therein).

There is some evidence that TCE is metabolized in the reproductive tract, and researchers have been able to demonstrate impairment of sperm fertilizing in mice and rats exposed to TCE orally and via inhalation in both *in vivo* and *in vitro* studies (Xu et al. 2004, DuTeaux et al. 2004). The mice were exposed under controlled conditions to very high concentrations, not likely to be encountered in community exposure (0-0.4% v/v TCE in drinking water or 5 000 000 µg/m^3). It has been postulated that the impairment may be attributed to TCE metabolites chloral hydrate (CH) and trichloroethanol (TCOH) which leads to oxidative damage to sperm (Scott and Chiu 2006*)*. One study found that the decreased fertilizing ability of sperm occurred in the absence of other changes such as testes/epididymides weight, sperm concentration or sperm motility (British Columbia Cancer Agency 2000).

In a study of occupationally exposed mechanics who sought treatment for fertility problems, TCE and its metabolites, CH and TCOH, were detected in all eight study subjects, and none was detected in the seminal fluid of the control subjects (Forkert et al. 2003). Trichloroacetic acid (TCA) (1/8 subjects) and dichloroacetic acid (DCA) (2/8 subjects) was detected in seminal fluid of only some workers. In the subject with the highest level of CH, TCE was relatively low. In the subject with the highest level of TCE detected, there were relatively low amounts of CH. This indicates that there is good correspondence between the amount of TCE in seminal fluid and the formation of metabolites in the male reproductive tract. This is good evidence that TCE is metabolized in the male reproductive tract, where metabolites are able to exert their effects.

Hepatic effects

Hepatotoxicity due to exposure to TCE has been observed in both animal and human studies (NRC 2006, ATSDR 1997). In rodents, TCE has elicited hepatocellular necrosis, liver enlargement and fatty infiltration following subchronic inhalation doses of 430 000 µg/m^3 and subchronic oral doses of 100 mg/kg_{bw}/d or higher (ATSDR 1997, US EPA 2009 and references therein). Few studies have examined non-cancer hepatotoxicity in rodents following chronic exposure (US EPA 2009). Changes in serum liver function tests and increases in serum bile acids following subchronic exposure to TCE have been observed in several occupational studies, however a LOAEL for these effects is uncertain due to imprecise quantification of exposure. Driscoll *et al*. (as cited in US EPA 2009) reported a LOAEL of less than 30 000 µg/m^3 but exposures were higher than this in other occupational studies (US EPA 2009 and references therein). Hepatitis accompanying severe skin reactions due to TCE exposure has been reported in workers (see further above under immunological effects).

Neurological effects

Neurological health effects have been reported in scientific literature from the use of TCE as an anesthetic, from controlled human experiments exposing humans at occupational exposure limits, and from epidemiological studies of workers and cases of accidental exposures. TCE was used as a surgical anesthetic and for treatment of painful symptoms of trigeminal neuralgia up until the 1950s. It was also used as an anesthetic during labour and delivery (Matheke and Felmly 1957) and in World War II (Tweedie and Snowdon 1990). No adverse effects from use for these purposes were noted in this literature search.

Although neurotoxicity of TCE is well documented in people, particularly with regard to effects related to central nervous system (CNS) depression (symptoms of CNS depression include drowsiness, reduced reaction time, clumsiness, slurred speech, etc.), there are relatively few studies on neurotoxicity following chronic exposure (NRC 2006). In addition to CNS depression, potential neurological effects of TCE include damage to the trigeminal nerve (Ruijten *et al*. 1991, where workers were exposed to TCE at concentrations of 100 000 µg/m^3 and greater), damage to the olfactory nerve, ototoxicity (observed in rodents at concentrations greater than 1 200 000 µg/m^3) (Vyskocil *et al*. 2008), motor discoordination, reduced attention span, and perturbations of neurotransmitter functions (NRC 2006). Other effects reported include impaired visual-motor coordination and decreased performance on tests of perception, memory, reaction time, and manual dexterity (ATSDR 1997). Possible mechanisms for neurological effects of TCE include changes in velocity of nerve conduction or changes to neurotransmitter systems (NRC 2006). Factors which control the reversibility of neurological effects elicited by TCE are uncertain (NRC 2006). Exposure levels, duration, and resulting effects are summarized in Table 6 below (ATSDR 1997).

Table 6 Air Concentrations of TCE, Duration of Exposure, and Resulting Neurological Effects

Air Concentrations of TCE		**Duration of**	**Effect**	**Study**
ppm	**µg/m^3**			
110	590 000	8-hour (two 4-hour exposures separated by 1.5 hours)	decreased performance on tests of perception, memory, reaction time, and manual dexterity	Salvini et al. 1971
200	1 000 000	3 days, 70 minutes each day	no change in reaction time or short-term memory function	Gamberale et al. 1976
100	500 000	5 days	psychological changes measured by standard psychometric tests	Triebig et al. 1977
200	1 000 000	5 days, 7 hours/day	normal motor and dexterity tests; fatigue, drowsiness	Stewart et al. 1970
38 to 172	204 000 to 924 000	Chronic, occupational exposure	sleepiness, dizziness, headache, and nausea	El Ghawabi et al. 1973
>17	>100 000	Chronic, occupational exposure	significant association between years of exposure and increase in masseter reflex latency (measure of trigeminal nerve function)	Ruitjen et al. 1991
1.5 to 32	8060 to 170 000	1-2 hours per day, 20 years, several accidental spills	headache, forgetfulness, vertigo, nausea, and loss of feeling in hands and feet persisting for 4 years after retirement	Kohlmuller and Kochen 1994 (case report)

Animal studies have provided some evidence for the relationship between TCE concentrations in air and neurotoxicity. Boyes *et al*. (2004) were able to replicate previous findings that TCE exposure can result in elevation of hearing threshold and mid-frequency hearing loss in rats. Ototoxicity manifests only in very high levels of exposure, in this study greater than 2000 ppm (10 000 000 µg/m^3). This is substantially higher than most occupational and community exposures. This study also found that inhalation of TCE reduced accuracy in discriminating signals and reduced the functional integrity of the visual system (as measured by reduced visual-evoked potential amplitudes).

Neurological effects elicited following acute exposure to concentrations of TCE greater than 1 000 000 µg/m^3 have included headaches, dizziness, nausea, nerve damage and unconsciousness (ATSDR 1997). However, such concentrations have not been observed in the community. In the past, TCE was used as an anesthetic in surgery and in childbirth due to its narcotic effects at very high concentrations. Some of the effects at high concentrations from acute exposures are summarized in Table 7 below:

Table 7 Threshold Toxicity Values for Acute Effects (UK Health Protection Agency 2008)

Exposure via inhalation

ppm	µg/m^3	Signs and symptoms
50 - 100	270000 - 540000	Headache, sluggishness, sleepiness, dulling of senses, dizziness, nausea and vomiting
100 - 600	804000 - 3200000	Respiratory irritation, irritability, restlessness, impaired concentration, euphoria
5000	27 000 000	Light anaesthesia
20 000	108 000 000	Deeper anaesthesia

Effects on eyes

ppm	µg/m^3	Signs and symptoms
5133 – 20 157	27 500 000 – 108 000 000	Eye irritation and reversible, superficial damage to the cornea

Note: This table was compiled by HPA using information from two sources

- International Programme on Chemical Safety, Environmental Health Criteria 50: Trichloroethylene, 1985.
- Trichloroethylene (HAZARDTEXT® Hazard Management). In: Klasco RK (Ed): TOMES® System.Thomson Micromedex, Greenwood Village, Colorado (accessed 02/2007)

6.0 Biomarkers of exposure to TCE

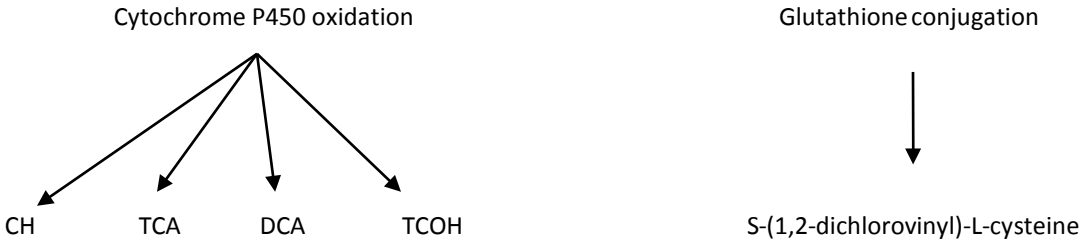
Biological markers of exposure to TCE include concentrations of TCE and its metabolites in body tissues and fluids, such as urine. These compounds have short biological half-lives and levels may vary depending on levels of metabolizing enzymes (Boyes et al. 2000). Urinary TCA has been used as a biological marker in occupational studies, however it only reflects relatively recent exposure (Anttila *et al*. 1995). The biological half-life of TCOH is longer in children and infants than adults, 8 days in adults, 10 days in children, 28 days in full-term infants, and 40 days in preterm infants (Renwick 1998).

Use and interpretation of biological markers should take into consideration variability between individuals that result from differences in physiology and pharmacokinetics of a population (Sohn et al. 2004). Two potential classes of biological measures will be examined; metabolites and gene mutations.

Metabolites

Toxicity and carcinogenicity have been attributed to internal exposure to TCE metabolites, which may be influenced by the dose of TCE and the level of metabolites in the body. TCE metabolites may also be formed from other sources, such as TCA and DCA that result from drinking water disinfection and TCA that is metabolized from exposure to the dry cleaning solvent perchloroethylene (Wu and Schaum 2000). These common exposures give rise to background levels of these metabolites. This is supported by results from the NHANES III survey that measured TCE in the blood of the general US population. Out of 677 samples, 13% had detectable concentrations of TCE in their blood (Ashley *et al*. 1994).

Metabolism of TCE occurs by two main pathways: cytochrome P450-dependent oxidation and glutathione conjugation. The following are metabolites that have been associated with the induction of cancers in specific target organs such as the liver, kidney, and lung in various animal studies



The formation of various TCE metabolites often depends on enzyme systems that also metabolize other drugs and environmental pollutants. These other exposures may affect levels of key enzymes, which can alter or enhance TCE's metabolism. Furthermore, enzyme activity can vary significantly between individuals, due to genetics or disease status. Sex and species differences in these enzyme systems also exist, which may account for the differences in carcinogenicity that have been found in animal studies. Differences in the biotransformation of TCE and the generation of these metabolites will result in different responses to this chemical, which poses challenges in using metabolites as a marker of exposure to TCE, extrapolating findings from animal studies for human exposure assessment and attributing a particular exposure to TCE-induced toxicity.

Metabolites formed from the metabolism of TCE, such as TCOH and TCA, have been used as markers of exposure in occupational studies of workers exposed to TCE (Xu *et al*. 2004). They would not be useful in the community for chronic low level exposure. In a community evaluation that arose from a TCE spill from a pipe manufacturing plant in Pennsylvania, only 2 out of 13 residents tested had detectable levels of TCE metabolites in their urine. Of these two residents, one was employed as a degreaser (who likely had higher levels of exposure) and the other had only very low levels present in the urine (2.5 µg/L detected; the lower limit of detection by the study method was 2 µg/L) (Landrigan *et al*. 1987). The ATSDR recommends TCOH in blood as the best marker of immediate exposure, while chronic exposure should be estimated by urinary TCA (ATSDR Case Studies in Environmental Medicine).

7.0 Biomarkers of effect of TCE (mutations of VHL gene)

Changes to a genome sequence can result in tumour formation (Shiao 2009). In their review of the literature on TCE genotoxicity, Tabrez and Ahmad (2009) found evidence that TCE metabolites bind to DNA and cause strand breaks at high concentrations. TCE metabolites can also induce non-genotoxic effects that can lead to chromosomal changes, such as hypomethylation, that can lead to tumour formation.

The von Hippel-Lindau (VHL) gene is a tumour suppressing gene; inactivation of this gene can result in the promotion of tumour development and this mode of action has been implicated in hereditary and sporadic clear cell renal carcinomas (Kaelin 2009). However, specificity of the VHL mutation spectra is lacking, and detecting a mutation in this gene cannot be used as proof of causation of tumour development for any particular exposure. Brauch *et al*. (2004) compared renal cell carcinoma characteristics between TCE-exposed and unexposed patients. They found that kidney tumours from the TCE-exposed patients had a higher VHL mutation rate than that of the unexposed patients (15/18 tumours had the somatic VHL mutation in TCE-exposed patients, while only 2/21 of the unexposed patients exhibited the somatic VHL mutation). A similar study conducted in France, however, did not observe a difference in the frequency of VHL mutations in exposed and unexposed populations (Charbotel *et al*. 2007).

Mutations in the VHL gene lack the specificity required to be useful as a biological marker of exposure or effect. Mutations in this gene may lead to the development of renal tumours, however these tumours may also occur as a result of exposure to a host of other carcinogenic exposures or risk factors. Exposure to N-nitroso compounds, which is associated with exposure to tobacco smoke, diuretic drugs, and dialysis, can generate a similar mutation pattern in the VHL gene (Sohn *et al*. 2004). Further, these exposures are also known to increase risk for renal cell carcinomas. To date, studies investigating the VHL mutation spectra have not included information regarding co-exposures to these major risk factors in exposed populations.

Genetic tests, due to lack of evidence for specificity to TCE exposure, are not likely to provide any interpretable information for residents.

8.1 What is the level of risk for my family?

Potential cancer risk is a function of both potential exposure and the potency of TCE as a carcinogen. Incremental lifetime cancer risk (ILCR) is an estimate of the extra potential risk of a cancer in a *population* due to a specific exposure. In order to estimate the potential ILCRs for the inhalation exposure of the Bishop Street community due to TCE in indoor air, both potential exposure and the carcinogenicity of TCE were quantified and then combined in a linear calculation. The specific variables, assumptions, and sources of uncertainty in the calculation of both exposure and toxicity are described further below.

Exposure

The variables used to estimate potential exposure were inhalation rate, hours per day spent indoors, body weight, averaging time (related to life expectancy), duration of exposure in years, and the average concentration of TCE in indoor air in the Bishop Street area. Table 8 below lists the variables used for each age group.

Exposures were estimated for each of five different age groups defined by Health Canada (2004b), and exposure was calculated as a lifestage-weighted lifetime average in order to account for higher potential doses during childhood. Inhalation rate, body weight, and averaging time were based on recommendations from Health Canada (2004b). The average number of hours spent indoors was estimated using summary statistics from the Canadian Human Activity Pattern Survey (Leech et al. 1996).

The duration of exposure was assumed to be forty years, which approximates the period from 1965 (shortly after the plant began operations) to 2005 (when investigation and mitigation of indoor air contamination began). The assumption of 40 years of exposure will overestimate the risk for people have moved into the neighbourhood more recently. In addition, the 40 year exposure was assumed to include exposure throughout childhood, i.e., residents of the Bishop Street area from 1965 to 2005 were assumed to be less than one year of age when their residence commenced. As childhood exposures are generally greater than those of adults when expressed on a body weight basis, this assumption will overestimate risk for those who did not spend their childhood years in the neighbourhood.

Table 8 Exposure Variables Used in Calculation of Incremental Lifetime Cancer Risk (ILCR)

Exposure Variable			**Age**			**Reference**
	infant, 0-0.5 y	**toddler, 0.5 y - 4 y**	**child, 5 y - 11 y**	**adolescent, 12 y - 19 y**	**adult, >20 y**	
inhalation rate, m^3/h	0.0875	0.3875	0.604166667	0.658333333	0.658333333	Health Canada 2004
exposure time, hours per day	24	17.184	17.184	16.272	15.432	Leech *et al*. 1996
exposure frequency, d per year	365	365	365	365	365	specific to this risk assessment
exposure duration, years	0.5	4.5	7	8	56	Health Canada 2004
body weight, kg	8.2	16.5	32.9	59.7	70.7	Health Canada 2004

averaging time, years	76	76	76	76	76	Health Canada 2004

The average inhaled concentration in the Bishop Street area over the period 1965-2005 was approximated by the average of average indoor air concentrations per dwelling measured prior to remediation and mitigation between 2005 and 2006. While this average is representative of the time period 2005-2006, using it as the average for earlier years contributes uncertainty to the estimated risk, although it likely overestimates average concentrations for the neighbourhood over the 40 year period.

Carcinogenicity of TCE

Estimates of the potential potency of TCE as a carcinogen have been made by multiple organizations including USEPA[1], WHO and Cal EPA as the upper bound estimate (approximately an upper 95% confidence limit) of increased cancer risk from lifetime exposure per unit of exposure. The increased risk is expressed either in terms of air concentration and referred to as an inhalation unit risk (IUR), or in terms of the reciprocal of a daily dose in mg per kg bodyweight per day and referred to as an inhalation cancer slope factor (CSF_i).

Potential cancer risks were calculated using both the unit risk from WHO (see Table 4) and the CSF_i from Cal EPA. The inhalation unit risks from WHO and Cal EPA are based on different studies and reflect different derivations. The IUR from WHO is based on applied dose and Leydig cell tumours in male rats, whereas the IUR from Cal EPA is a geometric mean of slope factors derived for metabolized dose for lymphoma, hepatic, pulmonary, Leydig cell and renal tumours.

Sources of uncertainty in both the WHO unit risk and the Cal EPA slope factor include:

- Both the unit risk and slope factor were derived for cancers elicited by TCE in controlled animal studies. The extent to which the potency of TCE as a carcinogen in those animal studies represents the potency of TCE as a carcinogen in people is uncertain.
- Default adjustments for enhanced lifestage susceptibility were used based on the potential mutagenicity of TCE. Different adjustments might be applied if additional chemical-specific information were available regarding the toxicokinetics or toxicodynamics of TCE in children versus adults.

The MOE Vapour Intrusion Target Level (VITL) of 0.5 $\mu g/m^3$ is based on a target cancer risk level of 1 in 1 million and a unit risk of 2×10^{-6} per 1 $\mu g/m^3$ (or 2 additional cancer cases for every 1 million people exposed to a TCE concentration of 1 $\mu g/m^3$ over the course of a lifetime). The unit risk originates from the California Department of Health Services and is included in the most recent compilation of cancer potency factors published by California Environmental Protection Agency (Cal EPA 2009b).

Incremental Lifetime Cancer Risk (ILCR)

Figure 4 compares the ILCRs estimated for different concentrations of TCE in inhaled air between the previous IUR used for Bishop Street (termed 'previous target' on the figure) and the current IUR (termed 'current VITL' on the figure). The ILCRs are predicted risks for a hypothetical individual based on the exposure assumptions outlined above, i.e., a 40-year exposure which includes the entirety of childhood. These two assumptions will contribute to overestimating the potential ILCR as there are people in the

Bishop Street community whose exposure lasted less than 40 years and/or did not include all of childhood. For example, in a population exposed to an average inhaled concentration of 250 µg/m^3, the corresponding ILCR in the figure is approximately 5 in 10 000. However, if exposure was for only 10 years, and did not include childhood, the ILCR would be lower than 5 in 10 000 (rather, it would be approximately 3.3 in 100 000, calculation not shown).

The risk for any individual person will be affected by the individual's specific exposure, constitutional and genetic susceptibility.

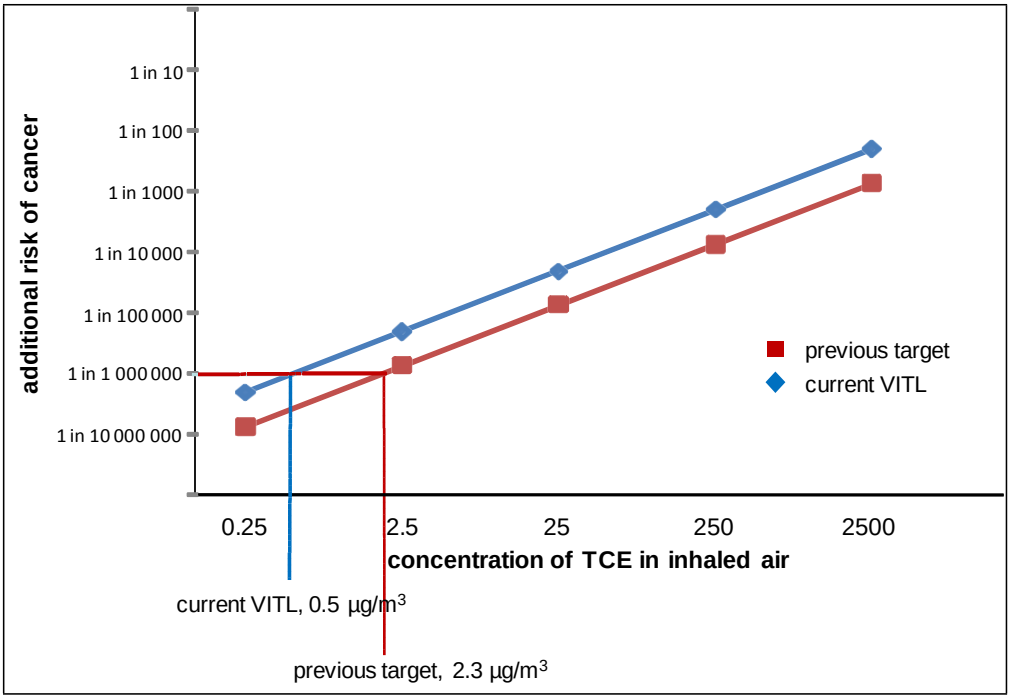


Fig. 4 Estimated Incremental Lifetime Cancer Risk versus TCE concentration

Further detail regarding the interaction between duration and concentration of exposure is provided in Tables 9 and 10 below, which provide ILCRs for different combinations of average inhaled concentration and duration of exposure. Potential ILCRs in Table 9 are based on exposures commencing from birth and include adjustments for enhanced susceptibility during earlier lifestages. Potential ILCRs in Table 10 are based on exposures that did not include any portion of childhood. The ILCRs are read according to the exponent value. For example, an ILCR of 1.7 x 10^{-7} is read as 1.7 cases of cancer in 10 million people, a potential ILCR of 1.7 x 10^{-6} is 1.7 cases in 1 million people, a potential ILCR of 1.7 x 10^{-5} is 1.7 cases in 100 000 people, and so forth.

Table 9: Potential Incremental Lifetime Cancer Risks for Inhalation Exposures to TCE Where Exposure Commenced During Childhood

Duration of Exposure, years

Air Concentration, µg/m^3	2	5	10	20	30	40
0.25	1.7 in 10,000,000	2.7 in 10,000,000	3.8 in 10,000,000	4.8 in 10,000,000	5.1 in 10,000,000	5.5 in 10,000,000
2.5	1.7 in 1,000,000	2.7 in 1,000,000	3.8 in 1,000,000	4.8 in 1,000,000	5.1 in 1,000,000	5.5 in 1,000,000
25	1.7 in 100,000	2.7 in 100,000	3.8 in 100,000	4.8 in 100,000	5.1 in 100,000	5.5 in 100,000
250	1.7 in 10,000	2.7 in 10,000	3.8 in 10,000	4.8 in 10,000	5.1 in 10,000	5.5 in 10,000
750	5.1 in 10,000	8.2 in 10,000	1.2 in 1,000	1.4 in 1,000	1.5 in 1,000	1.7 in 1,000
1250	8.4 in 10,000	1.4 in 1,000	1.9 in 1,000	2.4 in 1,000	2.6 in 1,000	2.7 in 1,000
1750	1.2 in 1,000	1.9 in 1,000	2.7 in 1,000	3.4 in 1,000	3.6 in 1,000	3.8 in 1,000
2500	1.7 in 1,000	2.7 in 1,000	3.8 in 1,000	4.8 in 1,000	5.1 in 1,000	5.5 in 1,000

Table 10: Potential Incremental Lifetime Cancer Risks (ILCR) for Inhalation Exposures to TCE Where Exposure Was During Adulthood Only

Duration of Exposure, years

Air Concentration, µg/m^3	2	5	10	20	30	40
0.25	6.6 in 1,000,000,000	1.7 in 100,000,000	3.3 in 100,000,000	6.6 in 100,000,000	9.9 in 100,000,000	1.3 in 10,000,000
2.5	6.6 in 100,000,000	1.7 in 10,000,000	3.3 in 10,000,000	6.6 in 10,000,000	9.9 in 10,000,000	1.3 in 1,000,000
25	6.6 in 10,000,000	1.7 in 1,000,000	3.3 in 1,000,000	6.6 in 1,000,000	9.9 in 1,000,000	1.3 in 100,000
250	6.6 in 1,000,000	1.7 in 100,000	3.3 in 100,000	6.6 in 100,000	9.9 in 100,000	1.3 in 10,000
750	2.0 in 100,000	5.0 in 100,000	9.9 in 100,000	2.0 in 10,000	3.0 in 10,000	4.0 in 10,000
1250	3.3 in 100,000	8.3 in 100,000	1.6 in 10,000	3.3 in 10,000	5.0 in 10,000	6.6 in 10,000
1750	4.6 in 100,000	1.2 in 10,000	2.3 in 10,000	4.6 in 10,000	7.0 in 10,000	9.3 in 10,000
2500	6.6 in 100,000	1.7 in 10,000	3.3 in 10,000	6.6 in 10,000	9.9 in 10,000	1.3 in 1,000

9.0 Additional questions from the public meeting, Nov. 1, 2010

My home was built in the 1920s. Does the age of your home affect the levels of TCE?

TCE vapours can enter a home through openings or cracks in the foundation. Openings such as sumps, unlined crawlspaces, or earthen floors can provide pathways for TCE vapours to migrate into the indoor space. Because TCE is slightly heavier than air, it can settle and accumulate in areas with lower air exchange rates or poor ventilation. In general, construction practices and materials have improved over

the decades and newer homes tend to be more resistant to vapour intrusion as a result. However, there are exceptions to these trends depending on site-specific circumstances, and thus assessment of a home is needed in order to determine whether subsurface vapour intrusion and significant indoor air contamination are occurring. Measurement of TCE concentration in the home is the most reliable way to determine the extent to which TCE vapour has migrated from soil into the home.

If the number of people per dwelling was increased (from 3 as per census data to an average of 4-5, as may characterize particular neighbourhoods or previous decades), or if multiple families have lived in the home since the 1950s, will this affect the calculation of cancer risk for this community? If the number of homes included in the sampling protocol is increased (by 200 homes this winter), will this affect the calculation of cancer risk for this community?

The estimate of potential cancer risk on an individual basis is *not* affected by the number of people who are exposed to TCE. This is because the estimate of potential cancer risk is based on the potency of TCE as a carcinogen, the concentration of TCE and the exposure assumptions outlined elsewhere in this report. However, the estimated number of cancers expected depends on the number of people who are exposed. This is because the estimate of the number of cancers expected is obtained by multiplying the cancer risk by a population size, e.g., if 1500 people have a cancer risk of 1 in 10 000 one would 'expect' 0.15 cases of cancer. Clearly one cannot have fraction of a case of cancer and our best interpretation would be that while a single case of cancer might occur, there probably wouldn't be any.

Based on the average pre-mitigation, per dwelling indoor air concentration of 52.3 $\mu g/m^3$ in 2005 and 2006, the incremental lifetime cancer risk (if exposed for 40 years, 1965-2005) is 1 to 2 in 10 000. Put another way, one would predict that 1 to 2 cancers attributable to TCE might occur in a group of 10 000 people who were exposed for 40 years, including during childhood, to an average concentration of 52.3 $\mu g/m^3$. In a population the size of the Bishop Street community (estimated at around 1500), less than 1 case (0.15) may be expected. Because TCE related cancers are not uniquely distinguishable from other cancers, one would not be able to identify a single additional case of cancer (or other diseases) in a community health study of the Bishop Street neighbourhood from the background number of cancers that occurs in any community even in the absence of any TCE exposure.

If the number of people per dwelling was increased from an average of about three persons per dwelling to an average of five per dwelling, this will increase the exposed population. Assuming 500 homes, the exposed population will now be 2500 persons. Taking into consideration the increased risk of one to two additional cancers in a population of 10 000, for a population of 2500 persons only a fraction of a cancer (0.25) outcome is expected. It would be very difficult to distinguish a fraction of a cancer due to TCE from the background incidence of cancer due to other causes. Even if the sample population were to be increased by 200 homes (to 700 homes), still only a fraction of a cancer is expected in the Bishop Street Community, based on the average TCE concentration in the 2005-2006 indoor air data, which are the highest recorded levels. The homes to be added to the sampling program are further away from the TCE plume in the groundwater, are expected to have a lower average exposure level, and thus are expected to have a lower risk. If additional air monitoring results warrant, the cancer risk estimates can be repeated using the new results.

Table 11 Effect of Changing Assumption of Number of Homes and Residents Exposed to TCE and Estimate of Predicted Cancers

Number of Homes	Number of Persons per Home	Average Indoor Air Concentration	Estimated Incremental Lifetime Cancer Risk	Number Exposed in the Bishop Street Community	Number of Cancers Predicted in the Bishop Street Community Due to Exposure to TCE as a Result of Subsurface Vapour Intrusion
500	3	52.3	1 in 10 000	1500	0.15
500	5	52.3	1 in 10 000	2500	0.25
700	5	52.3	1 in 10 000	3500	0.35

If multiple families have lived in a particular home over the course of the 40 years (1965 to 2005), this would mean that the duration of exposure estimated in the calculation of the ILCR, is an overestimate of the average duration of exposure for the community's residents (e.g., the average duration of exposure may be closer to 20 years than 40 years). An ILCR calculated with a lower duration of exposure per household would be less than 1 to 2 in 10 000, all other factors being equal.

What if my home had measurements of much greater concentrations than the average 52.3 µg/m^3?

Further details regarding the effect of different duration of exposure and exposure concentration on estimates of ILCR are provided in Section 8, specifically Tables 9 and 10.

How have other communities dealt with this type of contamination?

In the Beckwith Township, TCE was detected in a number of local private wells and there were concerns regarding exposure to TCE, vinyl chloride and dichloroethylene in drinking water. The McMaster Institute of Environment and Health investigated the feasibility of a health study that would provide residents with results that are helpful, scientifically valid, and statistically significant. There were approximately 250 homes potentially affected; based on an average of about 3 persons per household, the affected population appeared to be below 1000 persons. A review of epidemiological study designs concluded that cohort or case-control study designs would be most appropriate in a community setting. However, this population is about 6 to 2500 times less than the sample population required to detect a valid estimate of risk in a cohort study. For case control studies, the number of cases required exceeded the total Beckwith population. A health study was not recommended, as the results from such a study would not provide meaningful or helpful results. It was recommended that the PHU continue to monitor the environmental data and develop a communication and risk management strategy to engage the community on this issue.

10. Implications for possible health studies of the Bishop Street community

Decisions on whether or not to conduct community health studies are always influenced by local factors and not just by the probability of detecting outcomes related to a risk factor of immediate concern. Health studies of any neighbourhood in any community can give a snapshot of the health status of local residents and an enumeration of either self-reported health status or conditions for which medical care has been sought.

However, interpretation of small scale studies with respect to cause and effect, or the explanation for any patterns found presents challenges, and 'chance' is difficult to exclude as a possible explanation.

TCE exposure, especially in high concentrations may lead to the development of adverse health effects. Effects from very high exposures are well documented, however, these concentrations are higher than those measured in the community to date.

Chronic low level exposures, such as that of the Bishop Street Community, may contribute to the risk of cancer. However, based on the estimates outlined above, the risks from the TCE contamination in the Bishop Street neighbourhood are not expected to result in an excess of cancers that would be detectable through a community health study.

For endpoints other than cancer; we have been unable to identify any TCE related outcomes that could be linked detected in a health study of the Bishop Street neighbourhood.

Before embarking on any study it is wise to ask whether the results are likely to provide reliable answers to questions of importance to the community and whether the study has the potential to do more harm than good.

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