

## **1. Executive Summary**

ToxProbe Inc. has prepared this report for the Health Promotion and Environmental Protection Office of Toronto Public Health (TPH) with direction and advice offered by a Project Advisory Committee (PAC) composed of experts from community groups, the provincial government, academia and TPH. The following contaminants have been selected by the PAC for this assessment:

- 1,3-butadiene
- asbestos
- benzene
- cadmium
- chromium
- dioxins
- formaldehyde
- polycyclic aromatic hydrocarbons (PAHs)
- tetrachloroethylene
- trichloroethylene

Brief outlines of the contaminant's properties are provided in section 1.4 and more detailed profiles are contained in Appendix B. Sections 1.1 to 1.3 summarise the toxicological properties and potencies of the selected contaminants, as well as the occupational and environmental exposures in Toronto. More detailed information is available in sections 4 to 6. A summary of conclusions and recommendations is presented in section 1.5 and in greater detail in sections 7 and 8.

### **1.1. Cancer effects**

There is strong evidence to indicate that nine of the ten substances induce cancer. The International Agency for Research on Cancer (IARC), United States Environmental Protection Agency (US EPA) and Health Canada have all classified these nine substances as human carcinogens or probable human carcinogens. There is less agreement on tetrachloroethylene, which has been classified as “probably carcinogenic to humans” by IARC, “unlikely to be carcinogenic to humans” by Health Canada, and “on the continuum between a probable human carcinogen to a possible human carcinogen” by US EPA. The evidence considered by the three agencies suggests that this compound is possibly a weak carcinogen and an indirect carcinogen (tetrachloroethylene breaks down under anaerobic conditions to vinyl chloride, which is a potent carcinogen).

Some carcinogens are believed to induce cancer effects through a genotoxic event that results in an irreversible mutation in the DNA of a somatic cell. These carcinogens are called initiators. These mutagenic substances can initiate cancer even at very minute doses, even though the probability of adverse effects occurring at low doses is minimal. There is no level of exposure for these chemicals that is without some risk. On the other hand, some carcinogens are not mutagenic. Induction of cancer by these non-mutagenic substances involves other mechanisms, such as promotion. Non-mutagenic carcinogens are thought to have thresholds below which cancer risk is not expected to be increased.

There is relatively strong evidence to support the mutagenic property of five of the ten substances and/or their metabolites and therefore their potential to initiate cancer --1,3-butadiene, benzene, chromium (VI), formaldehyde, and polycyclic aromatic hydrocarbons (PAHs). There is evidence that both asbestos and cadmium are genotoxic, causing damage to the chromosomes, and possibly mutagenic. In the case of trichloroethylene and tetrachloroethylene, the evidence for mutagenicity is weak. Dioxin and related compounds are probably not mutagenic, although they are considered to be carcinogenic as promoters.

Among the initiators examined, carcinogenic PAHs and chromium (VI) appear to be the most potent carcinogens by inhalation exposure, followed by asbestos and cadmium. 1,3-butadiene and benzene are about 3 to 4 orders of magnitude less potent than PAHs and chromium (VI). Formaldehyde is a weak initiator but a strong promoter. Other than inhalation, dermal exposure to carcinogenic PAHs is of great concern while oral exposure to PAHs is of lesser importance. However, these comparisons are done without taking into consideration the weight of evidence supporting the identification of a chemical as a carcinogen. For example, while benzene is recognized as a human carcinogen, some individual PAHs are considered to be "probably" carcinogenic to humans.

The order might be different if the weight of evidence could be factored into the comparison. Among substances for which the evidence for mutagenicity is weak, dioxins and related compounds are likely the most potent carcinogens.

Section 4.0 provides the estimates of carcinogenic potency of the selected contaminants and the site and type of cancer they induce. Non-cancer effects are also listed.

## **1.2. Exposures in the workplace**

Exposure information for Ontario workplaces is currently not available. The readily available information on the levels of the selected contaminants in the workplace environment has been extracted from the

literature. However, this information is mostly out of date. Occupational exposures in the Toronto work environment are expected, in most instances, to be lower than these levels. On the other hand, this report contains estimates of the number of workers potentially exposed to contaminants in different industry sectors in Toronto. These sector- and contaminant-specific estimates are the first of their kind in Ontario. The estimates are based on the US and Finnish data from the 1980s. Exposed workers are defined as those potentially exposed at work to levels exceeding the typical ambient air levels.

Table 1.2.1 contains a listing of various contaminant-sector combinations, which were ranked among the top 20 in terms of the number of exposed workers. For example, more workers were potentially exposed to tetrachloroethylene in the clothing-making industry than to any other selected contaminant in any of the selected industries. In addition to sector-contaminant ranks, the table also lists other information such as the total number of workers potentially exposed above background levels of selected contaminants in a given sector and the rank of a sector.

ToxProbe recommends that future work be focused on the sectors and contaminants with the greatest number of workers potentially exposed in Toronto, which are listed in table 1.2.2. These exposures relate to tetrachloroethylene in the manufacture of wearing apparel, formaldehyde in the manufacture of furniture and fixtures, benzene in the wholesale and retail trade, restaurants and hotels industries, in personal and household services, as well as PAHs in the land transport industry. The one outcome in the prioritization exercise that may no longer be relevant to Toronto is the high ranking of benzene exposure in the wholesale and retail, restaurants and hotel sectors. The only obvious source of benzene in these sectors is indoor smoking. Smoking in public buildings and restaurants is restricted in Toronto; therefore it is likely that the actual number of workers exposed to benzene in these sectors could be much lower than predicted.

Given that the information is not based on Toronto-specific data, it is recommended that the current study be used only for planning and prioritizing of further Toronto-specific studies. One study that should be given high priority is the investigation of the prioritized sectors and contaminants to determine if workers are being exposed at levels of concern. This investigation is important because prioritization solely on the number of workers exposed may not necessarily reflect the true risk priority of a given contaminant in a given sector. Even if the number of workers exposed is relatively large, the health effects need not be significant so long as the level of exposure is low. Further details are provided in section 5.

**Table 1.2.1. Sectors with the greatest number of potentially exposed workers to selected contaminants**

	Asbestos	1,3-butadiene	benzene	cadmium	chromium (VI)	Formaldehyde	PAHs	Tetrachloroethylene	Trichloroethylene	Total exposed (x 1000)	Rank of # exposed	% sector workers	Percentage of Toronto workers
Manufacture of textiles					<b>10</b>					1.3	7	23	0.1
Manufacture of wearing apparel, except footwear						<b>8</b>	<b>12</b>	<b>1</b>		44	1	230	3.3
Manufacture of wood and wood and cork products,						<b>20</b>				0.49	20	12	0.04
Manufacture of furniture and fixtures						<b>5</b>				4.9	5	28	0.36
Manufacture of rubber products										1.1	9	8.2	0.08
Manufacture of other non-metallic mineral products				<b>15</b>						0.81	12	19	0.06
Manufacture of fabricated metal products					<b>16</b>					1.1	8	13	0.08
Manufacture of machinery except electrical					<b>18</b>					0.90	10	6.0	0.07
Construction	<b>9</b>							<b>19</b>		2.2	6	4.6	0.16
Wholesale and retail trade and restaurants and hotels	<b>6</b>		<b>4</b>				<b>17</b>			11	4	2.2	0.85
Land transport							<b>2</b>			30	2	140	2.2
Personal and household services	<b>13</b>		<b>3</b>		<b>14</b>		<b>11</b>	<b>7</b>		13	3	52	0.96
Total exposed (x 1000)	7.1	.18	1.5	2.5	5.9	8.1	3.3	4.5	.506				
Rank	5	9	3	7	6	4	2	1	8				
Percentage of Toronto workforce	0.53	0.01	1.1	0.18	0.45	0.61	2.5	3.4	0.04				

The top ten ranking industries are bolded and shaded.

**Table 1.2.2. Sectors and contaminants with highest above background incidence of exposure in Toronto. The most important exposures are in italics.**

Industry sector	Contaminants
Manufacture of wearing apparel, except footwear	<i>Tetrachloroethylene</i> , formaldehyde, PAHs
Manufacture of furniture and fixtures	<i>Formaldehyde</i>
Wholesale and retail trade and restaurants and hotels	<i>Benzene</i> , Asbestos, PAHs
Land transport	<i>PAHs</i>
Personal and household services	<i>Benzene</i> , Tetrachloroethylene, PAHs, Asbestos, Chromium (VI)

### **1.3. Environmental exposures**

It was not possible to obtain realistic emission estimates of the selected contaminants for the City of Toronto. Environment Canada's (2001a) National Pollutant Release Inventory (NPRI) and United States Environmental Protection Agency's (USEPA, 2001) Toxic Release Inventory (TRI) both focus on large point sources. Large point sources will also likely be the focus for the recently announced Ontario's Mandatory Monitoring and Reporting initiative (MOE, 2001). Toronto is affected primarily by mobile sources such as cars and trucks, area sources such as residential heating, and small but numerous point sources such as dry cleaning operations. This report provides the results of ranking generated by the Environmental Defence Fund (EDF) based on the United States TRI data (see section 6.1). TRI collects a wider range of data than NPRI and at present the TRI data set are preferred. The ranking prepared by EDF is not directly applicable to the Toronto situation. Many sources, which dominate TRI are not present in Toronto. On the other hand, many sources relevant to Toronto are not included in TRI. Nevertheless, the EDF ranking scheme identifies important industry emission sources for the selected contaminants that may be of concern to Toronto.

Environmental levels and estimated intakes of selected contaminants by inhalation and ingestion were mostly obtained from the Canadian Environmental Protection Act (CEPA) reports. The Ontario Ministry of the Environment (MOE) provided the levels of contaminants in Toronto's surface waters, sediment and drinking water. Although the results show that exposure by ingestion is usually larger than exposure by inhalation, the cancer potency by the inhalation route is generally greater for the selected contaminants. As a result, residents generally experience a higher risk from a given contaminant from inhalation exposure than from ingestion.

In order to compare the relative human health impact of various selected air contaminants, the levels of the contaminants were converted into toxic equivalency potentials (TEP) using the method developed by EDF.

TEP represents the number of pounds (or kilograms) of benzene (or toluene) that would have to be released into the air to pose approximately the same level of health risk as the reported release of a given contaminant. TEP is expressed in terms of benzene equivalents (for cancer risk) or toluene equivalents (for non-cancer health risk). Using these toxic equivalency potentials (TEPs), it was possible to estimate that benzene, chromium and PAHs account for the majority of the cancer risk posed by the selected contaminants by the inhalation exposure pathway. EDF did not develop TEPs for dioxins and asbestos and they were therefore not included in the comparison (see table 1.3.1). USEPA has withdrawn its dose response assessment for tetrachloroethylene and has yet to finalize the dose response assessment for dioxins and furans.

**Table 1.3.1 Ranking of Carcinogenic Potential of Ten Carcinogens in Toronto Air**

	<b>Benzene TEP</b>	<b>% benzene TEP</b>
1,3-Butadiene	0.11	2.7
Asbestos	-	-
Benzene	2.2	56
Cadmium	0.035	0.89
Chromium (VI)	0.88	23
Dioxins	-	-
Formaldehyde	0.0099	0.25
PAHs (B[a]P)	0.58	15
Tetrachloroethylene	-	-
Trichloroethylene	0.093	2.4
Total	3.9	100

*1 ng benzene per m<sup>3</sup> (1 microgram per cubic metre) of air corresponds to an added lifetime cancer risk of 4.1 in a million. 1 gram (g) is equivalent to 1,000,000 ng*

In terms of non-cancer effects, tetrachloroethylene is ranked second, after cadmium, among the ten substances. Dioxins are not included in the EDF’s ranking scheme for non-carcinogenic effects. Given that dioxins and furans are potent as tumour promoters and developmental toxicants, attention needs to be paid to this group of compounds because of the relatively high exposure from food particularly for people who consume large quantities of sport fish, breast-fed infants, and pregnant women.

The ranking exercise is limited to chemical release to the air and the results have to be interpreted with caution. According to EDF who developed the ranking scheme, TEP-weighted releases do not characterize the estimated increase in health risk associated with a chemical exposure and cannot be combined with information about an exposed population to predict the incidence of adverse effects. The scheme also does not take into account qualitative differences, such as the different types and locations of cancer that chemicals may cause, or the weight of evidence supporting the identification of a chemical as a carcinogen. Further uncertainty for the ranking in this report results from applying the TEP factors to the airborne contaminant levels in the outdoor air, based on the assumption that the air levels are proportional to the quantities released in air. This assumption may not hold because the contaminants may behave differently in the environment after being released to the air.

## **1.4. Selected contaminants**

The following briefly summarizes the uses, sources of release, and toxic properties of the 10 selected substances. More detailed descriptions are provided in Appendix B.

### **1.4.1. 1, 3-Butadiene**

1,3-Butadiene is used in the manufacture of synthetic rubber (styrene-butadiene polymer). Workers employed in the petrochemical, butadiene monomer and styrene-butadiene polymer industry are exposed to 1,3-butadiene.

In the USA, over 90% of 1,3-butadiene was released into the environment from mobile sources. Although this estimate is dated, it is likely that mobile sources continue to be important in the release of 1,3-butadiene today. Workers in the transport industry are expected to be exposed to 1,3-butadiene. The main health concern for exposure to 1,3-butadiene is cancer of the lymphohaematopoietic system. 1,3-Butadiene is a genotoxic carcinogen. Other health effects include effects on the heart, blood and lung, reproductive and developmental effects. Available data in humans indicate that the haematopoietic system is the critical target for butadiene-induced toxicity.

The cancer potency estimates by inhalation for this contaminant were recently revised by USEPA and Health Canada. The two estimates are basically the same, with the USEPA potency value at  $6.3 \times 10^{-6}$  per  $\mu\text{g}/\text{m}^3$ . This corresponds to a lifetime cancer risk of one in a million if individuals are exposed daily to 1,3-butadiene at  $0.16 \mu\text{g}/\text{m}^3$  over a lifetime. The current estimates are developed based on new human epidemiological data although the USEPA Integrated Risk Information System (IRIS) database continues to post the previous estimate that was based on the mouse data.

Environmentally, the predominant route of exposure to 1,3-butadiene is through inhalation. 1,3-Butadiene is present in the outdoor air at an average level of  $0.32 \mu\text{g}/\text{m}^3$  (range  $0.03\text{-}2.20 \mu\text{g}/\text{m}^3$ ) in Toronto. The concentration is expected to be higher at gasoline filling stations and in enclosed structures, such as parking garages and urban road tunnels (e.g.  $4\text{-}49 \mu\text{g}/\text{m}^3$  in parking garages). Most of the 1,3-butadiene present in the indoor air comes from cigarette smoking. Homes where smoking takes place indoors have higher levels of 1,3-butadiene, ranging from  $0.3$  to  $19.2 \mu\text{g}/\text{m}^3$  than smoke-free homes ( $0.04\text{-}1.0 \mu\text{g}/\text{m}^3$ ).

### **1.4.2. Asbestos**

Asbestos was once used extensively in a variety of building materials such as fire-retardant insulation, ceiling and floor tiles in Canada. Asbestos can be released from these materials to contaminate indoor air. Although asbestos is no longer used for these purposes in Canada, it is still used for some limited purposes in Canada and can still be found in some older buildings.

The main health concerns due to inhalation of asbestos fibres are asbestosis, lung cancer and mesothelioma (cancer of the thin membrane that surrounds the lungs and other internal organs). Gastro-intestinal cancer has been shown to be associated with both inhalation and oral exposures, however the risk is generally low. Asbestos exposure also leads to cardiovascular disease and depression of the immune system.

Asbestos is genotoxic causing damage to the chromosomes, and likely mutagenic causing large deletions in the DNA. The inhalation cancer potency of asbestos was estimated to be 0.23 per fibre/mL (fibres per milliliter) by USEPA. This corresponds to a lifetime cancer risk of one in a million if individuals are exposed daily to asbestos at an air level of  $4 \times 10^{-6}$  fibres/mL over a lifetime.

Inhalation is the major route of exposure for asbestos. While there is no Toronto-specific information on the levels of asbestos in the outdoor air, asbestos has been reported to be present at  $3 \times 10^{-6}$  to  $3 \times 10^{-4}$  fibres/mL (or 0.1 to 10 ng/m<sup>3</sup>) in urban areas. The outdoor air level in urban areas can range up to  $3 \times 10^{-3}$  fibres/mL (or 100 ng/m<sup>3</sup>). Note that 1 gram is equal to 1,000,000,000 nanograms (ng).

### **1.4.3. Benzene**

Benzene is released into the atmosphere from both natural and industrial sources. Major sources due to human activity that are potentially relevant to Toronto include automobile exhaust, automobile refueling operations and waste treatment plants. A major source of benzene indoors is cigarette smoking.

Benzene is a genotoxic carcinogen that is most clearly linked to acute myeloid leukemia (AML-leukemia), a cancer characterized by proliferation of the myeloid tissue (in bone marrow and spleen) and an abnormal increase in the number of white blood cells called granulocytes and their precursors, myelocytes and myeloblasts, in the circulating blood. Other health effects associated with long-term low-level exposure include toxic effects in the blood systems (reduction in different types of blood cells), reproductive effects (particularly in women) and depression of the immune system as a result of inhalation, oral or dermal exposure. Ingestion of benzene is known to cause gastrointestinal effects in humans. Exposure to high doses of benzene either through contact with air or through skin contact leads to eye irritation and skin damage.

USEPA has estimated the inhalation cancer potency for benzene at  $4.1 \times 10^{-6}$  per  $\mu\text{g}/\text{m}^3$  and the oral cancer potency at  $2.9 \times 10^{-2}$  per mg/kg body weight/day. These estimates correspond to a lifetime cancer risk of one in a million if individuals are exposed daily to an air level of  $0.24 \mu\text{g}/\text{m}^3$  by inhalation or orally to  $3.4 \times 10^{-2}$   $\mu\text{g}$  of benzene per kg body weight per day over a lifetime.

Inhalation is the major route of exposure for benzene. The levels of benzene in the outdoor air in Toronto range from 1.3 to 3.1  $\mu\text{g}/\text{m}^3$  with an average of 2.2  $\mu\text{g}/\text{m}^3$ . Indoor air levels may be even higher, particularly as a result of second hand tobacco smoke. Benzene is frequently found in groundwater and soil where there has been a gasoline spill in the past, such as from leaking underground gasoline tanks. The level of benzene exposure may be above the minimal level of concern.

#### **1.4.4. Cadmium**

In the USA, combustion of coal and oil is the main source that releases cadmium. Other important sources that are potentially relevant to Toronto include incineration of municipal waste, medical waste and sewage sludge. Emissions released during the production of plastics, pigments and batteries also contribute to overall cadmium exposure. Cadmium is also present in cigarette smoke. Even though the level of cadmium is low in cigarette smoke relative to the total annual cadmium emissions in the city, its close proximity to people, especially indoors, makes cigarette smoke an important source of cadmium in terms of its actual health impact.

Cadmium is a genotoxic carcinogen that can produce lung cancer in humans when inhaled. It does not appear to induce cancer when ingested. Other health effects resulting from either inhalation or oral exposure include kidney disorders and anaemia. The kidney is the main non-cancerous target of cadmium systemic toxicity with long-term exposure. On the other hand, anaemia is likely brought about by reduced gastrointestinal uptake of iron from the diet. Cadmium-induced anaemia is unlikely among populations that have adequate iron intakes.

US EPA has developed the cancer potency for cadmium based on human epidemiological data, while Health Canada chose to use animal data as its starting point. Their potency estimates differ by about an order of magnitude. On the other hand, WHO decided not to provide a potency estimate, because of the high level of uncertainty associated with the risk assessment. The USEPA inhalation cancer potency of  $1.8 \times 10^{-3}$  per  $\mu\text{g cadmium}/\text{m}^3$  air is recommended. Thus, daily exposure to  $5.6 \times 10^{-4}$   $\mu\text{g cadmium}/\text{m}^3$  air by inhalation over a lifetime corresponds to an added lifetime cancer risk of one in a million. This exposure limit based on cancer risk is lower than the exposure limit based on kidney dysfunction ( $0.01 \mu\text{g cadmium}/\text{m}^3$  air). The oral doses below which kidney effects are not expected are estimated by USEPA to be  $0.5 \mu\text{g cadmium per kg body weight per day}$  in water and  $1 \mu\text{g cadmium per kg body weight per day}$  in food.

Exposure to cadmium occurs mainly via food for all ages among the general population, ranging from  $0.21$  to  $0.51 \mu\text{g}$  of cadmium per kg body weight per day. For the smokers, cigarette smoking is an important source of cadmium exposure, contributing an additional  $0.053$ - $0.066 \mu\text{g}$  of cadmium per kg body weight per day. Exposure via the outdoor air is about 100 to 1000-fold lower than exposure from food. The intake from drinking water and soil are also relatively small when compared to intake from food. The average outdoor air concentration in Southern Ontario has been reported to be  $4.2 \times 10^{-4} \mu\text{g}/\text{m}^3$  (range:  $2.4 \times 10^{-4}$  to  $7.2 \times 10^{-4} \mu\text{g}/\text{m}^3$ ). Cigarette smoking adds substantially to the cadmium levels in the indoor air.

### 1.4.5. Chromium

Chromium exists in three forms.

- **Metallic chromium** (chromium (0)) Not much is known about the health effects of this form of chromium. However there is no reason to believe that chromium (0) is a major cause for concern.
- **Chromium (III)** is the form of chromium that is naturally found in the environment. Chromium (III) is an essential nutrient and is not considered to be carcinogenic.
- **Chromium (VI)** is released into the environment primarily as a result of industrial activity. Chromium (VI) is not an essential nutrient and induces lung cancer upon long-term exposure.

Electroplating, leather tanning, and textile industries release large amounts of chromium to surface waters. Coal burning may contribute to the emissions of chromium III and some chromium VI. Chromate manufacture can also be a major source for chromium (VI) but this source is not expected to be relevant in Toronto.

Chromium (VI) is a genotoxic carcinogen that can produce lung cancer when inhaled. However, at the present time there is no evidence that chromium (VI) is carcinogenic when ingested. Exposure to high levels of chromium in air (above 20 ng/m<sup>3</sup> chromium (VI)) can produce nosebleeds, ulcers, holes in the nasal septum and other respiratory effects. Exposure to low levels of chromium of any form can induce allergic dermatitis. Exposure to chromium (VI) may also produce reproductive effects.

There is agreement among regulators regarding the cancer potency of chromium (VI) by inhalation. The USEPA potency estimate of 1.2 x 10<sup>-2</sup> per µg chromium (VI)/m<sup>3</sup> is recommended. In essence, exposure to 8.3 x 10<sup>-5</sup> µg chromium (VI)/m<sup>3</sup> every day over a lifetime corresponds to an additional lifetime cancer risk of one in a million.

The general population of all age groups is exposed to chromium primarily from food (about 96%, primarily chromium (III)) and to a lesser degree from drinking water, soil and air. Cigarette smoking may increase total daily intake by 0.04 to 0.05 µg/kg/d. The mean airborne concentration of total chromium in 12 Canadian cities between 1987 and 1990 ranged from 3 x 10<sup>-3</sup> to 9 x 10<sup>-3</sup> µg/m<sup>3</sup>. Chromium (VI) comprises roughly 3-8% of total chromium in the urban outdoor air.

### 1.4.6. Dioxins and Dibenzofurans

In Ontario, medical waste incinerators are the most significant contributors of dioxins and furans. The next most important contributors are hazardous waste incinerators, followed by iron sintering, backyard barrel burning, steel manufacturing, diesel fuel combustion, base metal smelting, municipal waste incinerators, residential wood burning and coal-fired electrical generating station. Among these sources, diesel fuel combustion, wood burning and medical waste incineration may be most relevant to Toronto.

Dioxins and related compounds (including dibenzofurans and coplanar PCBs) induce a wide spectrum of responses in humans and animals. These responses are initiated by the binding of the compound to an Ah receptor protein in the cells, which triggers a series of events including alteration of normal cellular regulation leading to various health hazards. The spectrum of responses include cancer (multiple sites, particularly lung cancer and soft tissue sarcoma), chloracne (severe acne-like condition), reproductive and developmental effects, suppression of immune functions, and hormonal disruption. This represents a continuum of effects.

Dioxins and related compounds are not directly genotoxic. They are potent promoters. 2,3,7,8-tetrachlordibenzo-p-dioxin (TCDD) is the most toxic member and the toxicity of all other members is expressed as toxic equivalents (TEQ) of TCDD. Estimation of the cancer potency for dioxins is a controversial issue and the USEPA potency estimate for dioxins differs significantly from the estimates developed by WHO and Health Canada. USEPA assumed a non-threshold dose-response relationship and arrived at a cancer potency of approximately  $1 \times 10^{-3}$  per pg TCDD/kg/day. This corresponds to an added lifetime cancer risk of one in a million if individuals are exposed daily to  $1 \times 10^{-3}$  pg TEQ/kg/day for a lifetime. Both WHO and Health Canada consider dioxins and related compounds as threshold carcinogens and derived a tolerable daily intake of 10 pg TEQ/kg/day to protect humans from the carcinogenic properties of dioxins. The WHO and Health Canada approaches are recommended. (Note that 1 gram is equivalent to 1,000,000,000,000 picograms (pg)).

Altered development is among the most sensitive health endpoints resulting from dioxin exposure. Evidence in animals suggest that prenatal dioxin exposure has the potential to disrupt a large number of critical developmental events at specific developmental stages, ranging from death inside the womb, disruption of organ structure development, permanent impairment of organ function, alteration of learning behaviour and impaired reproductive system to immune suppression after birth. WHO has developed a tolerable daily intake of 1-4 pg TEQ/kg/day on the basis of reproductive and development effects.

The Canadian Council of the Ministers of the Environment (CCME) is currently developing *Canada-wide Standards* for dioxins and furans and is aiming for virtual elimination of this family of compounds.

Dioxins and related compounds can be transported a long distance in the air, persist in the environment and accumulate in the food chain. Food is the major source of exposure to dioxins and furans as they tend to bioaccumulate in the food chain. Age-specific estimates of average total exposure to dioxins and furans for Great Lakes basin residents range from 1.20 pg TEQ/kg/day in adults 20 years of age and older to 57.05 pg TEQ/kg/day in breast-fed infants under six months of age. Assuming a 70-year lifespan and being breast-fed as an infant, the daily intake for the Great Lakes Basin general population (including Torontonians),

averaged over a lifetime, is estimated to be 2.60 pg TEQ/kg/day. Since the fish in the Great Lakes contain substantial levels of dioxins and furans, individuals who eat a lot of sport fish are expected to have a high level of exposure. For example, adults 20 years of age or older, who eat an average 21.3 grams of Great Lakes sport fish per day would have a total exposure of 4.25 pg TEQ/kg/day.

Due to the effect of dioxin exposure at critical stages of development, the developing fetuses are the most sensitive subpopulations. Infants, particularly the breast-fed ones, are sensitive to the effect of dioxins because of their high levels of exposure. However, due to nutritional, immunological and psychological benefit of breast-feeding, Health Canada does not consider it reasonable to advise against breast-feeding.

### **1.4.7. Formaldehyde**

In the USA, more than half of formaldehyde releases to the environment originate from mobile sources. Humans can also be exposed to formaldehyde present in the indoor air due to off-gassing from building materials, especially pressed-wood products, consumer goods, environmental tobacco smoke and combustion appliances. A quantitative risk assessment would be required to determine which of these sources has greater impact on human health.

Formaldehyde is considered to have weak tumour initiating (genotoxic) and strong tumour promoting (non-genotoxic) properties. It is a highly reactive substance that is irritating to tissues with which it has direct contact and its effects are mostly experienced at the point of contact. For example, exposure to airborne formaldehyde leads to symptoms of irritation of the eyes and the upper respiratory tract. Skin irritation and allergic contact dermatitis can result from skin contact with liquid formaldehyde and the gastrointestinal tract can be irritated with oral exposure. Despite inconsistent evidence in humans, formaldehyde is considered a probable human carcinogen based on sufficient evidence that inhalation induces malignant nasal tumours in rats.

Both USEPA and Health Canada are currently reviewing the dose-response relationship for formaldehyde. The most recent cancer potency estimate proposed by USEPA is  $2.8 \times 10^{-7}$  per  $\mu\text{g}/\text{m}^3$ . This corresponds to an additional cancer risk level of one in a million for a lifetime exposure to  $3.6 \mu\text{g}/\text{m}^3$  of formaldehyde.

The most significant route of exposure to formaldehyde is inhalation, particularly while indoors. The average formaldehyde level present in the outdoor air in Canada is  $3.3 \mu\text{g}/\text{m}^3$ . The indoor air levels in homes and offices are generally higher than the outdoor levels due to off-gassing of formaldehyde from various home products and cigarette smoking. The average indoor air level of formaldehyde in the Canadian homes is estimated by CEPA to be  $35.9 \mu\text{g}/\text{m}^3$ . Assuming people spend 3 hours outdoors and 21 hours indoors on a daily basis, the mean 24-hr time-weighted average formaldehyde airborne level to which Canadians are exposed is estimated to be  $36 \mu\text{g}/\text{m}^3$ .

### **1.4.8. PAHs**

Toronto does not have large point sources of PAHs within its boundaries but there are significant area sources (home heating), mobile sources (car and truck traffic mostly) and a number of other smaller sources. PAHs are routinely found in Toronto soils, primarily as a result of past historical activities. Secondary tobacco smoke is an important source of PAH exposure for a large portion of the population.

PAHs have been shown to induce a number of toxic effects besides cancer. PAHs can irritate the respiratory tract, the eyes, and the skin in occupational settings. Extreme environmental conditions (e.g. heavy exposure to forest fire smoke) may also trigger these effects. Some PAH-rich mixtures are carcinogenic to both humans and animals. Individually, some PAHs are carcinogenic to animals while others are not. Some are genotoxic and others are not. Other effects include suppression of the immune system, disruption of the female and male reproductive systems, and impairment of fetal development. The doses required to induce developmental effects are generally similar or somewhat higher than those required for a carcinogenic response. Benzo[a]pyrene (B[a]P) is the most toxic member of the PAH family of compounds.

There are generally two approaches used to estimate the cancer potency of a PAH-rich mixture. One approach involves summing up the risk from exposure to individual PAHs, such as practised mostly in North America (Health Canada, USEPA, California EPA). This approach has been shown to underestimate the risk in many situations, probably because a typical mixture usually has hundreds of PAHs and the speciated approach considers only about a dozen PAHs. In Europe, PAH-rich mixtures are assessed as a whole (Netherlands, World Health Organization). The Ontario Ministry of the Environment (MOE) has thoroughly evaluated the two approaches and recommended that evaluation of PAH-rich mixtures be conducted on a whole mixture basis. The whole mixture approach is the model that ToxProbe recommends. MOE has established the cancer potency for B[a]PS (B[a]PS represents the potency of a PAH-rich mixture, expressed in terms of B[a]P content.) as  $2.3 \times 10^{-2}$  per  $\mu\text{g B[a]P/m}^3$  by inhalation, 2.9 per mg/kg/day by ingestion and 95 per mg/kg/day by dermal exposure. These values correspond to an added lifetime cancer risk of one in a million if individuals are exposed to a PAH-rich mixture that contains  $4.3 \times 10^{-5} \mu\text{g B[a]P/m}^3$  by inhalation, or yields an intake of  $3.4 \times 10^{-4} \mu\text{g B[a]P/kg/day}$  by ingestion or  $1 \times 10^{-5} \mu\text{g B[a]P/kg/day}$  by dermal absorption. (Note that 1 g is equivalent to 1000 mg which is equivalent to 1000  $\mu\text{g}$ .)

The average concentration of B[a]P in Toronto outdoor air is approximately  $3 \times 10^{-4} \mu\text{g/m}^3$ . The levels are generally higher in the winter ( $3.6 \times 10^{-4} \mu\text{g/m}^3$ ) than in the summer months ( $1.4 \times 10^{-4} \mu\text{g/m}^3$ ). Although food is the major source of exposure to B[a]P, since B[a]P is a more potent carcinogen when inhaled than ingested, the risk of stomach cancer from oral intake may not be higher than the risk of lung cancer due to inhalation exposure. In general, due to winter heating, the daily intake of B[a]P is about one order of magnitude higher in the winter than in the summer months. Because people spend more time indoors, the indoor air contributes more to the total daily intake of B[a]P. The exposure is further increased in situations where the residents supplement home heating with a fireplace and where cigarette smoking takes place in the homes.

### **1.4.9. Tetrachloroethylene**

Tetrachloroethylene may be important in Toronto because of its use in the dry-cleaning industry and clothing industry. Furthermore, tetrachloroethylene may biodegrade under anaerobic conditions into trichloroethylene and eventually into vinyl chloride (a potent carcinogen). Both trichloroethylene and vinyl

chloride are considered more toxic than tetrachloroethylene. All three contaminants are routinely found in the soil and groundwater of contaminated sites in southern Ontario.

According to Agency for Toxic Substances and Disease Registry (ATSDR), the pattern of tetrachloroethylene use in the USA are as follows: 55% for chemical intermediates, 25% for metal cleaning and vapour degreasing, 15% for dry cleaning and textile processing, and 5% for other unspecified uses. Since the chemical industry constitutes only a small proportion of Toronto industry, it is expected that dry cleaning and textile processing will contribute a greater proportion of the total emissions in Toronto as compared to the general USA use pattern. Dry cleaning use is important from an environmental perspective given the proximity of dry cleaning operations to commercial and residential buildings where people spend a lot of time.

Long term exposure to low levels of tetrachloroethylene has led to subtle neurological effects. Kidney effects have also been observed, especially in people occupationally exposed. There is strong evidence that tetrachloroethylene affects the liver in animals, however, evidence in humans is weaker. It is very likely that the tetrachloroethylene metabolic product responsible for liver toxicity in animals is relatively minor in humans.

Tetrachloroethylene is a weak mutagen in humans and the weight of evidence for its carcinogenicity is low as compared to the other nine substances considered. It appears that the mutagenic activities of tetrachloroethylene in the *in vivo* rodent tests are due to the activities of its glutathione conjugates. Glutathione conjugation is of less importance as a metabolic process in humans than in rodents. It is therefore expected that tetrachloroethylene may induce only minimal genotoxic effects in humans at low doses.

There is no consensus in the scientific community and regulatory agencies with respect to whether tetrachloroethylene induces cancer effects in humans. IARC has classified it as *probably carcinogenic to humans*. Health Canada has revised its classification downwards to *unlikely to be carcinogenic to humans*. Most agencies' positions lie somewhere between those of IARC and Health Canada. For example, the European Union considers tetrachloroethylene not classifiable as to its carcinogenicity. Though USEPA has proposed to classify tetrachloroethylene as a probable human carcinogen, the proposal was not supported by the Science Advisory Board of USEPA. US EPA's current official position regarding this contaminant is "on the continuum between a *probable human carcinogen (sufficient evidence from animals studies but inadequate evidence or no data from epidemiological studies)* and a *possible human carcinogen (limited evidence for carcinogenicity in animals, inadequate human carcinogenicity data)*". Health Canada has developed a potency estimate for tetrachloroethylene based on its adverse effects other than cancer. Despite IARC's classification (IARC is a WHO agency), WHO also chose to evaluate human health risk from exposure to tetrachloroethylene based on its critical toxic endpoints other than cancer. For the purposes of risk assessments and standard setting, the author supports the approach taken by Health Canada and WHO. However, for the purposes of this report, this compound can be treated as a possible carcinogen that may be weakly and perhaps indirectly carcinogenic.

The recommended potency estimates for tetrachloroethylene are the values developed by WHO for air and by USEPA for ingestion. These estimates suggest that exposure to an airborne concentration of 250  $\mu\text{g}/\text{m}^3$

daily by inhalation and a daily oral dose of 0.01 mg/kg/day are likely to be without any risk of adverse effects during a lifetime.

The average tetrachloroethylene levels in the outdoor air in eleven Canadian cities range from 0.2 to 5  $\mu\text{g}/\text{m}^3$ . The indoor air levels are about 5.1  $\mu\text{g}/\text{m}^3$ . Since people spend most of their time indoors, the time spent indoors makes the greatest contribution to the overall exposure to tetrachloroethylene, while the ingestion of drinking water (generally) makes a minor contribution. The use of household products that contain this compound and the residual tetrachloroethylene present in freshly dry-cleaned clothing are likely the predominant reason why the indoor air levels are generally higher than the ambient air levels.

#### **1.4.10. Trichloroethylene**

Degreasing operations are the biggest source of occupational exposures to trichloroethylene and the biggest source of emissions to the environment. Some trichloroethylene is released during household and industrial dry-cleaning. Trichloroethylene is also used as a solvent. Evaporation and losses from adhesives, paints and coatings may contribute to exposure indoors. Trichloroethylene may be biotransformed under suitable anaerobic conditions into vinyl chloride, which is a more potent carcinogen. These contaminants are routinely found in the soil and groundwater of contaminated sites in Southern Ontario

The data in support of mutagenicity of trichloroethylene are equivocal, consistent with a weak, indirect mutagen. Toxicants, which are not mutagenic are often assumed to have a threshold below which they have no effect. Nevertheless, Health Canada, California Environmental Protection Agency and World Health Organization all assume a no threshold dose-effect relationship for trichloroethylene.

Other health effects include depression of the central nervous system when inhaled and skin rashes on direct skin contact with trichloroethylene. Liver and kidney damage and developmental effects (behavioural and heart abnormalities in pups) have been observed in animals exposed by ingestion and inhalation. It is not clear how humans are compared to animals in terms of sensitivity to these effects.

Health Canada's cancer potency estimates are recommended. The cancer potency for inhalation is estimated at  $6.1 \times 10^{-7}$  per  $\mu\text{g}/\text{m}^3$  and for oral ingestion is  $1 \times 10^{-4}$  per mg/kg/day. These values correspond to an added lifetime cancer risk of one in a million if individuals are exposed daily to an airborne level of 1.6  $\mu\text{g}/\text{m}^3$  by inhalation or  $6.7 \times 10^{-3}$  mg/kg/day by ingestion.

Indoor air is the major source of exposure to trichloroethylene in the general population, while ambient air, drinking water and food make only minor contributions. The outdoor air levels in Toronto range from 0.32 to 2.8  $\mu\text{g}/\text{m}^3$ , however, the indoor air levels are higher averaging 1.4  $\mu\text{g}/\text{m}^3$ .

### **1.5. Conclusion and recommendations**

The adverse effects of the selected substances are generally well recognized, although there does not seem to be a regulatory consensus regarding the ability of tetrachloroethylene to induce cancer in humans.

There are also questions regarding the potency estimates derived by the various agencies for dioxins and PAHs. They can differ significantly. The report examines the evidence and makes specific recommendations in this area. ToxProbe recommends that the City periodically review the advances made in this area by leading regulatory bodies.

Very little up to date information is available regarding the exposure levels of the 10 selected substances in the workplace. The information from readily available reports from around the world is out of date and does not provide reliable estimates of exposure levels in Toronto's work environments. ToxProbe considers assessment of worker exposure to be a high priority. Reliable information about worker exposure is best obtained on an industrial sector-by-sector basis. Within each sector, specific processes and activities, which lead to high exposures, need to be identified. This report has identified the sectors expected to have the greatest number of workers exposed above background levels to the ten carcinogens in Toronto. These sectors include the transport industry, furniture manufacturing, clothing industry, personal and household services and others as listed in table 1.2.1. It is recommended that these sectors be the focus of any follow-up study.

ToxProbe recommends expanding estimation of the number of exposed workers to other carcinogens using the same method. CAREX lists 139 contaminants and mixtures. The expanded study needs to be methodologically compatible with the current one so that cross-study comparisons between contaminants and sectors can be made.

Ranking of the ten substances in terms of impact on human health due to environmental exposure is difficult without conducting a health risk assessment. Most of the contaminants examined act as non-threshold carcinogens while others act either as threshold carcinogens (e.g. dioxins) or have health effect other than cancer as the critical toxic endpoint (e.g. tetrachloroethylene). Furthermore, while air exposure is the major pathway for inducing health risk for most of the selected contaminants, food ingestion is the most important source for health risk due to dioxins and related compounds.

In terms of environmental exposure, obtaining good estimates of emissions from mobile sources such as cars and trucks, area sources such as home heating, and small point sources such as dry cleaning, is recommended to be the top priority. These sources are expected to have the greatest overall impact on human health in Toronto. For this reason, it is recommended that the City proceed on a sector-by-sector basis. The information contained in this report can be used to prioritize the emitting sectors for this exercise.

The second environmental priority is to obtain more reliable, Toronto-specific estimates of indoor air exposure. It needs to be stressed that the exposure that people receive by inhalation indoors often is the determining factor for the level of overall environmental health concern.

The third environmental priority is to determine the exposures from sources which are heavily influenced by lifestyle factors. For example, burning of wood in fireplaces can produce very high levels of PAHs and other contaminants both indoors and outdoors in the surrounding area. The exposure could lead to significant health risk to users and their neighbours. At present, the City may not have information on the number of households that use woodstoves and fireplaces, the duration and frequency of use. Consumption of home-grown produce on contaminated soil is another important source of exposure. In order to assess

this parameter, it would be desirable to establish the number of households consuming home-grown produce, the proportion of home-grown produce consumed annually and the range of contamination found in Toronto grown produce.

This report attempts not only to summarize the existing data, but also to make comparisons of impact where the data permit. The toxicity, release and human exposure of individual chemicals have been estimated in many jurisdictions. There has been less success in utilizing the available information to paint a comprehensive (big picture) picture of the state of occupational and environmental risk from these chemicals. Such an overview could be used to prioritize occupational and environmental issues in an informed manner. A systematic approach of this sort would also help to identify the data gaps better. Developing a systematic approach to environmental and occupational health based on good data would allow the City to accomplish more with its limited resources. Working towards developing such a big picture is strongly recommended. This is ToxProbe's main recommendation.

## **2. Background**

Toronto Public Health is a member of the Toronto Cancer Prevention Coalition. One of the working groups of the Coalition is focused on occupational and environmental carcinogens. The purpose of this project is to provide a comprehensive overview of the health effects and exposure information available on ten toxic substances that are expected to be common in Toronto workplaces and/or environment. The prepared report will provide the basis for a report to Toronto's Board of Health and may be used as a background report by the Coalition. The goal is to provide a qualitative evaluation of the health impact the selected carcinogens may have on Toronto populations at work, at home or during other activities in Toronto.

Dr. Pavel Muller of ToxProbe Inc. has prepared this report for the Health Promotion and Environmental Protection Office of Toronto Public Health (TPH).

### **3. Selection of Contaminants**

There are many ways by which contaminants can be prioritised. Factors that can be taken into consideration in the decision can include toxicological properties of the contaminants, the level of emissions from different industries found in Toronto (by means of emission factors), the size of the population affected and the magnitude of exposure of the exposed populations, the route of exposure, the persistence of the contaminants, adequacy of federal and provincial regulations, and the quality of the scientific knowledge.

The Project Advisory Committee has developed a list of contaminants to be assessed for their carcinogenic impact in Toronto. These contaminants are selected based on their carcinogenic potencies, the likelihood that there are sufficient sources within Toronto to justify investigation and other factors. The list of contaminants selected for evaluation is presented below.

- 1,3-butadiene
- asbestos
- benzene
- cadmium
- chromium
- polychlorinated dibenzo-p-dioxins (dioxins)
- formaldehyde
- PAHs
- tetrachloroethylene
- trichloroethylene

The properties of the selected contaminants are described in detail in Appendix A. Only selected relevant properties are examined in the main report.

## 4. Carcinogenic potential

### 4.1. *Weight of evidence for carcinogenicity*

Within the scientific literature, reports vary in their quality and some reports contradict each other. The International Agency for Research on Cancer (IARC) was the first organisation to develop a weight of evidence scheme for cancer agents. A panel of international experts systematically evaluates the evidence of carcinogenicity, classifies each agent and publishes a summary of the evidence which includes the rationale used to support the agent's classification. IARC is an agency of the World Health Organization (WHO).

Although the IARC ranking continues to be highly respected, other agencies have developed similar ranking schemes. Of these, the one published by the USEPA (1986) is probably the most influential. In 1996, USEPA replaced its ranking scheme based on letter ranks with a new descriptive scheme, which takes into account a wider range of data (see appendix A). The USEPA's 1986 scheme is still widely used, in part because the evaluations based on this earlier ranking scheme continue to be reported in the Integrated Risk Information System (IRIS) database. The ranking schemes by IARC and USEPA (1986) are quite similar. Although both organisations place a greater emphasis on good human epidemiological data than on animal data, USEPA has traditionally placed heavier emphasis on animal data than IARC. Even though the new USEPA (1996) ranking scheme has been in use for a few years, the number of agents ranked by this scheme is relatively small and thus it is not yet as widely used as the older scheme.

In Canada, Health Canada has developed a carcinogen-ranking scheme under the Canadian Environmental Protection Act (CEPA, 1994a) based on the IARC ranking scheme. CEPA's scheme consists of more categories and subcategories and is not very compatible with those of IARC and USEPA. CEPA distinguishes between genotoxic and non-genotoxic carcinogens, and gives the latter group a lower ranking when epidemiological evidence is inadequate.

Some US states, including California, have their own rankings. So do many European countries (see Moolenaar, 1994). A comparison of the key ranking schemes is summarised in table 4.1.1. Further details about the various ranking schemes are available in Appendix A.

**Table 4.1.1 Comparison of three well known weight of evidence classification schemes for carcinogens**

Strength/Type of Evidence	Weight of Evidence Classification		
	USEPA <sup>1</sup>	IARC (WHO) <sup>2</sup>	CEPA <sup>3</sup>
Strong human evidence	A	1	I
Some human + animal evidence	B1	2A	III B?
Little or no human evidence, strong animal evidence	B2	2B	II?
Weak evidence from human and animal data	C		III (except IIIb)?
Little evidence for or against carcinogenicity	D	3	VI
Good evidence for absence of carcinogenicity	E	4	V, (IV?)

Based on definitions obtained from the following sources.

1. USEPA (1986)
  2. IARC Monographs website
  3. CEPA (1994a)
- ? – Indicates imperfect fit

The carcinogenicity ranking of the selected contaminants is presented in table 4.1.2. In general, when ranking is available from more than one agency, there is a good agreement between the ranks assigned by the three agencies. The exception is tetrachloroethylene.

There is no consensus in the scientific community and regulatory agencies with respect to whether tetrachloroethylene induces cancer effects in humans. The judgement regarding tetrachloroethylene carcinogenicity ranges from probably carcinogenic to humans (IARC, 1995a; Cal EPA, 1991) to unlikely to be carcinogenic to humans (CEPA, 1996). Most agencies' positions lie somewhere between those of IARC and CEPA. For example, the European Union (Beck, 2000) considers tetrachloroethylene not classifiable as to its carcinogenicity. On the other hand, US EPA's official position (cited in ATSDR, 1995) is that tetrachloroethylene is on the continuum between group B2 (*probable human carcinogen*) and group C (*possible human carcinogen*).

There is a general agreement that the human data are by themselves insufficient to definitively identify tetrachloroethylene as a carcinogen. There is also a good agreement on the toxicity and carcinogenicity of tetrachloroethylene in rodents. The key area of contention for tetrachloroethylene relates to whether rodent data can be directly applied to humans.