



Ontario

Cancer Care Ontario

Action Cancer Ontario



Cancer Risk Factors in Ontario

Industrial Chemicals



INDUSTRIAL CHEMICALS

Risk factor/exposure	Cancer	The context where high risks were reported	Magnitude of risk*	Strength of evidence ^a
Acid mists, strong inorganic	Larynx	Occupational	1.2-2.5 ^a	Sufficient
	Lung	Occupational	...	Limited
Benzene	Leukemia (acute nonlymphocytic, acute myeloid)	Occupational	1.9-3.2 ^b	Sufficient
	Non-Hodgkin lymphoma	Occupational	...	Limited
		Environmental	...	
	Leukemia (acute lymphocytic, chronic lymphocytic)	Occupational	...	Limited
Multiple myeloma	Occupational	...		
1,3-Butadiene	Hematolymphatic organs	Occupational	1.1-3.0 ^{b,c}	Sufficient
Formaldehyde	Nasopharynx	Occupational	1.1-2.1 ^{d,e,f}	Sufficient
	Leukemia [†]	Occupational	1.1-1.9 ^g	
	Sinonasal	Occupational	...	Limited
Mineral oils, untreated or mildly treated	Skin	Occupational	1.2 ^a	Sufficient

Sources: ^aIARC, 2012; ^bKhalade et al., 2010; ^cDelzell et al., 2006; ^dBosetti et al., 2008; ^eBachand et al., 2010; ^fHauptmann et al., 2004; ^gZhang et al., 2009

* Relative risk (RR) estimate for persons exposed vs. unexposed.

... Magnitude of risk not shown in table if strength of evidence is "probable" or "limited."

[†] Association is particularly apparent for myeloid leukemia. Relative risk presented in the magnitude of risk column is therefore for myeloid leukemia only.

ACID MISTS, STRONG INORGANIC

Background

- » Strong acid mists may be produced from the use of strong inorganic acids, including sulfuric acid.¹⁵²
- » The major industries with exposure to strong inorganic acid mists are those involved in manufacturing phosphate fertilizer, isopropanol (isopropyl alcohol), synthetic ethanol, sulfuric acid, nitric acid and lead batteries.¹⁵²
- » The primary routes of occupational exposure to strong inorganic acid mists containing sulfuric acid are inhalation, ingestion and dermal contact, although exposure depends on factors such as particle size, proximity to the source and control measures in place.¹⁵²

- There is consistent evidence that strong inorganic acid mists cause cancer of the larynx¹⁵² and some evidence that acid mists may cause lung cancer.¹⁵²
- Workers exposed to acid mists are at a 1.2–2.5 times increased risk of laryngeal cancer.¹⁵² Evidence suggests a [dose-response](#) relationship with a combined measure of duration and intensity of exposure.¹⁵³
- The exact biologic mechanism by which strong inorganic acid mists induce cancer remains unknown; however, the high acidity from the mists may damage DNA.¹⁵²

BENZENE

Background

- » Benzene is a colourless, highly flammable liquid with a sweet odour.¹⁵⁴
- » Benzene is naturally found in petroleum products (e.g., crude oil and gasoline) and was formerly added to unleaded gasoline. Today, it is primarily used in the production of organic chemicals, such as styrene, phenol and chlorobenzenes.¹⁵²
- » Occupational exposure to benzene can occur in the rubber, paint (including paint applications), parts-manufacturing, crude-oil refining and chemical manufacturing industries.¹⁵² The primary route of occupational exposure is inhalation, but exposure can also occur through dermal absorption.^{152,154}
- » For the general population, the primary source of exposure is inhalation of tobacco smoke or ambient air contaminated with benzene (e.g., in areas with heavy traffic or surrounding gasoline-filling stations) or ingestion of food or water that is contaminated with benzene.¹⁵²

- Benzene causes acute myeloid leukemia (AML)/acute non-lymphocytic leukemia (ANLL).¹⁵² This finding is based on studies of occupational exposure, as well as some evidence from studies examining population exposure. There is some evidence for a positive association with other leukemias and lymphomas.¹⁵²
- Occupational benzene exposure is associated with a 2- to 3-fold increase in the risk of AML/ANLL.¹⁵⁵ Cohort studies have shown a dose-response relationship with benzene exposure and AML/ANLL in many industries and across several countries.¹⁵²
- Genotoxicity, particularly in pluripotent haematopoietic stem cells, is thought to be the main biologic mechanism through which benzene causes cancer.¹⁵²

1,3-BUTADIENE

Background

- » 1,3-butadiene is a colourless gas at room temperature used to produce synthetic rubbers and polymers that are used in many products, such as automobiles, construction materials, appliance parts, computers and telecommunication equipment, and household articles.¹⁵²
- » Significant sources of 1,3-butadiene in the environment include industrial emissions, while minor sources include vehicle exhaust, cigarette smoke and smoke from wood fires.¹⁵⁶ Forest fires are a natural source of 1,3-butadiene.¹⁵⁶
- » The primary route of human exposure is inhalation, with the highest level of exposure occurring in occupational settings. Much lower levels of butadiene are generally detected in ambient air.¹⁵²

- There is sufficient evidence that exposure to 1,3-butadiene causes cancer of the hematolymphatic organs.¹⁵²
- Workers exposed to 1,3-butadiene have an approximately 1–3 times greater risk of cancer of the hematolymphatic organs,¹⁵⁷ with the highest risks from studies of workers

first employed before 1950. Evidence for cancer in humans comes largely from [cohort studies](#) of workers belonging to the styrene-butadiene rubber industry for leukemia, including evidence for a [dose-response](#) relationship, and the butadiene-monomer industry for hematolymphatic malignancies in general.¹⁵²

- An [ecologic study](#) showed evidence of a [dose-response](#) relationship for environmental levels of butadiene and the risk of childhood leukemia.¹⁵⁸
- There is strong evidence that the biologic mechanism through which 1,3-butadiene induces cancer involves the formation of reactive epoxides that interact with DNA and cause mutations.¹⁵²

FORMALDEHYDE

Background

- » Formaldehyde is a colourless gas at room temperature with a pungent odour, primarily used for the production of resins, which are often used in wood- and plastic-production industries. It is also used as an intermediate in the manufacturing of industrial chemicals and in aqueous solution (known as formalin) as a disinfectant and preservative.¹⁵²
- » Formaldehyde occurs naturally in the environment, primarily at low concentrations in the air.¹⁵² Its primary source in ambient air is automobile exhaust but it can also be emitted from sources such as particle boards, carpets, paints and varnishes, and combustion processes.¹⁵²
- » Routes of occupational exposure include inhalation of formaldehyde gas and particulates¹³⁵ and absorption through the skin and eye following contact with formalin solutions or liquid resins.¹⁰⁸

- There is consistent evidence that formaldehyde exposure causes cancer of the nasopharynx and now sufficient evidence that it causes leukemia, particularly myeloid leukemia.^{152,159} Limited evidence suggests that formaldehyde exposure may also cause sinonasal cancer. The evidence for nasopharyngeal cancer comes from a large [cohort study](#) of industrial workers exposed to formaldehyde in the US, as well as several large [case-control studies](#).¹⁵² The evidence for leukemia comes from proportionate mortality studies of professional workers (e.g., embalmers, funeral parlour workers, pathologists) and from two large industrial [cohort studies](#).¹⁵²
- Occupational exposures to formaldehyde increase myeloid leukemia risk by 10%–90%,^{160,161} with the upper end of the range for occupations known to have high exposures. The strongest evidence for a [dose-response](#) relationship has been observed for peak exposure levels.¹⁵²
- Occupational exposures to formaldehyde increase nasopharyngeal cancer risk by 10%–30%,^{160,162} although the risk increases as much as 2-fold with high occupational exposure.¹⁶³ Significant [dose-response](#) relationships have been observed for peak exposure, cumulative exposure and duration of exposure (for differentiated squamous cell and unspecified epithelial nasopharyngeal cancer).¹⁵²
- There is strong evidence that [genotoxicity](#) is the biologic mechanism responsible for the development of nasopharyngeal cancer and that formaldehyde causes cellular replication, which promotes [carcinogenicity](#).¹⁵² [Genotoxicity](#) may also be the underlying biologic mechanism causing leukemia,¹⁵² although further research is needed in this area.

MINERAL OILS, UNTREATED OR MILDLY TREATED

Background

- » Mineral oils are complex mixtures of hydrocarbons prepared from crude petroleum oil; their exact composition and physical properties depend on the crude oil and refining processes used.¹⁶⁴
- » Mineral oils are used in many products, including lubricants (e.g., engine oils, machining fluids, transmission fluids) and non-lubricant products (e.g., agricultural spray oils, printing inks).¹⁶⁴
- » Occupations with opportunities for mineral oil exposure include metalworking, printing-press operating, and cotton- and jute-spinning, with inhalation and skin absorption as important routes of exposure.¹⁵² Non-occupational exposure is largely from ingestion of contaminated food.¹⁵²
- » In the past, mineral oils were untreated or only mildly refined. Because of advances in refining processes in recent decades, however, most mineral oils in use today are highly refined.¹⁵²

- Based on occupational exposures, untreated or mildly treated mineral oils cause skin cancer, specifically of the scrotum.¹⁵² This conclusion was largely based on case reports and case series from the early 1900s to the 1960s, and further supported by several epidemiological studies of occupational exposures. It is thus largely from periods when mildly treated oils were still in use.
- There is an approximately 20% increased risk of skin cancer from exposure to mildly treated mineral oils,¹⁵² with higher risks observed in older studies of scrotal cancer. An increased risk for all skin cancers is observed, although the strongest evidence is for melanoma. Studies have seen up to a 2 times higher risk for melanoma from exposure to mineral-oil based metalworking fluids.¹⁶⁵ Magnitudes of risk relevant to current exposures were difficult to determine due to the change in [carcinogenicity](#) of the mineral oils currently used.
- There is weak evidence for the biologic mechanism causing skin cancer.¹⁵² Further research needs to be conducted.
- Current refining procedures used for mineral oils have reduced the levels of polycyclic aromatic hydrocarbons and other contaminants, thereby reducing the [carcinogenicity](#) of the oil. Since there are limitations in accessing direct exposure to highly-treated mineral oils, the International Agency for Research on Cancer (IARC) concluded that there is insufficient evidence for the [carcinogenicity](#) of highly-treated mineral oils.¹⁵²

OTHER INDUSTRIAL CHEMICALS

This section highlighted the most commonly used workplace chemicals in Canada, but there are other chemicals that have been classified as [carcinogenic](#) by IARC.¹⁵² Bis(chloromethyl) ether, chloromethyl methyl ether (technical grade), and sulfur mustard, for example, cause lung cancer and aflatoxins and vinyl chloride cause liver cancer. Other chemicals classified as group 1 [carcinogens](#) include: 2-Aminobiphenyl, benzidine, 2-Naphthylamine, ortho-toluidine, 2,3,7,8-tetrachlorodibenzo-*para*-dioxin, aristolochic acid, dyes metabolized to benzidine, ethylene oxide, 4,4'-methylenebis (2-chloroaniline), 3,4,5,3',4'-pentachlorobiphenyl (PCB-126), 2,3,4,7,8-pentachlorodibenzofuran. More information on the evidence supporting these [carcinogens](#) including the associated cancers sites can be found in the recent IARC review of Group 1 [carcinogens](#).¹⁵²