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Canadian Soil Quality Guidelines

For n-Hexane:

Protection of Environmental and Human Health

Scientific Supporting Document

PN 1454

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NOTE TO READERS

This scientific supporting document provides the background information and rationale for the development of Canadian Soil Quality Guidelines for the protection of environmental and human health for n-hexane. They were developed under contract by Meridian Environmental and Equilibrium Environmental Inc., with further revisions by Health Canada and Environment Canada. For additional technical information regarding these guidelines, please contact:

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The Canadian Soil Quality Guidelines are developed by the Soil Quality Guidelines Task Group of the Canadian Council of Ministers of the Environment (CCME). Environment Canada serves as the federal member and technical secretariat to this Task Group. These guidelines are included as updates in the *Canadian Environmental Quality Guidelines*, which was published by CCME in October of 1999. The Canadian Environmental Quality Guidelines are available online at http://ceqg-rcqe.ccme.ca/.

This scientific supporting document is available in English only. Ce document scientifique du soutien n'est disponible qu'en anglais avec un résumé en français.

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TABLE OF CONTENTS

LIST OF APPENDICES

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Canadian environmental quality guidelines, developed under the auspices of the Canadian Council of Ministers of the Environment (CCME), are numerical concentrations or narrative statements recommended to support and maintain designated resource uses. Canadian soil quality guidelines can be used as the basis for consistent assessment and remediation of contaminated sites in Canada.

This report was prepared by Health Canada (Contaminated Sites Division, Safe Environments Programme) and Environment Canada (Existing Substance Division, National Guidelines and Standards Office), the latter acting as federal member and technical secretariat for the CCME Soil Quality Guidelines Task Group. The Guidelines were derived according to the procedures described in *A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME, 2006).

Following the introduction, Chapter 2 presents chemical and physical properties of n-hexane and a review of the sources and emissions in Canada. Chapter 3 discusses n-hexane's distribution and behaviour in the environment. Chapter 4 discusses the pharmacokinectics of n-hexane in mammals and aquatic life, the mode of action of n-hexane, and the toxicological effects of n-hexane in humans, mammalian species, avian species, soil-dependent biota and soil microbial processes. The above information is reflected in Chapters 5 and 6, which outlines the derivation procedure for the calculation of soil quality guidelines for n-hexane to protect environmental and human receptors, respectively, in four types of land uses: agricultural, residential/parkland, commercial, and industrial.

The following soil quality guidelines for n-hexane are recommended by CCME based on the available scientific data. An environmental soil quality guideline (SQG_E) could not be derived because there was insufficient information to calculate the required plant and invertebrate soil contact pathway (SQG_{SC}), however, soil quality guidelines were calculated for Soil and Food Ingestion (SQG_I; provisional), Freshwater Life (SQG_{FL}; provisional), and Livestock Watering (SQG_{LW}; provisional) pathways. The human health soil quality guidelines (SQG_{HH}) are 0.49 $mg \cdot kg^{-1}$ for coarse soil and 6.5 $mg \cdot kg^{-1}$ for fine soil, for agricultural and residential land use, and 6.5 $mg \cdot kg^{-1}$ for coarse soil and 41 $mg \cdot kg^{-1}$ for fine soil, for commercial and industrial land use. The final soil quality guideline (SQG_F) is the lowest value generated by the two approaches (SQG_E and SQG_{HH}), therefore, the the final SQGs for n-hexane for the protection of both environmental and human health are 0.49 $mg \cdot kg^{-1}$ for coarse soil and 6.5 $mg \cdot kg^{-1}$ for fine soil, for agricultural and residential land use, and 6.5 $mg \cdot kg^{-1}$ for coarse soil and 41 $mg \cdot kg^{-1}$ for fine soil, for commercial and industrial land use.

RÉSUMÉ

Les recommandations canadiennes pour la qualité de l'environnement, élaborées sous les auspices du Conseil canadien des ministres de l'environnement (CCME), sont des valeurs de concentrations ou des énoncés décrivant des conditions recommandées afin d'assurer le maintien et le développement durable d'utilisations désignées des ressources. On peut se fonder sur les *Recommandations canadiennes pour la qualité des sols* pour conformer l'évaluation et l'assainissement des lieux contaminés au Canada.

Le présent document a été préparé par Santé Canada (Division de sites contaminés, Programme de la sécurité des milieux) et l'Environnement Canada (Bureau national des recommandations et des normes), qui fournit des services de secrétariat technique au groupe de travail du CCME sur les recommandations pour la qualité des sols. On a élaboré ces recommandations selon les procédures décrites dans le *Protocole d'élaboration de recommandations pour la qualité des sols en fonction de l'environnement et de la santé humaine* (CCME, 2006).

Après une brève introduction, le chapitre 2 présente les propriétés chimiques et physiques du n-hexane, de même qu'un aperçu des sources et des émissions au Canada; le chapitre 3 traite de la distribution et du devenir de cette substance dans l'environnement; le chapitre 4 examine le pharmococinétique du n-hexane chez les mammifères et les espèces aquatiques, le mode d'action et les effets toxicologiques du n-hexane chez l'être humain, les mammifères, la faune aviaire, le biote qui dépend du sol et sur les processus microbiens. Les chapitres 5 et 6 servent à l'élaboration des recommandations pour la qualité des sols pour le n-hexane en vue de protéger la santé humaine, selon quatre types d'utilisations des terrains (agricole, résidentielle/parcs, commerciale et industrielle).

Le CCME énonce les recommandations canadiennes suivantes pour la qualité des sols relatives au n-hexane sur la base des données scientifiques disponibles. En l'absence des données voulues pour calculer les recommandations pour la qualité des sols fondées sur le contact avec le sol (RQS_{CS}) requises pour les plantes et les invertébrés, il n'a pas été possible d'élaborer une recommandation canadienne pour la qualité des sols en fonction de l'environnement (RQS_E). Toutefois, des recommandations pour la qualité des sols relatives à l'ingestion de sol et de nourriture (RQS_I ; provisoire) et des recommandations pour la qualité des sols en vue de la protection de la vie aquatique ((RQS_{VA}; provisoire) et de l'eau d'abreuvement (RQS_{EA} ; provisoire) ont été calculées. Les recommandations pour la qualité des sols en fonction de la santé humaine (RQS_{SH}) s'établissent à 0,49 $mg \cdot kg^{-1}$ de sol à texture grossière et à 6,5 $mg \cdot kg^{-1}$ de sol à texture fine pour les sols destinés à des usages agricole et résidentiel, et à 6,5 $mg \cdot kg^{-1}$ de sol à texture grossière et à 41 $mg \cdot kg^{-1}$ de sol à texture fine pour les sols destinés à des usages commercial et industriel. La recommandation définitive proposée pour la qualité des sols (RQS_D) est la plus faible valeur générée par les deux approches (RQS_E et RQS_{SH}). Les recommandations définitives relatives au n-hexane proposées pour la qualité des sols en vue de la protection de la santé de l'environnement et de la santé humaine s'établissent donc à 0,49 $mg \cdot kg^{-1}$ de sol à texture grossière et à 6,5 $mg \cdot kg^{-1}$ de sol à texture fine pour les sols destinés à des usages agricole et résidentiel, et à 6,5 $mg \cdot kg^{-1}$ de sol à texture grossière et à 41 $mg \cdot kg^{-1}$ de sol à texture fine pour les sols destinés à des usages commercial et industriel.

ACKNOWLEDGEMENTS

This scientific assessment for the development of Canadian Soil Quality Guidelines for n-hexane was prepared through the efforts of Equilibrium Environmental Inc., Meridian Inc., as well as Health Canada and Environment Canada staff. The assistance of the members of the CCME Soil Quality Guidelines Task Group in providing review comments, is also gratefully acknowledged.

1.0 INTRODUCTION

Canadian Soil Quality Guidelines are numerical concentrations or narrative statements that specify levels of toxic substances or other parameters in soil that are recommended to maintain, improve or protect environmental quality and human health. They are developed using formal protocols to ensure nationally consistent, scientifically defensible values. The guidelines are nationally endorsed through the Canadian Council of Ministers of the Environment (CCME).

This report reviews the sources and emissions of n-hexane, its distribution and behaviour in the environment, and its toxicological effects on humans and other mammals (i.e. rodents, and lagomorphs), avian species, aquatic life (i.e. fish, crustaceans, invertebrates, worms, molluscs, algae, fungi, and moss) and soil biota (i.e. invertebrates and plants). Guidelines are derived according to *A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME, 2006) for various land uses: agricultural, residential/parkland, commercial and industrial. In addition, various check mechanisms considering indirect pathways of exposure (e.g., nutrient and energy cycling check and off-site migration of contaminants via wind and water erosion) are used to provide protection for resources and receptors not otherwise considered in the derivation of soil quality guidelines.

Exposure to n-hexane is currently regulated by the *Canada-Wide Standard for Petroleum Hydrocarbons (PHC) in Soil* (CCME, 2008), under which n-hexane is considered a component of PHC fraction 1 (F1); however, due to the unique toxic potential of n-hexane, the F1 guidelines may not be protective of environmental and human health in all circumstances (e.g., if a high proportion of n-hexane is present, or if n-hexane contamination is not due to PHCs). Specific environmental and human health guidelines for n-hexane, similar to those developed for other F1 components (benzene, toluene, ethylbenzene and xylenes) are therefore considered warranted.

The following derived Canadian soil quality guidelines (SQGs) are considered valid for general guidance purposes and may be applied to any area in Canada; however, site-specific information, including building construction practices, soil properties and local background concentrations should always be considered in the application of these guidelines. In addition, because the SQGs may be applied differently in various jurisdictions, the reader should consult the appropriate authorities for guidance on the use of Canadian SQGs within a specific province or region. The guideline represents a limit below which no adverse impacts are expected, but site-specific information should always be considered in the application of these guidelines.

2.0 BACKGROUND INFORMATION

2.1 Physical and Chemical Properties

n-Hexane (CAS# 110-54-3) is a straight-chain saturated aliphatic hydrocarbon compound (or alkane) with the chemical formula C_6H_{14}. Four additional isomers exist with the same chemical formula. Synonyms for n-hexane include hexane, normal hexane, dipropyl and hexyl hydride (AENV, 2004a; ATSDR, 1999). Commercial and industrial grades of hexane are a mixture of n-hexane and other hydrocarbon compounds; these substances may be identified as hexanes or commercial hexane, or by trade names such as Skellysolve B or NCI-C60571 (NLM, 2005). It is a component of the F1 hydrocarbon fraction defined by CCME (2008).

At standard temperature and pressure, n-hexane is a clear and colourless liquid, with a mild petroleum-like odour detectable at 65 to 248 ppm (WHO, 2000; NLM, 2005; National Pollutant Inventory Substance Profile, 2005; ATSDR, 1999). Hexane mixtures have a characteristic, slightly unpleasant odour (WHO, 1991). n-Hexane is not highly soluble in water (solubility of 9.5 mg/L) and has a moderate tendency to partition into hydrophobic environments (log K_{OW} of 4.11; MacKay *et al*., 2006, Gustafsen *et al*., 1997). It is miscible with most organic solvents (WHO, 1991, 2000). In liquid form, n-hexane is less dense than water; vapours are heavier than air. n-Hexane is highly flammable, and vapour/air mixtures are explosive (WHO, 2000). It reacts with some forms of plastic, rubbers, and coatings (National Pollutant Inventory Substance Profile, 2005). Based on the Henry's Law Constant (1.69 to 1.83 atm-m^3/mol), n-hexane is expected to volatilize rapidly from water surfaces (AENV, 2004a).

The physical and chemical properties of n-hexane are listed in Table 2-1.

Table 2- 1 Physical and Chemical Properties of n-Hexane

Property	Value	References
CAS number	110-54-3	Gustafson *et al*., 1997
Molecular formula	C_6H_{14}	
Structural formula	CH_3-CH_2-CH_2-CH_2-CH_2-CH_3	
Physical State	Liquid	ATSDR, 1999
Relative molecular mass	86.17	Gustafson *et al*., 1997; NLM, 2005
Melting point	-94.3 ^oC	NLM, 2005
Boiling point	68.95^oC 68.7^oC	Gustafson *et al*., 1997 NLM, 2005
Odor Threshold :Water	0.0064 mg/L	Amoore and Hautala, 1983
Odor Threshold :Air	130 ppm	Amoore and Hautala, 1983
Critical temperature	507.38 K	NLM, 2005
Critical pressure	3012 kPa	NLM, 2005
Vapour pressure	0.199 atm 120 mm Hg @ 20 ^oC 190 mm Hg @ 30 ^oC	Gustafson *et al*., 1997 NLM, 2005 NLM, 2005
Specific gravity	0.6593 0.6548 at 25 ^oC	Gustafson *et al*., 1997 NLM, 2005
Vapour density	2.97 (air = 1)	NLM, 2005
Water Solubility	9.5 mg/L	Gustafson *et al*., 1997; NLM, 2005
Octanol-Water Partitioning Coefficient (Kow)	$10^{4.11}$	Gustafson *et al*., 1997 MacKay *et al*., 2006
Organic Carbon Partitioning Coefficient (Koc)	3410 mL/g	Gustafson *et al*., 1997
Henry's Law Constant	73.9 (unitless) 1.69 atm-m^3/mol 1.81 atm-m^3/mol 1.83 atm-m^3/mol	Gustafson *et al*., 1997 ATSDR, 1999 HSDB, 2005 NLM, 2005
Bioconcentration Factor in Fish	174 to 776 453	HSDB, 2005, ATSDR, 1999
Half life in water	volatilization 2.7 days (model river) volatilization 6.8 days (model lake)	ATSDR, 1999; Mackay *et al.*, 1993; HSDB, 2005
Half life in air	Photochemical reactions with hydroxl radicals 2.9 days	ATSDR, 1999; Mackay *et al.,* 1993; HSDB, 2005
Diffusivity in Air	0.2 cm^2/s	Gustafson *et al*., 1997
Diffusivity in Water	$7.77x10^{-6}$ cm^2/s	Gustafson *et al*., 1997
Saturation concentration in air	564 g/m^3 @ 20 ^oC	NLM, 2005

2.2 Analytical Methods

There are a variety of analytical methods available to quantify n-hexane in environmental matrices (refer to Table 2-2). Gas chromatography/flame ionization detector (GC/FID) and gas chromatography/mass spectrometry (GC/MS – US EPA Method 8260B) are commonly used to quantify n-hexane concentrations (ATSDR, 1999). Environmental samples with low concentrations of n-hexane may require a pre-concentrating step prior to GC analysis (ATSDR, 1999). Gas purge and trap, headspace extraction gas analysis and extraction with organic solvents are the three basic approaches for determining trace amounts of n-hexane in aqueous and other environmental media (ATSDR, 1999).

Table 2- 2 Analytical Methods for Determining n-Hexane in Environmental Samples

Sample Matrix	Preparation Method	Analytical Method	Sample Detection Limit	Percent Recovery	Reference
Water	Purge and trap	GC/FID	approximately 0.05 µg/L	not reported	Biziuk *et al.,* 1996
		capillary GC/MS	low to sub-ppb levels µg/L	90-120	Michael *et al.,* 1988
		capillary GC/FID	35-1,760 µg/L (gasoline)	77	Belkin and Hable, 1988
	Distillation; purge and trap	GC/FID	not reported	83-87	Kozloski, 1985
Water and soil	Headspace extraction	GC/MSD	0.5 µg/L	not reported	Roberts and Burton, 1984
Soil	Supercritical fluid extraction	capillary GC/FID	not reported	86-90 (trapping efficiency	Yang *et al.,* 1995
Sediment	Elevated temperature dynamic headspace extraction	capillary GD/FID, GC/ITD	20 ng/kg	not reported (bias 2 to 16 %)	Bianchi *et al.,* 1991

Notes:
FID = flame ionization detector; GC = gas chromatography; MS = mass spectrometry; ITD = ion trap detector

The high volatility of n-hexane makes reliable sampling challenging, since sample disturbance is likely to result in loss of the analyte, particularly from coarse or loose soils. The collection of undisturbed samples and the use of appropriate headspace-free containers are therefore critical for the evaluation of n-hexane concentrations in soil or water.

Currently, analyses for n-hexane in soil are not routinely performed in most jurisdictions. Based on discussions with a small sample of Canadian analytical laboratories, it is anticipated that analytical detection limits less than 0.02 mg/kg could be achieved in soil.

2.3 Production and Uses in Canada

n-Hexane is a naturally occurring component of crude oil and natural gas, and is therefore also found in many refined petroleum products. n-Hexane has been reported to comprise, on average, approximately 1.1% of gasoline (by weight) and 2.4% of JP-4 fuel oil (Potter and Simmons, 1998); modern high octane gasolines may include 3% n-hexane by weight (ATSDR, 1999). n-Hexane is also a component of glues, rubber cement, paints, coatings and adhesives (ATSDR, 1999; NLM, 2005), and is used in low temperature thermometers (NLM, 2005). High purity hexane is used as a laboratory reagent (ATSDR, 1999). Small amounts of n-hexane may also be emitted biogenically by marine phytoplankton (McKay *et al*., 1996), terrestrial plants (Rinnan *et al.,* 2005) and fungi (Ahearn *et al.,* 1996).

A major use of n-hexane is to extract vegetable oils from crops, including soybeans, canola, flaxseed, peanuts, safflower, corn germ and cottonseed, and in the production of defatted products such as defatted soy flour (ATSDR, 1999; WHO, 1991). Solvents containing n-hexane are also used as cleaning agents or degreasers for the printing, textile, furniture, shoemaking and leather industries (ATSDR, 1999), in rubber polymerization, and in the manufacture of polyoleins, elastomers, cosmetics and pharmaceuticals (NLM, 2005; WHO, 1991).

A total of 328 facilities reported n-hexane emissions to the National Pollutant Release Inventory (NPRI) in 2005, with total reported releases of 4558 tonnes (Environment Canada, 2007). The largest individual emitters (greater than 100 tonnes) included chemical producers, food manufacturers, petroleum facilities, oil sands mines, a manufacturer of adhesive tape and plastic film, and a steel foundry. These releases were predominantly to the atmosphere, mainly from stack/point sources or fugitive emissions. The NPRI tracks only large emitters, and therefore these releases do not represent the total amount of n-hexane entering the environment.

Major sources of n-hexane in soil include leaking petroleum storage tanks, or petroleum product spills during storage, transportation and handling. n-Hexane is particularly likely to be present in petroleum hydrocarbon-contaminated soils with a gasoline source. However, n-hexane may also enter soil from solvent spills and releases.

2.4 Concentrations in the Canadian Environment

2.4.1 Atmosphere

n-Hexane concentrations in ambient air at 39 monitoring stations across Canada between 1993 and 1995 ranged from less than the detection limit of 0.1 $\mu g/m^3$ to 242 $\mu g/m^3$, with a mean concentration of 2.03 ± 2.87 $\mu g/m^3$ (OMOE, 2005).

Half-hour average concentrations measured in Ontario between 1994 and 1996 ranged from the detection limit of 0.02 $\mu g/m^3$ to 110 $\mu g/m^3$. The highest concentrations were measured in the vicinity of Sarnia (110 $\mu g/m^3$ in 1994) and Vineland (95 $\mu g/m^3$ in 1996) (OMOE, 2005).

Ambient air quality monitoring was conducted at several locations in Quebec from 1995 to 1999. Average (annual) concentrations were 3.41 $\mu g/m^3$ at Pointe-aux Trembles (industrial setting),

1.53 μg/m^3 at rue Ontario, Montreal (urban setting), 2.56 μg/m^3 at rue Maisonneuve, Montreal (urban setting), 0.53 μg/m^3 at station Brossard, Montreal (suburban setting) and 0.23 μg/m^3 at Sainte-Françoise (rural setting) (Gouvernement du Québec, 2002).

Monitoring of n-hexane in ambient air has also been conducted in Alberta. Twenty-four hour average concentrations measured in 2001 ranged from 0.340 to 3.610 μg/m^3 with a mean of 1.078 μg/m^3 at the Calgary Central monitoring station, from 0.480 to 3.620 μg/m^3 (mean = 1.387 μg/m^3) at the Edmonton Central monitoring station, and from 0.740 to 25.55 μg/m^3 (mean = 5.443 μg/m^3) at the Edmonton East monitoring station (AENV, 2004b). A survey conducted in the Town of Banff in November 2002 reported one-hour average n-hexane concentrations on two sampling days of 0.87 μg/m^3 and 1.23 μg/m^3 (AENV, 2002). A monitoring program in the Fort Saskatchewan/Redwater area reported average 24-hour concentrations of 0.486 μg/m^3 for October and November 2001;, 0.223 μg/m^3 for March through May 2002, 0.270 μg/m^3 for June through July 2002, and 0.282 μg/m^3 for August 2002, with an overall maximum 24-hour concentration of 1.650 μg/m^3 (AENV, 2004b).

Monitoring at four Canadian rural locations in 1991 found monthly mean n-hexane concentrations to range from 0.07 to 0.5 μg/m^3 at Kejimkujik National Park, Nova Scotia, from 0.07 to 0.28 μg/m^3 at Lac la Flamme, Quebec, from 0.1 to 0.35 μg/m^3 at Egbert, Ontario, and from 0.035 to 0.32 μg/m^3 at Saturna Island, British Columbia (Bottenheim and Shepherd, 1995).

Only limited data were identified for n-hexane concentrations in indoor air in Canada. A Canada-wide study conducted in 1991-1992 found a mean concentration of 1.2 μg/m^3 and a maximum concentration of 124 μg/m^3 (Davis and Otson, 1996). The mean concentration in samples collected in Toronto from February to April 1996 was 5.24 μg/m^3 (Otson and Zhu, 1997).

A study of California office buildings (Daisey *et al.,* 1994) found a geometric mean n-hexane concentration of 1.9 μg/m^3, and indoor-to-outdoor air ratios ranging from 0.26 to 18. Concentrations can be much higher in poorly-ventilated occupational settings; concentrations exceeding 1750 μg/m^3 have been reported at some locations where n-hexane is used (ATSDR, 1999).

2.4.2 Soil/Sediments

n-Hexane may be present in soils contaminated with petroleum hydrocarbons, particularly soils contaminated with gasoline, or at the locations of hexane spills. No data were identified for n-hexane concentrations in uncontaminated soils or sediments. Soil vapour concentrations were measured in five volatile petroleum hydrocarbon (VPH) contaminated sites in western Canada. The concentrations of n-hexane ranged from <0.02 mg/m^3 to 24 mg/m^3 (Sevigny *et al*., 2003). Soil vapour concentrations for n-hexane were measured in eight US National Priorities List (NPL) contaminated sites. The concentrations of n-hexane ranged from 0.0067 mg/m^3 to 220,000 mg/m^3 (HazDat, 2008). n-Hexane was also identified in soil samples collected from three NPL contaminated sites. The concentration of n-hexane ranged from 0.316 mg/kg (subsurface topsoil, depth < 7.6 cm) to 0.72 mg/kg (subsurface soil, depth > 7.6 cm) (HazDat, 2008).

2.4.3 Water

There are few studies examining n-hexane concentrations in water. n-Hexane was measured in one groundwater monitoring well (0.0006 mg/L) and one public/municipal groundwater location (0.091 mg/L) in two contaminated sites (HazDat, 2008). No data were identified regarding background n-hexane surface water. n-Hexane is readily volatilized from water, and it is expected that n-hexane would volatilize in most municipal water treatment systems before entering water supply systems (ATSDR, 1999). Subsurface releases of n-hexane (e.g. gasoline releases from underground storage tanks) may result in n-hexane contamination of groundwater, where it may persist in anoxic conditions (ATSDR, 1999).

2.4.4 Biota/Food

No studies examining n-hexane concentrations in biota are currently available. Based on the properties of n-hexane, it is likely rapidly metabolized and is not expected to bioaccumulate.

n-Hexane is not routinely monitored in foods and no Canadian data are available. n-Hexane is commonly used to extract plant oils and in the production of defatted products such as defatted soy flour. Hexane concentrations in five brands of extra-virgin olive oil ranged from 19.1 ng/mL to 95.3 ng/mL (Overton and Manura, 1995). Mean hexane residues were <0.9 mg/kg in peanut oil and <1.5 mg/kg in sunflower oil (Hautfenne *et al*., 1987).

ATSDR (1999) suggested that n-hexane intake from food would likely be no more than 2.21 µg/kg-bw/day, but this estimate is based on very limited data.

2. 5 Existing Guidelines and Criteria in Various Media

Many regulatory agencies include n-hexane in their consideration of petroleum hydrocarbon mixtures, but do not explicitly define guidelines for n-hexane. There are currently no Canadian Environmental Quality Guidelines identifying acceptable concentrations of n-hexane in air, water, sediment, soil, or tissue residue. Environmental quality guidelines for n-hexane have been established by several provincial or state regulatory agencies (see Table 2-3).

The US Food and Drug Administration (FDA) has specified maximum residue limits (MRL) of 25 ppm for n-hexane in spice oleoresins, 25 ppm in modified hop extract for beer, and 5 ppm in fish protein isolate (FDA, 2006). Neither Health Canada nor the WHO have established MRLs for n-hexane; the WHO (1970) recommends that "use of hydrocarbon solvents should be restricted to that determined by good manufacturing practice, which is expected to result in minimal residues unlikely to have any significant toxicological effect."

Table 2- 3 Summary of Existing Guidelines and Criteria for n-Hexane

Jurisdiction	Medium	Guideline/Criterion	Reference
U.S.	Soil	570 mg/kg (residential) 2600 mg/kg (industrial)	ORNL, 2008
	Indoor Air	0.73 mg/m^3 (residential) 3.1 mg/m^3 (industrial)	
Michigan	Soil	58 mg/kg (protection of groundwater) 3.2x10^5 mg/kg (direct soil contact)	Michigan DEQ, 1994
	Groundwater	2.9 mg/L (drinking water value)	
Nebraska	Soil	85 mg/kg (residential direct contact) 480 mg/kg (industrial direct contact) 5.1 mg/kg (migration to groundwater)	Nebraska DEQ, 2006
	Groundwater	0.1 mg/L	
Maine	Indoor Air (Residential)	0.4 mg/m^3 (subchronic action level) 0.2 mg/m^3 (chronic action level)	Maine DEP,1998
Ontario	Ambient Air	2.5 mg/m^3 (24-hour average) 7.5 mg/m^3 (Point of Impingement)	OMOE, 2005
Quebec	Ambient Air	0.01 mg/m^3 (continuous lifetime daily exposure)	Gouvernment du Québec, 2002
Louisiana	Ambient Air	4.19 mg/m^3 (8-hour average)	Louisiana DEQ, 2003
New York State	Ambient Air	0.2 mg/m^3 (annual average)	NY DEC, 2003
North Carolina	Ambient Air	1.1 mg/m^3 (24-hour average)	NC ENR, 2007
Oklahoma	Ambient Air	17.628 mg/m^3 (24-hour average)	Oklahoma DEQ, 2006
Vermont	Ambient Air	4.29 mg/m^3 (24-hour average)	Vermont ANR, 2003
Washington State	Ambient Air	0.2 mg/m^3 (24-hour average)	Washington DOE, 1998

Chemicals Management Plan: N-hexane Screening Assessment Information:

Hexane was risk-assessed under the Canadian Environmental Proterction Act by both Health Canada and Environment Canada in August 2009 under the Chemical Management Plan (CMP). The screening assessment concluded that *n*-hexane is not entering the Canadian ambient environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health. The assessment looked at releases during production (refining) of hydrocarbons and handling, especially, of fuels, but contaminated sites were not specifically examined. The screening assessment reports are available from http://www.ec.gc.ca/substances/ese/eng/challenge/batch4/batch4_110-54-3_en.pdf or http://www.ec.gc.ca/substances/ese/fre/challenge/batch4/batch4_110-54-3_fr.pdf

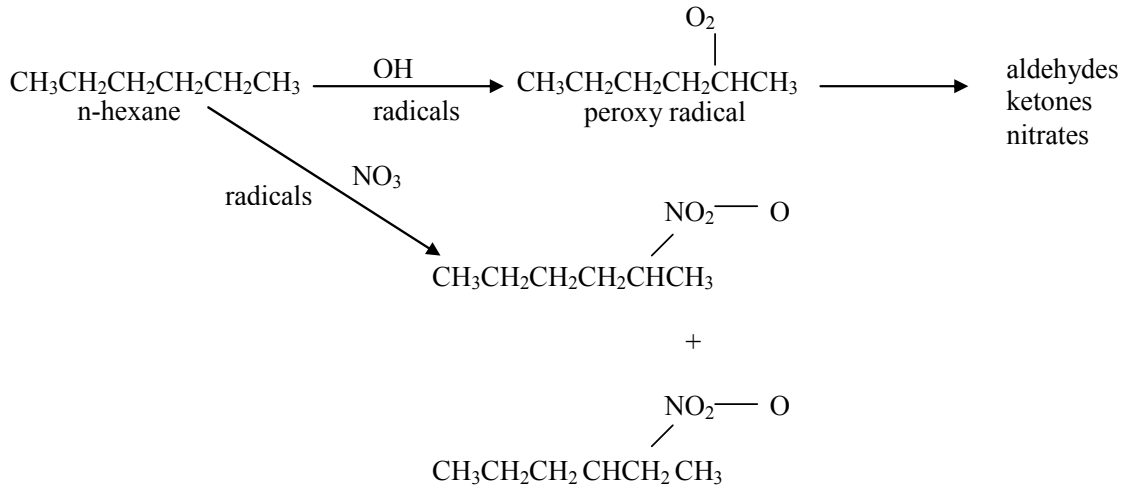
3.0 ENVIRONMENTAL FATE AND BEHAVIOUR

The transport and partitioning of n-hexane in the environment are governed by its physical properties, including water solubility, octanol/water partition coefficient (log K_{OW}), Henry's law constant, vapour pressure, and organic carbon partition coefficient (log K_{OC}). Values for these properties are provided in Table 2-1.

3.1 Atmosphere

n-Hexane has a relatively high vapour pressure (153 mm Hg at 25°C) and is therefore expected to be present almost entirely in the vapour phase in the atmosphere (NLM, 2005). The proposed decomposition of n-hexane in air is shown in Figure 3-1. The primary mechanism of n-hexane degradation in the atmosphere is believed to be reaction with photochemically-produced hydroxyl radicals; the estimated half-life of this reaction is approximately two to three days (ATSDR, 1999; NLM, 2005; WHO, 1991). Hexane does not absorb ultraviolet light (290 nm) and is not expected to undergo direct photolysis (ATSDR, 1999).

Figure 3- 1 Degradation of n-Hexane in Air by Free Radicals



Source: Atkinson, 1985.

Theoretically, n-hexane can react with nitrogen oxides to produce ozone precursors; however, the potential for n-hexane to produce smog is considered to be very low compared to other alkanes and chlorinated organic compounds (ATSDR, 1999). n-Hexane is resistant to hydrolysis (ATSDR, 1999) and is not expected to physically affect the atmosphere, cause ozone depletion, or affect precipitation patterns (WHO, 1991).

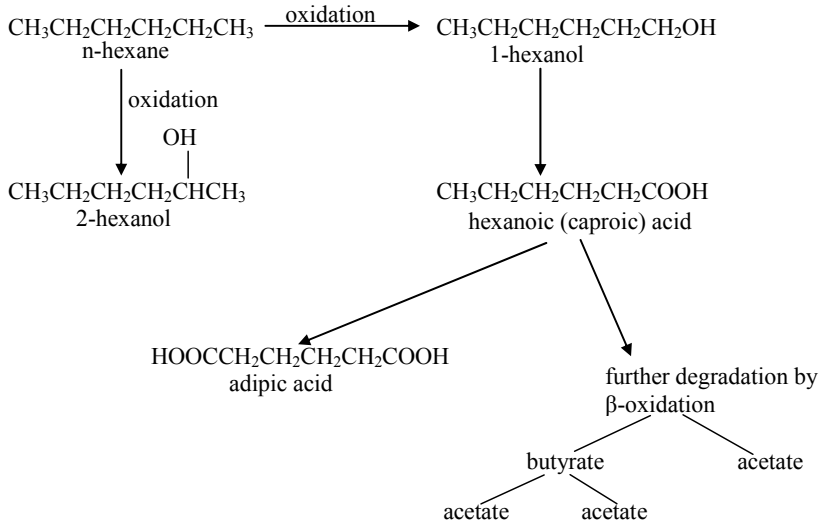
3.2 Soil and Sediment

The high vapour pressure and Henry's Law constant for n-hexane indicate that it is likely to volatilize rapidly from surficial soils. Adsorption to soil particles is considered moderate, given

the relatively low Koc (AENV, 2004b; ATSDR, 1999); however, n-hexane may persist in deeper soils, particularly if the oxygen content is low or nutrients are limited (ATSDR, 1999). The relatively low water solubility of n-hexane indicates that relatively little will dissolve in surface water or groundwater. n-Hexane is less dense than water and will be present as a light non-aqueous phase liquid at high concentrations (above solubility limits) (Feenstra *et al*., 1991; Hunt *et al.*, 1988; ATSDR, 1999). Since it is likely to float on the water table and is only moderately adsorbed to soil particles, n-hexane contamination is expected to be mobile and spread along the top of the saturated zone.

Volatilization is believed to be much more rapid than chemical or biochemical degradation; however, n-hexane can be converted into primary alcohols, aldehydes and ultimately fatty acids (ATSDR, 1999). n-Hexane biodegradation products and metabolic pathways (as determined in a pure culture of *Pseudomonas*) are shown in Figure 3-2. Aerobic degradation is often assumed to be higher for low molecular weight aliphatics than heavier hydrocarbons; however, in field studies, aerobic degradation of n-hexane vapours in soil is slower than for n-octane or n-decane, with a first-order decay rate constant of approximately 0.24 d^{-1} (Höhener *et al*., 2003). Degradation rates are affected by numerous factors, including oxygen, soil properties, and microbial communities.

Figure 3- 2 Aerobic Biodegradation of n-Hexane in Sediment and Soil



Source: Heringa et al., 1961

In an activated sludge inoculum, n-hexane and 12 other components of gasoline were degraded completely in less than 30 days (Solano-Serena *et al.,* 2000). In a separate experiment, high octane gasoline (100 µl/L or 7,550 µg/L based on density of octane gasoline of 0.755 g/cm^3 at 15°C) including n-hexane (1.36 µL/L or 0.89 mg/L based on a density of 0.655; HSDB, 2005) was incubated with natural flora in groundwater at 13°C. After 192 hours, biodegradation reduced n-hexane concentrations by 46% (Verschueren, 1983; HSDB, 2005).

3.3 Water

The high vapour pressure and Henry's Law constant for n-hexane indicate that it is likely to volatilize rapidly from water surfaces. In mathematical models developed by EPA, the volatilization half-lives of n-hexane were less than 3 hours in rivers (any degree of turbulent mixing) and shorter than 6.8 days in lakes (standing bodies of water) (AENV, 2004a; ATSDR, 1999; HSDB, 2005). n-Hexane is slightly soluble in water. It is readily absorbed by the lipid phase of aquatic organisms, which can facilitate its transport in the environment (National Pollutant Inventory Substance Profile, 2005). Biodegradation of n-hexane in surface water or groundwater has been shown to occur in laboratory and field studies, particularly under aerobic conditions (McClay *et al*., 1995; Rosenberg *et al*., 1992; ATSDR, 1999).

Based on these properties, n-hexane is not expected to persist in most surface water unless there is an on-going source. However, it may persist in groundwater, particularly under anaerobic or low-nutrient conditions (ATSDR, 1999).

3.4 Biota

3.4.1 Soil Microbes

Several types of bacteria have been observed to metabolize n-hexane. Aerobic catabolism is believed to be the dominant mechanism of n-hexane degradation in soils with adequate oxygen (Leahy and Colwell, 1990). However, in some soils oxygen and nutrient concentrations may not be adequate for aerobic degradation.

Certain denitrifying bacteria are able to oxidize n-hexane anaerobically (Rabus *et al*, 2001), forming (1-methylpentyl) succinate, which in turn is converted to methyl-branched fatty acids (Wilkes *et al*., 2002) and eventually CO_2 (Wilkes *et al*., 2006). Each species of denitrifying bacteria metabolizes a specific range of alkanes, and only certain species can metabolize n-hexane (Ehrenreich *et al*., 2000), indicating that microbial community composition may affect degradation rates. Sulphate-reducing and iron(III)-reducing bacteria have also been shown to metabolize alkanes, including n-hexane, anaerobically (Harayama *et al*., 2004).

3.4.2 Terrestrial Plants

No information was identified on metabolic pathways of n-hexane in plants. Phytoremediation has been applied for sites with petroleum hydrocarbon contamination. Maize growing normally in petroleum hydrocarbon-contaminated soil did not accumulate saturated alkanes (Chaîneau *et al*., 1997) The presence of plants reduced diesel fuel concentrations in arctic soils, particularly lighter alkanes; however, plants did not appear to significantly bioaccumulate these compounds (Palmroth *et al*., 2002).

n-Hexane may also be produced and biogenically emitted by terrestrial plants (Rinnan *et al*., 2005) and fungi (Ahearn *et al*., 1996).

3.4.3 Terrestrial Invertebrates

No specific information was found on metabolism of n-hexane by terrestrial invertebrates. Blue crabs have been shown to take up and discharge n-alkanes, but not metabolize them (Geiszler *et al*., 1977). However, the relevance of this study to terrestrial invertebrates is unknown.

3.5 Bioconcentration

n-Hexane is unlikely to be concentrated in biota, based on values for log K_{OC} and log K_{OW} (Swarm *et al*., 1983). A bioconcentration factor (BCF) of n-hexane in fathead minnow was calculated to be 453 and it was concluded that the bioconcentration and bioaccumulation potential for n-hexane in aquatic and terrestrial food chains is low (AENV, 2004b; ATSDR, 1999). Syracuse Research Corporation (SRC) estimated a BCF of 200 (HSDB, 2005), from a log K_{OW} of 3.09 (Hansch *et al.,* 1995) and a regression-derived equation (Meylan *et al.,* 1999; HSDB, 2005). SRC concluded that the potential for bioconcentration in aquatic organisms is high (HSDB, 2005), which contrasts with the conclusion of AENV (2004) and ATSDR (1999). Beek (2000) considers a BCF range of 100 to 1000 to be indicative of a high potential for bioaccumulation. Based on estimated BCFs of 453 and 200 for n-hexane, the potential for bioconcentration of in aquatic life may be considered high from these definitions. The Canadian Council of Ministers of the Environment stated in, *Protocol for the Derivation of Canadian Tissue Residue Guidelines for the Protection of Wildlife that Consume Aquatic Biota* (CCME, 1999a) that a substance with a bioconcentration or bioaccumulation factor of less than 5000 (or a log K_{OW} of < 5) would not tend to concentrate or accumulate in aquatic biota. This criterion is also used for assessing bioaccumulation of substances under the federal Toxic Substances Management Policy and has been selected as an appropriate criterion for evaluating n-hexane bioavailability for the purposes of the development of this SQG. Based on the log K_{OW} and estimated BCFs, significant bioconcentration/bioaccumulation is not expected for n-hexane.

4.0 BEHAVIOUR AND EFFECTS IN HUMANS, EXPERIMENTAL ANIMALS AND BIOTA

4.1 Absorption, Distribution, Metabolism and Excretion

4.1.1 Mammals

Absorption

Inhaled n-hexane may be absorbed via the lungs. A significant proportion of the inhaled dose is not absorbed and is exhaled as unchanged n-hexane in rats (Bus *et al*., 1982). Absorption of n-hexane (87 to 122 ppm for periods of up to 4 hours) in a group of Japanese men and women aged 18 to 25 averaged 27.8 ± 5.3% with retention as low as 5.6 ± 6.2% (Nomiyama and Nomiyama, 1974). Mutti *et al*. (1984) estimated that the absorption rate of n-hexane in the lungs was approximately 17% in humans. Human volunteers exposed to 102 or 204 ppm n-hexane for 4 hr absorbed approximately 20 to 25% of the inhaled dose (Veulemans *et al.*, 1982).

n-Hexane is also absorbed following oral exposure, although few studies were identified where bioavailability was quantified. In human volunteers administered 0.24 or 0.81 mg/kg n-hexane by gastrointestinal tube, n-hexane was detected in exhaled air and the metabolite 2,5-hexanedione was excreted in urine (Baelum *et al.*, 1998). Guinea pigs administered a single 660 mg/kg bolus of n-hexane orally, had a peak blood concentration of 200 µg/mL after 30 minutes (Couri *et al*., 1978).

n-Hexane, as liquid or vapour, may also be absorbed following dermal exposure. Percutaneous transfer of n-hexane has been demonstrated using isolated preparations of human skin (Loden, 1986). After an initial period of rapid absorption into the skin, the steady-state percutaneous n-hexane transfer rate was 0.83 µg-cm^2/hr, 100-fold lower than other chemicals such as benzene and ethylene glycol. Application of neat n-hexane to approximately 1% of the total skin surface area of Fischer-344 rats resulted in significant dermal absorption, with peak blood n-hexane concentrations of 8 µg/mL four hours post-application (Morgan *et al.*, 1991). Dermal absorption from aqueous solutions was also observed, with blood concentrations correlating with dissolved n-hexane concentrations (Morgan *et al.*, 1991).

A rat dermal n-hexane vapour permeability constant of 0.031 cm/hr was estimated based on whole-body exposure to high vapour concentrations of n-hexane (60,000 ppm) (McDougal *et al.*, 1990). Steady-state blood n-hexane concentrations of 0.7 µg/mL (10-fold lower than for dermal application of neat n-hexane; Morgan *et al*., 1991) were achieved within an hour (McDougal *et al.*, 1990). Dermal absorption of n-hexane vapours has been estimated to account for approximately 0.1% of the total internal dose as compared to pulmonary absorption (McDougal *et al.*, 1990)[1].

1 As the experimental data indicate that inhalation, oral and dermal absorption of n-hexane occurs, a multi-route exposure assessment for n-hexane in drinking water was carried out in order to estimate the total dose that may be attributed to the drinking water supply. This assessment is based on physical and

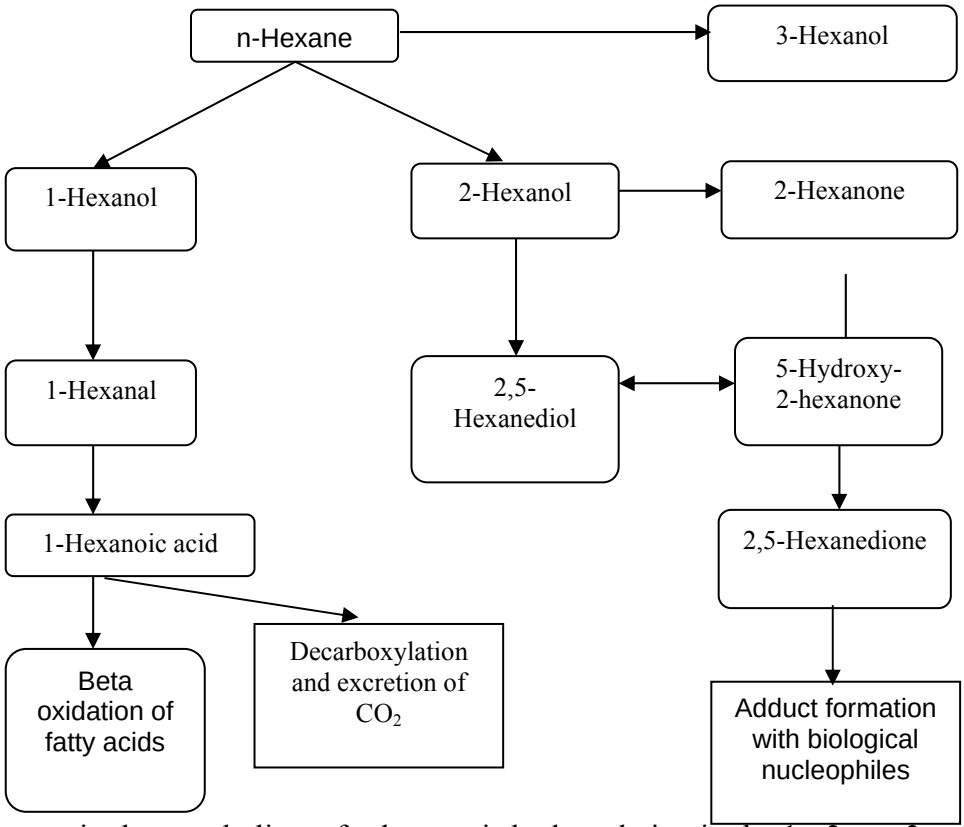
Distribution

In rats, n-hexane is distributed to most tissues including the kidney, liver, lung, brain and testes, (Baker and Rickert, 1981) as well as peripheral nerves. Steady-state concentrations are generally proportional to tissue lipid content, and were achieved in less than one hour with exposures of up to 10 000 ppm n-hexane (Baker and Rickert, 1981).

Metabolism

n-Hexane is metabolized into both non-neurotoxic and neurotoxic metabolites by cytochrome P-450 enzymes located primarily in the liver, with significant metabolism also occurring in other tissues including lung, brain, and skeletal muscle (Crosbie *et al*., 1997). The metabolism of n-hexane is summarized in Figure 4-1.

Figure 4- 1 Primary Metabolic Pathways for n-Hexane



The first step in the metabolism of n-hexane is hydroxylation in the 1-, 2-, or 3- position leading to formation of 1-hexanol, 2-hexanol, and 3-hexanol, respectively. The primary metabolite in rats and humans is 2-hexanol. Rats exposed to 1-hexanol do not develop neurotoxicity, whereas rats exposed to 2-hexanol develop neuropathy (Perbellini *et al*., 1978).

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chemical properties of n-hexane for standard conditions of bathing and showering, rather than experimental data. See Appendix IV.

n-Hexane is further metabolized to 2,5-hexanedione through several intermediate metabolites (see Figure 4-1) with progressively greater toxic potencies, as shown below (Anderson and Dunham, 1984; Misumi and Nagano, 1984; Krasavage *et al.*, 1980; Perbellini, *et al.*, 1978):

n-hexane < 2-hexanol < 2-hexanone < 5-hydroxy-2-hexanone < 2,5-hexanedione

One important metabolite not shown in Figure 4-1 is 4,5-dihydroxy-2-hexanone, the second most abundant metabolite excreted in the urine of rats exposed to n-hexane. Formation of this metabolite may be a detoxification pathway for 2,5-hexanedione or its precursor, 5-hydroxy-2-hexanone (Fedke and Bolt, 1987). The toxicity of n-hexane is attributed to its metabolites, and in particular 2,5-hexanedione, rather than the parent compound (ATSDR, 1999).

Excretion

There are three primary excretion routes for *n*-hexane: exhalation of unchanged n-hexane (Baelum *et al*., 1998); exhalation as metabolic CO_2 following metabolism to 1-hexanol and subsequent decarboxylation; and elimination of metabolites in urine (Bus *et al*., 1982). Fecal excretion of n-hexane does not appear to be a significant elimination pathway (Bus *et al*., 1982; DiVincenzo *et al.*, 1977). Rats administered radiolabelled 2-hexanone (a metabolite of n-hexane) via gavage excreted 1.4% of the total dose in feces and 40% in urine (DiVincenzo *et al*., 1977).

n-Hexane metabolites (e.g., 1-hexanol, 2-hexanol, 2,5-hexanedione) are excreted in urine primarily as glucuronide conjugates (Baker and Rickert, 1981).

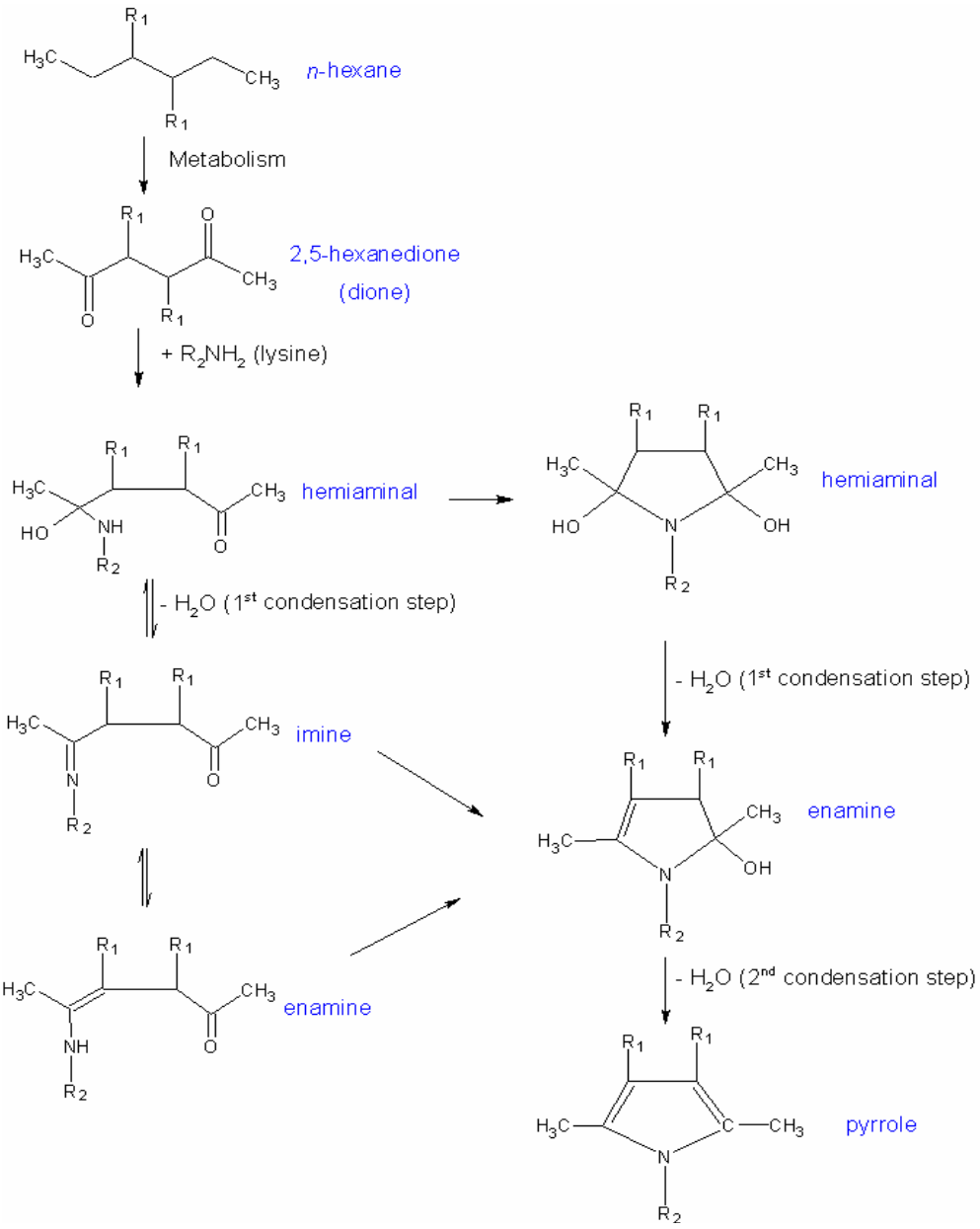
4.1.2 Aquatic Life

Fish are exposed to n-hexane from water contacting the skin and passing over the gills during respiration, and following ingestion of n-hexane in food (Vandermeulen, 1987). Due to the low solubility of n-hexane in water, concentrations in fish tissue are expected to be equivalent to concentrations of n-hexane in the surrounding water (Vincoli, 1997). No information was available in the literature regarding the bioavailability of n-hexane in other aquatic life (i.e. crustaceans, invertebrates, molluscs, etc).

4.2 Mechanism of Action

Several mechanisms of action for the neurotoxic metabolite of n-hexane (2,5-hexanedione) have been proposed for rodent and avian species. It is postulated that 2,5-hexanedione binds to biological nucleophiles (*e.g.*, the side chain of lysine amino acids) resulting in the formation of pyrrole adducts. The formation of pyrrole adducts and subsequent pyrrole-mediated protein crosslinking may alter the rate of transport of neurofilament proteins in the axons of nerve cells (Pyle *et al.*, 1992). This mechanism may also be responsible for observed effects on the testes of male rodents. Pyrrole formation between 2,5-hexanedione and biological molecules has been correlated with neurotoxic potency. A proposed reaction mechanism leading to the formation of pyrroles is provided in Figure 4-2.

Figure 4- 2 Hypothesized Reaction for the Binding of 2,5-Hexanedione to Amino Acids



Source: DeCaprio et al., 1987. Note: R_2 – biological molecule with a nitrogen group

Protein binding and formation of pyrrole adducts between 2,5-hexanedione and γ-amino groups has been demonstrated *in vitro* using synthesized amines (*e.g.*, ethanolamine) and biological molecules (*e.g.*, serum globulin, bovine serum albumin, and lysine; DeCaprio *et al.*, 1982). Protein binding to and pyrrole formation with serum globulin and neurofilament proteins has been demonstrated in rats and hens following multiple exposures to 2,5-hexanedione *in vivo* (Pyle *et al.*, 1992; DeCaprio *et al.*, 1987; DeCaprio *et al.*, 1983).

4.3 Mammalian Toxicology

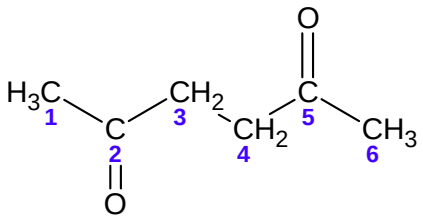
Inhalation and oral exposures to n-hexane are known to produce neurological, reproductive, and visual system toxicity. Respiratory effects associated with inhalation exposure to n-hexane have been demonstrated in animal studies at concentrations greater than those required to elicit neurological and reproductive toxicity. These endpoints are introduced below.

4.3.1 Neurotoxicity

Epidemiological studies conducted during the 1960s to 1980s described a novel sensori-motor peripheral neuropathy occurring in workers exposed to petroleum-based solvents containing n-hexane. Symptoms of the sensori-motor neuropathy include paraesthesia and weakness in the legs, sensory impairment to touch and pain, paralysis of arms and legs, poor reflexes and reduced nerve conduction velocity. The neurotoxic syndrome developed in Japanese sandal making workers (Yamamura, 1969; Yamada, 1964), Italian shoemakers (Abbritti *et al.*, 1976; Mutti *et al.*, 1982), Taiwanese press proofing workers (Wang *et al.*, 1986), and American tungsten carbide milling workers (Sanagi *et al.*, 1980) following exposures of less than a year in duration to 25 years or more. In the 1990s, similar neurotoxic effects were noted among workers in a leather coat and shoe production facility (Oge *et al.*, 1994), a luggage factory (Yuasa *et al.*, 1996), and in automotive repair shops (Harrison *et al.*, 2001). The identification of n-hexane as a causative agent in these cases was complicated by the presence of numerous other compounds, some of which also possessed neurotoxic activity.

Studies with laboratory rats identified n-hexane as a putative etiological agent for the observed neurotoxicity (Spencer *et al.*, 1980). Rats exposed to n-hexane via inhalation developed a syndrome similar to that seen in cases of occupational neurotoxicity. Histopathological changes in peripheral nerves were later shown to be similar in humans and experimental animals (Chang *et al*., 1993).

Detailed toxicokinetic and biochemical studies have correlated the neurotoxicity of n-hexane to the formation of a γ-diketone metabolite (2,5-hexanedione) (Pyle *et al*., 1992). This symmetrical diketone structure reacts with biological tissue forming adducts that ultimately lead to neurotoxicity (Pyle *et al*., 1992; DeCaprio *et al*., 1987; DeCaprio *et al*., 1983). The structure of 2,5-hexanedione is shown below.



Neurotoxicity associated with n-hexane inhalation exposure in an occupational setting has been observed at n-hexane concentrations ranging from 50 ppm to 2,500 ppm (US EPA, 2005). In animal studies, neurotoxicity has been demonstrated to be associated with subchronic inhalation exposure to n-hexane concentrations ranging from 500 ppm to 5,000 ppm (US EPA, 2005; ATSDR, 1999).

4.3.2 Vision

Adverse effects on the human optic tract may occur following n-hexane exposure, characterized by blurred vision, maculopathy, and impaired colour discrimination (Chang, 1987). Experimentally exposed animals developed characteristic histopathological changes (*i.e.*, axonal swelling) in the optic tract (Spencer *et al.*, 1980). Abnormal evoked neuronal potentials have been reported in humans exposed to solvents containing n-hexane and in experimental animals exposed to pure n-hexane (Chang, 1987). A possible correlation between n-hexane exposure and potentiation of visual failure in individuals with Leber Hereditary Optic Neuropathy (hereditary loss of vision linked to maternal mitochondria DNA mutations) has been suggested (Carelli *et al*., 2007); however, further work is required before statements of causality can be made.

4.3.3 Reproductive Toxicity

Adverse effects on the testes are seen in experimental animals exposed to n-hexane and 2,5-hexanedione (Boekelheide *et al*., 2003). Sprague Dawley rats exposed to 5000 ppm n-hexane for 16 h/d (daily for 8 days or 6 d/wk for up to 6 weeks) demonstrated signs of toxicity in the germinal epithelium and abnormalities in primary spermatocytes and sperm maturation (De Martino *et al*., 1987). The authors reported testicular effects could be observed prior to the development of clinical neurotoxicity. Both exposure durations resulted in focal spermatocyte degeneration with greater effect on early meiotic prophase or metaphase in comparison to pachytene spermatocytes. The 6-week exposure was associated with atrophy of the seminiferous tubules and testicular lesions. Testicular toxicity has also been observed in rats exposed to 1000 ppm n-hexane daily for 61 days, as evidenced by a loss of germinal cells and damage to Sertoli cells (Nylen *et al*., 1989). The available epidemiological data are inadequate to evaluate whether testicular effects are relevant to humans.

Rats exposed to 200, 1000, or 5000 ppm n-hexane for 20 h/d for 5 days prior to mating were assessed for reproductive effects (Mast *et al.*, 1988b). Short-term exposure of males to n-hexane was not associated with significant effects on litter size or resorptions (Mast *et al.*, 1988b). A subsequent study by Mast *et al*. (1988c) found no abnormal sperm characteristics or morphology in B6C3F1 mice following short-term n-hexane exposure.

Pregnant Sprague-Dawley rats exposed to 1000 or 5000 ppm n-hexane for 20 h/d had significantly less pregnancy-associated weight gain than controls and fetal body weight gain was significantly reduced (Mast, 1987). No effect on maternal or fetal weight gain was observed at 200 ppm (Mast, 1987). Similar effects on maternal and fetal weight gain were seen in CD-1 mice, although only effects on the fetus were considered significant (Mast *et al.,* 1988a). Litter numbers were reduced in CD-1 mice exposed to 5000 ppm n-hexane for 20 h/d during pregnancy (Mast *et al.*, 1988a). Exposure to n-hexane was associated with a greater percentage of intrauterine deaths, although this effect was not dose-dependent. The incidence of late

resorptions was positively correlated with n-hexane concentration, and reached statistical significance at the highest dose (5000 ppm for 20 h/d). Developmental effects were also observed in offspring of pregnant rats and mice exposed to high doses of n-hexane. Pregnant rats exposed to 5000 ppm n-hexane for 20 h/d produced live fetuses with reduced ossification of sternebrae 1 to 4 (Mast, 1987), and similarly exposed pregnant mice produced live fetuses with a greater incidence of supernumerary ribs (Mast *et al.*, 1988a).

The limited data available did not indicate significant reproductive toxic effects in males, or in females at doses that were not maternally toxic. A NOAEL for developmental toxicity of 200 ppm n-hexane was identified (Mast *et al.,* 1998a). Multigenerational reproductive and developmental toxicity studies are lacking.

4.3.4 Respiratory Effects

In a subchronic inhalation exposure study, male New Zealand rabbits were exposed to 3,000 ppm of n-hexane in an inhalation chamber 8 h/d, 5 d/wk, for 24 weeks. After a further 120 days in clean air, examination of lungs revealed exposure-related lesions, which consisted of air space enlargement centred on respiratory bronchioles and alveolar ducts, scattered foci of pulmonary fibrosis, and papillary tumours of non-ciliated bronchiolar epithelial cells. Death occurred in 2 of the 12 male rabbits. Before death, the rabbits showed signs of difficulties in breathing, which include gasping, lung rales, and mouth breathing (Lungarella *et al*., 1984). New Zealand rabbits exposed to 3,000 ppm of n-hexane in an inhalation chamber 8 h/d for 8 days showed morphological changes in lung parenchyma characterized by centriacinar emphysema and scattered micro hemorrhages (Lungarella *et al*., 1980).

Milder respiratory effects have been observed in mice exposed to 1000 ppm and 10,000 ppm of n-hexane (Dunnick *et al*., 1989; NTP, 1991). Exposure levels at which respiratory effects were observed in mice and rabbits are greater than levels at which neurotoxicity has been observed in rats.

4.3.5 Carcinogenicity and Genotoxicity:

A 2-year inhalation study of commercial hexane (a mixture containing at least 52% n-hexane and other related hydrocarbons) showed an increase in combined hepatocellular adenomas and carcinomas in female B6C3F1 mice (Daughtrey *et al*., 1999; Biodynamics, 1993a; Biodynamics, 1993b). Neither treated male mice nor F344 rats of either sex had increased tumour incidences. This commercial hexane study was considered inappropriate for characterizing the carcinogenicity of pure n-hexane as commercial n-hexane contains various hydrocarbons, the toxic effects of which have not been fully evaluated (USEPA, 2005).

Further work is required before the genotoxicity and carcinogenicity of n-hexane can be adequately evaluated. The US EPA has therefore classified the available data on n-hexane as "inadequate for an assessment of the human carcinogenic potential" (USEPA, 2005).

The International Agency for Research on Cancer (IARC) has not classified n-hexane with respect to carcinogenicity.

4.3.6 Sensitive subpopulations

The US EPA (2005) identified certain subpopulations that may be at greater risk of n-hexane toxicity. Adults may be more susceptible than children, as n-hexane neurotoxicity appeared earlier and was more severe in adult rats than weanlings. This difference may be a function of weanling neuronal axons as being shorter and smaller in diameter compared to those in adult rats (Howd *et al.*, 1982). In addition, differences in the development and maturity of metabolic enzymes (including CYP2E1, responsible for the formation of the toxic 2,5-hexanedione metabolite) between adults and children have been demonstrated (Vieira *et al.*, 1996**;** Johnsrud *et al.*, 2003). Individuals with polymorphisms in the CYP2E1 gene may also be more susceptible to n-hexane toxicity due to altered metabolism (Zhang *et al.,* 2006).

Additionally, possible associaton between CYP2E1 gene polymorphisim and Parkinson Disease (PD) has been shown by Shahabi et al (2009) in a Swedish population. The authors concluded that additional investigation is necessary to further study the importance of this polymorphism for CYP2E1 activity and susceptibility to PD. In some other individual human case studies by Pezzoli et al (1989, 1995, 1996), and experimental animal studies (Pezzoli et al 1990) evidence of PD was shown after exposure to n-hexane. In another study by Vanacore et al (2000), chronic exposure to a commercial hexane mixture (17 working years) was also associated with PD in a 55 year-old patient. Further neurophysiological and neuropsychological tests indicated central nervous system effects from n-hexane exposure. Due to various limitations in those studies, however, direct causal linkage is very difficult to establish. Based on studies available to date in animals and humans, individuals with PD may be susceptible to n-hexane and other solvent exposure.

4.4 Avian Toxicology

Pigeons exposed by inhalation to 3,000 ppm of n-hexane (5 h/d, 5 d/wk for 17 weeks) showed no functional, electrophysiological or pathological changes (Foa *et al*., 1976). Similarly, hens exposed to 1,000 ppm of n-hexane vapours exhibited no signs of toxicity (Abou-Donia *et al*., 1991). Following oral administration of two doses of 2,000 mg/kg-day administered 21 days apart, Leghorn chickens developed signs of mild leg weakness followed by full recovery after 2 to 4 days. No deaths or decreases in body weight were noted at this concentration. A 19% decrease in body weight was observed in 12 month old female Leghorn chickens administered 100 mg/kg-day of n-hexane via gavage for 90 consecutive days (Abou-Donia *et al*., 1982).

Dermal exposures have also been associated with neurological effects in avian species. Subclinical neuropathy was reported in chickens exposed percutaneously to 35.2% hexane mixture (Spencer *et al*., 1980). Histological damage to nerves in chickens was demonstrated following dermal exposure to a mixture of 1 g/kg-day of n-hexane for 65 days (Franchini *et al*., 1978).

4.5 Effects on Soil Dependent Biota

Hordeum vulgare (barley) and *Daucus carota sativus* (carrot) were exposed to 4.5 to 6.3 mmol/L (388 to 543 mg/L) and 4.5 to 7.8 mmol/L (388 to 675 mg/L) of n-hexane fumigation (air spray

application), respectively. Injury to both plant species was observed at 1 day and 28 days, respectively (Currier and Peoples, 1954). Exposure to n-hexane vapours resulted in increased permeability in plant leaves. The application of slight pressure on the leaf resulted in darkening as a consequence of cell sap filling intercellular spaces on the leaf. In addition, dark areas appeared in the leaves in the absence of pressure, followed by loss of turgor, complete wilting, and plant death (Currier and Peoples, 1954). Membrane damage has also been observed in ornamental crop species exposed to n-hexane (Vincoli, 1997).

Soaking *Hordeum vulgare* (barley) roots in 0.69 mmol/L (59.46 mg/L) of n-hexane for 0.25 day produced loss of root cell viability, with the apical meristem being most resistant (Currier and Peoples, 1954). As plant roots are more adapted to absorbing polar substances and leaves to absorbing non-polar substances, plant roots may have a greater resistance to hydrocarbon exposure than leaves (Crafts, 1948).

In 24-hour toxicity tests of various hydrocarbon compounds, the rotifers *Brachionus calyciflorus* (freshwater species) and *Brachionus pilcatilis* (saltwater species) were most sensitive to n-hexane, with LC_{50} values of 68.3 mg/L and 154.3 mg/L, respectively (Ferrando *et al*., 1992). Rotifers are found in a variety of habitats including, mosses and lichens, leaf litter and moist soils, however, experiments on soil-dwelling rotifers could not be found.

There was 0 % mortality of the earth worm *Eisenia andrei* after exposure to 210 ppm n-hexane in artificial soil for 14 days (Gaëlle Triffault-Bouchet, Développement durable, Environnement et Parcs, Québec, pers. comm. 2008). A concentration of 1.42 ppm n-hexane produced a 95% avoidance response in sandy soil and an 80% avoidance response in loamy soil for the earthworm *Eisenia andrei* (Gaëlle Triffault-Bouchet, Développement durable, Environnement et Parcs, Québec, pers. comm. 2008). The worms had a choice to enter, and move freely between, a total of six enclosures containing either spiked or control soils over a three day period.

4.6 Effects on Soil Microbial Processes

Limited data were found concerning the effect of n-hexane on soil microorganisms. n-Hexane was toxic to over 20 methyltrophic organisms in a 50 mg suspension of municipal sewage sludge at an n-hexane concentration of 500 mg/L (Gerhold and Malaney, 1966). The oxidation of n-hexane to its corresponding methyl ketone, 2-pentanone and the corresponding alcohol, 2-pentanol was also observed within 24 hours (Gerhold and Malaney, 1966).

4.7 Human Exposure Limits

4.7.1 Inhalation Exposure

n-Hexane inhalation exposure limits are available from various regulatory agencies. Summaries of guidelines developed by the US EPA, ATSDR, and California EPA are provided below. The toxicological reference values retained for the purpose of the derivation of SQGs are identified in section 6.1.

US EPA

An updated reference concentration (RfC) value of 0.7 mg/m^3 was developed by the US EPA (2005, 2008) based upon the results of Huang *et al*. (1989). This RfC has been selected for the derivation of the soil quality guideline for n-hexane. Huang *et al*. (1989) demonstrated exposure concentration- and duration-dependant behavioural, neurophysiological, and neuropathological effects in Wistar rats exposed to n-hexane. Various other supporting studies were also reviewed (Mast, 1987; Ono *et al*.,1981; Takaeuchi et al 1980, 1981; Bus *et al*., 1979).

The RfC was based upon the Huang *et al.* (1989) study, in which rats (8/group) were exposed to 0, 500, 1200, or 3000 ppm (0, 1762, 4230, 10,574 mg/m^3) *n*-hexane (>99% pure) 12 h/d, 7 d/wk for 12 weeks. A benchmark concentration limit (BMCL) of 430 mg/m^3 (122 ppm) was calculated for the critical effect of peripheral neuropathy (decreased motor nerve conduction velocity [MCV]) and adjusted for continuous exposure (24 h/d, 7 d/wk) to obtain a Point of Departure (POD) value of 215 mg/m^3. An overall uncertainty factor of 300 (x 10 for intraspecies variation in susceptible populations, and x 3 each for interspecies variation, extrapolation from less-than lifetime to chronic exposure, and database deficiencies) was applied to the POD to derive an RfC of 0.7 mg/m^3.

In April 2008 the US EPA amended US EPA (2005) to include updated benchmark dose modelling of the Huang *et al*. (1989) data. The updated analysis did not change the inhalation RfC, with the US EPA providing the following explanation.

> "The scale intercept was inadvertently not added back in after estimating MCVs from figure 2 of the Huang *et al.* (1989) data at the time of derivation of the RfC for n-hexane. The corrected mean MCV values from the Huang *et al.* (1989) data were run in the 2008 version of the USEPA's BMDS version 1.4.1.C. Although modified data sets were used, the BMD modelling results provided similar BMCLs. Therefore, no revision to the POD (215 mg/m^3) and derivation of RfC (0.7 mg/m3) were carried out." (USEPA, 2008).

ATSDR

A chronic minimal risk level (MRL) of 0.6 ppm (2.1 mg/m^3) for n-hexane was developed by ATSDR based on an epidemiological study by Sanagi *et al.* (1980) of tungsten carbide alloy production workers exposed to n-hexane (8 hr time-weighted average [TWA] of 58 ± 41 ppm) and acetone (TWA of 39 ± 30 ppm) for periods of 1 to 12 yr (mean 6.2 yr). The 8-hour time-weighted average exposure concentration of 58+/-41 ppm was considered a LOAEL for reduced

maximal motor nerve conduction velocity and increased residual latency of motor nerve conduction. An overall uncertainty factor of 100 (x 10 for use of a LOAEL and x 10 for intraspecies variability) was applied to the LOAEL resulting in a MRL of 0.6 ppm. Acetone has been demonstrated to potentiate n-hexane neurotoxicity. ATSDR reports that, while it is not clear whether co-exposure to acetone contributed to the n-hexane neurotoxicity observed in the key study, the likelihood of potentiation is small.

California EPA

The California Environmental Protection Agency (CalEPA) developed a chronic reference exposure level (REL) of 7 mg/m^3 for n-hexane. The REL was based on an inhalation study in which male mice were exposed to n-hexane 24 hours per day, six days per week for one year (Miyagaki, 1967). The critical health effect was peripheral neuropathy and a NOAEL of 100 ppm was identified. The NOAEL was adjusted to 57.9 ppm for continuous exposure. An overall uncertainty factor of 30 (x 3 for interspecies variability and x 10 for intraspecies variability) was applied to the adjusted NOAEL resulting in an REL of 2 ppm or 7 mg/m^3.

4.7.2 Oral Exposure

The US EPA Region 9 has adopted the US EPA Health Effects Assessment Summary Tables (HEAST) (USEPA, 1997) oral reference dose (RfD) of 0.06 mg/kg-d for n-hexane. The RfD is based on a study in which rats were exposed to n-hexane by gavage five days per week for 90 days (Krasavage *et al*., 1980) and examined for neuropathy and testicular atrophy. The neurological endpoint chosen for the study was severe hind-limb weakness or paralysis as the onset of earlier, more subtle signs of neuropathy is reportedly more difficult to establish. A LOAEL of 570 mg/kg-d is reported by USEPA (1997) for neurotoxicity and testicular atrophy. An uncertainty factor of 10,000 was applied to the LOAEL to develop the RfD of 0.06 mg/kg-d, which was not adjusted for continuous exposure. However, the authors of the key study report that clinical signs of neuropathy and testicular atrophy were observed only at the high dose of 3,980 mg/kg. The authors report that body weight gain was affected at all dose levels (including the low dose of 580 mg/kg); however, the significance of this finding is not reported. Furthermore, there are several weaknesses associated with the key study, including an inadequate number of animals in each dose group, a high rate of mortality in the mid- and high-dose groups and a lack of a clear dose-response.

US EPA (2005) considers the current toxicological database regarding the oral toxicity of n-hexane insufficient for the development of an oral toxicity reference value.

An interim oral tolerable daily intake (TDI) of 0.1 mg/kg bw per day was developed by Equilibrium (2008) for Health Canada. The interim oral TDI was based upon data from subchronic rat studies (Ono *et al*., 1979, 1981). Two endpoints of neurotoxicity (motor nerve conduction velocity and mixed nerve conduction velocity) in rats were considered in the development of the oral TDI. The rationale for this approach is described in detail in Equilibrium (2008).

The calculated point of departure (POD) value relied on the use of repeated measures data from a meta-analysis of studies (Ono *et al*., 1979, 1981). A POD value of 8 mg/kg-d based on a 5%

reduction in mixed nerve conduction velocity was determined for the derivation of a lifetime TDI, after adjustment to an equivalent lifetime exposure. An uncertainty factor of 90 was applied (x 10 for sensitive individuals; x 3 for interspecies toxicokinetic differences; and x 3 for limitations of the oral dataset, including a small number of data points and the use of repeated measures data). The lifetime TDI for oral exposure to n-hexane was calculated to be 0.1 mg/kg-d (Equilibrium, 2008).

Given the statistical uncertainties and limitations in data analysis associated with this approach, the value of 0.1 mg/kg-day is considered an interim value. The confidence in this oral POD value is considered weak since it was derived from data containing limited exposure doses for a maximum of 4 weeks. For a detailed oral exposure data analysis, the reader should refer to the *Supporting Document for the Development of a Human Health-Based Soil Quality Guideline for n-Hexane* prepared for Health Canada by Equilibrium Environmental (2008).

The Equilibrium Environmental (2008) interim oral tolerable daily intake (TDI) of 0.1 mg/kg bw per day was used to derive the soil quality guideline. The interim oral TDI was selected for SQG derivation due to a low level of confidence in the HEAST RfD (USEPA, 1997). Furthermore, the interim oral TDI was based on a more sensitive neurological endpoint than that selected by USEPA (1997).

5.0 DERIVATION OF ENVIRONMENTAL SOIL QUALITY GUIDELINES

5.1 Soil Quality Guideline for Soil Contact

No acceptable toxicity studies could be found that exposed invertebrates or plants to n-hexane in soil. Therefore, a soil contact guideline could not be derived.

5.2 Soil Quality Guideline for Soil and Food Ingestion for Primary Consumers

The minimum data requirements for deriving a soil quality guideline for soil and food ingestion (SQG_I) for protection of grazing livestock and wildlife are three studies; two oral mammalian studies and one oral avian study. Appendix I summarizes the available wildlife and livestock toxicity studies. Only a single chicken toxicity study was found to be acceptable for guideline derivation purposes; as a result, the derived SQG_I presented below should be considered as provisional since the minimum data requirements were not met.

5.2.1 Daily Threshold Effective Dose

Abou-Donia *et al*. (1982) administered 100 mg/kg bw/day n-hexane orally to three leghorn laying chickens (*Gallus gallus domesticus*) for 90 days. Chickens were considered relevant for livestock/wildlife soil and food ingestion guideline development as a surrogate for avian wildlife receptors. After 90 days n-hexane administration and a 30 day recovery period, the body weight of the n-hexane treatment chickens were significantly lower than that of controls. The chickens also displayed leg weakness during oral administration with a recovery shortly after administration stopped. At higher concentrations, adverse effects on the reproductive and nervous system in rats and mice have been observed.

An uncertainty factor of between one and five can be applied to the toxicity study with the lowest effects dose using expert judgment and consideration of whether the dose is considered "biologically relevant", whether the effects are based on acute lethal or sublethal toxicity, and/or the number of taxonomic groups represented by the toxicological dataset. An uncertainty factor or 4 was applied to the study of Abou-Donia *et al.* (1982) for the following reasons; minimum data requirements were not met; it is unknown if chickens represent a species that are the most sensitive to n-hexane; the use of a single dose level; the adverse effects were considered biologically relevant and low, however, it was not possible to quantify the effect.

The daily threshold effect dose for primary consumers ($DTED_{1C}$), livestock or wildlife, was calculated using the following equation (CCME, 2006):

$$DTED_{1C} = \frac{Lowest\ ED_{1C}}{UF}$$

where,

$DTED_{1C}$ = daily threshold effect dose of primary consumer (mg/kg bw_{1C}-day)
ED_{1C} = lowest effect dose (mg/kg bw_{1C}-day); 100
UF = uncertainty factor; 4

Substituting the appropriate values in the above equation yielded a $DTED_{1C}$ of 25 mg/kg bw_{1C}-day.

5.2.2 Soil and Food Ingestion Rate

The soil and food ingestion guideline for the protection of primary consumers was calculated using body weight and soil and food ingestion rates for chickens. Abou-Donia *et al.* (1982) reported the chicken body weight as 1.7 kg, which is within the range provided by CCME (1999c) of 1.6 to 2.3 kg. USEPA (1999) reported a soil ingestion rate for chickens of 0.02 kg dry weight/day. CCME (1999c) reported a food ingestion rate of 0.11 kg/d to 0.15 kg/d. The average (median) value of 0.13 kg/d for this range was selected.

5.2.3 Bioavailability Factor

There was a lack of information on the bioavailability of n-hexane from ingested soil for livestock and wildlife. Therefore, for primary consumers, the bioavailability of soil-adsorbed contaminants was assumed to be 1 (CCME, 2006).

5.2.4 Bioconcentration Factor

There were no data available to estimate the bioconcentration factor (BCF) of n-hexane from soil to plants. The BCF was, therefore, calculated based on a K_{OW} value of 4.11 (refer to Table 2-1) and the CCME (2006) equation below:

$$\log BCF_1 = 2.53 - 0.4965 \log K_{ow}$$

where,

BCF_1 = chemical specific bioconcentration factor
$\log K_{ow}$ = octanol water partitioning coefficient; 4.11 - see Table 2-1

Substituting the appropriate values in the above equation yielded a BCF_1 of 3.1.

5.2.5 Calculation of Soil Quality Guideline for Ingestion for Primary Consumers

Soil and food ingestion of contaminants by primary consumers was calculated using the equation provided by CCME (2006):

$$SQG_{1C} = \frac{0.75 \times DTED_{1C} \times BW_{1C}}{(SIR_{1C} \times BF) + (FIR_{1C} \times BCF_1)}$$

where,

SQG_{1c} = soil quality guideline for soil and food ingestion for the primary consumer (mg/kg)
0.75 = allocation factor (dimensionless)

$DTED_{1c}$ = daily threshold effect dose (mg/kg bw_{1C}-day); 25 – calculated above
BW_{1c} = body weight for chickens (kg); 1.7 (Abou-Donia *et al.*, 1982)
SIR_{1c} = soil ingestion rate for chickens (kg dw soil/day); 0.02 (USEPA, 1995)
FIR_{1c} = food ingestion rate for chickens (kg dw food/day); 0.13 (CCME, 1999c)
BF = bioavailability factor; 1.0 (CCME, 2006)
BCF_1 = bioconcentration factor; 3.1 – calculated above

Substituting the appropriate values into the equation yielded a guideline of 75 mg/kg was calculated for the protection of primary consumers for soil and food ingestion for both fine- and coarse-grained soil. A guideline for secondary consumers was not developed since available data suggest n-hexane does not bioaccumulate in the food chain.

5.3 Soil Nutrient and Energy Cycling Check

Insufficient data were available from the literature search to evaluate the guideline check regarding potential effects of n-hexane on soil nutrient and energy cycling.

5.4 Protection of Freshwater Life

The protection of freshwater life (surface water) from contact with contaminated groundwater due to soil contamination applies to all land uses. The Soil Quality Guideline for the Protection of Freshwater Life (SQG_{FL}) is derived by using the Canadian Water Quality Guideline (CWQG) for the Protection of Aquatic Life to back calculate a soil concentration that will not result in an exceedance of the CWQG once the contaminant has migrated from soil, to groundwater, and ultimately to surface water (CCME, 2006). Currently, however, there is no CWQG for n-hexane. The Soil Quality Guidelines Task Group decided to deviate from standard protocol in developing a Toxicity Reference Value (TRV) for the protection for Aquatic Life (freshwater) in order to derive a value for the SQG_{FL} pathway. The methodology for deriving the TRV is based as closely as possible on *A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life 2007* (CCME 2007) since the soil protocol (CCME 2006) provides no guidance on deriving aquatic life guidelines. The process for deriving the TRV is explained in the following text.

A literature search was conducted for studies investigating the toxicity of n-hexane to freshwater organisms. The literature search built upon a recent review of aquatic toxicity data by Alberta Environment (Equilibrium Environmental Inc. 2009). A complete summary of the studies evaluated is provided in Appendix II.

The aquatic toxicity studies were evaluated according to CCME's protocol for the derivation of aquatic life guidelines (CCME 2007). An additional consideration for study acceptability was that n-hexane is volatile, and the experimental design should account for potential losses of n-hexane over the test duration. Of the 14 studies presented in Appendix II, only two were of acceptable quality and considered further for TRV development (see Table 5-1 for summaries of the two studies). Primary reasons for which studies in Appendix II were rejected include n-

hexane volatility being inadequately addressed, and reported effect concentraions exceeding n-hexane solubility limit of 9.5 mg/L (see Table 2-1). Other common reasons include unreported test concentrations, statistics, and/or replications, and studies with poorly reported abiotic test parameters. The following studies reported in Equilibrium Environmental Inc. (2009) were not evaluated because they were written in German or Japanese; Bringmann and Kuhn 1977, 1982; Juhnke and Luedemann 1978; Tsiuji et al. 1986 (note that Equilibrium Environmental reported effect concentrations from these studies above n-hexane solubility).

Table 5- 1: Summary of data used in the development of a provisional protection of aquatic life (freshwater) Toxicity Reference Value.

Species	Endpoint and duration	Life stage	Effect Concentration (mg/L)	Exposure type	Reference
Pimephales promelas (fathead minnow)	96h-LC50	31 d	2.50	Flow-through	Geiger 1990
Daphnia magna (water flea)	48h-LC50	neonates	3.88	Static*	Bobra et al. 1983

* Authors attempted to address volatilization loss from water by removal of air space in exposure chambers as explained in Bobra et al. (1983), and Abernathy et al. (1986).

The study from Geiger *et al.* (1990) in Table 5-1 was selected as the key study to develop the TRV because standard toxicity test methods were employed, treatment concentrations were measured, reporting of abiotic factors were complete, the experimental design was a flow-though, and the test species was the more sensitive of the two studies. The experimental design in Bobra et al. (1980) did provide adequate replication, number of test concentraions, control mortality, and minimized losses due to volatilization, however, the effect concentrations were calculated based on reported n-hexane solubility (roughly 9.5 mg/L), reporting of abiotic factors was incomplete, and the test organism was not as sensitive.

Modelled estimates of n-hexane toxicity are presented in Table 5-2 for comparison purposes with observed effects seen in Table 5-1.

Table 5- 2: Modelled aquatic toxicity of n-hexane

Species	Endpoint and duration	Effect Concentration (mg/L)	Reference
Pseodokirchneriella subcapitata (green algae)	72h-EC_{50} (growth inhibition)	7.76	AIEPS
Tetrahymena pyriformis (ciliate)	LC50	0.98	Computox (Kaiser, 1993)
Tetrahymena pyriformis (ciliate)	24h (and greater)-IC_{50} (growth inhibition)	202	AIEPS
Daphnia magna (water flea)	48h–LC50	16.21	AIEPS
Pimephales promelas (fathead minnow)	96h–LC50	12.24	AIEPS
Pimephales promelas (fathead minnow)	LC50	1.54	Computox (Kaiser, 1993)

The available data presented in Table 5-1 were insufficient to derive a TRV similar to a CWQG (CCME 2007). Minimum data requirements for the development of a CWQG includes two fish species (one salmonid and one non-salmonid), two aquatic invertebrates (at least one planktonic), and two aquatic plant or algal studies if the substance is considered to be phyto-toxic; in order to develop a TRV similar to a Type B2 aquatic life guideline for n-hexane, additional data would be required for one salmonid fish species and one invertebrate species (CCME 2007).

The method for calculating long-term Type B2 guideline from CCME (2007) was modified to derive the TRV by deviating from the minimum data requirements (as explained above). The TRV is calculated as follows;

$$TRV = LC_{50} \text{ or } EC_{50} x\ SF$$

where,

TRV = Toxicity Reference Value for the protection for Aquatic Life (freshwater) (mg/L)

LC_{50} or EC_{50} = lowest observed lethal concentration for 50% of test organisms, or effective concentration for 50% of test organisms (mg/L); 2.50 mg/L from Geiger et al. (1990)

SF = safety factor of 0.05 to derive long term guideline for nonpersistent substances (i.e. $t_{1/2}$ in water < 8 weeks) (CCME 2007)

Thus, we obtain a Toxicity Reference Value of 0.125 mg/L for the protection of aquatic life (freshwater) from n-hexane. This value is only being used as a parameter in which to develop the SQG_{FL}, the TRV should not be construed as, or used as, a Canadian Water Quality Guideline for the Protection of Aquatic Life.

To derive the soil quality guideline for the protection of freshwater life, it was assumed that a surface water body is located 10 m from a contaminated site (CCME, 2006). There are four dilution factors (DFs), 1 to 4 which account for the following environmental fate and transport processes (CCME, 2006):

1. partitioning of the substance from soil to pore water (leachate);
2. transport of the leachate from the base of contamination to the groundwater table;
3. mixing of leachate with groundwater; and,
4. transport of the substance in groundwater down-gradient to a discharge point.

DF4 (Saturated Groundwater Zone) was calculated using the following equation:

$$C_w(x,y,z,t) = \left(\frac{C_{gw}}{4}\right)\exp\left\{\left(\frac{x}{2\partial_x}\right)\left[1-\left(1+\frac{4L_s\partial_x}{v}\right)^{1/2}\right]\right\} erfc\left[\frac{x-vt\left(1+\frac{4L_s\partial_x}{v}\right)^{1/2}}{2(\partial_x vt)^{1/2}}\right]$$

$$\left\{erf\left[\frac{(y+Y/2)}{2(\partial_y x)^{1/2}}\right]-erf\left[\frac{y-Y/2}{2(\partial_y x)^{1/2}}\right]\right\}$$

$$v=\frac{K_H i}{n_e R_f};\quad R_f = 1+\frac{\rho_b}{n}K_d$$

where,

- C_w = allowable chemical concentration in water at receptor (mg/L); 0.125 mg/L (i.e. Toxicity Reference Value derived as above)
- x = distance from source to receptor (m); 10 (CCME, 2006)
- x,y,z = Cartesian coordinates relating source and receptor (m); y, z assumed to be 0
- t = time since contaminant release (years)
- C_{gw} = allowable chemical concentration in groundwater at source (mg/L)
- ∂_x = longitudinal dispersivity tensor = 0.1x; (0.1 x 10 m = 1)
- ∂_y = lateral dispersivity tensor = 0.1∂_x (0.1 x 1 = 0.1)
- L_s = decay constant (y^{-1}) in saturated zone (see calculation below)

$$L_s = \frac{0.693}{t_{1/2S}}\left(e^{-0.07d}\right)$$

where,

- d = depth from surface to groundwater surface (m); 3 (CCME, 2006)
- $t_{1/2S}$ = biodegradation half-life in saturated zone (y; conservative assumption of

1,000 years used);

- v = velocity of contaminant (m/y; see equation above)
- K_H = hydraulic conductivity in the saturated zone (m/y); 32 for fine soil; 320 for coarse soil (CCME, 2006)
- i = hydraulic gradient (unitless); 0.028 for fine and coarse soils (CCME, 2006)
- n = total porosity of soil = 1 - ρ_b/2.65 (unitless); 0.47 for fine soil; 0.36 for coarse soil (CCME, 2006)
- n_e = effective soil porosity (unitless); generally assumed to be the same as total soil porosity (n)
- Y = source width perpendicular to groundwater flow (m); 10 (CCME, 2006)
- R_f = retardation factor (unitless) (see equation above)
- ρ_b = soil bulk density in saturated zone (g/cm^3); 1.4 for fine soil; 1.7 for coarse soil (CCME, 2006)
- K_d = distribution coefficient (cm^3/g); for non-dissociating organic compounds - K_{oc} x f_{oc}; which is 17.1 cm^3/g; see Table 2-1 for K_{oc} value and Table B-1 for f_{oc} value (CCME, 2006)

Limited data were available regarding the decay of n-hexane in groundwater. The n-Hexane content in a high-octane gasoline mixture was reduced 46% in 192 hours (Verschueren, 1983). Other studies suggest complete n-hexane degradation within 30 days (Solano-Serena *et al*., 2000). No data were available for n-hexane in anoxic or nutrient poor environments. The half-life of n-hexane in groundwater may be longer if significant hydrocarbon contamination is present resulting in anoxic conditions or the consumption of available nutrients. In the absence of data for anoxic and nutrient poor conditions, a conservative assumption of a long (> 1000 years) half-life for n-hexane was assumed. A half-life of 1000 years is sufficiently long, such that use of a greater half-life in the calculations would not result in a change to the DF4 (C_{gw}/C_w).

DF4 (transport of the substance in groundwater down-gradient to a discharge point) is a function of time (t) and "t" was determined iteratively by solving the equation with various values of "t". Based on the worst-case result, "t" was assumed to be 3300 years. Substituting the appropriate values and rounding to three significant digits yielded DF4 (C_{gw}/C_w) values of 1.16 and 1.02 for fine and coarse soil, respectively.

DF3 (Mixing Zone Unsaturated/Saturated) was calculated using the following equation:

$$C_z = C_{gw}\left\{1+\left(\frac{Z_d K_H i}{IX}\right)\right\}$$

where,

- C_z = allowable chemical concentration in leachate at the water table (mg/L)
- C_{gw} = allowable chemical concentration in groundwater at the source (mg/L) – calculated above
- Z_d = average thickness of mixing zone (m) – calculated below
- K_H = hydraulic conductivity in the saturated zone (m/y); 32 for fine soil; 320 for coarse soil (CCME, 2006)
- i = hydraulic gradient (unitless); 0.028 (CCME, 2006)

I = infiltration rate (m/y) = precipitation minus runoff and evapotranspiration; 0.2 for fine soil; 0.28 for coarse soil (CCME, 2006)
X = length of source parallel to groundwater flow (m); 10 (CCME, 2006)

The calculation of an average thickness for the mixing zone was based on the following equation:

$Z_d = r + s$; Z_d cannot exceed d_a

where,

r = mixing depth available due to dispersion and diffusion (m) 0.01 X which is 0.1
X = length of source parallel to groundwater flow (m); 10 (CCME, 2006)
s = mixing depth available due to infiltration rate and groundwater flow rate (m) – calculated below

$$s = d_a \left\{ 1 - e^{-\frac{2.178 XI}{K_H i d_a}} \right\}$$

where,

d_a = depth of unconfined aquifer (m); 5 (CCME, 2006)
I = infiltration rate (m/y) = precipitation minus runoff and evapotranspiration; 0.2 for fine soil; 0.28 for coarse soil
K_H = hydraulic conductivity in the saturated zone (m/y); 32 for fine soil; 320 for coarse soil (CCME, 2006)
I = hydraulic gradient (unitless); 0.028 (CCME, 2006)

Substituting the appropriate values and rounding to three significant digits yielded DF3 (C_z/C_{gw}) values of 2.44 and 3.36 for fine and coarse soil.

For generic guideline development, it was assumed that n-hexane is in contact with groundwater (CCME, 2006). Therefore, the allowable chemical concentration of leachate at the source (C_L) equals the allowable chemical concentration in leachate at the water table (C_z), which is 0.35 mg/L and 0.44 mg/L for fine and coarse soil respectively.

A soil quality guideline for the protection of freshwater life was calculated using the following equation (DF1):

$$SQG_{GW} = C_L \left\{ K_d + \left(\frac{\theta_w + H' \theta_a}{\rho_b} \right) \right\}$$

where,

SQG_{GW} = soil quality guideline for the protection of groundwater (mg/kg); (i.e. SQG_{FL})
C_L = allowable leachate concentration at source (mg/L) – calculated

above

K_d = distribution coefficient (cm^3/g) – calculated above

θ_w = water filled porosity (unitless); 0.168 for fine soil; 0.119 for coarse soil (CCME, 2006)

H' = dimensionless Henry's Law constant = H x 42.32 mol/m^3-atm

H = Henry's Law constant ($atm\text{-}m^3/mol$); see Table 2-1; 1.78; (average taken from 1.69, 1.81, and1.83)

θ_a = air-filled porosity (unitless); 0.302 for fine soil; 0.241 for coarse soil; (CCME, 2006)

ρ_b = soil bulk density in contaminant partitioning zone (g/cm^3); 1.4 for fine soil; 1.7 for coarse soil (CCME, 2006)

Substituting the appropriate values and rounding to 1 significant digits yielded soil quality guidelines for the protection of freshwater life (SQG_{FL}) of 11.6 mg/kg for fine and 12.3 mg/kg for coarse soil.

5.5 Protection of Livestock Watering

A soil quality guideline protective of livestock watering was calculated by setting the allowable receptor groundwater concentration in equation DF4 equal to a livestock watering threshold value (CCME, 2006). In the absence of Canadian Water Quality Guidelines for for Livestock Watering for n-hexane, an allowable livestock watering threshold (LWT) value was calculated based on the equation provided below (CCME, 2006):

$$LWT = \frac{DTED \times BW}{WIR}$$

where,

LWT = calculated livestock watering threshold value (mg/L)

DTED = daily threshold effect dose (mg/kg bw_{1C}-day); 25 – calculated above

BW = body weight for chickens (kg); 1.7 kg (Scott *et al.,* 1976)

WIR = livestock water ingestion rate (L/d); 0.37 (CCME, 1999c)

The body weight and water consumption rate for chickens was used. CCME (1999c) reported a water consumption rate for chickens of 0.12 to 0.61 L/d; the average value (0.37 L/d) for this range was selected. Abou-Donia *et al.* (1982) reported the chicken body weight as 1.7 kg, which is within the range provided by CCME (1999c) of 1.6 to 2.3 kg. No adjustment was made to account for potential differences in bioavailability between the toxicological study and a water exposure medium.

Substituting the appropriate values into the equation yielded a livestock watering threshold of 115 mg/L for fine and coarse soil.

For the calculation of a soil quality guideline protective of livestock watering, groundwater dilution factors (DF1 to 3) were used. It was assumed that dugouts or wells could be installed within the contaminated area and therefore lateral transport through the saturated zone (DF4) was not considered (CCME, 2006). Therefore, the allowable chemical concentration in

groundwater at the source (C_{gw}) is equal to the allowable chemical concentration at receptor (C_w), which is the livestock watering threshold of 115 mg/L for fine and coarse soil. Using the equation provided above resulted in DF3 (C_z) values of 281 mg/L for fine soil and 386 mg/L for coarse.

For generic guideline development, it was assumed that n-hexane is in contact with groundwater (CCME, 2006). Therefore, transport through the unsaturated zone (DF2) was not considered and the allowable chemical concentration (C_L) equals the allowable chemical concentration in leachate at the water table (C_z). The allowable chemical concentration (C_L) is 281 mg/L and 386 mg/L for fine and coarse soil, respectively.

A soil quality guideline protective of livestock watering was calculated using the equation (DF1) provided above. Substituting the appropriate values yields a soil quality guideline protective of livestock watering of 9391 mg/kg for fine soil and 10 749 mg/kg for coarse soil.

5.6 Protection of Irrigation Watering

A soil quality guideline protective of irrigation watering is typically calculated by setting the allowable receptor groundwater concentration in equation DF4 equal to the irrigation watering guideline provided by the Canadian Water Quality Guidelines (CCME, 2006). No guideline was available for n-hexane, and available data were reviewed to determine if they were sufficient to derive an irrigation watering guideline using protocols provided by CCME (1999c). Minimum data set requirements must be met which include: 1) at least three studies on three or more cereals, tame hays, or pasture crops grown in Canada; and, 2) of the above studies, at least two must be chronic tests (entire growing season) that consider sensitive and biologically relevant endpoints (CCME, 1999c). In cases where minimum data set requirements are not met, an interim irrigation watering guideline can be derived provided at least two studies on two or more cereals, tame hays, or pasture crops grown in Canada are available. Only one study was identified where the minimum lethal concentration of n-hexane was reported for barley soaked or dipped in n-hexane solution. The data were therefore considered insufficient to derive an irrigation water guideline for n-hexane. In the absence of irrigation water guideline information for n-hexane, the soil quality guideline for the protection of irrigation water cannot be derived (CCME, 2006).

5.7 Offsite Migration Check

The movement of soil from industrial and commercial sites to adjacent more sensitive land uses was considered in the offsite migration check. However, this check mechanism cannot be applied to volatile organic compounds (CCME, 2006) and therefore was not calculated for n-hexane.

5.8 Sources of Uncertainty

Several key sources of uncertainty were identified in the process of deriving the ecological soil quality guidelines. There is a general lack of toxicological data for soil dependent biota. Also, there was a lack of toxicity data for nutrient and energy cycling and grazing herbivores. Available data suggest n-hexane is susceptible to biodegradation in groundwater; however, no biodegradation half-lives were available for anoxic or nutrient deficient environments. The

biodegradation of n-hexane was not considered in the derivation of a guideline protective of groundwater uses.

6.0 DERIVATION OF HUMAN HEALTH SOIL QUALITY GUIDELINES

Human health soil quality guidelines provide concentrations of contaminants in soil at or below which no appreciable risks to human health are expected. For compounds for which the critical effect is believed to have a threshold of exposure, two key factors are considered in the setting of soil guidelines in Canada (CCME, 2006). First, it is recognized that, exclusive of hazardous waste sites or any other point source of pollution, everyone is exposed to a "background" level of contamination that cannot be avoided. For n-hexane, this background exposure arose primarily from food. In setting soil guidelines for n-hexane, the background estimated daily intake (EDI) was subtracted from the Tolerable Daily Intake (TDI) before guidelines were derived.

Secondly, CCME (2006) recommends a multimedia approach to guidelines development whereby guidelines for one medium are established recognizing that guidelines for other media may also be required. Guidelines must be established in a manner such that total simultaneous exposure at the guideline levels for all media will not result in exposure which exceeds the TDI. Therefore, in order to set soil guidelines for threshold contaminants, some portion of the residual tolerable daily intake (rTDI = tolerable daily intake [TDI] – estimated daily intake [EDI] or background intake) must be attributed to soil to account for potential exposure via four other primary exposure media (water, air, food and consumer products). With five primary media to which people are exposed - air, water, soil, food, and consumer products - 20% of the residual tolerable daily intake for threshold (non-carcinogenic) contaminants is apportioned to each of these media. In cases in which the mechanism of toxicity varies by exposure route, it is possible to derive SQGs using TDIs for each exposure route (i.e. soil ingestion only, dermal contact only, and particulate inhalation only). The final direct human health-based soil guideline (SQG_{DH}) for direct contact with soil is then the lowest of the calculated values for each direct exposure pathway.

Human health Canadian soil quality guidelines are defined for agricultural, residential/parkland, commercial and industrial land uses according to the *A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME, 2006).

6.1 Exposure Limits for Human Receptors

A reference concentration (RfC) of 0.7 mg/m^3 based on US EPA (2008) was used for the derivation of the SQGs. This RfC was adopted as a daily life time tolerable concentration (TC).

A Tolerable Daily Intake (TDI) of 0.1 mg/kg bw/d was assumed for oral exposure to n-hexane based on Equilibrium (2008).

6.2 Relative Absorption Factors

A relative absorption factor of 1 was assumed for inhalation exposures to n-hexane. For oral and dermal exposures, no data were identified regarding the relative bioavailability of n-hexane in soil compared to the toxicological study (food administration of olive oil; Ono *et al*., 1981). As a result, a relative absorption factor of 1 was assumed for oral and dermal exposures.

6.3 Estimated Daily Intakes/Background Concentrations

There are insufficient data to undertake a formal multimedia assessment to accurately estimate n-hexane background exposures (i.e., exclusive of hazardous waste sites or any other point source of pollution). It is likely background n-hexane exposure originates primarily from foods (and cooking oils, in particular), and that background exposure from soil and water ingestion is negligible. The ATSDR (1999) estimated dietary daily intake (EDI) rate of 0.00221 mg/kg bw/d was adopted as the dietary EDI for all age groups for SQG development.

Background soil and water n-hexane concentrations were assumed to be negligible. The mean n-hexane concentration measured by Environment Canada between 1993 and 1995 (2.03 $\mu g/m^3$) was adopted as a background outdoor air concentration, since this is the only Canada-wide data set available and is consistent with values measured in regional studies. Due to limited data on Canadian indoor air concentrations and the expectation that indoor air concentrations to a large extent originate from outdoor air sources (Daisey *et al*., 1994), the outdoor concentration is also applied as a background indoor air concentration.

An EDI has been calculated for each of five age classes of the Canadian general population as prescribed in CCME (2006); these EDIs are summarized in APPENDIX III.

6.4 Defined Land Uses

Agricultural lands are characterized by the presence of a farm with a family, including children, where residents consume the produce, meat, and milk produced on-site, and groundwater may be used as potable water. In a residential/parkland setting, the most sensitive receptor may have access to a backyard, and it is assumed that up to 10% of produce is grown on-site. In both cases, the most sensitive receptor is the toddler, due to it being the age category with the largest exposure to mass unit ratio.

Commercial sites include such places as shopping malls and places of business. Access to the site is not restricted, and since some commercial properties may include daycare facilities, the critical receptor is the toddler. Commercial sites do not include any areas where manufacturing takes place, nor areas where individuals may reside.

Exposure at a commercial site is assumed to be 10 h/d, 5 d/wk and 48 wk/y. Since access to commercial sites is not assumed to be 24-hours, exposure assumptions are appropriately less than for residential land use. Discretion should be used in employing the commercial land use classification – in scenarios where unrestricted 24-hour access by children or toddlers, or residential occupancy by any individual is possible, the residential/parkland classification may

be more appropriate.

Industrial lands typically have limited or restricted access to the public so that adult, occupational exposure will predominate. The most common exposure scenario is expected to be unintentional soil ingestion by an adult. The potential for off-site migration of contaminants (i.e. via soils and dust) may need to be evaluated for industrial land use scenarios.

In an industrial scenario, occupational exposure will be the primary route of exposure, hence the use of an adult receptor. Exposure for an adult at an industrial site is assumed to be 10 h/d, 5 d/wk and 48 wk/y. Examples of industrial lands could be manufacturing plants.

6.5 Direct Human Health-Based Soil Guideline Derivation

Direct contact with contaminated soil includes soil ingestion, dermal contact with soil, and particulate inhalation; however, particulate inhalation does not need to be evaluated for volatile chemicals (CCME, 2006). These exposures are normally combined, unless it can be demonstrated that the mechanisms of toxicity differ between the exposure routes considered.

Exposure for commercial and industrial scenarios is amortized over the days per week and weeks per year exposed at the site, but not hours per day since the soil ingestion and dermal contact exposures are assumed to occur as discrete events and not at a constant rate over a 24 hour period.

The direct human health-based soil guideline (SQG_{DH}) is calculated using the following equation (CCME, 2006):

$$SQG_{DH} = \frac{(TDI - EDI) \times SAF \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET} + BSC$$

where,

SQG_{DH}	=	direct human health-based soil quality guideline (mg/kg)
TDI	=	tolerable daily intake (mg/kg bw/day); 0.1 (toddler & adult) (Section 6.1)
EDI	=	estimated daily intake (mg/kg/day); 0.0033 (toddler), 0.0027 (adult) (Table 3)
SAF	=	soil allocation factor (unitless); 0.2 (toddler & adult) (CCME, 2006)
BW	=	body weight (kg); 16.5 (toddler), 70.7 (adult) (CCME, 2006)
BSC	=	background soil concentration (mg/kg); 0 (Table 3)
AF_G	=	relative absorption factor for gut (unitless); 1 (toddler & adult) (CCME, 2006)
AF_S	=	relative absorption factor for skin (unitless); 1 (toddler & adult) (CCME, 2006)
SIR	=	soil ingestion rate (kg/day); 0.00008 (toddler), 0.00002 (adult) (CCME, 2006)
SR	=	soil dermal contact rate (kg/day); 0.000069 (toddler), 0.000011 (adult) – *see below*
ET	=	exposure term (unitless) – days per week/7 x weeks per year/52; 1 (toddler), 0.659341 (adult) (CCME, 2006)

Soil Dermal Contact Rate:

$$SR = (SA_H DL_H + SA_O DL_O)EF$$

where,

SA_H = exposed surface area of hands (m^2); 0.043 (toddler), 0.089(adult) (CCME, 2006)

SA_O = area of exposed body surfaces other than hands (m^2); 0.258 (toddler), 0.250 (adult) (CCME, 2006)

DL_H = dermal loading of soil to hands (kg/m^2-event); 0.001 (toddler & adult) (CCME, 2006)

DL_O = dermal loading of soil to other surfaces (kg/m^2-event) ; 0.0001 (toddler & adult) (CCME, 2006)

EF = exposure frequency (events/d); 1 (toddler & adult) (CCME, 2006)

The toddler is used as the critical receptor for the agricultural, residential and commercial land uses, while an adult is used as the critical receptor for the industrial land use, consistent with the CCME (2006) protocol.

Based on the above, the direct human health-based soil guidelines (SQG_{DH}) for n-hexane are as follows:

- Agricultural and Residential Land Uses: $RSQG_{DH}$ = 2,140 mg/kg
- Commercial Land Uses: $CSQG_{DH}$ = 3,250 mg/kg
- Industrial Land Uses: $ISQG_{DH}$ = 15,600 mg/kg

6.6 Guideline for the Protection of Indoor Air Quality

Soil guidelines for the protection of indoor vapour inhalation are calculated using a vapour intrusion model developed by Johnson and Ettinger (1991). Guidelines are calculated separately for coarse-grained and fine-grained soils. For Agricultural and Residential land use, guidelines are derived for two building scenarios: a slab-on-grade building and a building with a basement. Only the slab-on-grade building scenario is considered for guidelines for commercial and industrial land use. The soil quality guideline for the protection of indoor air quality (SQG_{IAQ}) is calculated using the following equation (CCME, 2006):

$$SQG_{IAQ} = [(TC - C_a)\{\theta_w + (K_{OC})(f_{OC})(\rho_b) + (H')(\theta_a)\}(SAF)(DFi)(10^3 g/kg)]/[(H')(\rho_b)(ET)(10^6 cm^3/m^3)] + BSC$$

Where: SQG_{IAQ} = soil quality guideline for the protection of indoor air quality

TC = tolerable concentration (mg/m^3); 0.7 (see Section 6.1)

C_a = background indoor air concentration (mg/m^3) 0.002 (see 2.4.1, indoor air assumed to be similar to ambient air)

SAF = allocation factor (unitless) 0.2 (CCME, 2006)

θ_a = vapour-filled porosity (unitless) = effective porosity (n) – moisture-filled porosity; 0.241 (coarse), 0.302 (fine) (CCME, 2006)

θ_w = moisture-filled porosity (unitless); 0.119 (coarse), 0.168 (fine) (CCME, 2006)

n = soil porosity (unitless); 0.36 (coarse), 0.47 (fine) (CCME, 2006)

K_{OC} = organic carbon partition coefficient (mL/g); 3410 (see Table 2-1)

f_{OC} = soil organic carbon fraction in contaminant partitioning zone (g/g) 0.005 (CCME, 2006)
ρ_b = soil dry bulk density in contaminant partitioning zone (g/cm^3); 1.7 (coarse), 1.4 (fine) (CCME, 2006)
H' = unitless Henry's Law Constant = H/RT 73.9 (see Table 2-1)
H = Henry's Law Constant (atm-m^3/mol) 1.78 (see Table 2-1)
DF_i = dilution factor from soil gas to indoor air (unitless): ***see derivation below***
ET = exposure term (unitless) 1(residential, agricultural), 0.27 (commercial, industrial
BSC = background soil concentration (mg/kg), 0 (see Table 3)

Calculation of DF for indoor infiltration pathway:

$$DF_i = \frac{1}{\alpha}$$

DF_i = dilution factor from soil gas concentration to indoor air concentration (unitless)
α = attenuation coefficient, see calculation below.
= (contaminant vapour concentration in the building)/(vapour concentration at the contaminant source)

$$D_T^{eff} \approx D_a \left(\frac{\theta_a^{10/3}}{n^2} \right)$$

D_T^{eff} = overall effective porous media diffusion coefficient based on vapour-phase concentrations for the region between the source and foundation (cm^2/s)
D_a = pure component molecular diffusivities in air (cm^2/s) 0.2 (See Table 2-1)_
θ_a = vapour-filled porosity (unitless); 0.241 (coarse), 0.302 (fine) (CCME, 2006)
n = total soil porosity (unitless); 0.36 (coarse), 0.47 (fine) (CCME, 2006)

$$Q_B = L_B W_B H_B (ACH) / (3600\ s/h)$$

Q_B = building ventilation rate (cm^3/s)
L_B = building length (cm); 1225 (residential, agricultural), 2000 (commercial, industrial) (CCME, 2006)
W_B = building width (cm); 1225 (residential, agricultural), 1500 (commercial, industrial) (CCME, 2006)
H_B = building height, including basement (cm) 488 (residential, agricultural), 300 (commercial, industrial) (CCME, 2006)
ACH = air exchanges per hour (h^{-1}); 0.5 (residential, agricultural), 0.9 (commercial, industrial)

$$Q_{soil} = \frac{2\pi\ \Delta P\, k_v\ X_{crack}}{\mu \ln\left[\frac{2\left(Z_{crack}\right)}{r_{crack}}\right]}$$

Q_{soil} = volumetric flow rate of soil gas into the building (cm^3/s)
ΔP = pressure differential ($g/cm \cdot s^2$); 40 (residential, agricultural), 20 (commercial industrial) (CCME, 2006)
k_v = soil permeability to vapour flow (cm^2); 6×10^{-8} (coarse), 1×10^{-9} (fine) (CCME, 2006)
X_{crack} = length of idealized cylinder (cm); 4900 (residential, agricultural), 7000 (commercial, industrial) (CCME, 2006)
μ = vapour viscosity ($g/cm \cdot s$); 0.000173
Z_{crack} = distance below grade to idealized cylinder (cm); 244 (basement), 11.25 (slab-on-grade) (CCME, 2006)
r_{crack} = radius of idealized cylinder (cm); 0.2 (residential, agricultural), 0.26 (commercial, industrial) (CCME, 2006)

$$\alpha = \frac{\left(\frac{D_T^{eff} A_B}{Q_B L_T}\right) \exp\left(\frac{Q_{soil} L_{crack}}{D^{crack} A_{crack}}\right)}{\exp\left(\frac{Q_{soil} L_{crack}}{D^{crack} A_{crack}}\right) + \left(\frac{D_T^{eff} A_B}{Q_B L_T}\right) + \left(\frac{D_T^{eff} A_B}{Q_{soil} L_T}\right)\left[\exp\left(\frac{Q_{soil} L_{crack}}{D^{crack} A_{crack}}\right) - 1\right]}$$

D_T^{eff} = effective porous media diffusion coefficient (cm^2/s); see calculation above
A_B = building area – floor and subgrade walls (cm^2); 2.7×10^6 (residential basement), 1.5×10^6 (residential slab-on-grade), 3.0×10^6 (commercial, industrial, slab-on-grade) (CCME, 2006)
Q_B = building ventilation rate (cm^3/s); see above calculation
L_T = distance from contaminant source to foundation (cm); 30 (CCME, 2006)
Q_{soil} = volumetric flow rate of soil gas into the building (cm^3/s); see calculation above
L_{crack} = thickness of the foundation (cm); 11.25 (CCME, 2006)
D_{crack} = effective vapour-pressure diffusion coefficient through the crack (cm^2/s); assumed to be equal to D_T^{eff} ; see calculation above
A_{crack} = area of cracks through which contaminant vapours enter the building (cm^2); 994.5 (residential, agricultural), 1846 (commercial, industrial) (CCME, 2006)

For the effective diffusion coefficient through cracks in foundations (D_{crack}), it is assumed that a coarse, granular material is used as the base for the floor and footings and that the cracks are filled with coarse soil, even if the native soil is fine/medium textured. Consequently, D_{crack} will be the same as D_T^{eff} for coarse soils, regardless of the surrounding soil texture.

Soil quality guidelines for the protection of indoor air quality (SQG_{IAQ}) are summarized in Table 6-1, according to land use, building characteristics, and soil texture.

Table 6- 1 Soil Quality Guidelines for the Protection of Indoor Air Quality (SQG_{IAQ})

Land Use	SQG_{IAQ} (mg/kg)	
Soil Type	**Coarse Grained**	**Fine Grained**
Agricultural/Residential (slab-on-grade)	0.49	6.5
Agricultural/Residential (basement)	0.75	6.8
Commercial/Industrial (slab-on-grade)	6.5	41

6.7 Guideline for the Protection of Potable Groundwater

Soil guidelines for the protection of potable groundwater are developed using a model incorporating components for partitioning between soil and pore water, unsaturated zone transport, dilution of pore water at the water table, and saturated zone transport (CCME, 2006). For the derivation of Tier 1 guidelines for the potable groundwater pathway, contamination is assumed to be in contact with the water table and it is assumed that a water well could be installed at the edge of a remediated site; therefore the unsaturated zone transport and saturated zone transport components are not used. The soil quality guideline for the protection of potable groundwater (SQG_{PW}) is calculated using the following equation (CCME, 2006):

Soil/Leachate Partitioning (DF1)

$$SQG_{GW} = C_L\left\{K_d + \left(\frac{\theta_w + H'\theta_a}{\rho_b}\right)\right\}$$

SQG_{GW} = soil quality guideline for the protection of potable groundwater (mg/kg)
C_L = allowable leachate concentration at source (mg/L) – calculated below
K_d = distribution coefficient (cm^3/g); $K_{oc}xf_{oc}$=17.05 (Table 2-1 and CCME, 2006)
θ_w = water filled porosity (unitless); 0.119 (coarse), 0.168 (fine) (CCME, 2006)
H' = dimensionless Henry's Law constant; H x 42.32
H = Henry's Law constant (atm-m^3/mol) 1.78 (see Table 2-1)
θ_a = air-filled porosity (unitless); 0.241 (coarse), 0.302 (fine) (CCME, 2006)
ρ_b = soil bulk density (g/cm^3); 1.7 (coarse), 1.4 (fine) (CCME, 2006)

Unsaturated Groundwater Zone (DF2)
Note – for generic guideline development, contamination is assumed to be in contact with groundwater, and DF2 = 1 ($C_L = C_z$)
Mixing Zone Unsaturated/Saturated (DF3)

$$C_z = C_{gw}\left\{1 + \left(\frac{Z_d K_H i}{IX}\right)\right\}$$

C_z = allowable chemical concentration in leachate at the water table (mg/L)
C_{gw} = allowable chemical concentration in groundwater at the source (mg/L) – calculated below
Z_d = average thickness of mixing zone (m) – calculated below

K_H = hydraulic conductivity, saturated zone (m/y); 320 (coarse), 32 (fine) (CCME, 2006)
i = hydraulic gradient (unitless) 0.028 (CCME, 2006)
I = infiltration rate (m/y) = precipitation minus runoff and Evapotranspiration; 0.28(coarse), 0.20(fine) (CCME, 2006)
X = length of source parallel to groundwater flow (m); 10 (CCME, 2006)

Calculation of average thickness of mixing zone:

$Z_d = r + s$; Z_d cannot exceed d_a

r = mixing depth available due to dispersion and diffusion (m)
= 0.01 X; X=10 (CCME, 2006)
X = length of source parallel to groundwater flow (m); 10 (CCME, 2006)
s = mixing depth available due to infiltration rate and groundwater flow rate (m)

$$s = d_a \left\{ 1 - e^{-\frac{2.178 XI}{K_H i d_a}} \right\}$$

d_a = depth of unconfined aquifer (m); 3 (CCME, 2006)
I = infiltration rate (m/y) = precipitation minus runoff and evapotranspiration; 0.28(coarse), 0.20(fine) (CCME, 2006)
K_H = hydraulic conductivity in the saturated zone (m/y); 320 (coarse), 32 (fine) (CCME, 2006)
i = hydraulic gradient (unitless); 0.028 (CCME, 2006)

Saturated Groundwater Zone (DF4)
Note: for a receptor located at the edge of the contaminant source, DF4 = 1 (Cgw = Cw)

Cw = allowable chemical concentration in water at receptor (mg/L) (i.e., drinking water guideline or source guidance value for groundwater)

There are currently no Guidelines for Canadian Drinking Water Quality (GCDW) for n-hexane, and calculation of GCDWs is outside the jurisdiction of CCME. If there is no GCDW for the contaminant being evaluated, e.g. n-hexane, then an allowable concentration in potable water (Source Guidance Value for Groundwater) can be derived according to CCME (2006). The source guidance value for groundwater (SGVG) presented here is calculated using the same principles and procedures as used by Health Canada (1994 and 2005) to allow the calculation of the soil quality guideline drinking water check. This value should not be interpreted, however, as a Guideline for Canadian Drinking Water Quality

Therefore, an allowable concentration in potable water (Cw) can be obtained by deriving a source guidance value for groundwater using the following equation (CCME, 2006):

$$SGVG = \frac{TDI \times BW \times WF}{WIR}$$

SGVG = source guidance value for groundwater (mg/L)

TDI = interim tolerable daily intake (mg/kg/d);0.1 (see section 6.1)
WF = water allocation factor (unitless); 0.2
BW = body weight (kg); 70.7 (CCME, 2006))
WIR = water ingestion rate (L/d) (6.25 L-eq)*

* See Appendix IV for a detailed calculation of water ingestion rate via multi-route exposure (ingestion and inhalation/dermal uptake during showering and bathing).

Based on the above default and calculated values, the source guidance value for groundwater is estimated to be 0.23 mg/L.

Consistent with CCME (2006) guidance and Health Canada (1995), the allowable concentration in potable water is based upon an adult body weight of 70.7 kg and equivalent water ingestion rate of 6.25 L/d, based on multi-route exposure. The drinking water allocation factor is analogous and equivalent to the soil allocation factor. As for the soil allocation factor, a water allocation of 0.2 is applied.

The soil quality guideline for protection of potable water (SQG_{PW}) is 21 mg/kg for both fine and coarse soils. This value was derived by multiplying the dilution factors (DF1, DF2, DF3, and DF4), as calculated above, with the source guidance value for groundwater (SGVG = Cw).

6.8 Consumption of Contaminated Produce, Meat, and Milk

The plant, milk and livestock consumption pathway (SQG_{FI}) was not included in the derivation of the n-hexane soil quality guidelines, as significant bioaccumulation or bioconcentration of n-hexane is not expected. Furthermore, there is currently insufficient information to evaluate this pathway quantitatively for the development of an n-hexane soil quality guideline. At sites where appreciable amounts of garden produce are consumed, a lower soil quality guideline value may need to be considered.

6.9 Off-Site Migration of Soil/Dust

The soil quality guideline for off-site migration (SQG_{OM}) is not required for volatile chemicals (CCME, 2006) and accordingly is not calculated for n-hexane.

6.10 Consideration of Additional Exposure Pathways

For most sites, the exposure pathways described in Section 6 are considered sufficient for developing human health soil quality guidelines. However, other exposure pathways may exist and should be evaluated if there is concern that they may also adversely affect humans. Comments received from one reviewer during the public review of the draft Canadian Soil Quality Guideline for n-hexane, in February 2009, suggested that workers may be at risk from vapours migrating into trenches from contaminated soil due to the high volatility of n-hexane, high sensitivity of humans to direct inhalation exposure, and the possibility of limited air flow in trenches. Although this exposure pathway would not likely be the determining factor for the selection of the final Soil Quality Guideline for n-hexane, it may have more importance on a site-specific basis if various (i.e. potentially more sensitive) soil quality guideline pathways do not

apply and have been "turned off". The Soil Quality Guidelines Task Group (SQGTG) contracted Meridian Environmental Inc. to recommend a methodology based on available models, and derive a Soil Quality Guideline for Management considerations (SQG_M) that would protect workers in trenches from the effects of n-hexane vapours.

In the end, the SQGTG decided that the health of workers is best addressed by Occupational Health and Safety guidance from the appropriate jurisdiction for the site which includes risks associated with entry into a confined space. The rest of this section is intended to be a "lessons learned" from our experience in deriving an "effects on workers in trenches" management guideline in case site practitioners, after consulting OHS guidance, feel that a site-specific risk assessment is needed to properly address this exposure scenario for n-hexane.

Effects on Workers in Trenches

Models for the infiltration of contaminant vapours into trenches and excavations (or volatilization to outdoor air models that could be adapted to trenches) were reviewed (Meridian Environmental Inc., 2010). The purpose of the review was to select an approach for calculating the SQG_M based on the following criteria; the ease of use and application, flexibility for different exposure scenarions including parameterization for different trench scenarios, and reliability and scientific defensibility of the final predictions. The Jury model (Jury *et al.* 1983 and 1990) was selected due to more current regulatory acceptance and validation testing, as well as satisfying the SQGTG's assumed exposure scenario of a soil contaminant source that is in contact with the trench base, sidewalls or both (vapours from groundwater or pooling in the trench were not considered). USEPA (1996, 2002) and Ontario Ministry of the Environment both incorporate the Jury model in developing acceptable soil concentrations. Briefly the process is as follows: the starting point is setting an allowable air chemical concentration in the trench (i.e. hazard benchmark). This is used to back-calculate an allowable volatilization flux from soil to the trench: the Jury model is then used to calculate an allowable soil concentration (i.e. SQG_M) from the allowable flux.

Sensitivity analysis of this approach showed that the most sensitive model parameters were the air exchange rate (positive linear relationship with allowable soil concentration), width of the trench (doubling of width doubles allowable soil concentration), and time since contamination. (i.e. in this case, the worker exposure period). A time-weighted average over an 8 hour workday was used as the exposure period (i.e. workers would be protected over the course of an average work day, occurring at roughly the half way point). Human exposure was assumed to begin at 8 minutes after the initial trench excavation. It is unlikely that workers would be in the trench immediately after excavation due to the time required to properly shore the trench and ensure that entry is safe; furthermore, time is required to excavate the full length of the trench, and parts of the trench would likely be exposed for several minutes or even hours. Therefore it is recommended that the first few minutes be excluded in the calculation of the allowable soil concentration (i.e. exposure is from t = 8 minutes to t = 8 hours and 8 minutes). A benefit of excluding the first few minutes is that the models (e.g. Jury) predict high initial vapour flux, which if included in the calculation would result in lower allowable soil concentrations. The distance of the trench to the soil contamination (from 30 cm to 1 cm) and difference in soil type, e.g. fine vs. coarse, had little effect on the calculated allowable soil concentration, while altering excavation lengths or depth had no effect (see Meridian Environmental Inc., 2010 for a full description of model review, selection, paramaterization, and sensitivity analysis).

Selection of the Tolerable Concentration (i.e. setting the allowable air concentration) strongly influences the allowable soil concentration, and may be the biggest challenge in being able to conclude that workers are protected. It is expected that the exposure in trenches would likely be for an acute or sub-chronic duration for working age adults. Using a chronic or sub-chronic TC and the assumed exposure of period of t = 8 minutes to 8 hours and 8 minutes may not adequately protect workers from acute exposures due to immediate entry into a newly dug trench. This potential acute hazard should be evaluated using an acute TC and short exposure period (e.g. t = 0 mintes to t = 15 minutes). Due diligence is also needed to ensure that the selected TC is appropriate for use in the SQG_M scenario and assumptions described above.

Additional concerns for workers in trenches may also need to be addressed, including hypoxic conditions in the trench due to n-hexane, or other hydrocarbon, biodegradation (e.g. release of CO_2) and fumes associated with risks of entry into a confined space.

Free Phase Formation

The presence of free phase, particularly mobile free phase, is generally considered to be undesirable at sites, since a free phase acts as a source of future contamination and may result in effects on indoor air quality or water quality not accounted for by the three-phase partitioning models used in the calculation of Tier 1 levels. Most jurisdictions have specific management requirements that apply to a free phase of contaminant.

Theoretically, free-phase hydrocarbon can form in soil once a constituent exceeds its solubility limit in soil water, which is reached at a total soil concentration determined by the partitioning isotherm applicable to the particular soil and substance under consideration. In practice, lower molecular weight constituents tend to partition strongly into any residual (immobile) hydrocarbon phase if present. Where the contaminant is relatively insoluble in water and quite viscous, it may also be important to consider if the presence of the free phase alone can pose a risk to the environment. Some considerations may be whether the free phase contaminant can partition into the vapour or groundwater phases to pose a significant risk along those pathways or whether it is essentially acting as an occluded or trapped phase within the soil matrix. Therefore, when considering free phase formation of individual constituents, it is important to keep in mind the role the carrier organic phase may play if it is only one constiuent of a larger contaminant matrix.

If one considers the solubility limit of the constituent to determine the free phase formation, the pure phase solubility limit can be used to determine the potential for free phase formation or;

$$C_{sat} = \frac{S}{\rho_b} x\left(K_{oc} f_{oc} \rho_b + H^{'} \theta_a + \theta_w\right)$$

Where,
C_{sat} = *soil saturation limit (mg/kg)*
S = *pure phase solubility limit (mg/L) (9.5; table 2-1)*
ρ_b = *soil bulk density (g/cm^3) (1.7 coarse soil, 1.4 fine soil; CCME (2006))*

K_{oc} = organic carbon partition coefficient (mL/g) (3410; table 2-1)
f_{oc} = fraction of organic carbon (g/g) (0.005; CCME (2006))
H' = dimensionless Henry's Law constant (73.9; table 2-1)
Θ_a = vapour filled porosity (unitless) (0.241 coarse, 0.302 fine; CCME (2006)) and,
Θ_w = moisture filled porosity (0.119 coarse, 0.168 fine; CCME (2006))

Substituting these values yields a solubility limit of 261 mg/kg and 315 mg/kg n-hexane for coarse and fine soil respectively.

7.0 RECOMMENDED CANADIAN SOIL QUALITY GUIDELINES

According to the CCME soil protocol (CCME, 2006), both environmental (SQG_E) and human health (SQG_{HH}) soil quality guidelines are developed for four land uses: agricultural, residential/parkland, commercial, and industrial. The lowest value generated by the two approaches for each of the four land uses is recommended by the CCME as the final Canadian Soil Quality Guideline (SQG_F). An SQG_E could not be calculated as there was insufficient data to derive an ecological soil contact guideline. Therefore, the recommended final Canadian Soil Quality Guidelines for the protection of ecological and human health are 0.49 $mg \cdot kg^{-1}$ for coarse soil and 6.5 $mg \cdot kg^{-1}$ for fine soil for agricultural and residential land use, and 6.5 $mg \cdot kg^{-1}$ for coarse soil and 41 $mg \cdot kg^{-1}$ for fine soil for commercial and industrial land use. Table 7-1 and 7-2 summarizes the soil quality guideline values derived for all exposure pathways and land uses utilized in the determination of the Canadian Soil Quality Guidelines for n-hexane for fine and coarse soil, respectively.

In addition to producing toxic responses in human and ecological receptors, contaminants may have other effects. If there is evidence that a contaminant may cause significant environmental effects beyond toxicity to human and ecological receptors, then this evidence should be evaluated (CCME, 2006). The CCME protocol requires management considerations and allows for adjustment of the guideline based on a management consideration. The jurisdictional authority where the site is located should be consulted for their policy on management considerations with respect to n-hexane. Other concerns with respect to n-hexane could include, but are not limited to;

- Policies on free-phase liquid formation
- Threat of explosion or fire hazards
- Occupational health and safety limits for workers exposed to potential hexane sources

Table 7- 1 Soil Quality Guidelines for n-Hexane for Fine Soil

	Land Use			
	Agricultural	**Residential/ Parkland**	**Commercial**	**Industrial**
	mg/kg	**mg/kg**	**mg/kg**	**mg/kg**
Guideline[a]	6.5	6.5	21	21
Human health guidelines/check values				
SQG_{HH}[b] (or provisional SQG_{HH})	6.5	6.5	21	21
Direct contact (SQG_{DH})	2,140[c]	2,140[c]	3,250[c]	15,600[c]
Protection of indoor air quality – basement (SQG_{IAQ})	6.8	6.8	-	-
Protection of indoor air quality – slab-on-grade (SQG_{IAQ})	6.5	6.5	41	41
Protection of potable water (SQG_{PW})	21	21	21	21
Off-site migration check[d] (SQG_{OM-HH})	-	-	NA	NA
Produce, meat and milk check[e] (SQG_{FI})	NC	NC	-	-
Environmental health guidelines/check values				
SQG_E[f] (or provisional SQG_E)	NC	NC	NC	NC
Soil contact (SQG_{SC})	NC	NC	NC	NC
Soil contact confidence rank	-	-	-	-
Soil and food ingestion (SQG_I)	75[g]	-	-	-
Protection of freshwater life (SQG_{FL})	11.6[h]	11.6[h]	11.6[h]	11.6[h]
Livestock Watering (SQG_{LW})	9400[c,g]	-	-	-
Irrigation Water (SQG_{IR})	NC	-	-	-
Nutrient and energy cycling check[i] (SQG_{NEC})	NC	NC	NC	NC
Off-site migration check (SQG_{OM-E})	-	-	NA	NA
SQG_M (non-toxicity considerations)	NC	NC	NC	NC
Interim soil quality criterion (CCME 1991)	No value	No value	No value	No value

Notes: NA = not applicable; NC = not calculated; SQG_E = soil quality guideline for environmental health; SQG_{HH} = soil quality guideline for human health; - = guideline/check value was not calculated because it was not part of the exposure scenario for this land use; SQG_F = final recommended soil quality guideline for protection of ecological and human health.

[a]Data are sufficient and adequate to only calculate an SQG_{HH},and not an SQG_E. Therefore the recommended soil quality guideline is set as the SQG_{HH} and represents a *de novo* guideline for this land use, derived in accordance with the soil protocol (CCME 2006).

[b]The SQG_{HH} is the lowest of the human health guidelines and check values.

[c] Free-phase formation, a circumstance deemed unacceptable by many jurisdictions, occurs when a substance exceeds its solubility limit in soil water. The concentration at which this occurs is dependent on a number of factors, including soil texture, porosity, and aeration porosity. Under the assumptions used for this guideline free-phase formation will likely occur at concentrations greater than 315 $mg \cdot kg^{-1}$ in fine soil and 261 $mg \cdot kg^{-1}$ in coarse soil. Contact jurisdiction for guidance.

[d]Given the volatility and biodegradability of n-hexane, it is unlikely that significant amounts would remain after wind or water transport of soil, and so this pathway was not evaluated.

[e]This check is intended to protect against chemicals that may bioconcentrate in human food. n-Hexane is not expected to exhibit this behaviour, and so this pathway was not evaluated.

[f]The SQG_E could not de derived because there was insufficient/inadequate data to calculate the required soil contact guideline.

[g]Provisional guideline.

[h]This guideline is considered provisional because there was no Canadian Water Quality Guideline for the Protection of Aquatic Life available for its derivation, as required in CCME (2006). As a substitute, a freshwater life Toxicity Reference Value was estimated based on the limited n-hexane toxicity data available. This value is presented for users to consider applying at their own discretion.

[i]Data are insufficient/inadequate to calculate the nutrient and energy cycling check for this land use.

Table 7- 2 Soil Quality Guidelines for n-Hexane for Coarse Soil

	Land Use			
	Agricultural	**Residential/ Parkland**	**Commercial**	**Industrial**
	mg/kg	**mg/kg**	**mg/kg**	**mg/kg**
Guideline[a]	0.49	0.49	6.5	6.5
Human health guidelines/check values				
SQG_{HH}[b] (or provisional SQG_{HH})	0.49	0.49	6.5	6.5
Direct contact (SQG_{DH})	2,140[c]	2,140[c]	3,250[c]	15,600[c]
Protection of indoor air quality – basement (SQG_{IAQ})	0.75	0.75	-	-
Protection of indoor air quality – slab-on-grade (SQG_{IAQ})	0.49	0.49	6.5	6.5
Protection of potable water (SQG_{PW})	21	21	21	21
Off-site migration check[d] (SQG_{OM-HH})	-	-	NA	NA
Produce, meat and milk check[e] (SQG_{FI})	NC	NC	-	-
Environmental health guidelines/check values				
SQG_E[f] (or provisional SQG_E)	NC	NC	NC	NC
Soil contact (SQG_{SC})	NC	NC	NC	NC
Soil contact confidence rank	-	-	-	-
Soil and food ingestion (SQG_I)	75[g]	-	-	-
Protection of freshwater life (SQG_{FL})	12.3[h]	12.3[h]	12.3[h]	12.3[h]
Livestock Watering (SQG_{LW})	10,750[c,g]	-	-	-
Irrigation Water (SQG_{IR})	NC	-	-	-
Nutrient and energy cycling check[i] (SQG_{NEC})	NC	NC	NC	NC
Off-site migration check (SQG_{OM-E})	-	-	NA	NA
SQG_M (non-toxicity considerations)	NC	NC	NC	NC
Interim soil quality criterion (CCME 1991)	No value	No value	No value	No value

Notes: NA = not applicable; NC = not calculated; SQG_E = soil quality guideline for environmental health; SQG_{HH} = soil quality guideline for human health; - = guideline/check value was not calculated because it was not part of the exposure scenario for this land use; SQG_F = final recommended soil quality guideline for protection of ecological and human health

[a]Data are sufficient and adequate to only calculate an SQG_{HH},and not an SQG_E. Therefore the recommended soil quality guideline is set as the SQG_{HH} and represents a *de novo* guideline for this land use, derived in accordance with the soil protocol (CCME 2006).

[b]The SQG_{HH} is the lowest of the human health guidelines and check values.

[c]Free-phase formation, a circumstance deemed unacceptable by many jurisdictions, occurs when a substance exceeds its solubility limit in soil water. The concentration at which this occurs is dependent on a number of factors, including soil texture, porosity, and aeration porosity. Under the assumptions used for this guideline free-phase formation will likely occur at concentrations greater than 315 $mg \cdot kg^{-1}$ in fine soil and 261 $mg \cdot kg^{-1}$ in coarse soil. Contact jurisdiction for guidance.

[d]Given the volatility and biodegradability of n-hexane, it is unlikely that significant amounts would remain after wind or water transport of soil, and so this pathway was not evaluated.

[e]This check is intended to protect against chemicals that may bioconcentrate in human food. n-Hexane is not expected to exhibit this behaviour, and so this pathway was not evaluated.

[f]The SQG_E could not de derived because there was insufficient/inadequate data to calculate the required soil contact guideline.

[g]Provisional guideline.

[h]This guideline is considered provisional because there was no Canadian Water Quality Guideline for the Protection of Aquatic Life available for its derivation, as required in CCME (2006). As a substitute, a freshwater life Toxicity Reference Value was estimated based on the limited n-hexane toxicity data available. This value is presented for users to consider applying at their own discretion.

[i]Data are insufficient/inadequate to calculate the nutrient and energy cycling check for this land use.

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Appendix I. Selected and consulted Ecological Toxicity studies for n-hexane

Organism	Effect	Duration	Media or exposure route	Endpoint	Concentration or dose	Ranking	Reference
Plant and invertebrate toxicity studies							
Hordeum vulgare (Barley)	mortality		SL	minimum lethal concentration	59.46 mg/L	consulted	Currier and Peoples, 1954
Eisenia andrei (earthworm)	avoidance	72 hr	soil	80-95%	1.46 ppm	consulted	Gaëlle Triffault-Bouchet, MDDEP, Québec, pers. comm.
Eisenia andrei (earthworm)	mortality	14 d	soil	0%	210 ppm	consulted	Gaëlle Triffault-Bouchet, MDDEP, Québec, pers. comm.
Brachionus calyciflorus (rotifer)	neonate - mortality		FW	LC_{50}	68.3 mg/L	consulted*	Snell, 1991
Brachionus calyciflorus (rotifer)	neonate - mortality		FW	LC_{50}	68 mg/L	consulted*	Snell *et al*., 1991a
Brachionus calyciflorus (rotifer)	neonate - mortality		FW	LC_{50}	57.9 – 78.7 mg/L (mean = 68.3)	consulted*	Ferrando, *et al*., 1992
Brachionus plicatilis (rotifer)	neonate - mortality		SW	LC_{50}	154 mg/L	consulted*	Snell *et al*., 1991b
Brachionus plicatilis (rotifer)	neonate - mortality		SW	LC_{50}	145.5 – 160.0 mg/L (mean = 154.3)	consulted*	Ferrando *et al*., 1992
Mammal or avian toxicity studies							
Gallus gallus domesticus (Leghorn chicken)	Weight loss	dose at day 0 and 21	oral, 2 doses over 90 days	17%	1000 (mg/kg bw/d)	consulted	Abou-Donia *et al.,* 1982
Gallus gallus domesticus (Leghorn chicken)	Weight loss	dose at day 0 and 21	oral, 2 doses over 90 days	2%	2000 (mg/kg bw/d)	consulted	Abou-Donia *et al.,* 1982
Gallus gallus domesticus (Leghorn chicken)	mild leg weakness	dose at day 0 and 21	oral, 2 doses over 90 days	ND	2000 (mg/kg bw/d)	consulted	Abou-Donia *et al.,* 1982
Gallus gallus domesticus (Leghorn chicken)	weight	90 d	oral, daily	ND	100 (mg/kg bw/d)	Selected	Abou-Donia *et al.,* 1982

Appendix I. Mammal or avian toxicity studies continued.

Organism	Effect	Duration	Media or exposure route	Endpoint	Concentration or dose	Ranking	Reference
Gallus gallus domesticus (Leghorn chicken)	leg weakness	90 d	oral, daily	ND	100 (mg/kg bw/d)	selected	Abou-Donia *et al.,* 1982
Sprague Dawley rats	Reproductive	1wk, 6d/wk, 16hr/d	inhalation	LOAEL	5000 ppm	consulted	De Martino *et al*., 1987
Rats	Testicular	61 days	Inhalation	LOAEL	1000 ppm	consulted	Nylen *et al*., 1989
Pregnant Sprague-Dawley rats	pregnancy and fetal weight gain	20 h/d	Inhalation	LOAEL	1000 or 5000 ppm	consulted	Mast, 1987
Pregnant Sprague-Dawley rats	no effect	20 h/d	Inhalation	NOAEL	200 ppm	consulted	Mast, 1987
New Zealand Rabbit	nasal discharge, gasping, and lung rales	14d, 5d/wk, 8hr/d	inhalation	LOAEL	3000 ppm	consulted	Lungarella *et al*., 1984
New Zealand Rabbit	lacrimation, hyperemia of conjunctiva	24wk, 5d/wk, 8hr/d	dermal	LOAEL	3000 ppm	consulted	Lungarella *et al*., 1984
New Zealand Rabbit	lacrimation, hyperemia of conjunctiva	1wk, 5d/wk, 8hr/d	dermal	LOAEL	3000 ppm	consulted	Lungarella *et al*., 1984
Rabbit	ataxia and restlessness	4 hr	dermal	-	2 – 5 ml/kg	consulted	Bingham *et al*., 2001
Rabbit	mortality	4hr	dermal	-	5 ml/kg	consulted	Bingham *et al*., 2001

Notes: EC_{50} = effective concentration for 50% of the test population; FW = freshwater; LC_{50} = lethal concentration for 50% of the test population; LOAEL – lowest observed effect level; ND = Not determined; NOAEL – no observed adverse effect level; SL = solution – dipped or soaked route of exposure; ; SW = saltwater
*In the absence of soil contact data, freshwater and saltwater data have been presented.

Appendix II: Selected and consulted freshwater toxicity studies for n-hexane.

Organism	Effect	Duration	Endpoint	Effect Concentration (mg/L)	Exposure type	Rank	Reference
Chlamydomonas angulosa (green algae)	Phtosynthesis (CO_2 uptake)	3 - h	IC_{50}	8.1	Static	Unacceptable	Hutchinson et al. (1980)
Chlorella vulgaris (green algae)	Phtosynthesis (CO_2 uptake)	3 - h	IC_{50}	12.84	Static	Unacceptable	Hutchinson et al. (1980)
Daphnia magna (water Flea)	Mortality	48-h	LC50	3.88	Static	Secondary	Bobra et al. 1983
Brachionus calyciflorus (rotifer)	Mortality	24-h	LC50	68.3	Static	Unacceptable	Ferrando and Andreu-Moliner 1992
Brachionus plicatilis (rotifer)	Mortality	24-h	LC50	154	Static	Unacceptable	Ferrando and Andreu-Moliner 1992
Pimephales promelas (fathead minnow)	Mortality	96-h	LC50	2.5	Flow through	Primary	Geiger et al. 1990
Tilapia mossambica (Tilapia)	Mortality	96-h	LC5	40	Static	Unacceptable	Ghatak et al. 1988
Tilapia mossambica (Tilapia)	Mortality	96-h	LC50	113	Static	Unacceptable	Ghatak et al. 1988
Tilapia mossambica (Tilapia)	Mortality	96-h	LC95	185.5	Static	Unacceptable	Ghatak et al. 1988
Cyclops viridis (copepod)	Mortality	96-h	LC5	<5.0	NR	Unacceptable	Panigrahi and Konar 1989
Cyclops viridis (copepod)	Mortality	96-h	LC50	732.5	NR	Unacceptable	Panigrahi and Konar 1989
Cyclops viridis (copepod)	Mortality	96-h	LC95	1 503.8	NR	Unacceptable	Panigrahi and Konar 1989

Organism	Effect	Duration	Endpoint	Effect Concentration (mg/L)	Exposure type	Rank	Reference
Thiara tuberculata (snail)	Mortality	96-h	LC5	<125.0	NR	Unacceptable	Panigrahi and Konar 1989
Thiara tuberculata (snail)	Mortality	96-h	LC50	1 900	NR	Unacceptable	Panigrahi and Konar 1989
Thiara tuberculata snail)	Mortality	96-h	LC95	3 965	NR	Unacceptable	Panigrahi and Konar 1989
Chironomid larvae	Mortality	96-h	LC5	150	NR	Unacceptable	Panigrahi and Konar 1989
Chironomid larvae	Mortality	96-h	LC50	595	NR	Unacceptable	Panigrahi and Konar 1989
Chironomid larvae	Mortality	96-h	LC95	1 040	NR	Unacceptable	Panigrahi and Konar 1989
Tetrahymena elliotti (ciliate)	Mortality	18-h	LC100	9.05	Static	Unacceptable	Rogerson et al.1983
Brachionus calyciflorus (rotifer)	Mortality	24-h	LC50	68.3	Static	Unacceptable	Snell 1991
Brachionus calyciflorus (rotifer)	Mortality	24-h	LC50	68.0	Static	Unacceptable	Snell et al. 1991
Anabaena variabilis (blue-green algae)	Growth reduction	14-d	IC_{50}	43 100*	NR	Unacceptable	Stratton 1987
Anabaena inaequalis (blue-green algae)	Growth reduction	14-d	IC_{50}	11 100*	NR	Unacceptable	Stratton 1987
Anabaena cylindrical (blue-green algae)	Growth reduction	14-d	IC_{50}	15 100*	NR	Unacceptable	Stratton 1987
Anabaena sp. (blue-green algae)	Growth reduction	14-d	IC_{50}	14 300*	NR	Unacceptable	Stratton 1987
Nostoc sp. (blue-green algae)	Growth reduction	14-d	IC_{50}	52 300*	NR	Unacceptable	Stratton 1987

Organism	Effect	Duration	Endpoint	Effect Concentration (mg/L)	Exposure type	Rank	Reference
Chlorella pyrenoidosa (green algae)	Growth reduction	14-d	IC_{50}	17 400*	NR	Unacceptable	Stratton and Smith 1988
Vibrio fischeri (bacteria)	Biolumination inhibition	15 min	IC_{50}	174 000	Static	Unacceptable	Zhao et al. 1998

NR = not reported

*effect concentrations originally reported as (%v/v), which were converted into mg/L using the density of hexane at 25°C (reported experimental temperature).

Appendix III. Mean Estimated Daily Intake for n-Hexane in the Canadian Population

(mg/kg bw/day)

Exposure Route	Infant	Toddler	Child	Teen	Adult
Food Ingestion[a]	0.00221	0.00221	0.00221	0.00221	0.00221
Soil Ingestion[b]	0	0	0	0	0
Water Ingestion[c]	0	0	0	0	0
Air Inhalation[d]	0.00052	0.001144	0.000895	0.000537	0.000454
Total Ingestion Exposure	0.00221	0.00221	0.00221	0.00221	0.00221
Total Inhalation Exposure	0.00052	0.001144	0.000895	0.000537	0.000454
Total EDI	0.00273	0.003354	0.003105	0.002747	0.002664

a – ATSDR 1999
b – background soil concentration assumed to be 0 mg/kg
c – background water concentration assumed to be 0 mg/kg
d – based on average concentration in air of 0.00203 mg/m^3 and receptor characteristics defined by Health Canada (Table 4)

Appendix IV Multi-route Exposure Assessment: Determination of the Equivalent Water Ingestion Rate

In addition to oral ingestion of drinking water, the dermal and inhalation routes of exposure (via bathing and showering) to volatile organic compounds (VOC) are considered significant if they potentially contribute to at least 10% of the drinking water consumption level (Krishnan, 2004). In order to assess total exposure to n-hexane via drinking water, the relative contributions of multi-exposure pathways were calculated based on the methodology described in Krishnan and Carrier (2008). Exposure to a volatile substance in drinking water, using this methodology, is expressed as litre-equivalents (L-eq) of consumption per day.

For n-hexane the L-eq values estimated for the different routes of exposure – oral ingestion (1.5 L), dermal exposure via showering or bathing (2.96 L-eq), and inhalation exposure via showering or bathing (1.79 L-eq) were summed. A total of 6.25 L-eq was therefore used to calculate a Soil Quality Guideline for the protection of the potable water source. In the following sections, detailed explanations are provided on Tier I and Tier II calculations for dermal and inhalation exposure to n-hexane via showering and bathing.

Dermal Exposure:

To determine whether dermal exposure potentially contributes significantly to total exposure to n-hexane in drinking water, Tier 1 calculations were carried out. This is a determination of whether or not this route of exposure may contribute a minimum of 10% of the drinking water consumption level (i.e., 10% of 1.5 L = 0.15 L).

To meet a Tier 1 level of 0.15 L-eq, the skin permeability coefficient (K_p) for n-hexane would need to be greater than 0.024 cm/h. To estimate K_p for n-hexane, the US EPA (2000)2 equation based on the molecular weight and the octanol-water partition coefficient, was used, as shown in equation (1). Since the estimated K_p for n-hexane of 0.47 cm/h is greater than 0.024 cm/h, exposure to n-hexane via dermal absorption from bathing or showering is considered significant.

$$\log K_p = -2.72 + 0.71 \log K_{ow} - 0.0061\ MW \qquad (1)$$

where:

K_p is the skin permeability coefficient (cm/hr);

K_{ow} is the octanol-water partition coefficient (log K_{ow}= 4.11);

MW is the molecular weight (=86.17).

Tier 2 calculations (Krishnan and Carrier 2008) are then used to estimate the litre-equivalent value. Based on the Tier 2 calculations, a value of 2.96 L-eq value was estimated for the dermal route of exposure, as shown in equation (2):

2 EPI Suite v3.20, © 2000 U.S. Environmental Protection Agency, Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm

Dermal L-eq = 6.3 x Kp (2)

Where: K_p is the skin permeability coefficient, as calculated above.

Inhalation exposure:

The two-tier assessment described by Krishnan and Carrier (2008) was also used to evaluate the inhalation route of exposure. Similar to the approach used for dermal exposure, Tier 1 of the assessment determines whether the inhalation of n-hexane during bathing or showering is likely to contribute at least 10% of the drinking water consumption level. For a Tier 1 level of 0.15 L-eq, the air to water n-hexane concentration ($F_{air:water}$) value would need to be greater than 0.00063. Using the estimated Henry's law constant (K_{aw}) obtained from the U.S. EPA's EPI Suite program3, the $F_{air:water}$ value for n-hexane was estimated to be 0.007588, as shown in equation (3).

$$F_{air:water} = (0.61 \times K_{aw})/[1 + (80.25 \times K_{aw})] \quad (3)$$

where:

$F_{air:water}$ is the air:water n-hexane concentration;

K_{aw} is the unitless Henry's law constant (=6.98);

0.61 is based on a 61% transfer efficiency;

80.25 is the ratio of the volume of air in an average bathroom (6420 L) to the average volume of water (80 L) used during the showering/bathing event (Krishnan, 2004).

Since the $F_{air:water}$ value is greater than the Tier1 level of 0.00063, exposure to n-hexane via inhalation from bathing or showering is considered to be significant. Based on the Tier 2 calculations, a value of 1.79 L-eq value was estimated for the inhalation route of exposure using equation (4):

$$\text{Inhalation L-eq} = F_{air:water} \times Q_{alv} \times t \times F_{abs} \quad (4)$$

where:

$F_{air:water}$ is the ratio (partitioning) of air to water benzene concentrations;

Q_{alv} is the adult alveolar ventilation rate, assumed to be 675 L/h;

t is the exposure duration, assumed to be 0.5 h;

3 EPI Suite v3.20, © 2000 U.S. Environmental Protection Agency, Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm

F_{abs} is the fraction absorbed, assumed to be 0.5.

Using the above approach, the litre-equivalent exposure was calculated as 2.96 L-eq for the dermal route and 1.79 L-eq for the inhalation route. Adding these values to the standard Canadian drinking water consumption rate of 1.5 L/day results in a total litre-equivalent daily exposure of **6.25 L-eq.**

It should be noted that this multi-route exposure assessment is a conservative approach used to estimate the contribution that both the dermal and inhalation routes of exposure make towards total exposure. Using physiologically based pharmacokinetic (PBPK) modelling to estimate the litre-equivalent contributions to the total daily dose from the dermal and inhalation pathways do not take into account exposure to n-hexane metabolites. Therefore, the approach does not place any "toxicological" weight on a particular route of exposure due to metabolite production.

References:

Krishnan, K and Carrier, R (2008) Approaches for Evaluating the Relevance of Multiroute Exposures in Establishing Guideline Values for Drinking Water Contaminants',Journal of Environmental Science and Health, Part C,26:3,300 —316

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