APPENDIX 23A TOXICITY PROFILES

23A.1 Introduction

This appendix is concerned with identifying and describing the acute (i.e., 10-minute, 1-hour, 8-hour, daily) and chronic (i.e., annual) exposure limits used in the assessment of potential human health risks associated with the release of the COPCs by the proposed Petro Canada Sturgeon Project (the Project).

To distinguish toxicity, chemicals are categorized into one of two types depending on the nature of the toxic response. The largest category is threshold chemicals. For these chemicals a certain threshold or minimum dose is required before any toxicity is expressed. Once the threshold dose is exceeded, some form of toxic response is produced, the magnitude of which increases with increasing dose. The threshold phenomenon applies to virtually all types of toxic responses and chemicals, except for some carcinogens and some forms of cancer. 'Non-threshold' chemicals are a select group of substances which potentially can produce cancer through genetically mediated mechanisms. Regulatory policies in effect in many jurisdictions suggest that no safe dose level exists for this type of carcinogen and that the threshold phenomenon does not apply.

The toxicity assessment ultimately requires an understanding of the toxic effects that can be caused by the COPCs. Knowledge about this is typically obtained through reviewing scientific literature that describes the responses witnessed in:

- laboratory animals or volunteer human subjects following administration of the chemicals at various doses for varying periods of time under controlled conditions
- as part of community health studies (i.e., epidemiological investigations) examining the incidence of disease in relation to chemical exposures

Of particular importance is the need to narrow the information for the determination of a NOAEL, which refers to the dose of the chemical that produces no obvious response in the most sensitive health endpoint when tested in the most sensitive species. The NOAEL can then be used to derive an exposure limit or 'safe' level of exposure through the application of 'uncertainty' or safety factors that provide an added level of protection. The exposure limit refers to the dose of the chemical that is without effect on even the most sensitive subjects and is calculated as follows:

$$\text{Exposure Limit} = \frac{\text{NOAEL}}{\text{Uncertainty Factor(s)}}$$

The uncertainty factor can vary from 10-fold to several thousand-fold, to ensure adequate protection of any exposed populations. The most common forms of uncertainty factors are listed in Table 23A-1. It is common practice to apply a 10-fold uncertainty factor to account for possible differences in sensitivity between species (i.e., interspecies differences), and a further 10-fold uncertainty factor to accommodate differences in sensitivity between individuals within the same species (i.e., intra-species differences). Uncertainty factors are required mainly because of the practical constraints that apply to conventional toxicological research (i.e., the study of the harmful effects of chemicals). The most common research species are laboratory rodents (e.g., rats, mice, guinea pigs, rabbits), mainly because of their large numbers, low cost, and the ease with which they can be housed and handled. The use of the 10-fold interspecies factor accommodates the uncertainty in extrapolating the laboratory rodent data to the human condition. It assumes that humans will be 10 times more responsive to the chemical than even the most sensitive laboratory animals. The use of the 10-fold intra-species factor recognizes the fact that the test populations of laboratory animals used in toxicity studies are specially bred to confer genetic uniformity. These animals tend to respond to chemicals in a similar manner, with

only limited differences in responses between individual animals. Using the intra-species uncertainty factor respects the heterogeneity that exists among human populations and is intended to accommodate sensitive individuals who might be especially vulnerable to chemical exposures.

Table 23A-1: Summary of Commonly Used Uncertainty Factors in Determining Exposure Limits

Nature of Uncertainty	Size	Comments
Differences in sensitivity between species	10-fold	Used to accommodate the uncertainty surrounding the use of laboratory animal data to predict the responses that might be observed among humans. It conservatively assumes that people are 10 times more sensitive to the chemical than the most sensitive laboratory animal species.
Differences in sensitivity within a single species	10-fold	Used to account for the fact that some individuals within a population may show higher sensitivity to chemicals than the average person. It acts as an added measure to ensure the protection of such sensitive individuals, and assumes these individuals are 10 times more responsive. Its use is generally confined to assessments involving human receptors. For ecological receptors, convention specifies that it is the health of the population as a whole, and not the individual, that is of primary concern.
LOAEL[1] to NOAEL	10-fold	Used when a NOAEL is not demonstrated in the most sensitive laboratory animal species. It permits the LOAEL observed in the sensitive test species to be translated to a NOAEL, from which an exposure limit can then be derived. It assumes that if the lowest dose administered in the most definitive toxicity study had been 10-fold lower, no responses would have been observed in the test species.
Subchronic to chronic	10-fold	Reserved for cases in which exposures are expected to occur for long periods, and chronic toxicity data, involving repeated exposures of test animals to the chemical for much of their lifespan, are unavailable. It permits the use of subchronic data, involving exposures over shorter periods, to predict the responses that might be observed after more prolonged exposure.

NOTE:
[1]Refers to the lowest dose of the chemical that produces an observable adverse response in the most sensitive health endpoint when tested in the most sensitive species.

As indicated previously, the exposure limit represents the dose of the chemical that is expected to be without effect on even the most refers to the dose of the chemical that produces no obvious response in the most sensitive health endpoint when tested in the most sensitive species sensitive subjects. Typically, exposure limits are differentiated on the basis of the duration of exposure recognizing the variability in toxic responses that might be seen with the same chemical following an acute (short-term) vs. chronic (long-term) exposure. Differing terminology can be assigned to exposure limits depending on the source of exposure (e.g.., air, water, food) and the regulatory jurisdiction involved. Often, generic terminology will apply, with the following terms and descriptions used.

- RfC – Refers to the safe levels of airborne chemicals in which the primary (and almost exclusive) avenue of exposure is through inhalation (e.g., gases, vapours, aerosols, suspended dusts). The RfC is expressed as a concentration of the chemical in air (e.g., µg/m3).
- RfD – Refers to the safe levels of threshold-type chemicals to which exposure occurs through multiple pathways, both primary and secondary. It is most commonly expressed as the dose of the chemical per unit body weight of the receptor per day (i.e., µg/kg·bw/d).
- RsD/RsC – Reserved for non-threshold carcinogens, and refers to the dose or concentration of the carcinogen that corresponds to a socially acceptable incremental increase in the incidence of cancer, typically set at one extra case in a population of 100,000 people.

In some cases, reliance must be placed on a further guiding principle, which states that the molecular structure of a chemical has a distinct bearing on its reactivity, biological activity and toxicity. This principle allows the toxicity of a chemical for which little or no toxicological information exists to be predicted on the basis of information available on another chemical of similar molecular structure. The second chemical is often termed a surrogate, and the term ‘read across’ has been coined to describe the principle. The principle is also often applied to groups of chemicals of similar structure in which toxicity data on many of the individual constituents of the group might be lacking. In such cases, all of the constituents are assumed to share the same toxic potency as the most toxic chemical in the group for which toxicity information is known.

As exposure to chemicals typically does not occur in isolation, consideration was given to the potential health risks that might be presented by chemicals acting in combination. The interaction between chemicals can take many forms, all of which are of toxicological interest and some of which might be relevant to assessing potential health risks. The most common forms of interaction are:

- additivity (1 + 1 = 2)
- synergism (1 + 1 = 3)
- antagonism (1 + 1 =1)
- potentiation (1 + 0 = 1)

Toxicological interactions among chemicals depend on the chemicals present, their mode of action, and their concentrations. Of the four types of interactions, additivity is most plausible. It requires that the chemicals act through similar mechanisms and affect the same target tissue. For example, the effects of irritants will often be added if the chemicals are given in combination. As per Health Canada’s guidance, chemical interactions were assumed to be additive in nature (Health Canada 2004a).

A complete list of the COPCs that were identified as part of the HHRA is provided in Table 23A-2, along with chemical groupings used in the HHRA. COPCs were assessed individually if an exposure limit had been developed by a leading scientific authority and regulatory agency as an objective, guideline or standard for the protection of air quality and human health. Selection of each exposure limit required that the limits be:

- protective of the health of the general public based on the current scientific understanding of the health effects known to be associated with exposures to the COPC
- protective of sensitive individuals, including children and the elderly, through the incorporation of safety factors
- established or recommended by reputable scientific or regulatory authorities
- supported by adequate documentation

When these criteria were satisfied by more than one objective, guideline or standard, the most stringent exposure limit was typically selected. Otherwise, the rationale for selection of an alternate limit is provided.

23A.1.1 Selection of Acute Exposure Limits

On an acute-basis, the sources of the exposure limits used in the HHRA include:

- the AAQOs developed by Alberta Environment (AENV 2005)
- the Acute MRLs for Hazardous Substances developed by the Agency for Toxic Substances and Disease Registry (ATSDR 2005a)
- the Acute RELs recommended by the California Office of Environmental Health Hazard Assessment (OEHHA 2000)
- summary of Ontario REG. 419/05 Standards and POI Standards, AAQCs of the Ontario Ministry of the Environment (OMOE 2005a)
- the Air Quality Guidelines for Europe (Second Edition) developed by the World Health Organization (WHO 2000)

If an acute exposure limit that meets the four selection criteria (listed above) could not be identified from any of these regulatory agencies, then the search was expanded to include:

- the Intermediate MRLs for Hazardous Substances developed by the Agency for Toxic Substances and Disease Registry (ATSDR 2005a)
- the TLVs developed by the American Conference of Governmental Industrial Hygienists (ACGIH 1991, 2006b)
- the TEEL-0 s provided by the United States Department of Energy Subcommittee on Consequence Assessment and Protective Actions (U.S. DOE 2005)

Table 23A-2 Chemicals of Potential Concern

Chemical	Surrogate Chemical (if applicable)	Chemical Constituent(s)
1,3-Butadiene	NA	1,3-Butadiene
2-Chloronaphthalene	NA	2-Chloronaphthalene
2-Methylnaphthalene	NA	2-Methylnaphthalene
Acenaphthene group	Acenaphthene	Acenaphthene; acenaphthylene
Acetaldehyde	NA	Acetaldehyde
Acrolein	NA	Acrolein
Aliphatic C_5-C_8 group	n-Hexane (acute only)[1]	(1.alpha)-1,2,4-Trimethyl-cyclopentane; (1.alpha)-1,2,3-trimethyl-cyclopentane; (1.alpha-cis)-1,2,3-trimethyl-cyclopentane; (1.alpha-trans)-1,2,3-trimethyl-cyclopentane; 1-ethyl-cyclopentene; 1-ethyl-1-methyl-cyclopentane; 1-ethyl-2-methyl-cyclopentane; 1-ethyl-2-hexene; 1-ethyl-3-methyl-cyclopentane; 1-heptene; 1-hexene; 1-methyl-cyclohexene; 1-methyl-cyclopentene; 1-methyl-1,4-cyclohexadiene; 1-methyl-2-methylene-cyclopentane; 1-methyl-2-(1-methylpentyl)-cyclopropane; 1-methyl-4-methylene-cyclohexane; (1-methylethyl)-cyclopentane; (1-methylethylidene)-cyclopentane; 1-pentene; 1,1-dimethyl-cyclohexane; 1,1-dimethyl-cyclopentane; 1,1-dimethyl-cyclopropane; 1,1'-oxybis-hexane; 1,1,2-trimethyl-cyclopentane; 1,2-dimethyl-cyclohexene; 1,2-dimethyl-cyclopentane; 1,2-dimethyl-1,3-cyclopentadiene; 1,2-dimethyl-3-methylene-cyclopentane; 1,2-dimethyl-3-methylene-cyclopropane; 1,2,3,4-tetramethyl-cyclobutene; 1,2,4-trimethyl-cyclopentane; 1,3-bis(methylene)-cyclopentane; 1,3-cyclohexadiene; 1,3-cyclopentadiene; 1,3-dimethyl-cyclohexene; 1,4-cyclohexadiene; 1,4-hexadiene; 1,5-dimethyl-cyclopentene; 2-ethyl-4-methyl-1-pentene; 2-heptene; 2-hexene; 2-methyoxy-2-hexene; 2-methoxy-2-methyl-propane; 2-methyl-butane; 2-methyl-heptane; 2-methyl-hexane; 2-methyl-pentane; 2-methyl-1-butene; 2-methyl-1-heptene; 2-methyl-1-hexene; 2-methyl-1-pentene; 2-methyl-1,3-butadiene; 2-methyl-2-butene; 2-methyl-2-hexene; 2-methyl-2-pentene; 2-methyl-2,4-hexadiene; (2-methylbutyl)-cyclopentane; 2-octene; 2-pentene; 2,2-dimethyl-butane; 2,2-dimethyl-pentane; 2,2-dimethyl-propane; (2,2-dimethylpropylidene)-cyclopropane; 2,2,3-trimethyl-butane; 2,2,4-trimethyl-pentane; 2,3-dimethyl-hexane; 2,3-dimethyl-pentane; 2,3-dimethyl-1-butene; 2,3-dimethyl-1,3-pentadiene; 2,3-dimethyl-1,4-hexadiene; 2,3-dimethyl-2-butene; 2,3-pentadiene; 2,3,3-trimethyl-pentane; 2,3,3-trimethyl-1,4-pentadiene; 2,3,4-trimethyl-pentane; 2,3,4-trimethyl-2-pentene; 2,4-dimethyl-heptane; 2,4-dimethyl-hexane; 2,4-dimethyl-pentane; 2,4-dimethyl-1-pentene; 2,4-dimethyl-2-pentene; 2,4-hexadiene; 2,4,4-trimethyl-2-pentene; 2,5-dimethyl-1-hexene; 2,5-dimethyl-2,4-hexadiene; 3-ethoxy-3-methyl-1-butyne; 3-ethyl-cyclopentene; 3-ethyl-hexane; 3-ethyl-pentane; 3-ethyl-2-pentene; 3-ethyl-2,2-dimethyl-pentane; 3-hexyne; 3-methyl-cyclohexene; 3-methyl-cyclopentene;

Table 23A-2 Chemicals of Potential Concern (cont'd)

Chemical	Surrogate Chemical (if applicable)	Chemical Constituent(s)
Aliphatic C_5-C_8 group (cont'd)	n-Hexane (acute only)[1] (cont'd)	3-methyl-heptane; 3-methyl-hexane; 3-methyl-pentane; 3-methyl-1-heptene; 3-methyl-1-hexene; 3-methyl-1-pentene; 3-methyl-2,4-hexadiene; 3-methylene-pentane; 3,3-dimethyl-1-butene; 3,3-dimethyl-1,4-pentadiene; 3,4-dimethyl-1-pentene; 3,4,4-trimethyl-2-pentene; 4-methyl-cyclohexene; 4-methyl-heptane; 4-methyl-1-hexene; 4-methyl-1,3-pentadiene; 4-methyl-2-pentene; 4-methylene-heptane; 4,4-dimethyl-cyclopentene; 5,5-dimethyl-1,3-cyclopentadiene; 6-methyl-1-heptene; azido-cyclohexane; bicycle[4,1,0]hept-2-ene; cis-1-butyl-2-methyl-cyclopropane; cis-1-ethyl-2-methyl-cyclopentane; cis-1-ethyl-3-methyl-cyclopentane; cis-1,2-dimethyl-cyclohexane; cis-1,2-dimethyl-cyclopentane; cis-1,2-dimethyl-cyclopropane; cis-1,3-dimethyl-cyclohexane; cis-1,3-dimethyl-cyclopentane; cycloheptane; cyclohexane; cyclohexene; cyclooctane; cyclopentane; cyclopentene; (e)-1,3-pentadiene; (e)-2-heptene; (e)-2-hexene; (e)-2-octene; (e)-2-pentene; (e)-3-hexene; (e)-3-methyl-1,3,5-hexatriene; (e)-3-methyl-2-pentene; (e)-3-methyl-3-hexene; (e)-3-octene; (e)-3,4-dimethyl-2-pentene; (e)-5-methyl-2-hexene; (e,e)-2,4-heptadiene; (e,e)-1,3,5-heptatriene; ethyl-cyclohexane; ethyl-cyclopentane; ethylidene-cyclopentane; heptane; isopropyl-cyclobutane; isopropyliden-cyclobutane; methyl-cyclobutane; methyl-cycloheptane; methyl-cyclohexane; methyl-cyclopentane; methylene-cyclohexane; methylene-cyclopentane; n-hexane; octane; pentane; propyl-cyclopentane; trans-1-ethyl-3-methyl-cyclopentane; trans-1,2-dimethyl-cyclohexane; trans-1,2-dimethyl-cyclopentane; trans-1,2-dimethyl-cyclopropane; trans-1,3-dimethyl-cyclohexane; trans-1,3-dimethyl-cyclopentane; trans-1,4-dimethyl-cyclohexane; trimethylmethylene-cyclopropane; (z)-1,3-pentadiene; (z)-2-hexene; (z)-2-pentene; (z)-3-methyl-2-pentene; (z)-3-methyl-3-hexene; (z)-3,4-dimethyl-2-pentene; (z)-4-methyl-2-pentene; (z)-4,4-dimethyl-2-pentene
Aliphatic C_9-C_{16} group	n-Decane (acute only)[1]	(1.alpha)-1,2,3-Trimethyl-cyclohexane; (1.alpha)1,2,4-trimethyl-cyclohexane; (1.alpha)1,3,5-trimethyl-cyclohexane; 1-butyl-cyclohexene; 1-ethyl-1-methyl-cyclohexane; 1-methyl-2-pentyl-cyclopropane; 1-methyl-2-propyl-cyclopentane; 1-methyl-2,4-diethyl-cyclohexane; 1-methyl-3-propyl-cyclooctane; 1-methyl-3-(1-methylethyl)-cyclopentane; 1-methyl-4-(1-methylethyl)-cyclohexane; 1-methyl-4-(1-methylethyl)-cyclohexene; 1,1-dimethyl-2-propyl-cyclohexane; 1,1,2-trimethyl-cyclohexane; 1,1,3-trimethyl-cyclohexane; 1,2-diethyl-1-methyl-cyclohexane; 1,2-diethyl-3-methyl-cyclohexane; 1,2,3-trimethyl-cyclohexane; 1,2,4-trimethyl-cyclohexane; 1,5-diisopropyl-2,3-dimethyl-cyclohexane; 2-ethyl-1-decene; 2-ethyl-1-dodecene; 2-ethyl-1-methyl-3-propyl-cyclobutane; 2-methyl-decane; 2-methyl-nonane; 2-methyl-octane; (2-methylbutyl)-cyclopentane; 2,2-dimethyl-decane; 2,2-dimethyl-1-isopropenyl-cyclopentane; 2,2,3-trimethyl-hexane; 2,2,3,4-tetramethyl-pentane; 2,2,4-trimethyl-hexane; 2,2,4,6,6-pentamethyl-heptane; 2,2,6-trimethyl-decane; 2,3-dihydro-1-methyl-1h-indene; 2,3-dihydro-1h-indene; 2,3-dimethyl-heptane; 2,3-dimethyl-octane; 2,3,3-trimethyl-decane; 2,3,4-trimethyl-hexane; 2,3,5-trimethyl-decane; 2,3,5-trimethyl-hexane; 2,4-dimethyl-heptane; 2,4-dimethyl-2,4-heptadiene; 2,4,4-trimethyl-1-hexene;

Table 23A-2 Chemicals of Potential Concern (cont'd)

Chemical	Surrogate Chemical (if applicable)	Chemical Constituent(s)
Aliphatic C_9-C_{16} group (cont'd)	n-Decane (acute only)[1] (cont'd)	2,5-dimethyl-decane; 2,5-dimethyl-dodecane; 2,5-dimethyl-heptane; 2,5-dimethyl-undecane; 2,5,6-trimethyl-octane; 2,6-dimethyl-heptane; 2,6-dimethyl-octane; 2,6-dimethyl-1-heptene; 2,6,6-trimethyl-octane; 2,6,8-trimethyl-decane; 2,6,11-trimethyl-dodecane; 3-(deuteromethyl)-3,6-di-1,5-heptadiene; 3-ethyl-heptane; 3-ethyl-2-methyl-heptane; 3-ethyl-3-heptene; 3-ethyl-3-methyl-hexane; 3-ethyl-4,4-dimethyl-2-pentene; 3-methyl-octane; 3-methyl-undecane; (3-methylbutyl)-cyclopentane; 3-methyl-nonane; 3-methyl-5-propyl-nonane; 3,3-diethyl-pentane; 3,3-dimethyl-undecane; 3,3,4-trimethyl-decane; 3,3,5-trimethyl-decane; 3,3,5-trimethyl-heptane; 3,3,5-trimethyl-1-hexene; 3,3,6-trimethyl-decane; 3,4-nonadiene; 3,4,4-trimethyl-2-hexene; 3,5-dimethyl-undecane; 3,5,5-trimethyl-1-hexene; 3,6-dimethyl-octane; 3,7-dimethyl-nonane; 3,9-dimethyl-undecane; 4-ethyl-octane; 4-methyl-heptane; 4-methyl-octane; 4-methyl-1-decene; 4-propyl-heptane; 4-(1-methylethyl)-heptane; 4,4-dimethyl-heptane; 4,4-dimethyl-undecane; 4,5-dimethyl-nonane; 4,5-nonadiene; 4,6,8-trimethyl-1-nonene; 5-butyl-nonane; 5-ethyl-undecane; 5-methyl-undecane; 5-(1-methylpropyl)-nonane; 5-(2-methylpropyl)-nonane; 6-methyl-1-octene; 6,6-dimethyl-undecane; bicycle[5.1.0]octane; butyl-cyclohexane; butyl-cyclooctane; cis-1-ethyl-2-methyl-cyclohexane; cis-1-ethyl-4-methyl-cyclohexane; cis-1,1,3,5-tetramethyl-cyclohexane; cis-1,2-di(1,1-dimethylethyl)cyclopropane; cis-3,4-dimethyl-1,5-heptadiene; cis-4-methyl-2-undecene; cis-5-methyl-3-undecene; decane; decyl-cyclohexane; hexadecane; hexyl-cyclohexane; methyl-cyclodecane; nonane; octahydro-1-methyl-pentalene; octahydro-2-methyl-pentalene; octyl-cyclohexane; propyl-cyclohexane; trans-1-ethyl-2-methyl-cyclohexane; trans-1-ethyl-4-methyl-cyclohexane; trans-1,1,3,4-tetramethyl-cyclopentane; trans-3,4-dimethyl-1,5-heptadiene; trans-4-methyl-2-undecene; trans-5-methyl-3-undecene; (z)-3-methyl-4-nonene; (z)-5-methyl-2-decene
Aliphatic C_{17}-C_{34} group	Heptadecane	1,3,5-Trimethyl-2-octadecyl-cyclohexane; 1,4-dimethyl-2-octadecyl-cyclohexane; 3-methyl-4-meth-bicyclo[3.2.1]oct-2-ene; eicosyl-cyclohexane; heptadecane
Aliphatic alcohol group	Methanol	1-Heptanol; 1-hexanol; 2-butyl-1-octanol; 2-cyclohexen-1-ol; 2,3,4,5-tetramethylcyclopent-2-en-1-ol; 3-methyl-1-butanol; 3,3-dimethylcyclobutyl methanol; 9-dodecenol; bicyclo[2.2.1]heptan-1-ol; bicyclo[2.2.2]octan-1-ol; (z)-2-methyl-3-octen-2-ol
Aliphatic aldehyde group	Propionaldehyde	2-Methyl-propanal; 2-methyl-2-butenal; 3,3-dimethyl-hexanal; propylhydrazone-propanal; (z)-4,4-dimethyl-2-pentenal
Aliphatic ketone group	Methyl ethyl ketone	1-(2-Furanyl)-ethanone; 1,3-cylopentanedione; 2-methyl-cycloheptanone; 2-methyl-1-penten-3-one; 2,3-dimethyl-cyclohexanone; 3-hexanone; 3-methyl-cyclopentanone; 4-heptanone; 4-octanone; 5-methyl-4-hepten-3-one; cis- 2,3-dimethyl-cyclobutanone; trans-2,3-dimethyl-cyclobutanone

Table 23A-2 Chemicals of Potential Concern (cont'd)

Chemical	Surrogate Chemical (if applicable)	Chemical Constituent(s)
Ammonia	NA	Ammonia
Aromatic C_9-C_{16} group	Naphthalene (acute only)[1]	(1-methylpropyl)-benzene; 1-ethyl-2,3-dimethyl-benzene; 1-ethyl-3-methyl-benzene; 1-ethyl-4-methyl-benzene; 1-methyl-2-(1-methylethyl)-benzene; 1-methyl-2-propyl-benzene; 1-methyl-3-propyl-benzene; 1-octadecene; 1,2-diethyl-benzene; 1,2-dimethyl-benzene; 1,2,3-trimethyl-benzene; 1,2,3,5-tetramethyl-benzene; 1,2,4-trimethyl-benzene; 1,3,5-trimethyl-benzene; 2-methylnaphthalene; acenaphthene; acenaphthylene; isopropylbenzene; n-butylbenzene; n-propylbenzene; naphthalene; p-isopropyltoluene; sec-butylbenzene; tert-butylbenzene
Aromatic C_{17}-C_{34} group	3-Methylcholanthrene (acute only)[1]	2,3-Dihydro-1-methyl-1H-indene; 2,3-dihydro-1H-indene; 3-methylcholanthrene; 7,12-dimethylbenz(a)anthracene; cis-octahydro-1h-indene; perylene
Benzaldehyde	NA	Benzaldehyde
Benzene	NA	Benzene
Benzo(a)pyrene WMM group	Benzo(a)pyrene	Benzo(a)pyrene and equivalents
Benzo(a)pyrene IPM group	Benzo(a)pyrene	Anthracene; benz(a)anthracene; benzo(a)pyrene; benzo(b)fluoranthene; benzo(e)pyrene; benzo(g,h,i)perylene; benzo(k)fluoranthene; chrysene; dibenz(a,h)anthracene; fluoranthene; fluorene; indeno(1,2,3-cd)pyrene; phenanthrene; pyrene
Carbon monoxide	NA	Carbon monoxide
Carbon disulphide group	Carbon disulphide	Allyl sulphide; butyl sulphide; carbon disulphide; carbonyl sulphide; ethyl sulphide
Cyclohexane	NA	Cyclohexane
Dichlorobenzenes	1,4-Dichlorobenzene	Dichlorobenzenes
Ethylbenzene	NA	Ethylbenzene
Formaldehyde	NA	Formaldehyde
n-Hexane	NA	n-Hexane
Hydrogen sulphide	NA	Hydrogen sulphide
Isopropylbenzene	NA	Isopropylbenzene
Methylene chloride	NA	Methylene chloride

Table 23A-2 Chemicals of Potential Concern (cont'd)

Chemical	Surrogate Chemical (if applicable)	Chemical Constituent(s)
Naphthalene	NA	Naphthalene
Nitrogen dioxide	NA	Nitrogen dioxide
Particulate matter	NA	Particulate matter
Propylene oxide group	Propylene oxide	2-Ethyl-3-methyl-oxetane; propylene oxide
Styrene	NA	Styrene
Sulphur dioxide	NA	Sulphur dioxide
Sulphuric acid	NA	Sulphuric acid
Toluene	NA	Toluene
Xylenes	NA	Xylenes

NOTES:

[1] A surrogate was not required for the aliphatic C5-C8 group, aliphatic C9-C16 group, aromatic C9-C16 group and aromatic C17-C34 group on a chronic basis since CCME (2000a) provides chronic exposure limits for the chemical groups.

NA – not applicable

23A.1.2 Selection of Chronic Exposure Limits

The sources of the chronic exposure limits used in the HHRA include the regulatory agencies outlined by Health Canada in the "*Federal Contaminated Site Risk Assessment in Canada*" (Health Canada 2004a):

- the Minimum Risk Levels for Hazardous Substances developed by the Agency for Toxic Substances and Disease Registry (ATSDR 2005a)
- the Toxicological Reference Values (TRVs) and Health-Based Guidance Values established by Health Canada (Health Canada 2004b,c)
- the Maximum Permissible Risk Levels established by the Netherlands National Institute of Public Health and the Environment (RIVM 2001)
- the Integrated Risk Information System (IRIS) developed by the U.S. Environmental Protection Agency (U.S. EPA 2006)
- the Air Quality Guidelines for Europe (Second Edition) developed by the World Health Organization (WHO 2000)

As in the acute assessment, chronic exposure limits were required to satisfy the four selection criteria listed above. If a chronic exposure limit that met each of these criteria was not available from the aforementioned agencies, the search for a chronic exposure limit expanded to the following agencies:

- the chronic RELs recommended by the California Office of Environmental Health Hazard Assessment (OEHHA 2005)
- documentation of the Threshold Limit Values and Biological Exposure Indices (Sixth Edition) developed by the American Conference of Governmental Industrial Hygienists (ACGIH 1991, 2006b)

23A.2 Toxicity Profiles

23A.2.1 1,3-Butadiene

23A.2.1.1 Acute Exposure Limit

Table 23A-3: Summary of Acute Inhalation Exposure Limits for 1,3-Butadiene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	60	½ hour, 1-hour	OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
- not applicable

The ACGIH provides a TLV-TWA occupational exposure limit of 2 ppm (4.4 mg/m^3) for 1,3-butadiene that is developed to be protective of a worker repeatedly exposed during an 8-hour workday and a 40-hour workweek (ACGIH 1991, 2006b). The ACGIH does not consider the acute toxicity of 1,3-butadiene in its derivation of the TWA because the ACGIH regards the measures that control the risk of fire and explosion sufficient to minimize the potential for adverse acute effects. Instead, the ACGIH based the TWA on the development of cancer in human and animal populations exposed to 1,3-butadiene. Specifically, the ACGIH considered the levels of 1,3-butadiene reported in industry during the 1980s (i.e., less than 25 ppm) to represent low risk with respect to cancer. An uncertainty factor of 10 was applied to the TWA to account for intra-species variability in the derivation of a short-term limit.

Although the study team does not support the use of chronic toxicity data in the derivation of an acute limit, no other acute guideline with supporting documentation was identified. Thus, a 24-hour exposure limit of 440 µg/m^3 was used in the acute effects assessment of 1,3-butadiene.

23A.2.1.2 Chronic Exposure Limit(s)

Table 23A-4: Summary of Chronic Inhalation Exposure Limits for 1,3-Butadiene

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	1.7	RsC	Health Canada (2004c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	0.3	RsC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

NOTE:
– not applicable

Health Canada (2000) classifies 1,3-butadiene as a human carcinogen via inhalation based on an observed increase in leukemia in both epidemiological studies and investigations in experimental animals. The RsC was developed from a tumorigenic concentration (TC_{01}) of 1.7 mg/m^3 that is based on the incidence of leukemia in 15,649 workers in an epidemiological study (Health Canada 2004c). The RsC of 1.7 µg/m^3 represents the daily dose via inhalation that is associated with an increased cancer risk of one in 100,000.

The U.S. EPA bases its inhalation unit risk of 3 x 10^{-5} per µg/m^3 (i.e., RsC = 0.3 µg/m^3) on the Health Canada analysis of the leukemia incidence rates in styrene-butadiene rubber workers (U.S. EPA 2006). Although the risk estimates for the two agencies are based on the same epidemiological study, the U.S. EPA made a number of adjustments in the derivation of their unit risk, including:

- accounting for the difference in the amount of air inhaled per day between a worker exposed for an 8-hour work shift and the general public exposed for an entire 24-hour period (10 m^3/d versus 20 m^3/d)
- considering the increased incidence of getting leukemia as opposed to dying from leukemia (i.e., Health Canada based its risk estimates on the excess probability of dying from leukemia, not of getting leukemia)

- the application of an adjustment factor of two, as animal data suggests that 1,3-butadiene may be a multi-site carcinogen and female animals may present additional tumour types. Extrapolation of risk based upon male data only may underestimate the overall cancer risk to the general population (U.S. EPA 2006)

In light of this, the current assessment adopted the more stringent RsC published by the U.S. EPA to evaluate the potential long-term health risks associated with 1,3-butadiene.

A chronic oral exposure limit was not required for the assessment of 1,3-butadiene as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and was not incorporated into the multiple exposure pathway model.

23A.2.2 2-Chloronaphthalene

23A.2.2.1 Acute Exposure Limit

Table 23A-5: Summary of Acute Inhalation Exposure Limits for 2-Chloronaphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
– not available

An acute criterion or guideline is not provided by any of the above regulatory agencies for 2-chloronaphthalene. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for 2-chloronaphthalene.

The U.S. DOE (2005) provides a TEEL-0 (i.e., threshold concentration below which most people will experience no appreciable risk of health effects) of 0.2 mg/m^3 for 2-chloronaphthalene. While TEELs are intended to be compared to 15-minute time-weighted average concentrations (U.S. DOE 2005), in the current HHRA they were compared to the 1-hour predicted ground-level air concentration. Therefore, the TEEL-0 was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TEEL-0 is adjusted to a concentration of 150 $\mu g/m^3$. An uncertainty factor of 10 was applied to the duration-adjusted TEEL-0 to account for intra-species variability. Thus, a 1-hour limit of 15 $\mu g/m^3$ was adopted as the short-term exposure limit for this assessment.

The U.S. DOE does not provide scientific basis for the TEEL-0 value. As a result, the study team is unable to comment on the scientific merit of these limits and will make no assertions as to the adequacy of the study upon which it may be based. The adjusted TEEL-0 thus should be considered provisional and its toxicological relevance limited.

23A.2.2.2 Chronic Exposure Limit(s)

Table 23A-6: Summary of Chronic Inhalation Exposure Limits for 2-Chloronaphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	1	RfC	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
NOTE: – not available			

The RIVM has developed a provisional TCA for 2-chloronaphthalene of 1 $\mu g/m^3$ based on a LOAEC of 1.3 mg/m^3 for small liver effects (RIVM 2001). Rats were exposed via inhalation to di- and tri-chloronaphthalenes for 16 hours per day for 134 days. The LOAEC was adjusted to account for discontinuous exposure (16 hours/24 hours). An uncertainty factor of 1,000 was applied to the duration-adjusted LOAEC to account for extrapolation of the LOAEC for the di- and tri-chloronaphthalenes to a NOAEC for the monochloronapthalenes (3-fold), interspecies differences (10-fold), intra-species differences (10-fold) and for database restrictions (3-fold). The RIVM considers this TCA to be provisional due to limitations associated with the data, and evidence that suggests that the higher chlorinated naphthalenes (i.e., di- and tri-chloronaphthalenes) are more toxic than the monochloronaphthalenes after inhalation exposure.

A chronic oral exposure limit was not required for the assessment of 2-chloronaphthalene as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and was not incorporated into the multiple exposure pathway model.

23A.2.3 2-Methylnaphthalene

23A.2.3.1 Acute Exposure Limit

Table 23A-7: Summary of Acute Inhalation Exposure Limits for 2-Methylnaphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
- not available

An acute criterion or guideline is not provided by any of the above regulatory agencies for 2-methylnaphthalene. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for 2-methylnaphthalene.

The ACGIH has developed a TLV-TWA occupational exposure limit for 1-methylnaphthalene and 2-methylnaphthalene. The ACGIH TWA of 0.5 ppm (3 mg/m^3) is based on irritation to the upper respiratory tract of mice (ACGIH 2006a). A 50% reduction in respiratory rate (RD_{50}) was identified in mice at concentrations of 129 mg/m^3 of 1-methylnaphthalene and 67 mg/m^3 of 2-methylnaphthalene. The ACGIH considers chemical concentrations that are 0.03 x RD_{50} to be protective of respiratory irritation in the workplace. On this basis, the maximum acceptable concentration should be 4 mg/m^3 for 1-methylnaphthalene and 2 mg/m^3 for 2-methylnaphthalene. The ACGIH (2006a) recommends a TWA 0.5 ppm (3 mg/m^3).

The TWA was divided by an uncertainty factor of 10 to account for intra-species variability in deriving the short-term limit. Thus, a 24-hour acute exposure limit of 300 $\mu g/m^3$ was used in the acute effects assessment of 2-methylnaphthalene.

23A.2.3.2 Chronic Exposure Limit(s)

Table 23A-8: Summary of Chronic Inhalation Exposure Limits for 2-Methylnaphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	-	-	OEHHA (2005)
NOTE: – not available			

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for 2-methylnaphthalene. Consequently, the toxicity search was expanded to include the OEHHA (2005, see Table 23A-8) and chronic oral criteria or guidelines provided by any of the above regulatory agencies for 2-methylnaphthalene (see Table 23A-9).

Table 23A-9: Summary of Chronic Oral Exposure Limits for 2-Methylnaphthalene

Regulatory Agency	Value ($\mu g/kg$ bw/d)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	40	RfD	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	4	RfD	U.S. EPA (2006)
WHO	-		WHO (2000)
NOTE: – not available			

The U.S. EPA has developed an oral RfD of 4 µg/kg bw/d for pulmonary alveolar proteinosis based on a subchronic oral bioassay (U.S. EPA 2006). The lower 95% confidence interval on the benchmark dose associated with a 5% extra risk ($BMDL_{05}$) for pulmonary alveolar proteinosis in male and female mice was used as the point of departure for the RfD. The U.S. EPA applied an uncertainty factor of 1,000 to the $BMDL_{05}$ to account for interspecies variability (10-fold), intra-species variability (10-fold), and database deficiencies (10-fold).

As a chronic inhalation limit for 2-methylnaphthalene was not available, the chronic oral limit identified previously was modified to an equivalent inhalation limit of 14 $\mu g/m^3$ based on the following adjustments and assumptions:

- inhalation bioavailability of 100% (assumed)
- oral bioavailability of 80% (RAIS 2006)
- adult body weight of 70.7 kg (Health Canada 2004a)
- adult inhalation rate of 15.8 m^3/d (Health Canada 2004a)

This RfC of 14 μg/m^3 was used in the chronic inhalation effects assessment.

A chronic oral exposure limit was not required for the assessment of 2-methylnaphthalene, as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and was not incorporated into the multiple exposure pathway model.

23A.2.4 Acenaphthene Group

Surrogate: Acenaphthene

23A.2.4.1 Acute Exposure Limit

Table 23A-10: Summary of Acute Inhalation Exposure Limits for Acenaphthene

Regulatory Agency	Value (μg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
– not available

An acute criterion or guideline is not provided by any of the above regulatory agencies for acenaphthene. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for acenaphthene.

The ATSDR provides an intermediate MRL of 0.6 mg/kg bw/d for hepatic effects in mice. The MRL is based on an oral LOAEL of 175 mg/kg bw/d in mice (ATSDR 1995, 2005a). The ATSDR applied an uncertainty factor of 300 to the study LOAEL to account for use of a minimum LOAEL (3-fold), extrapolation from mice to humans (10-fold), and human variability (10-fold). The use of an intermediate LOAEL when characterizing acute exposure is considered to be conservative, as a higher exposure over a shorter time-period (i.e., acute exposure) presumably could occur without risk of adverse effects. The MRL of 0.6 mg/kg bw/d is equivalent to an air concentration of 830 μg/m^3, with adjustment made for chemical bioavailability, described below. This 24-hour exposure limit was used in the acute effects assessment.

23A.2.4.2 Chronic Exposure Limit(s)

Table 23A-11: Summary of Chronic Inhalation Exposure Limits Acenaphthene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	-	-	OEHHA (2005)

NOTE:
– not available

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for acenaphthene. Consequently, the toxicity search was expanded to include the OEHHA (2005, see Table 23A-11) and chronic oral criteria or guidelines provided by any of the above regulatory agencies for acenaphthene (see Table 23A-12).

Table 23A-12: Summary of Chronic Oral Exposure Limits Acenaphthene

Regulatory Agency	Value (μg/kg bw/d)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	50	RsD[1]	RIVM (2001)
U.S. EPA	60	RfD	U.S. EPA (2006)
WHO	-	-	WHO (2000)

NOTE:
[1]Represents the daily dose that is associated with an increased cancer risk of one in 100,000.
– not available

The RIVM provides an RsD of 50 μg/kg bw/d based on the multiplication of the cancer risk of benzo(a)pyrene by the carcinogenic potency of acenaphthene (RIVM 2001). However, the RIVM acknowledges that the IPCS could not reliably classify acenaphthene for genotoxicity owing to inconsistent results and could only classify the carcinogenicity of acenaphthene as questionable. To date, the IARC has not evaluated acenaphthene. Based on the limited evidence supporting the carcinogenicity of acenaphthene, the acenaphthene group was included as a threshold chemical (i.e., non-carcinogen) in the chronic assessment.

The U.S. EPA has developed an RfD of 60 µg/kg bw/d for hepatotoxicity based on the same ATSDR subchronic study discussed under the Acute Exposure Limit (U.S. EPA 2006). In this case, the U.S. EPA identified an oral dose of 175 mg/kg bw/d as the NOAEL, and of 350 mg/kg bw/d as the LOAEL. The U.S. EPA applied an uncertainty factor of 3,000 to the NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), use of a subchronic study for chronic RfD derivation (10-fold), and lack of adequate data in a second species and reproductive and developmental data (3-fold).

Given that there were no available inhalation guidelines for acenaphthene, the oral RfD derived by the U.S. EPA was used for the inhalation assessment, with adjustments made for chemical bioavailability. The chronic oral limit identified previously was modified to an equivalent inhalation limit of 83 µg/m^3 based on the following adjustments and assumptions:

- inhalation bioavailability of 100% (assumed)
- oral bioavailability of 31% (RAIS 2006)
- adult body weight of 70.7 kg (Health Canada 2004a)
- adult inhalation rate of 15.8 m^3/d (Health Canada 2004a)

This RfC of 83 µg/m^3 was used in the chronic inhalation effects assessment.

A chronic oral exposure limit was not required for the assessment of the acenaphthene group because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and was not incorporated into the multiple exposure pathway model.

23A.2.5 Acetaldehyde

23A.2.5.1 Acute Exposure Limit

Table 23A-13: Summary of Acute Inhalation Exposure Limits for Acetaldehyde

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	90	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	500	½-hour, 1-hour	OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
- not available

The AENV recommends a 1-hour AAQO for exposure to acetaldehyde of 90 µg/m^3 (AENV 2005). However, this objective was adopted from the Texas Natural Resource Conservation Commission, which is odour based (TCEQ 2003). Given that this guideline is not health-based, it was not used in the current assessment.

The OMOE provides both a ½-hour and 24-hour standard of 500 µg/m^3, presumably because the short-term toxicity of acetaldehyde is more dependent on concentration than duration of exposure (OMOE 2005a, CEPA 2000a). These AAQOs were not used in the acute effects assessment because they do not have adequate supporting documentation.

Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for acetaldehyde.

The ACGIH provides a TLV-Ceiling of 25 ppm (45 mg/m^3) for eye and upper respiratory tract irritation (ACGIH 1996, 2006b). A TLV-Ceiling represents the chemical concentration that should not be exceeded at any part of the working exposure. Sensitive individuals are reported to experience eye irritation at concentrations as low as 25 ppm of acetaldehyde after a

15-minute exposure, with most people only experiencing irritation at concentrations greater than 50 ppm. On this basis, the ACGIH developed the TLV-Ceiling of 25 ppm (45 mg/m^3).

While this TLV-Ceiling is based on 15-minute exposure, in the current HHRA they were compared to the 1-hour predicted ground-level air concentration. Therefore, the TLV-Ceiling was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TLV-Ceiling is adjusted to a concentration of 34 mg/m^3.

An uncertainty factor of 100 was applied to the TLV-Ceiling to account for intra-species variability (10-fold) and the apparent use of a LOAEL (10-fold). Thus, a 1-hour limit of 340 µg/m^3 was adopted as the short-term exposure limit for this assessment.

23A.2.5.2 Chronic Exposure Limit(s)

Table 23A-14: Summary of Chronic Inhalation Exposure Limits for Acetaldehyde

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	390	RfC	Health Canada (2004c)
	17.2	RsC	
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	9	RfC	U.S. EPA (2006)
	5	RsC	
WHO	-	-	WHO (2000)

NOTE:
– not available

Both Health Canada and IARC classify acetaldehyde as possibly carcinogenic to humans (CEPA 2000a; IARC 1999). As a result, acetaldehyde was included as a carcinogen in the chronic effects assessment.

An RsC of 17.2 µg/m^3 was developed from a tumorigenic concentration (TC_{05}) of 86 mg/m^3, which was associated with a 5% increase in nasal adenocarcinomas and squamous cell carcinomas (combined) in the most sensitive sex (males) of Wistar rats exposed for up to 28 months (Health Canada 2004c; CEPA 2000a). The TC_{05} was derived by Health Canada using a multistage model, with adjustment for intermittent to continuous exposure (6 hours/24 hours x 5 days/7 days). The RsC represents the daily dose via inhalation that is associated with an increased cancer risk of one in 100,000.

The U.S. EPA (2006) also presents a quantitative estimate of carcinogenic risk from inhalation exposure. Its inhalation unit risk of 2.2 x 10^{-6} per µg/m^3 equates to an RsC of 5 µg/m^3 (corresponding to a risk level of one in 100,000). This unit risk was not used for the current assessment for the following reasons.

- The U.S. EPA last reviewed its limit in 1991, while the Health Canada value is more recent (published in 2000).
- The Health Canada and U.S. EPA limits are based on studies conducted by the same researchers. However, the Health Canada limit is based on a 1986 study by Woutersen et al. (1986), which is more recent than the work completed by Woutersen and Appelman in 1984, upon which the U.S. EPA limit is based.
- The scientific rationale for the Health Canada limit is considerably more detailed than what the EPA provides in support of its limit.

Therefore, the Health Canada RsC of 17.2 µg/m^3 was selected for the chronic inhalation assessment of acetaldehyde.

A chronic oral exposure limit was not required for the assessment of acetaldehyde, because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multiple exposure pathway model. As well, acetaldehyde is expected to remain in the medium to which it is discharged (i.e., air). Fugacity modelling predicts that when acetaldehyde is released into ambient air, the distribution of mass is 97.1% in air, 2.6% in water and 0.3% in soil (CEPA 2000a).

23A.2.6 Acrolein

23A.2.6.1 Acute Exposure Limit

Table 23A-15: Summary of Acute Inhalation Exposure Limits for Acrolein

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	6.9	1-hour	ATSDR (2005a)
OEHHA	0.19	1-hour	OEHHA (2000)
OMOE	0.24 0.08	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

NOTE:
– not available

The OMOE (2004, 2005a) provides a 24-hour standard of 0.08 µg/m^3 for acrolein based on a LOAEL of 920 µg/m^3 for nasal lesions in rats (Feron et al. 1978) and histological lesions in the upper respiratory tract of rats (Kutzman 1981; Kutzman et al. 1985).

Feron et al. (1978) observed nasal lesions in rats during a subchronic inhalation study, while Kutzman (1981) and Kutzman et al. (1985) reported histological lesions in the upper airways of rats exposed 6 hours per day, 5 days per week for 62 days. The OMOE (2004) adjusted the studies' LOAEL for continuous exposure (6 hours/24 hours x 5 days/7days) to a concentration

of 164 µg/m^3. In addition, the OMOE (2004) calculated the $LOAEL_{HEC}$ using the RGDR as described by the U.S. EPA and OEHHA.

$$RGDR_{ET} = \frac{(V_E/SA_{ET})_A}{(V_E/SA_{ET})_H}$$

$$RGDR_{ET} = \frac{0.2\ m^3/day/15\ cm^2}{20\ m^3/day/200\ cm^2}$$

Where:

$RGDR_{ET}$ = regional gas dosimetry ratio in the extrathoracic region

V_E = minute volume in rats $(V_E)_A$ or humans $(V_E)_H$

SA_{ET} = extrathoracic surface area in rats $(SA_{ET})_A$ or humans $(SA_{ET})_H$

The rat $LOAEL_{ADJ}$ was then multiplied by the $RGDR_{ET}$ to yield a $LOAEL_{HEC}$ of 23 µg/m^3, as follows:

$$LOAEL_{HEC} = LOAEL_{ADJ} \times RGDR_{ET}$$

$$LOAEL_{HEC} = 164\ \mu g/m^3 \times 0.14$$

A cumulative uncertainty factor of 300 was applied to the $LOAEL_{HEC}$ in the derivation of the proposed 24-hour standard to account for use of a LOAEL (3-fold), interspecies variation (3-fold), extrapolating from subchronic to chronic exposure (3-fold), and intra-species variation (10-fold).

However, derivation of an acute (i.e., 24-hour) criterion from a subchronic LOAEL is considered unnecessary (and inappropriate) since a higher exposure over a shorter time-period presumably could occur without risk of adverse effects. Thus, the uncertainty factor of 3 to account for "extrapolating from subchronic to chronic exposure" could be removed, resulting in a 24-hour standard of 0.23 µg/m^3. Nevertheless, the study LOAEL is still based on subchronic exposure and thus was not used in the short-term effects assessment of acrolein.

The OEHHA provides an acute REL of 0.19 µg/m^3 based on a LOAEL of 0.06 ppm for eye irritation in 36 healthy human workers exposed to acrolein for 5 minutes (Darley et al. 1960; OEHHA 1999a, 2000). In deriving the REL, the OEHHA adjusted the LOAEL to a 1-hour concentration of 0.005 ppm using a modified Haber's Law.

$$C_{ADJ}^{\ n} \times T_{ADJ} = C^n \times T$$

$$C^1 \times 60\ minutes = 0.06^1\ ppm \times 5\ minutes$$

Where:

C_{ADJ} = duration-adjusted concentration

T_{ADJ} = desired time of exposure (60 minutes)

C = concentration of exposure (0.06 ppm)

T = time of exposure (5 minutes)

n = chemical-specific modification factor designed to account for the toxicity of a chemical being concentration and/or deputation dependant (1)

The OEHHA applied an uncertainty factor of 60 to the duration-adjusted LOAEL to account for uncertainty in the LOAEL (6-fold) and intra-species variation (10-fold).

The OEHHA used an "n" value of 1 in its adjustment for less than 1-hour exposure (OEHHA 2000). Ideally, the magnitude of n is determined by evaluating the concentration versus response relationships for several different exposure durations (OEHHA 2000). The time-concentration-response relationship will depend on the time-frame considered as well as the endpoint measured. Thus, there are many "n" values for a single chemical that are applicable to different endpoints. The OEHHA provides an example using ammonia which has an "n" value of 4.6 for irritation and 2 for lethality (OEHHA 1999b). In the case of acrolein, an "n" value of 1.2 is reported for lethality. An "n" value was not reported for irritation. As such, in all likelihood by defaulting to an "n" value of 1 the OEHHA is overestimating the actual short-term toxicity of acrolein. The study team suggests examining the range of 1-hour concentrations calculated using more probable values of n for irritation, such as 1.2 (actual value identified for lethality) to 2. An "n" value of 2 was calculated by the OEHHA as the whole number closest to the midpoint of the range of "n" values reported for 40 gases and vapours.

Using an "n" value of 1.2 or 2 in combination with the cumulative uncertainty factor of 60 applied by the OEHHA in the original REL derivation, an acute exposure limit of 0.29 $\mu g/m^3$ or 0.66 $\mu g/m^3$ is calculated. This range of 1-hour exposure limits was used in the acute effects assessment for acrolein.

23A.2.6.2 Chronic Exposure Limit(s)

Table 23A-16: Summary of Chronic Inhalation Exposure Limits for Acrolein

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	0.4	RfC	Health Canada (2004c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	0.02	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

Health Canada provides a tolerable concentration of 0.4 $\mu g/m^3$ based on the lower benchmark concentration of 0.14 mg/m^3 associated with a 5% increase in non-neoplastic lesions in the nasal respiratory epithelium of rats (Health Canada 2004c; CEPA 2000b; Cassee et al. 1996). A safety factor of 100 was incorporated to account for interspecies variation (10-fold) and intra-species variation (10-fold). The limit was further adjusted by Health Canada to account for continuous exposure (6 hours/24 hours).

The U.S. EPA (2006) provides an inhalation RfC of 0.02 $\mu g/m^3$ based upon a subchronic (i.e., 3 month) rat inhalation study conducted by Feron et al. in 1978. The U.S. EPA adjusted the study LOAEL of 900 $\mu g/m^3$ by accounting for "less than continuous exposure" (i.e., 6 hours/24 hours x 5 days/7 days) and the RDGR (factor of 0.14 to determine a human equivalency concentration). The resultant $LOAEL_{HEC}$ of 20 $\mu g/m^3$ was then divided by an uncertainty factor of 1,000 to account for extrapolation from rat to human (3-fold), intra-species variability (10-fold), subchronic to chronic (10-fold), and for use of a minimal LOAEL (3-fold).

Effects attributable to acrolein inhalation appear to be primarily associated with the level of exposure, and less dependent on the duration of exposure. An adaptive response to the irritant

effects of acrolein has been suggested to occur over time (U.S. EPA 2003). For the reason that the U.S. EPA's use of the "subchronic to chronic" uncertainty factor likely results in an overestimation of the toxicity of acrolein, and because Health Canada's tolerable concentration is based on a benchmark concentration model (which is generally preferred over the standard method of applying uncertainty factors to a LOAEL or NOAEL), the current assessment adopted Health Canada's tolerable concentration of 0.4 µg/m^3 for its chronic inhalation limit.

A chronic oral exposure limit was not required for the assessment of acrolein as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multiple exposure pathway model.

23A.2.7 Aliphatic C5-C8 Group

Surrogate: n-Hexane (acute only)

23A.2.7.1 Acute Exposure Limit

Table 23A-17: Summary of Acute Inhalation Exposure Limits for n-Hexane

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	n-hexane mixture: 7,500 2,500 n-hexane and n-hexane isomers only: 22,500 7,500	 ½-hour 24-hour ½-hour 24-hour	 OMOE (2005a) OMOE (2005a) OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE provides a ½-hour standard of 7,500 µg/m^3 and a 24-hour standard of 2,500 µg/m^3 for an n-hexane mixture (OMOE 2005a,b). These standards were developed from a NOAEL of 204 mg/m^3 for polyneuropathy in humans (Sanagi et al. 1980). The NOAEL was revised to a HEC of 73,000 µg/m^3 by the OMOE and an uncertainty factor of 30 was applied to account for individual sensitivity (10-fold) and potential interaction with other hydrocarbon solvents in commercial n-hexane (3-fold) (OMOE 2005b). The 24-hour exposure limit of 2,500 µg/m^3 was used for the acute effects assessment of the aliphatic C5-C8 group since the aliphatic group includes a variety of organic compounds with six to eight carbon atoms joined together in a straight or branched chain and is not limited to n-hexane and its isomers.

23A.2.7.2 Chronic Exposure Limit(s)

In the case of the aliphatic and aromatic petroleum hydrocarbon groups, the search for chronic inhalation and oral exposure limits was limited to three regulatory agencies: CCME (2000a), MA DEP (2003) and TPHCWG (1997). These agencies have developed chronic exposure limits for the aliphatic and aromatic groups as a whole.

Table 23A-18: Summary of Chronic Inhalation Exposure Limits for the Aliphatic C5-C8 Group

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
CCME	18,400	RfC	CCME (2000a)
MA DEP	200	RfC	MA DEP (2003)
TPHCWG	18,400	RfC	TPHCWG (1997)

The CCME (2000a) provides an RfC of 18,400 $\mu g/m^3$ for the C5-C8 aliphatic group based on the neurotoxic endpoint of commercial hexane. This exposure limit was adopted from the TPHCWG (1997) and was developed from the NOAEL of 10,307 mg/m^3 for two (rat and mice) chronic bioassays involving lifetime exposure. The NOAEL was adjusted for continuous exposure (6 hours/24 hours and 5 days/7 days) to a concentration of 1,840 mg/m^3. An uncertainty factor of 100 was applied by the TPHCWG to account for interspecies (10-fold) and intra-species (10-fold) variability. The TPHCWG (1997) recommends using the RfC derived for commercial hexane over an RfC specific to n-hexane (as is the case of the MA DEP RfC) as it is more representative of the C5-C8 aliphatic fraction. According to the TPHCWG, using n-hexane alone results in an overestimation of the toxicity of the fraction since n-hexane is the most toxic of the group's constituents, it is uniquely toxic, and its interaction with other petroleum compounds influences its toxicity. On this basis, the RfC for commercial hexane will be used to evaluate the risks associated with this petroleum mixture. This RfC corresponds to an inhalation dose of 4,100 µg/kg bw/d based on an average adult body weight of 70.7 kg and an inhalation rate of 15.8 m^3/d (Health Canada 2004a).

The MA DEP (2003) RfC of 200 $\mu g/m^3$ was developed from toxicity data specific to n-hexane, which is considered overly conservative and inappropriate when characterizing the toxicity of the aliphatic C5-C8 group as a whole. Furthermore, the MA DEP RfC was adopted from the 1993 U.S. EPA RfC for n-hexane, which was updated in 2005 to a value of 700 $\mu g/m^3$ for peripheral neuropathy in a subchronic rat inhalation study (U.S. EPA 2006).

Based on the Environment Canada (2006) physical and chemical screening, the aliphatic C5-C8 group was assessed via multiple exposure pathways.

Table 23A-19: Summary of Chronic Oral Exposure Limits the Aliphatic C5-C8 Group

Regulatory Agency	Value (µg/kg bw/d)	Type	Reference
CCME	5,000	RfC	CCME (2000a)
MA DEP	40	RfC	MA DEP (2003)
TPHCWG	5,000	RfC	TPHCWG (1997)

The CCME (2000a) RfD of 5,000 µg/kg bw/d based on the neurotoxicity of commercial hexane was selected for use in the chronic oral effects assessment. As in the chronic inhalation assessment, this RfD was adopted from the TPHCWG (1997). The TPHCWG developed the oral RfD from the inhalation limit (discussed above), assuming an adult body weight of 70 kg, a breathing rate of 20 m^3/d, and 100% absorption.

The MA DEP recommends an oral RfD of 40 µg/kg bw/d based on reduced body weight and neurotoxicity (MA DEP 2003). In a subchronic gavage study, a LOAEL of 570 mg/kg bw/d was

identified in rats exposed to n-hexane. The LOAEL was adjusted for discontinuous exposure (5 days/7 days) to a concentration of 407 mg/ kg bw/d. An uncertainty factor of 10,000 was applied to the duration-adjusted LOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), subchronic to chronic extrapolation (10-fold) and use of a LOAEL (10-fold). As in the chronic inhalation assessment (discussed above), use of an RfD developed on the basis of n-hexane toxicity alone is overly conservative and inappropriate when characterizing the toxicity of the aliphatic C5-C8 group as a whole. In addition, the degree of uncertainty identified by the MA DEP with the application of a 10,000-fold uncertainty factor does not imply a high degree of confidence in the limit. Thus, the CCME RfD of 5,000 µg/kg bw/d was used in the chronic oral effects assessment of this aliphatic group.

For incorporation in the multiple exposure pathway model, inhalation bioavailability was assumed to be 100% (no specific data were identified in the literature regarding the amount of C5-C8 aliphatic that is absorbed via inhalation) and (RAIS 2006). As well, an oral bioavailability in humans of 80% and a dermal bioavailability of 10% was assumed for this assessment based on n-hexane (RAIS 2006).

23A.2.8 Aliphatic C9-C16 Group

Surrogate: n-Decane (acute only)

23A.2.8.1 Acute Exposure Limit

Table 23A-20: Summary of Acute Inhalation Exposure Limits for n-Decane

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	60,000	1-hour	OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE has developed a 1-hour AAQC of 60,000 $\mu g/m^3$ for n-decane (OMOE 2005a). Although this exposure limit is based on health and odour considerations, the specific basis is not provided. As a result, the study team is unable to comment on the scientific merit of this limit.

However, there are no published guidelines with supporting documentation available for acute exposure to n-decane and thus the 1-hour exposure limit of 60,000 $\mu g/m^3$ was used in the acute effects assessment.

23A.2.8.2 Chronic Exposure Limit(s)

In the case of the aliphatic and aromatic petroleum hydrocarbon groups, the search for chronic inhalation and oral exposure limits was limited to three regulatory agencies: CCME (2000a), MA DEP (2003) and TPHCWG (1997). These agencies have developed chronic exposure limits for the aliphatic and aromatic groups as a whole.

Table 23A-21: Summary of Chronic Inhalation Exposure Limits for the Aliphatic C9-C16 Group

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
CCME	1,000	RfC	CCME (2000a)
MA DEP	200	RfC	MA DEP (2003)
TPHCWG	1,000	RfC	TPHCWG (1997)

The CCME (2000a) provides an RfC of 1,000 $\mu g/m^3$ for the aliphatic C9-C16 group, which was adopted from the TPHCWG (1997). The RfC is based on the hepatic and haematological effects of de-aromatized petroleum streams and JP-8 Jet Fuel, which together cover the entire range of the fraction. Two separate studies were examined by the TPHCWG.

- Study #1 (Phillips and Egan 1984): Sprague-Dawley rats were exposed to 0, 300 or 900 ppm of C10-C11 isoparaffinic solvent for 6 hours per day, 5 days per week, for 12 weeks. The NOAEL of 900 ppm (5,226 mg/m^3) was adjusted for intermittent exposure (6 hours/24 hours x 5 days/7 days) to a concentration of 933 mg/m^3. An uncertainty factor of 1,000 was applied to the duration-adjusted NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). The result is an RfC of 0.9 mg/m^3.
- In the same study, Sprague-Dawley rats were exposed to 0, 300 or 900 ppm of de-aromatized white spirit vapours (DAWS) for 6 hours per day, 5 days per week, for 12 weeks. The study NOAEL of 5,485 mg/m^3 was adjusted for intermittent exposure (6 hours/24 hours x 5 days/7 days) to a concentration of 979 mg/m^3. An uncertainty factor of 1,000 was applied to the adjusted NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). The result is an RfC of 1.0 mg/m^3.
- Study #2 (Matti et al. 1991): Mice and rats were exposed to JP-8 vapours continually for 90 days. A NOAEL of 1,000 mg/m^3 was identified and an uncertainty factor of 1,000 was applied to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). The result is an RfC of 1.0 mg/m^3.

Based on these two studies (RfCs range between 0.9 and 1.0 mg/m^3), an RfC of 1,000 $\mu g/m^3$ was selected by the TPHCWG (1997).

In part, the MA DEP (2003) based its RfC on Study #1 (Phillips and Egan 1984) of the TPHCWG studies. However, the concentration the TPHCWG defined as a NOAEL was reported to be a LOAEL by the MA DEP. As a result, the MA DEP applied an additional uncertainty factor of 3 in the derivation of the RfC to account for the use of a LOAEL, resulting in RfCs of 0.3 mg/m^3 instead of 0.9 or 1.0 mg/m^3. In addition to Study #1, the MA DEP considered a subchronic inhalation study that exposed rats to 0, 2,620 or 5,253 mg/m^3 (0, 400 or 800 ppm) of DAWS for 6 hour per day, 5 days per week for 6 months (Lund et al. 1995). Following a 2-6 month exposure-free period, neurophysiological, neurobehavioural, and microscopic pathologic examinations were performed. Exposure-related changes in sensory evoked potentials were observed and a decrease in motor activity during dark periods was reported. According to the authors, a 6-month exposure to DAWS can result in long-lasting and possibly irreversible effects in the nervous system of the rat. The LOAEL of 2,620 mg/m^3 (400 ppm) was adjusted for continuous exposure (6 hours/24 hours x 5 days/7 days) to a concentration of 468 mg/m^3. An uncertainty factor of 3,000 was applied by MA DEP to account for interspecies

variability (10-fold), intra-species variability (10-fold), adjusting from a LOAEL to a NOAEL (10-fold), and use of a subchronic study (3-fold). The result is an RfC of 0.2 mg/m^3.

Based on these two studies the MA DEP (2003) established an RfC of 200 μg/m^3 for neurotoxicity.

The study team concluded, upon review of the Phillips and Egan (1984) study, that the MA DEP accurately interpreted the exposure concentration of 300 ppm as a LOAEL, and not a NOAEL as the TPHCWG and CCME reported. Phillips and Egan (1984) observed increase kidney weights and alterations in kidney structure in male rats in the low and high exposure groups for both the C10-C11 isoparaffinic solvent- and DAWS-exposed male rats. The effect appeared to be dose related and time dependant (Phillips and Egan 1984). As a result, the MA DEP RfC of 200 μg/m^3 was selected for the chronic inhalation effects assessment of the aliphatic C9-C16 group. This RfC corresponds to an inhalation dose of 45 μg/kg bw/d based on an average adult body weight of 70.7 kg and an inhalation rate of 15.8 m^3/d (Health Canada 2004a).

Based on the Environment Canada (2006) fate and persistence screening the aliphatic C9-C16 group was assessed via multiple exposure pathways.

Table 23A-22: Summary of Chronic Oral Exposure Limits the Aliphatic C9-C16 Group

Regulatory Agency	Value (μg/kg bw/d)	Type	Reference
CCME	100	RfC	CCME (2000a)
MA DEP	100	RfC	MA DEP (2003)
TPHCWG	100	RfC	TPHCWG (1997)

An RfD of 100 μg/kg bw/d is provided by the CCME (2000a) for the C9-C16 aliphatic group, which was adopted from the TPHCWG (1997). The RfD is based on both a LOAEL and a NOAEL for hepatic and haematological effects in rats exposed to de-aromatized aliphatics (C9-C13). Two separate studies were examined by the TPHCWG.

- Study #1: Rats were dosed orally with C9-C12 aliphatics including isoparaffins, naphthenes and n-alkanes for 90 days. A LOAEL of 500 mg/kg bw/d was identified based on observed reversible liver and haematological effects. An uncertainty factor of 5,000 was applied to the study LOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), use of a subchronic study (10-fold), and use of a LOAEL versus a NOAEL (5-fold). The result is an RfD of 0.1 mg/kg bw/d.
- Study #2: Rats were exposed to C10-C13 aliphatics including isoparaffins, naphthenes and n-alkanes for 13 weeks. A NOAEL of 100 mg/kg bw/d was identified. The TPHCWG (1997) applied an uncertainty factor of 1,000 to the study NOAEL to account for intra-species variation (10-fold), interspecies variation (10-fold), and use of a subchronic study (10-fold). The result is an RfD of 0.1 mg/kg bw/d.

An RfD of 0.1 mg/kg bw/d was selected from the aforementioned studies by the TPHCWG (1997). In addition to the above studies, the TPHCWG considered toxicity data for JP-8 Jet Fuel and C11-C17 isoparaffinic solvent, which were less conservative.

Similar to the TPHCWG, the MA DEP (2003) RfD of 100 μg/kg bw/d was developed from three separate studies.

- Study #1 (Anon 1991a): Rats were orally dosed with 0, 500, 2,500 or 5,000 mg/kg bw/d of C9-C12 isoparaffins, n-alkanes and naphthalenes for 90 days. A LOAEL of 500 mg/kg bw/day was identified for changes in serum chemistry and liver weight. An uncertainty factor of 5,000 was applied to the LOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), use of a subchronic study (10-fold) and use of a LOAEL (5-fold). The result is an RfD of 0.1 mg/kg bw/d.
- Study #2 (Anon 1991b): Rats were orally treated with 0, 100, 500 or 1,000 mg/kg bw/d of C10-C13 isoparaffins, n-alkanes and naphthalenes for 13 weeks. A NOAEL of 100 mg/kg bw/d was identified for changes in serum chemistry and liver weight. An uncertainty factor of 1,000 was applied to the adjusted NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). The result is an RfD of 0.1 mg/kg bw/d.
- Study #3 (Anon 1990): Rats were orally treated with 0, 100, 500 or 1,000 mg/kg bw/d of C11-C17 isoparaffinic solvent for 13 weeks. A NOAEL of 100 mg/kg bw/d was identified based on observed liver effects. An uncertainty factor of 1,000 was applied to the adjusted NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). The result is an RfD of 0.1 mg/kg bw/d.

As in the TPHCWG (1997) assessment, an RfD of 0.1 mg/kg bw/d was selected from the above studies by the MA DEP (2003). Thus, an RfD of 100 μg/kg bw/d was used in the chronic oral effects assessment for the aliphatic C9-C16 group.

For incorporation in the multiple exposure pathway model, inhalation, oral and dermal bioavailability was assumed to be 100% since no data were identified in the literature regarding the amount of aliphatic C9-C16 or any of the individual constituents that is absorbed via inhalation.

23A.2.9 Aliphatic C17-C34 Group

23A.2.9.1 Acute Exposure Limit

Table 23A-23: Summary of Acute Inhalation Exposure Limits for Heptadecane

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

An acute criterion or guideline is not provided by any of the above regulatory agencies for heptadecane. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for heptadecane.

The U.S. DOE (2005) provides a TEEL-0 (i.e., threshold concentration below which most people will experience no appreciable risk of health effects) of 15 mg/m^3 for heptadecane. While TEELs are intended to be compared to 15-minute time-weighted average concentrations (U.S. DOE 2005), in the current HHRA they were compared to the 1-hour predicted ground-level air concentration. Therefore, the TEEL-0 was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TEEL-0 is adjusted to a concentration of 11,000 µg/m^3. An uncertainty factor of 10 was applied to the duration-adjusted TEEL-0 to account for intra-species variability. Thus, a 1-hour limit of 1,100 µg/m^3 was adopted as the short-term exposure limit for this assessment.

The U.S. DOE does not provide scientific basis for the TEEL-0 value. As a result, the study team is unable to comment on the scientific merit of these limits and will make no assertions as to the adequacy of the study upon which it may be based. The adjusted TEEL-0 thus should be considered provisional and its toxicological relevance limited.

23A.2.9.2 Chronic Exposure Limit(s)

In the case of the aliphatic and aromatic petroleum hydrocarbon groups, the search for chronic inhalation and oral exposure limits was limited to three regulatory agencies: CCME (2000a), MA DEP (2003) and TPHCWG (1997). These agencies have developed chronic exposure limits for the aliphatic and aromatic groups as a whole.

As stated in the acute effects assessment, appropriate inhalation toxicity data were not identified for the individual constituents or fractions in the C17-C34 carbon range (CCME 2000a). According to CCME, this could be the result of the hydrocarbons in this group not being volatile and thus inhalation is not a likely exposure pathway. Nevertheless, C17-C34 aliphatics will be emitted to the atmosphere from the proposed facility and thus require an inhalation limit.

Based on the Environment Canada (2006) physical and chemical screening the aliphatic C17-C34 group was assessed via multiple exposure pathways.

Table 23A-24: Summary of Chronic Oral Exposure Limits the Aliphatic C17-C34 Group

Regulatory Agency	Value (µg/kg bw/d)	Type	Reference
CCME	2,000	RfC	CCME (2000a)
MA DEP	2,000	RfC	MA DEP (2003)
TPHCWG	2,000	RfC	TPHCWG (1997)

An RfD of 2,000 µg/kg bw/d is provided by the CCME (2000a) for the C17-C34 aliphatic group based on liver granuloma formation. The RfD was adopted from TPHCWG (1997), which derived the limit from a study that administered white mineral oil to rats for 90 days. A NOAEL of 200 mg/kg bw/d was identified for the low molecular weight oils (aliphatic C17-C34). The TPHCWG (1997) applied an uncertainty factor of 100 to the study NOAEL to account for interspecies variation (3-fold), intra-species variation (10-fold), and use of a subchronic study

(3-fold). The inhalation exposure limit of 9,000 μg/m^3 was derived from the oral exposure limit based on an average adult body weight of 70.7 kg and an inhalation rate of 15.8 m^3/d (Health Canada 2004a). No adjustments were made for relative bioavailability.

Since the MA DEP (2003) provides an equivalent RfD to the TPHCWG and CCME, this RfD of 2,000 μg/kg bw/d and subsequent RfC of 9,000 μg/m^3 were used as the chronic exposure limits for the aliphatic C9-C18 group.

For incorporation in the multiple exposure pathway model, inhalation, oral and dermal bioavailability were assumed to be 100% since no data were identified in the literature regarding the amount of aliphatic C17-C34 or any of the individual constituents that is absorbed via inhalation.

23A.2.10 Aliphatic Alcohol Group

Surrogate: Methanol

23A.2.10.1 Acute Exposure Limit

Table 23A-25: Summary of Acute Inhalation Exposure Limits for Isopropanol and Methanol

Regulatory Agency	Value (μg/m^3)	Averaging Time	Reference
Isopropanol			
AENV	7,850	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	3,200	1-hour	OEHHA (2000)
OMOE	22,000 7,300	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)
Methanol			
AENV	2,600	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	3,200	1-hour	OEHHA (2000)
OMOE	12,000 4,000	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The AENV (2005) provides AAQOs for isopropanol and methanol which were adopted from the Texas Natural Resource Conservation Commission, but no specific basis is provided. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of the aliphatic alcohol group.

The OMOE (2005a) has established guidelines for various alcohols; however, isopropanol is the only chemical for which supporting documentation is provided. The OMOE (2005c) provides a ½-hour standard of 22,000 μg/m^3 and a 24-hour AAQC of 7,300 μg/m^3 for isopropanol. The ½-hour standard is based on odour perception, while the 24-hour standard is based on adverse renal effects in a two year chronic inhalation study with male rats. A NOAEL of 500 ppm was

identified and adjusted for intermittent exposure (6/24 hours x 5/7 days) to a concentration of 90 ppm. An uncertainty factor of 30 was applied to the duration-adjusted NOAEL to account for intra-species variation (10-fold) and interspecies variation (3-fold). Interspecies variation is typically accounted for by a factor of 10 and consists of two components – pharmacokinetics and pharmacodynamics. However, sufficient evidence exists to indicate that the pharmacokinetics of isopropanol in humans and rats are similar. On this basis, the uncertainty factor was reduced to 3 (OMOE 2005c).

The OEHHA (2000) has established acute RELs for both isopropanol and methanol. The acute REL of 3,200 µg/m^3 for isopropanol is based on a NOAEL of 200 ppm for mild irritation of the eyes, nose and throat in ten human subjects exposed to isopropanol vapour for 4 minutes (OEHHA 1999c). The NOAEL was adjusted to a 1-hour concentration of 13 ppm (4 minutes/60 minutes) and an uncertainty factor of 10 was applied to the adjusted NOAEL to account for intra-species variation. As discussed earlier with respect to acrolein, the adjustment of the study NOAEL to a 1-hour concentration does not account for atmospheric conditions, resulting in an overly conservative exposure limit.

A common methodology for deriving 1-hour concentrations from 4-minute concentrations is as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{4-minute concentration}}{(\text{60 minutes/4 minutes})^{0.2}}$$

The exponent for the 4-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the LOAEL is adjusted to a concentration of 116 ppm. Application of an uncertainty factor of 10 to account for intra-species variability results in an acute exposure limit of 28,000 µg/m^3.

The OEHHA has established an acute REL of 28,000 µg/m^3 for methanol based on subtle neurologic effects in male volunteers (OEHHA 1999d, 2000). Twelve healthy male volunteers were exposed to 250 mg/m^3 (192 ppm) methanol for 75 minutes and administered 20 neurobehavioural and neurophysiological tests before, during, and after exposure. To obtain the REL, the NOAEL of 192 ppm was extrapolated to a 1-hour concentration of 214 ppm and the OEHHA applied an uncertainty factor of 10 to account for intra-species variability.

The OEHHA 1-hour REL of 28,000 µg/m^3 derived for methanol was used in the acute effects assessment of the aliphatic alcohol group. The exposure limit derived by the OMOE for isopropanol was not used in the current assessment as it was based on a chronic inhalation study and therefore is not applicable for deriving an acute guideline.

23A.2.10.2 Chronic Exposure Limit(s)

Table 23A-26: Summary of Chronic Inhalation Exposure Limits for the Isopropanol and Methanol

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Isopropanol			
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	7,000	RfC	OEHHA (2005)
Methanol			
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	4,000	RfC	OEHHA (2005)

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for isopropanol or methanol. Consequently, the toxicity search was expanded to include the OEHHA (2005) for isopropanol and methanol (see Table 23A-26).

The OEHHA (2005) provides chronic RELs for both isopropanol (7,000 $\mu g/m^3$) and methanol (4,000 $\mu g/m^3$). The chronic inhalation REL for methanol was employed in the current assessment since it is the more conservative of the two available chronic inhalation guidelines.

The REL for methanol is based on a NOAEL of 1,000 ppm for developmental effects in mice (OEHHA 2005). Pregnant mice were exposed to methanol 7 hours per day on days 6 to 15 of gestation. The most sensitive developmental toxicity endpoint of abnormal cervical ribs was associated with a benchmark concentration with a 5% added risk above background (BMC_{05}) of 305 ppm. The BMC_{05} was adjusted to continuous exposure (7 hours/24 hours) and a HEC was calculated assuming a regional gas dose ratio of 1.0, resulting in a BMC_{05}(HEC) of 89 ppm. The OEHHA (2005) applied an uncertainty factor of 30 to account for interspecies variability (3-fold) and intra-species variability (10-fold). The chronic REL of 4,000 $\mu g/m^3$ was used in the chronic inhalation effects assessment.

A chronic oral exposure limit was not required for the assessment of the aliphatic alcohol group since the persistence and bioaccumulation parameters for isopropanol and methanol did not exceed any of Environment Canada's (2006) screening parameters and thus was not incorporated into the multiple exposure pathway model.

23A.2.11 Aliphatic Aldehyde Group

Surrogate: Propionaldehyde

23A.2.11.1 Acute Exposure Limit

Table 23A-27: Summary of Acute Inhalation Exposure Limits for Propionaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

An acute criterion or guideline is not provided by any of the above regulatory agencies for propionaldehyde. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for propionaldehyde.

The ACGIH has developed a TLV-TWA occupational exposure limit for propionaldehyde. Propionaldehyde (or propanal, C_3H_6O) is similar in structure to 2-methylpropanal (C_4H_8O). For this reason, the exposure limits for the aliphatic aldehyde group were based on the known toxicity of propionaldehyde.

The ACGIH TLV-TWA of 20 ppm (47,500 $\mu g/m^3$) is based on irritation to the upper respiratory tract of mice (ACGIH 2002, 2006b). A 50% reduction in respiratory rate (RD_{50}) was identified in two strains of mice at concentrations greater than 20,000 ppm. The ACGIH considers chemical concentrations that are 0.01 to 0.03 x RD_{50} to be protective of respiratory irritation in the workplace. On this basis, the TWA of 20 ppm was calculated.

The TWA was divided by an uncertainty factor of 10 to account for intra-species variability in deriving the short-term limit. Thus, a 24-hour acute exposure limit of 4,750 $\mu g/m^3$ was used in the acute effects assessment of the aliphatic aldehyde group.

23A.2.11.2 Chronic Exposure Limit(s)

Table 23A-28: Summary of Chronic Inhalation Exposure Limits for the Propionaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	-	-	OEHHA (2005)

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for propionaldehyde. Consequently, the toxicity search was expanded to include the OEHHA (2005, see Table 23A-28) and chronic oral criteria or guidelines provided by any of the above regulatory agencies for propionaldehyde (see Table 23A-29).

Table 23A-29: Summary of Chronic Oral Exposure Limits Propionaldehyde

Regulatory Agency	Value ($\mu g/kg$ bw/d)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)

Finally, the toxicity search was extended to occupational exposure values established by the ACGIH. The same ACGIH TLV–TWA occupational exposure limit of 47,500 $\mu g/m^3$ that formed the basis of the acute exposure limit was used to derive the chronic inhalation exposure limit (ACGIH 2002, 2006b). However, the TLV–TWA was adjusted from an 8-hour time-weighted average occupational exposure to continuous exposure using the following calculation (U.S. EPA 2002):

$$TLV\text{–}TWA_{adj} = TLV\text{–}TWA \times \frac{MV_{ho}}{MV_h} \times \frac{Exp_{ho}}{Exp_h}$$

Where:

$TLV\text{–}TWA_{adj}$ = chemical-specific TLV–TWA for chronic exposure via inhalation ($\mu g/m^3$)

TLV–TWA = chemical-specific TLV–TWA ($\mu g/m^3$)

MV_{ho} = amount of air used by a worker during an 8-hour work period (10 m^3/d)

MV_h = amount of air used by an individual in the general population during a day (20 m^3/d)

Exp_{ho} = days per week a worker is exposed (5 days)

Exp_{h} = days per week an individual in the general population is exposed (7 days)

An uncertainty factor of 10 was applied to the TLV–TWA_{adj} to account for intra-species variability, resulting in an RfC of 1,700 µg/m^3. This RfC was used in the chronic inhalation effects assessment of the aliphatic aldehyde group.

A chronic oral exposure limit was not required for the assessment of the aliphatic aldehyde group since the persistence and bioaccumulation parameters for propionaldehyde did not exceed any of Environment Canada's (2006) screening parameters and thus was not incorporated into the multiple exposure pathway model.

23A.2.12 Aliphatic Ketone Group

Surrogate: Methyl ethyl ketone

23A.2.12.1 Acute Exposure Limit

Table 23A-30: Summary of Acute Inhalation Exposure Limits for Methyl Ethyl Ketone

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	13,000	1-hour	OEHHA (2000)
OMOE	3,000 1,000	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

Although the OMOE (2005a) provides ½-hour and 24-hour standards for methyl ethyl ketone, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of methyl ethyl ketone.

The OEHHA provides an acute REL of 13,000 µg/m^3 for methyl ethyl ketone based on eye, nose and throat irritation in four healthy human volunteers (OEHHA 1999e, 2000). A LOAEL of 270 ppm was reported for 2-hour exposure. An uncertainty factor of 60 was applied to the study LOAEL to account for intra-species variation (10-fold) and use of a LOAEL (6-fold). Use of a LOAEL is typically accounted for by a factor of 10; however, the LOAEL is based on mild irritation and thus OEHHA considered a factor of 6 to be adequate. This REL was selected as the 1-hour exposure limit for the aliphatic ketone group.

23A.2.12.2 Chronic Exposure Limit(s)

Table 23A-31: Summary of Chronic Inhalation Exposure Limits for Methyl Ethyl Ketone

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	5,000	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA (2006) provides an RfC of 5,000 $\mu g/m^3$ for methyl ethyl ketone based on developmental effects. This RfC is developed from a lowest-exposure-concentration (LEC) of 5,202 mg/m^3 for reduced fetal birth rate in a mice exposed 7 hours per day on days 6 through 15 of gestation (Schwetz et al. 1991; Mast et al. 1989). The LEC was adjusted for intermittent exposure (7 hours/24 hours) to a value of 1,517 mg/m^3. An uncertainty factor of 300 was applied to account for intra-species variability (10-fold), interspecies extrapolation (3-fold) and database deficiencies (10-fold). The uncertainty factor for interspecies extrapolation embodies two areas of uncertainty: pharmacokinetics and pharmacodynamics. In this assessment, the pharmacokinetic component is addressed by the calculation of the HEC according to the procedures in the RfC methodology. Accordingly, only the pharmacodynamic area of uncertainty remains as a partial factor for interspecies uncertainty and thus a partial uncertainty factor was incorporated. This inhalation RfC of 5,000 $\mu g/m^3$ was selected as the chronic exposure limit for the aliphatic ketone group.

A chronic oral exposure limit was not required for the assessment of the aliphatic ketone group since the persistence and bioaccumulation parameters for methyl ethyl ketone did not exceed any of Environment Canada's (2006) screening parameters and thus it was not incorporated into the multiple exposure pathway model.

23A.2.13 Ammonia

23A.2.13.1 Acute Exposure Limit

Table 23A-32: Summary of Acute Inhalation Exposure Limits for Ammonia

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	1,400	1-hour	AENV (2005)
ATSDR	1,200	24-hour	ATSDR (2005a)
OEHHA	3,200	1-hour	OEHHA (2000)
OMOE	300, 3,600 (interim) 100	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

Although the OMOE (2005a) provides ½-hour and 24-hour standards for ammonia, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of ammonia.

The ATSDR (2005a, 2004a) provides an acute MRL of 1.7 ppm (1,200 μg/m^3) for mild irritation of the eyes, nose and throat in humans exposed to ammonia gas. Sixteen human volunteers were exposed to 50, 80, 110 or 140 ppm for 2 hours. The testing was repeated with a 1-week interval. During exposure, each volunteer recorded subjective feelings every 15 minutes. Immediately prior to and following exposure, vital capacity, forced expiratory volume, and forced inspiratory volume were measured. A LOAEL of 50 ppm was reported. The LOAEL was not adjusted to a 24-hour exposure since the effects observed were local irritation effects and thus not time-dependent but rather concentration-dependent (ATSDR 2004a). An uncertainty factor of 30 was applied to the LOAEL to account for use of a (minimal) LOAEL (3-fold) and human variation (10-fold). This acute MRL was used as a 24-hour exposure limit in the acute effects assessment for ammonia.

23A.2.13.2 Chronic Exposure Limit(s)

Table 23A-33: Summary of Chronic Inhalation Exposure Limits for Ammonia

Regulatory Agency	Value (μg/m^3)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	70	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	100	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The ATSDR provides a chronic MRL of 0.1 ppm (70 μg/m^3) based on the respiratory effects of ammonia (ATSDR 2005a). Sense of smell, prevalence of respiratory symptoms, eye and throat irritation, and lung function parameters were measured in humans exposed for an average of 12.2 years in a soda ash plant (ATSDR 2004a). The cohort included 52 workers and 35 controls. The subjects were assessed on the first and last workday of their workweek. Exposure levels were determined by sampling exposed and control workers over one work shift. The average sample collection period was 8.4 hours. The mean time-weighted average exposure concentration of 9.2 ppm (6.4 mg/m^3) was identified as the NOAEL. The NOAEL was adjusted for continuous exposure (8 hours/24 hours x 5 days/7 days) and divided by an uncertainty factor of 10 for the protection of sensitive individuals. As well, a modifying factor of 3 was used to account for the lack of reproductive and developmental studies (ATSDR 2004a).

The U.S. EPA (2006) has developed an RfC of 100 μg/m^3 based on the same study (Holness et al. 1989) as the ATSDR (2004a). The minor difference between the limit values of the U.S. EPA and the ATSDR arises from a different way of extrapolating working-week exposure conditions to continuous exposure conditions and the final rounding of the U.S. EPA RfC. The U.S. EPA converted the NOAEL from an 8-hour time-weighted average occupational exposure to continuous exposure using the following calculation:

$$NOAEL_{HEC} = NOAEL \times \frac{MV_{ho}}{MV_h} \times \frac{Exp_{ho}}{Exp_h}$$

Where:

$NOAEL_{HEC}$ = NOAEL in the human population from continuous exposure to ammonia (mg/m^3)

NOAEL = NOAEL for discontinuous exposure in an occupational setting (6.4 mg/m^3)

MV_{ho} = amount of air used by a worker during an 8-hour work period (10 m^3/d)

MV_h = amount of air used by an individual in the general population during a day (20 m^3/d)

Exp_{ho} = days per week a worker is exposed (5 days)

Exp_h = days per week an individual in the general population is exposed (7 days)

An uncertainty factor of 30 was applied to the $NOAEL_{HEC}$ of 2.3 mg/m^3 to account for intra-species variability (10-fold) and database inadequacy (3-fold). Database deficiencies included the lack of chronic data, the proximity of the LOAEL to the NOAEL, and the lack of reproductive and developmental toxicology studies. A partial uncertainty factor of 3 was deemed to be adequate by the U.S. EPA since studies in rats have not demonstrated an increase in blood ammonia levels at exposures of 32 ppm and only minimal increases at 300-1,000 ppm, suggesting that no significant distribution is likely to occur at the HEC level. The result is an RfC of 76 $\mu g/m^3$ for ammonia; however, the U.S. EPA rounds this limit up to 100 $\mu g/m^3$. For the chronic inhalation effects assessment the non-rounded RfC of 76 $\mu g/m^3$ was used.

A chronic oral exposure limit was not required for the assessment of ammonia since the persistence and bioaccumulation parameters for ammonia did not exceed any of Environment Canada's (2006) screening parameters and thus it was not incorporated into the multiple exposure pathway model.

23A.2.14 Aromatic C9-C16 Group

Surrogate: Naphthalene (acute only)

23A.2.14.1 Acute Exposure Limit

Table 23A-34: Summary of Acute Inhalation Exposure Limits for Naphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	36 22.5	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE (2005a) has developed a ½-hour POI of 36 $\mu g/m^3$ and an AAQC of 22.5 $\mu g/m^3$ for a 24-hour averaging period for naphthalene. The ½-hour POI is based on odour perception. Although the 24-hour criterion is based on health consideration, the specific basis of its derivation remains unknown. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for naphthalene.

The ACGIH (1991, 2006b) recommends a short-term exposure limit (STEL) of 15 ppm (79 mg/m^3) based on ocular irritation as a result of occupational naphthalene exposure. The STEL equates to a 15-minute air concentration that should not be exceeded at any time during a work day. The 15-minute STEL can be adjusted to an equivalent 1-hour concentration using the following equation:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the STEL is then adjusted to a concentration of 60 mg/m^3. A cumulative uncertainty factor of 100 was applied to the duration-adjusted STEL to account for intra-species variability (10-fold) and the apparent use of a LOAEL (10-fold). Thus, a 1-hour limit of 600 µg/m^3 was adopted as the short-term exposure limit for this assessment.

23A.2.14.2 Chronic Exposure Limit(s)

In the case of the aliphatic and aromatic petroleum hydrocarbon groups, the search for chronic inhalation and oral exposure limits was limited to three regulatory agencies: CCME (2000a), MA DEP (2003) and TPHCWG (1997). These agencies have developed chronic exposure limits for the aliphatic and aromatic groups as a whole.

Table 23A-35: Summary of Chronic Inhalation Exposure Limits for the Aromatic C9-C16 Group

Regulatory Agency	Value (µg/m^3)	Type	Reference
CCME	200	RfC	CCME (2000a)
MA DEP	50	RfC	MA DEP (2003)
TPHCWG	200	RfC	TPHCWG (1997)

The CCME (2000a) proposes a chronic RfC for C9-C16 aromatics of 200 µg/m^3 based on increased liver and kidney weights in male rats exposed to high flash aromatic naphtha (HFAN), which is primarily composed of 9-carbon aromatic compounds. The RfC was adopted from the TPHCWG (1997) and derived from a study that exposed rats to a mixture of C9 aromatics at concentrations of 0, 450, 900 or 1,800 mg/m^3 for 6 hours per day, 5 days per week for 12 months (Clark et al. 1989). A NOAEL of 900 mg/m^3 was derived and converted to continuous exposure (6 hours/24 hours x 5 days/7 days). An uncertainty factor of 1,000 was applied to the duration-adjusted NOAEL of 160 mg/m^3 to account for the most sensitive (10-fold), interspecies variability (10-fold), and use of a subchronic study (10-fold).

The MA DEP (2003) provides an RfC of 50 µg/m^3 based on the same Clark et al. (1989) study as the TPHCWG and the CCME. However, the MA DEP applies an extra 3-fold uncertainty factor for database deficiency. The partial uncertainty factor was applied to account for the lack of toxicity information on non-PAH compounds in the C9-C16 aromatic fraction range (MA DEP 2003).

For the purpose of assessing chronic inhalation effects, the TPHCWG and CCME both consider there to be an adequate database for the derivation of an RfC that is representative of the C9-C16 aromatics. As a result, the CCME RfC of 200 µg/m^3 was used in the chronic inhalation

effects assessment. This RfC equates to an inhaled dose of 45 µg/kg bw/d based on an average adult body weight of 70.7 kg and an inhalation rate of 15.8 m^3/d (Health Canada 2004a).

Table 23A-36: Summary of Chronic Oral Exposure Limits for the Aromatic C9-C16 Group

Regulatory Agency	Value (µg/kg bw/d)	Type	Reference
CCME	40	RfD	CCME (2000a)
MA DEP	30	RfD	MA DEP (2003)
TPHCWG	40	RfD	TPHCWG (1997)

The CCME (2000a) recommends an oral RfD of 40 µg/kg bw/d for the C9-C16 aromatics based on the most commonly reported RfD value of eight individual compounds for which the U.S. EPA has established oral RfDs (isopropylbenzene, acenaphthene, biphenyl, fluorene, anthracene, fluoranthene, naphthalene, pyrene). The CCME adopted this value from the TPHCWG (1997), who examined the aforementioned RfDs for liver and kidney effects together with toxicity data for naphthalenes/methylnaphthalenes to determine the RfD of 0.04 mg/kg bw/d. At the time of the TPHCWG assessment, four of the eight individual compounds (isopropylbenzene, naphthalene, fluorene and fluoranthene) had RfDs of 0.04 mg/kg bw/d, while the remaining compounds had RfDs ranging from 0.03 mg/kg bw/d to 0.3 mg/kg bw/d (TPHCWG 1997).

Alternatively, the MA DEP (2003) selected the U.S. EPA RfD for pyrene of 0.03 mg/kg bw/d to represent the entire range of compounds. The U.S. EPA RfD is based on kidney effects (renal tubular pathology, decreased kidney weights) observed in a subchronic mouse oral bioassay and has not been updated since the MA DEP assessment (U.S. EPA 2006).

Although the U.S EPA (2006) has revised the isopropylbenzene (0.1 mg/kg bw/d) and naphthalene (0.02 mg/kg bw/d) RfDs since the TPHCWG's assessment, it is important that the RfD of the group reflect the toxicity of the group as a whole and not a single compound within the group. On this basis, the CCME (2000a) oral RfD of 40 µg/kg bw/d was used in the chronic oral effects assessment of the C9-C16 aromatics.

In order to incorporate the aromatic C9-C16 group in the multiple exposure pathway model, bioavailability was assessed via a surrogate (naphthalene) for the various exposure pathways (i.e., inhalation, ingestion and dermal contact). No specific data were identified in the literature regarding the amount of the aromatic C9-C16 group that is absorbed via inhalation; therefore it was conservatively assumed that 100% of the inhaled group is absorbed. Oral bioavailability in humans was assumed to be 80% and dermal bioavailability was assumed to be 13% for this assessment (RAIS 2006).

23A.2.15 Aromatic C17-C34 Group

Surrogate: 3-Methylcholanthrene (acute only)

23A.2.15.1 Acute Exposure Limit

Table 23A-37: Summary of Acute Inhalation Exposure Limits for 3-Methylcholanthrene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

An acute criterion or guideline is not provided by any of the above regulatory agencies for 3-methylcholanthrene. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for 3-methylcholanthrene.

The U.S. DOE (2005) provides a TEEL-0 of 0.2 mg/m^3 for 3-methylcholanthrene. While TEELs are intended to be compared to 15-minute time-weighted average concentrations (U.S. DOE 2005), in the current HHRA they are compared to the 1-hour predicted ground-level air concentration.

Therefore, the TEEL-0 was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{\text{(60 minutes/15 minutes) 0.2}}$$

The exponent for the 15-minute multiplier of 0.2 used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TEEL-0 is adjusted to a concentration of 0.15 mg/m^3. An uncertainty factor of 10 was applied to the duration-adjusted TEEL-0 to account for intra-species variability. Thus, a 1-hour limit of 15 $\mu g/m^3$ was used in the acute effects assessment.

The U.S. DOE provides no scientific basis for its TEEL-0. As a result, the study team is unable to comment on the scientific merit of this limit and will make no assertions as to the adequacy of the study upon which it may be based. The adjusted TEEL-0 is considered provisional and limited reliance should be placed on its toxicological relevance.

23A.2.15.2 Chronic Exposure Limit(s)

In the case of the aliphatic and aromatic petroleum hydrocarbon groups, the search for chronic inhalation and oral exposure limits was limited to three regulatory agencies: CCME (2000a), MA DEP (2003) and TPHCWG (1997). These agencies have developed chronic exposure limits for the aliphatic and aromatic groups as a whole.

According to CCME (2000a), appropriate inhalation toxicity data were not identified for the individual constituents or fractions in the C17-C34 carbon range. The CCME suggests that this could be the result of the hydrocarbons in this group not being volatile and inhalation not being the likely exposure pathway. The MA DEP (2003) does not provide an RfC for exposure to C19-C32 aromatics either. The MA DEP attributes this to the limited volatility of the group. Nevertheless, the C17-C34 aromatics will be emitted to the atmosphere from the proposed facility and thus requires an inhalation limit. Given that a chronic inhalation limit is not provided by CCME (2000a), MA DEP (2003) or TPHCWG (1997), the toxicity search was expanded to include the chronic oral criteria or guidelines provided by any of these regulatory agencies (see Table 23A-37).

Table 23A-38: Summary of Chronic Oral Exposure Limits for the Aromatic C17-C34 Group

Regulatory Agency	Value (µg/kg bw/d)	Type	Reference
CCME	30	RfD	CCME (2000a)
MA DEP	30	RfD	MA DEP (2003)
TPHCWG	30	RfD	TPHCWG (1997)

The CCME (2000a) recommends an oral RfD of 30 µg/kg bw/d for the aromatic C17-C34 fraction. This RfD was adopted from the TPHCWG (1997) and is based on the nephrotoxicity of pyrene. There are no previously developed RfDs or appropriate data for compounds within the C17-C34 fraction. The RfD for pyrene was derived from a NOAEL of 75 mg/kg bw/d with an uncertainty factor of 1,000 applied to the NOAEL to account for interspecies variability (10-fold), intra-species variability (10-fold), and use of a subchronic study (10-fold). A modifying factor of 3 was also applied to the RfD because of the lack of adequate toxicity data. The oral RfD provided by CCME (2000a) was converted to a RfC of 130 µg/m^3 based on the following adjustments and assumptions:

- inhalation bioavailability and oral bioavailability of 100% (assumed)
- adult body weight of 70.7 kg (Health Canada 2004a)
- adult inhalation rate of 15.8 m^3/d (Health Canada 2004a)

As no data were identified in the literature regarding the absorption of aliphatic C17-C34 group or any of the individual constituents, oral and dermal bioavailability were also assumed to be 100% in the multiple exposure pathway model.

23A.2.16 Benzaldehyde

23A.2.16.1 Acute Exposure Limit

Table 23A-39: Summary of Acute Inhalation Exposure Limits for Benzaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

An acute criterion or guideline is not provided by any of the above regulatory agencies for benzaldehyde. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for benzaldehyde.

The U.S. DOE (2005) provides a TEEL 0 of 6 mg/m^3 for benzaldehyde. While TEELs are intended to be compared to 15 minute time-weighted average concentrations (U.S. DOE 2005), in the current HHRA they were compared to the 1-hour predicted ground-level air concentration. Therefore, the TEEL-0 of 6 mg/m^3 was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TEEL-0 is adjusted to a concentration of 4.5 mg/m^3. An uncertainty factor of 10 was applied to the duration-adjusted TEEL-0 to account for intra-species variability. Thus, a provisional 1-hour limit of 450 $\mu g/m^3$ was used in the acute effects assessment.

The U.S. DOE does not provide the scientific basis for its TEEL-0. As a result, the study team is unable to comment on the scientific merit of this limit and will make no assertions as to the adequacy of the study upon which it may be based. The adjusted TEEL-0 should be considered provisional and limited reliance placed on its toxicological relevance.

23A.2.16.2 Chronic Exposure Limit(s)

Table 23A-40: Summary of Chronic Inhalation Exposure Limits Benzaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	-	-	OEHHA (2005)

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for benzaldehyde. Consequently, the toxicity search was expanded to include the OEHHA (2005, see Table 23A-40) and chronic oral criteria or guidelines provided by any of the above regulatory agencies for benzaldehyde (see Table 23A-41).

Table 23A-41: Summary of Chronic Oral Exposure Limits Benzaldehyde

Regulatory Agency	Value (µg/kg bw/d)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	100	RfD	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA (2006) assessment of benzaldehyde reports an RfD of 0.1 mg/kg bw/d based on a NOAEL of 200 mg/kg bw/d for stomach lesions and kidney toxicity in a subchronic oral toxicity study in rats (U.S. EPA 2006). The NOAEL was dose-adjusted for gavage schedule of 5 days per week to a concentration of 143 mg/kg bw/d (i.e., 5 days/7 days). An uncertainty factor of 1,000 was applied to the NOAEL to account for interspecies variation (10-fold), intra-species variation (10-fold), and extrapolation from subchronic to chronic exposure (10-fold). The result is a chronic exposure limit of 100 µg/kg bw/d for benzaldehyde.

The chronic exposure limit of 100 µg/kg bw/d is equivalent to an air concentration of 360 $\mu g/m^3$, based on the following adjustments and assumptions:

- inhalation bioavailability of 100% (assumed)
- oral bioavailability of 80% (RAIS 2006)
- adult body weight of 70.7 kg (Health Canada 2004a)
- adult inhalation rate of 15.8 m^3/d (Health Canada 2004a)

This RfC of 360 $\mu g/m^3$ was used in the chronic inhalation effects assessment.

A chronic oral exposure limit was not required for the assessment of benzaldehyde because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and was not incorporated into the multiple exposure pathway model.

23A.2.17 Benzene

23A.2.17.1 Acute Exposure Limit

Table 23A-42: Summary of Acute Inhalation Exposure Limits for Benzene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	30	1-hour	AENV (2005)
ATSDR	28.8	24-hour	ATSDR (2005a)
OEHHA	1,300	6-hour	OEHHA (2000)
OMOE	-	-	OMOE (2005a)
WHO	-	-	WHO (2000)

The current assessment used the AENV 1-hour exposure limit of 30 $\mu g/m^3$ (AENV 2005). Alberta's AAQO was adopted from the Texas Natural Resource Conservation Commission, but the specific basis of the derivation remains unknown. Although supporting documentation is not available, this AAQO was used in the current short-term assessment of benzene in air, as per discussions with Alberta Health and Wellness. As a result, the study team is unable to comment on the scientific merit of this limit and will make no assertions as to the adequacy of the study upon which it may be based.

23A.2.17.2 Chronic Exposure Limit(s)

Table 23A-43: Summary of Chronic Inhalation Exposure Limits for Benzene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	3	RsC	Health Canada (2004b)
ATSDR	9.6	RsC	ATSDR (2005a)
RIVM	20	RsC	RIVM (2001)
U.S. EPA	30 1.3 to 4.5	RfC RsC	U.S. EPA (2006) U.S. EPA (2006)
WHO	1.7	RsC	WHO (2000)

An RsC of 3 $\mu g/m^3$ is reported by Health Canada (2004b) based on an inhalation unit risk of 0.0033 per mg/m^3. This RsC represents the daily dose via inhalation that is associated with an increased cancer risk of one in 100,000.

The WHO (2000) provides an RsC of 1.7 $\mu g/m^3$, which is associated with an increased cancer risk of one in 100,000. Using multiplicative risk estimates and a cumulative exposure model, a unit risk for lifetime exposure of 1.4 to 1.5 x 10^{-5} per ppb was derived with the Paustenbach exposure matrix and 2.4 x 10^{-5} per ppb with the Crump and Allen exposure matrix (WHO 2000). These unit risks equate to a range of 4.4 x 10^{-6} per $\mu g/m^3$ to 7.5 x 10^{-6} per $\mu g/m^3$. From this the WHO (2000) selected a representative unit risk of 6 x 10^{-6} per $\mu g/m^3$.

The U.S. EPA (2006) presents a range of potential carcinogenic risks from inhalation of benzene. Its inhalation unit risks of 2.2 x 10^{-6} to 7.8 x 10^{-6} per $\mu g/m^3$ equate to an RsC of 1.3 to 4.5 $\mu g/m^3$ (corresponding to risk levels of one in 100,000). Given that the Health Canada RsC

falls in the middle of this range, the RsC of 3 μg/m^3 was selected as the exposure limit for the current assessment.

Based on Environment Canada's (2006) physical and chemical screening, benzene was not assessed via multiple exposure pathways. Thus, a chronic oral exposure limit was not required for the current assessment.

23A.2.18 Benzo(a)pyrene Group

Surrogate: Benzo(a)pyrene (acute only)

23A.2.18.1 Acute Exposure Limit

Table 23A-44: Summary of Acute Inhalation Exposure Limits for Benzo(a)pyrene

Regulatory Agency	Value (μg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	0.0033 0.0011	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The only regulatory agency that has a public acute exposure limit for benzo(a)pyrene is the OMOE (2005a), which provides a ½-hour POI of 0.0033 μg/m^3 and a 24-hour standard of 0.0011 μg/m^3 for benzo(a)pyrene. These limits are based on the carcinogenic potential for benzo(a)pyrene and were derived based on an annual exposure limit of 0.00022 μg/m^3 for protection against carcinogenic effects using a simple extrapolation factor generally considered to be overly conservative. This limit was not used in the acute effects assessment for the benzo(a)pyrene group, as it did not account for the influence of duration of exposure on the carcinogenic action of a chemical. As a result, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for benzo(a)pyrene.

The U.S. DOE (2005) provides a TEEL-0 of 0.2 mg/m^3 for benzo(a)pyrene (coal tar pitch volatiles). While TEELs are intended to be compared to 15-minute time-weighted average concentrations (U.S. DOE 2005), in the current HHRA they are compared to the 1-hour predicted ground-level air concentration. Therefore, the TEEL-0 was adjusted from 15-minute exposure to 1-hour exposure as follows:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes/15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier of 0.2 used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the TEEL-0 is adjusted to a concentration of 0.15 mg/m^3. An uncertainty factor of 10 was applied to the duration-adjusted TEEL-0 to account for intra-species variability. Thus, a 1-hour limit of 15 μg/m^3 was used in the acute effects assessment.

The U.S. DOE provides no scientific basis for its TEEL-0. As a result, the study team is unable to comment on the scientific merit of this limit and will make no assertions as to the adequacy of the study upon which it may be based. The adjusted TEEL-0 is considered provisional and limited reliance should be placed on its toxicological relevance.

23A.2.18.2 Chronic Exposure Limit(s)

As recommended in OMOE (1997), the assessment of carcinogenic PAHs can be based on two approaches: (1) the WMM and (2) the IPM. The WMM approach is based on the conservative assumption that the potency of the PAH fraction of any environmental mixture is proportional to the benzo(a)pyrene content of the mixture (OMOE 1997). The WMM was derived from the methodology of the OMOE (1997), using the concentration of benzo(a)pyrene together with the toxic potency of the PAH-WMM group. The cancer slope factor for oral exposure to benzo(a)pyrene was estimated by OMOE, based on an examination of the composition and toxic potency of PAH mixtures derived from many different sources (e.g.., coal tar, coke oven emissions, diesel emissions and wood burning). The unit risk for inhalation exposure to benzo(a)pyrene was developed based on a weight-of-evidence review of numerous epidemiology and rodent toxicity studies of benzo(a)pyrene. Critical effects included lung cancer and genitourinary tract cancer in humans. This approach, used in conjunction with the IPM, ensures that potential risks are not underestimated in the current assessment (OMOE 1997).

The IPM health risks are based on the sum of attributable risks for each individual PAH. The first step in the IPM requires an estimate of the inhalation potency of benzo(a)pyrene and other PAHs relative to benzo(a)pyrene. This step involves the use of Toxic Equivalency Factors (TEFs) to denote the cancer potency of specific PAH compounds relative to the potency of benzo(a)pyrene (Bostrom et al. 2002). TEFs allow large groups of compounds with a common mechanism of action such as PAHs to be assessed when limited data is available for all but one of the compounds (i.e., benzo(a)pyrene). Table 23A-45 shows the TEFs used in the current assessment of PAHs via the IPM approach.

Table 23A-45: Relative Potency of Individual PAHs Compared with Benzo(a)pyrene

Compound[1]	TEF
Anthracene	0.0005
Benz(a)anthracene	0.005
Benzo(a)pyrene	1
Benzo(b)fluoranthene	0.1
Benzo(e)pyrene	0.002
Benzo(g,h,i)perylene	0.02
Benzo(k)fluoranthene	0.05
Chrysene	0.03
Dibenz(a,h)anthracene	1.1
Fluoranthene	0.05
Fluorene	0.0005
Indeno(1,2,3-cd)pyrene	0.1
Phenanthrene	0.0005

Table 23A-45: Relative Potency of Individual PAHs Compared with Benzo(a)pyrene (cont'd)

Compound[1]	TEF
Pyrene	0.001
NOTE: [1]All compounds for which TEFs were identified in Larsen and Larsen (1998) were assessed as a part of the IPM approach.	
SOURCE: Larsen and Larsen (1998).	

For the chronic assessment, benzo(a)pyrene was evaluated along with all other carcinogenic PAHs. The exposure limits used in this assessment are summarized in Table 23A-46 and are recommended by either WHO (2000), OMOE (1997), or Health Canada (2004b).

Table 23A-46: Summary of Chronic Inhalation Exposure Limits for Benzo(a)pyrene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	0.32	RsC	Health Canada (2004b)
ATSDR	-	-	ATSDR (2005a)
RIVM	0.00012	RsC	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	0.00012	RsC	WHO (2000)

The WHO (2000) recommends an inhalation unit risk of 0.087 per $\mu g/m^3$ based on a benzo(a)pyrene concentration of 1 $\mu g/m^3$ in air as a component of benzene-soluble coke-oven emissions. This RsC of 0.00012 $\mu g/m^3$ is associated with an acceptable incremental lifetime cancer risk of development of lung tumours of one in 100,000. This RsC was selected for the chronic effects assessment of the benzo(a)pyrene (WMM) group. It is equivalent to an inhaled dose of 0.000026 $\mu g/kg$ bw/d based on the following assumptions:

- inhalation bioavailability and oral bioavailability of 100% (assumed)
- adult body weight of 70.7 kg (Health Canada 2004a)
- adult inhalation rate of 15.8 m^3/d (Health Canada 2004a)

The Health Canada (2004b) provided an inhalation unit risk of 0.0033 per $\mu g/m^3$. This RsC of 0.32 $\mu g/m^3$ is associated with an acceptable incremental lifetime cancer risk of development of lung tumours of one in 100,000. This RsC was selected for the chronic effects assessment of the benzo(a)pyrene (IPM) group and is equivalent to an inhaled dose of 0.072 $\mu g/kg$ bw/d (based on the above adjustments).

Although Health Canada (2004b) has established inhalation unit risks for benzo(b)fluoranthene, benzo(k)fluoranthene, and indeno(1,2,3-cd)pyrene, these TRVs were not used in the current assessment of PAHs. The IPM approach provides a more conservative assessment of the potential cancer risk to humans than the inhalation unit risk values for the same end point (i.e., cancer). As well, the scientific basis for these inhalation unit risk values is unknown.

Table 23A-47: Summary of Chronic Oral Exposure Limits for Benzo(a)pyrene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	0.0043	RsC	Health Canada (2004b)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The Health Canada (2004b) provided an oral slope factor of 2.3 per mg/kg bw/d based on the Canadian Guidelines for Drinking Water Quality. This RsD of 0.0043 per µg/kg bw/d is associated with an acceptable incremental lifetime cancer risk of development of stomach tumours of one in 100,000. This RsD was selected for the chronic effects assessment of the benzo(a)pyrene (IPM) group.

For the benzo(a)pyrene (WMM) group, the toxicity search was expanded to include the OMOE (1997). The OMOE (1997) provides an RsD of 0.0034 µg/kg bw/d for stomach tumours. This RsD is associated with an acceptable incremental lifetime cancer risk of one in 100,000 and was used in the chronic oral effects assessment for the benzo(a)pyrene (WMM) group.

The bioavailability of benzo(a)pyrene was assessed for the various exposure pathways (i.e., inhalation, ingestion and dermal contact). In order to incorporate the benzo(a)pyrene group in the multiple exposure pathway model, bioavailability was assessed via a surrogate (i.e., benzo(a)pyrene) for the various exposure pathways (i.e., inhalation, ingestion and dermal contact). No specific data were identified in the literature regarding the amount of benzo(a)pyrene that is absorbed via inhalation; therefore it was conservatively assumed that 100% of the inhaled group is absorbed. Oral bioavailability in humans was assumed to be 31% and dermal bioavailability was assumed to be 13% for this assessment (RAIS 2006).

23A.2.19 Carbon Disulphide Group

Surrogate: Carbon disulphide

23A.2.19.1 Acute Exposure Limit

Table 23A-48: Summary of Acute Inhalation Exposure Limits for Carbon Disulphide

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	30	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	6,200	6-hour	OEHHA (2000)
OMOE	330	½-hour, 24-hour	OMOE (2005a)
WHO	100	24-hour	WHO (2000)

The AENV (2005) provides a 1-hour average AAQO for carbon disulphide, however it is based on odour and thus was not employed in the short-term assessment of carbon disulphide in air.

The WHO (2000) provides a 24-hour guideline for carbon disulphide of 100 µg/m^3. This guideline is based on the lowest concentration at which adverse effects were observed in occupational exposure. However, the lowest observed concentration of 10 mg/m^3 is based on a 10 to 15 year duration of exposure and therefore is not appropriate for the derivation of an acute exposure limit. Thus, this guideline was not used in the short-term assessment of the carbon disulphide group.

The OMOE (2005a) provides an acute 24-hour AAQC for carbon disulphide of 330 µg/m^3, however this criteria is based on odour and therefore was not employed in the short-term assessment of carbon disulphide in air.

The OEHHA (1999f, 2000) acute REL of 6,200 µg/m^3 for carbon disulphide is based on reproductive, developmental and CNS effects in rats. Pregnant rats were exposed via inhalation to concentrations of 0, 100, 200, 400, and 800 ppm for 6 hours per day on days 6 to 20 of gestation. Significant reductions in fetal weight were reported at 400 ppm and the NOAEL was identified as 200 ppm (620 mg/m^3). A cumulative safety factor of 100 was applied to the NOAEL to account for interspecies differences (10-fold) and intra-species differences (10-fold). The acute REL of 6,200 µg/m^3 was used in the acute effects assessment as a 1-hour exposure limit.

23A.2.19.2 Chronic Exposure Limit(s)

Table 23A-49: Summary of Chronic Inhalation Exposure Limits for Carbon Disulphide

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	100	RfC	Health Canada (2004c)
ATSDR	930	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	700	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The chronic inhalation exposure limit of 100 µg/m^3 was based on the tolerable concentration (TC_{05}) for inhalation exposure recommended for carbon disulphide by Health Canada (Health Canada 2004b; CEPA 2000c). This TC_{05} was derived from the lower benchmark concentration of 20 mg/m^3, associated with a 5% adverse response for peroneal motor nerve conduction velocity in occupationally exposed workers (Johnson et al. 1983; CEPA 2000c). The TC_{05} was adjusted by Health Canada for intermittent exposure of 8 hours per workday and 5 days per workweek (8 hours/24 hours x 5 days/7 days). A safety factor of 50 was also applied by Health Canada in the derivation of the human exposure limit to account for intra-species variation (10-fold) and for potential effects on neurobehavioral development (5-fold). The resultant TC_{05} of 100 µg/m^3 was used as the chronic inhalation exposure limit for carbon disulphide.

The carbon disulphide group was not assessed through the secondary pathways since its physical and chemical parameters did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006). On this basis, a chronic oral exposure limit was not required for this assessment.

23A.2.20 Carbon Monoxide

23A.2.20.1 Acute Exposure Limit

The AENV provides a 1-hour AAQO of 15,000 µg/m^3 and an 8-hour AAQO of 6,000 µg/m^3 for CO (AENV 2005). These AAQOs were adopted from the CEPA/FPAC Working Group on Air Quality Objectives and Guidelines, who recommends maximum desirable, acceptable and tolerable objectives for CO. The Alberta objectives are based on the maximum desirable levels (i.e., the lowest objective). These objectives were developed to protect the subpopulation sensitive to cardio-respiratory effects (CEPA/FPAC 1994).

As there were no 24-hour guidelines available, the acute assessment was completed on a 1-hour and 8-hour basis only.

23A.2.20.2 Chronic Exposure Limit(s)

No regulatory exposure limits were available for chronic exposure to CO. The critical effect of CO exposure is the formation of carboxyhemoglobin (COHb) in blood. As COHb concentrations reach a steady-state after six to eight hours of exposure, CO exposure for longer periods of time (i.e., chronic exposure) is not expected to cause accumulation of COHb in the blood (WHO 2000).

Epidemiological studies have identified associations between ambient low-level CO concentrations and various health effects (Burnett et al. 2000; Moolgavkar 2000). However, the results across studies are inconsistent and it has been suggested that CO might represent only a surrogate compound for particulate emissions from mobile sources (Sarnat et al. 2001; Schwartz 1999).

CO was assessed only for the inhalation route of exposure as the principal health effects are strictly related to inhalation.

23A.2.21 Cyclohexane

23A.2.21.1 Acute Exposure Limit

Table 23A-50: Summary of Acute Inhalation Exposure Limits for Cyclohexane

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	18,300 6,100	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE has updated the criteria for cyclohexane and recommends a ½-hour standard of 18,300 µg/m^3 and 24-hour standard of 6,100 µg/m^3 for cyclohexane (OMOE 2005a,e). These criteria were developed from a NOAEL of 6,886 mg/m^3 for reduced pup weights in the F_1 and F_2 generations in a reproductive and developmental inhalation study (Kreckmann et al. 2000; OMOE 2005e). The NOAEL was revised to a HEC of 1,722 mg/m^3 and the lower confidence of

the benchmark concentration (BMCL) was then derived (1,822 mg/m^3). An uncertainty factor of 300 was applied to the BMCL to account for intra-species variability (10-fold), interspecies variability (3-fold), and database deficiencies due to the lack of chronic studies specifically examining developmental neurotoxicity and hepatic effects (10-fold) (OMOE 2005e). An uncertainty factor of three was considered adequate as opposed to the typical value of 10 because a HEC was calculated from the rat NOAEL to account for pharmacokinetic variation. This results in the 24-hour standard of 6,100 µg/m^3 for cyclohexane.

Derivation of an acute (i.e., 24-hour) criterion from a long-term study examining reproductive and developmental effects is generally considered conservative, as a higher exposure over a shorter time-period (i.e., acute exposure) presumably could occur without risk of adverse effects. On this basis, the OMOE's incorporation of an uncertainty factor of 10 to account for "database deficiencies due to the lack of chronic studies specifically examining developmental neurotoxicity and hepatic effects" is considered unnecessary (OMOE 2005e). Removal of this 10-fold uncertainty factor results in an acute criterion of 61,000 µg/m^3. This 24-hour RfC was used in the short-term assessment of cyclohexane.

Because the OMOE 24-hour standard of 6,100 µg/m^3 (which includes the 10-fold uncertainty factor for database deficiencies due to the lack of chronic studies) is higher then the 24-hour standard of 2,500 µg/m^3 for the aliphatic C5-C8 group (which includes cyclohexane), cyclohexane was not included in the acute effects assessment as an individual COPC. Instead, it was assessed on an acute-basis as a constituent of the C5-C8 aliphatic group.

23A.2.21.2 Chronic Exposure Limit(s)

Table 23A-51: Summary of Chronic Inhalation Exposure Limits for Cyclohexane

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	-	-	Health Canada (2004c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	6,000	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA has established an RfC of 6,000 µg/m^3 based on a NOAEL of 6,886 mg/m^3 for developmental toxicity in rats (U.S. EPA 2006). The NOAEL in the reproductive toxicity assay (6-hour exposure per day) was duration-adjusted to derive an exposure level corresponding to 24-hour daily exposure by multiplying by a factor of 6/24. A default value of 1 was used in calculating the HEC, as the available animal and human values cannot be distinguished statistically. Thus, the HEC values for cyclohexane were set equal to the duration-adjusted exposure concentration of 1,822 mg/m^3. Finally, the RfC was derived by dividing the HEC benchmark concentration limit by the product of uncertainty factors (300) to account for interspecies variability (3-fold), intra-species variability (10-fold), and database deficiencies (10-fold). A factor of 3 was applied for interspecies since the pharmacokinetic component was addressed by the calculation of the HEC according to the RfC methodology for a category 3 gas. Accordingly, only the pharmacodynamic area of uncertainty remains as a partial factor for interspecies uncertainty (U.S. EPA 2006).

Cyclohexane was not assessed through the secondary pathways since its physical and chemical parameters did not exceed any of the persistence and bioaccumulation parameters

established by Environment Canada (2006). On this basis, a chronic oral exposure limit was not required for this assessment.

23A.2.22 Dichlorobenzenes

Surrogate: 1,4-Dichlorobenzene

23A.2.22.1 Acute Exposure Limit

Table 23A-52: Summary of Acute Inhalation Exposure Limits for 1,4-Dichlorobenzene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	12,000	24-hour	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	285 95	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE (2005a) provides ½-hour and 24-hour standards for 1,4-dichlorobenzene; however, no scientific basis is provided. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of dichlorobenzenes.

The ATSDR has developed an acute inhalation MRL for 1,4-dichlorobenzene of 12,000 $\mu g/m^3$ based on a NOAEL of 15 ppm for eye and nose irritation in occupationally exposed workers (ATSDR 2004b, 2005a). The study consisted of 58 men who had worked in unspecified industrial operations involving the handling of 1,4-dichlorobenzene for 8 hours per day, 5 days per week for a period of 8 months to 25 years (average 4.75 years). An uncertainty factor of 10 was applied to the NOAEL to account for intra-species variability. This MRL was used as a 24-hour exposure limit in the acute effects assessment of dichlorobenzene in air.

23A.2.22.2 Chronic Exposure Limit(s)

Table 23A-53: Summary of Chronic Inhalation Exposure Limits for 1,4-Dichlorobenzene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	95	RfC	Health Canada (2004b)
ATSDR	120	RfC	ATSDR (2005a)
RIVM	670	RfC	RIVM (2001)
U.S. EPA	800	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The chronic inhalation exposure limit of 95 $\mu g/m^3$ was based on the tolerable concentration for inhalation exposure recommended for 1,4-dichlorobenzene by Health Canada (2004b). Although this tolerable concentration is based on health considerations, the specific basis of its

derivation remains unknown. As a result, the study team is unable to comment on the scientific merit of this limit and did not use it in the long-term assessment of dichlorobenzenes.

The ATSDR provides a chronic inhalation MRL for 1,4-dicholobenzene of 0.02 ppm (120 $\mu g/m^3$) based on nasal olfactory epithelial lesions (of moderate or greater severity) in female rats (ATSDR 2005a,b). A NOAEL of 19.8 ppm was identified in a two-year inhalation study in which groups of 50 male and female F344/DuCrj rats and 50 male and female Crj:BDF1 mice were exposed to 0, 19.8, or 298.4 ppm of 1,4-dichlorobenzene for 6 hours per day, five days per week for 104 weeks. The NOAEL was adjusted for intermittent exposure (6 hours/24 hours x 5 days/7 days) to a concentration of 3.54 ppm. The $NOAEL_{ADJ}$ was converted to a HEC using the RGDR.

$$RGDR_{ET} = \frac{(V_E/SA_{ET})_A}{(V_E/SA_{ET})_H}$$

$$RGDR_{ET} = \frac{0.24\ m^3/day/15\ cm^2}{20\ m^3/day/200\ cm^2}$$

Where:

$RGDR_{ET}$ = regional gas dosimetry ratio in the extrathoracic region

V_E = minute volume in rats $(V_E)_A$ or humans $(V_E)_H$

SA_{ET} = extrathoracic surface area in rats $(SA_{ET})_A$ or humans $(SA_{ET})_H$

The rat $NOAEL_{ADJ}$ was then multiplied by the $RGDR_{ET}$ to yield a $NOAEL_{HEC}$ of 3.54 ppm, as follows:

$$NOAEL_{HEC} = NOAEL_{ADJ} \times RGDR_{ET}$$

$$NOAEL_{HEC} = 3.54\ ppm \times 0.16$$

Finally, an uncertainty factor of 30 was applied to the $NOAEL_{HEC}$ to account for interspecies variability (3-fold) and intra-species variability (10-fold). A 3-fold uncertainty factor was used instead of the 10-fold default value for extrapolation from rats to humans because the calculation of a HEC addresses one of the two areas of uncertainty encompassed in an interspecies uncertainty factor. The HEC adjustment addresses the pharmacokinetic component of the extrapolation factor, leaving the pharmacodynamic area of uncertainty. This RfC of 120 $\mu g/m^3$ was used in the chronic inhalation assessment for dichlorobenzenes.

A chronic oral exposure limit was not required for the assessment of dichlorobenzene as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multiple exposure pathway model.

23A.2.23 Ethylbenzene

23A.2.23.1 Acute Exposure Limit

Table 23A-54: Summary of Acute Inhalation Exposure Limits for Ethylbenzene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	2,000	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	1,400 1,000	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

An AAQO of 2,000 $\mu g/m^3$ for a 1-hour average exposure was recommended by AENV (2005). This limit was adopted from the Texas Natural Resource Conservation Commission based on odour perception, but no specific basis was provided. Given that this objective is not health based, the AENV AAQO was not used in the short-term assessment of ethylbenzene.

The OMOE (2005a) provides a lower ½-hour standard based on odour and a health-based 24-hour standard for ethylbenzene. However, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of ethylbenzene.

The toxicity search was therefore expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for ethylbenzene.

An acute exposure limit for ethylbenzene of 4,340 $\mu g/m^3$ corresponds to the MRL recommended for intermediate inhalation exposure to ethylbenzene by the ATSDR (1999a, 2005a). This MRL was derived from a NOAEL of 97 ppm for developmental effects in Wistar mice following inhalation exposure for 7 hours per day, 5 days per week for 3 weeks. The ATSDR applied an uncertainty factor of 100 to the study NOAEL to account for interspecies (10-fold) and intra-species variation (10-fold). Use of an intermediate NOAEL when characterizing acute exposure is typically considered conservative, because a higher exposure over a shorter period (i.e., acute exposure) presumably could occur without the risk of adverse effects. The use of this intermediate MRL as a 24-hour exposure limit is considered appropriate, as the health effects associated with ethylbenzene have been observed to be concentration dependant, rather than duration-dependant.

23A.2.23.2 Chronic Exposure Limit(s)

Table 23A-55: Summary of Chronic Inhalation Exposure Limits for Ethylbenzene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	770	RfC	RIVM (2001)
U.S. EPA	1,000	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The RIVM (2001) provides a TCA of 770 $\mu g/m^3$ based on kidney and liver effects in rats and mice. A NOAEL of 430 mg/m^3 was identified in the 1992 semi chronic NTP study (NTP 1996). The RIVM adjusted the NOAEL of intermittent applied an uncertainty factor of 100 to the NOAEL to account for interspecies variation (10-fold) and intra-species variation (10-fold). An uncertainty factor was not applied to the NOAEL by the RIVM for use of a subchronic study because the chronic NTP study reported a higher NOAEL of 1,075 mg/m^3.

The U.S. EPA assessment of ethylbenzene reports an RfC of 1,000 $\mu g/m^3$ based on a NOAEL of 434 mg/m^3 for developmental toxicity in rats and rabbits (U.S. EPA 2006). Wistar rats and New Zealand white rabbits exposed to concentrations of 0, 100, or 1,000 ppm (434 or 4,342 mg/m^3) for 6 to 7 hours per day, 7 days per week during days 1-19 and 1-24 of gestation, respectively. According to the U.S. EPA methodology, a NOAEL based on developmental effects is not adjusted for intermittent exposure. A $NOAEL_{HEC}$ was calculated assuming a default value of 1.0 since b:a lambda values are unknown for the experimental animal species (a) and humans (h) (U.S. EPA 2006). An uncertainty factor of 300 was applied to the study $NOAEL_{HEC}$ to account for interspecies variation (3-fold), intra-species variation (10-fold), and the absence of multigenerational reproductive and chronic studies (10-fold). A 3-fold uncertainty factor for interspecies variability was considered appropriate by the U.S. EPA since the HEC adjustment addresses the pharmacokinetic component of the extrapolation factor, leaving the pharmacodynamic area of uncertainty.

The TCA provided by RIVM was not used in the chronic inhalation effects assessment because it is based on a NOAEL from a subchronic study, rather than based on a NOAEL from a chronic study (i.e., U.S. EPA). As a result, the U.S. EPA RfC of 1,000 $\mu g/m^3$ was used in the chronic inhalation effects assessment for ethylbenzene.

A chronic oral exposure limit was not required for the assessment of ethylbenzene because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multi-media exposure model.

23A.2.24 Formaldehyde

23A.2.24.1 Acute Exposure Limit

Table 23A-56: Summary of Acute Inhalation Exposure Limits for Formaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	65	1-hour	AENV (2005)
ATSDR	49.3	2-hour	ATSDR (2005a)
OEHHA	94	1-hour	OEHHA (2000)
OMOE	65	½-hour, 24-hour	OMOE (2005a)
WHO	100	½-hour	WHO (2000)

The ATSDR has developed an acute inhalation MRL for formaldehyde of 49.3 $\mu g/m^3$ (0.04 ppm) based on a LOAEL of 0.4 ppm for nasal and eye irritation (ATSDR 1999b, 2005a). Occupationally exposed patients with skin hypersensitivity to formaldehyde and unexposed (control) patients, all of whom were non-smokers, were separated into two groups. Group 1 included 7 male and 3 female volunteers with skin hypersensitivity to formaldehyde and group 2 included 11 healthy males with no history of allergic diseases. Nasal washings were performed in both groups immediately before and after a 2-hour exposure to 0 (placebo) or 0.5 mg/m^3 (0.4 ppm) formaldehyde, and again 4 and 18 hours after the exposure period. In both groups, the placebo did not result in any effects on nasal wash cellular contents or symptom score. Exposure to 0.4 ppm formaldehyde showed statistically significant increased average symptom scores compared with average placebo scores, in both groups. As well, eosinophil counts and albumin levels were elevated in both groups. After 18 hours, symptom scores, eosinophil counts and albumin levels were no longer elevated. A cumulative uncertainty factor of 10 was incorporated by the ATSDR (1999b) to account for the use of a minimal LOAEL (3-fold) and to account for intra-species variability (3-fold). An uncertainty factor of 3 was considered adequately protective of human variability as the observed symptoms of irritation were observed in a potentially sensitive group of subjects. This 2-hour MRL was conservatively used as the 1-hour exposure limit in the acute effects assessment for formaldehyde.

23A.2.24.2 Chronic Exposure Limit(s)

Table 23A-57: Summary of Chronic Inhalation Exposure Limits for Formaldehyde

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	9.5 1.9	RfC RsC	CEPA (2001) CEPA (2001)
ATSDR	9.8	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	0.8	RsC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The IARC has classified formaldehyde as being carcinogenic to humans (Group 1) on the basis of sufficient evidence in humans and in experimental animals (IARC 2004). As well, Health Canada provides a tumorigenic concentration (TC_{05}) for formaldehyde of 9.5 mg/m^3 (CEPA 2001). This TC_{05} represents the total intake associated with a 5% increase in incidence of nasal squamous tumours in rats exposed to formaldehyde for up to 24 months (Monticello et al. 1996). The TC_{05} corresponds to an RsC of 1.9 µg/m^3, which is associated with an increased cancer risk of one in 100,000.

The U.S. EPA (2006) last reviewed its RsC derivation for formaldehyde in 1991, which was 4 years before the publication of the critical study used in the Health Canada assessment. The U.S. EPA based its inhalation unit risk on an inhalation study by Kerns et al. (1983) that examined the incidence of squamous cell carcinomas in rats exposed to formaldehyde. The U.S. EPA unit risk of 1.3 x 10^{-5} per µg/m^3 equates to an RsC of 0.8 µg/m^3 (associated with a one in 100,000 excess cancer risk).

When considering the combined incidence of nasal tumours in rats exposed to formaldehyde from the Kerns et al. and Monticello et al. studies, the concentration of formaldehyde associated with a 5% increase in tumour incidence is approximately 7.3 mg/m^3, which is very close to the Health Canada TC_{05} of 9.3 mg/m^3. As Health Canada identified the Monticello et al. (1996) study as the study that best characterizes the exposure-response of formaldehyde (CEPA 2001) and the U.S. EPA was unable to review the Monticello et al. (1996) study in its assessment, the tolerable concentration based on its results alone was used in the current assessment.

A chronic oral exposure limit was not required for the assessment of formaldehyde, because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multi-media exposure model. Formaldehyde tends to remain in the medium to which is discharged, in this case air (CEPA 2001).

23A.2.25 Hydrogen Sulphide

23A.2.25.1 Acute Exposure Limit

Table 23A-58: Summary of Acute Inhalation Exposure Limits for Hydrogen Sulphide

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	14 4	1-hour 24-hour	AENV (2005) AENV (2005)
ATSDR	280	½-hour	ATSDR (2005a)
OEHHA	42	1-hour	OEHHA (2000)
OMOE	30	½-hour, 24-hour	OMOE (2005a)
WHO	150	24-hour	WHO (2000)

The AENV (2005) provides 1-hour and 24-hour AAQOs for hydrogen sulphide of 14 µg/m^3 and 4 µg/m^3, respectively. As well, the OMOE (2005a) recommends a ½-hour standard and 24-hour AAQC of 30 µg/m^3. However, all of these guidelines were odour-based rather than health-based and thus were not used in the acute effects assessment for hydrogen sulphide.

The OEHHA (1999g, 2000) provides an acute REL of 42 µg/m^3 based on physiological responses to odour. Sixteen individuals were exposed to increasing concentrations of hydrogen sulphide until their odour threshold was reached. The LOAEL was based on the range of odour thresholds of 0.012-0.069 ppm that was identified among the individuals. The geometric mean of the odour thresholds (0.03 ppm) was used to develop the acute REL. An uncertainty factor of 1 was applied to the geometric mean, resulting in an acute REL of 0.03 ppm (42 µg/m^3). Again this exposure limit was not used in the acute effects assessment because it was based on odour-perception.

A 24-hour guideline of 150 µg/m^3 has been developed by the WHO (2000) for hydrogen sulphide. A LOAEL of 15 mg/m^3 was identified for eye irritation. An uncertainty factor of 100 was applied to LOAEL by the WHO; however, the basis of the uncertainty factor is unknown. Due to the lack of adequate supporting documentation, the study team is unable to comment on the scientific merit of this limit and thus did not use it in the short-term assessment of hydrogen sulphide.

The ATSDR provides an acute inhalation MRL for hydrogen sulphide of 0.2 ppm (280 µg/m^3) (ATSDR 2004c, 2005a). This MRL was developed based on a LOAEL of 2 ppm for changes in airway resistance and specific airway conductance in excess of 30% in two of the 10 individuals examined. The test subjects all had bronchial asthma requiring medication for 1-13 years, but none of the subjects had severe asthma. The subjects were exposed for ½-hour and their respiratory function in response to a histamine challenge was assessed prior to and following exposure. Although the two subjects showed changes in airway resistance and specific airway conductance, no statistically significant alterations in lung function were observed at this concentration. The ATSDR (2004b) applied an uncertainty factor of 10 to account for the use of a minimal LOAEL (3-fold) and intra-species variability (3-fold). This acute MRL was used as a 1-hour exposure limit in the acute effects assessment for hydrogen sulphide.

23A.2.25.2 Chronic Exposure Limit(s)

Table 23A-59: Summary of Chronic Inhalation Exposure Limits for Hydrogen Sulphide

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	2	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA has developed an RfC of 2 µg/m^3 for nasal lesions of the olfactory mucosa (U.S. EPA 2006). This RfC is based on a NOAEL of 13.9 mg/m^3 for olfactory loss in adult male CD rats following inhalation exposure to hydrogen sulphide for 6 hours per day, 7 days per week for 10 weeks. The NOAEL was adjusted for intermittent exposure (6 hours/24 hours) to a concentration of 3.48 mg/m^3. The $NOAEL_{ADJ}$ was converted to a HEC using the RGDR.

$$RGDR_{ET} = \frac{(V_E/SA_{ET})_A}{(V_E/SA_{ET})_H}$$

$$RGDR_{ET} = \frac{0.19 \text{ litres/minute/15 cm}^2}{13.8 \text{ litres/minute/200 cm}^2}$$

Where:

$RGDR_{ET}$ = regional gas dosimetry ratio in the extrathoracic region

V_E = minute volume in rats $(V_E)_A$ or humans $(V_E)_H$

SA_{ET} = extrathoracic surface area in rats $(SA_{ET})_A$ or humans $(SA_{ET})_H$

The $NOAEL_{ADJ}$ was then multiplied by the $RGDR_{ET}$ to yield a $NOAEL_{HEC}$ of 0.64 mg/m^3, as follows:

$$NOAEL_{HEC} = NOAEL_{ADJ} \times RGDR_{ET}$$

$$NOAEL_{HEC} = 3.48 \text{ mg/m}^3 \times 0.184$$

Finally, an uncertainty factor of 300 was applied to the $NOAEL_{HEC}$ to account for intra-species variability (10-fold), interspecies extrapolation (3-fold), and for subchronic exposure (10-fold). A 3-fold uncertainty factor was used instead of the 10-fold default value for extrapolation from rats to humans because the calculation of a HEC addresses one of the two areas of uncertainty encompassed in an interspecies uncertainty factor. The HEC adjustment addresses the pharmacokinetic component of the extrapolation factor, leaving the pharmacodynamic area of uncertainty. This RfC of 2 µg/m^3 was used in the chronic inhalation effects assessment for hydrogen sulphide.

A chronic oral exposure limit was not required for the assessment of hydrogen sulphide since it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multi-media exposure model.

23A.2.26 Isopropylbenzene

23A.2.26.1 Acute Exposure Limit

Table 23A-60: Summary of Acute Inhalation Exposure Limits for Isopropylbenzene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	500	1-hour	AENV (2005)
ATSDR	--	--	ATSDR (2005a)
OEHHA	--	--	OEHHA (2000)
OMOE	100 400	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	--	--	WHO (2000)

The OMOE (2005a) has developed a ½-hour standard of 100 $\mu g/m^3$ and a 24-hour standard of 400 $\mu g/m^3$. However, these standards are based on U.S. EPA's chronic exposure limit of 400 $\mu g/m^3$ for increased kidney and adrenal weights in rats exposed to isopropylbenzene for 13 weeks (U.S. EPA 2006). The study team is of the opinion that use of a chronic endpoint in the derivation of short-term exposure limit is an overly conservative methodology since a higher exposure over a shorter time-period (i.e., acute exposure) presumably could occur without risk of adverse effects.

The AENV (2005) provides an AAQO of 500 $\mu g/m^3$ for a 1-hour averaging period, which was adopted from the Texas Natural Resource Conservation Commission (TCEQ 2003). However, the Texas effects screening level of 500 $\mu g/m^3$ is based on odour effects and therefore was not used in the acute effects assessment.

Since none of the acute criteria or guidelines provided above were determined to be appropriate for the acute effects assessment, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for isopropylbenzene.

The ACGIH (1991, 2006b) provides a TLV-TWA of 50 ppm (246 mg/m^3) for isopropylbenzene based on animal studies citing irritation and CNS effects. The TLV-TWA is considered to be below the level predicted to be irritating to humans and considerably less than levels causing acute nervous system changes. An uncertainty factor of 100 was applied to the TLV-TWA to account for intra-species variability (10-fold) and interspecies variability (10-fold) in the derivation of a short-term limit. Thus, a 24-hour exposure limit of 2,460 $\mu g/m^3$ was used in the acute effects assessment of isopropylbenzene.

23A.2.26.2 Chronic Exposure Limit(s)

Table 23A-61: Summary of Chronic Inhalation Exposure Limits for Isopropylbenzene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	--	--	Health Canada (2004b,c)
ATSDR	--	--	ATSDR (2005a)
RIVM	--	--	RIVM (2001)
U.S. EPA	400	RfC	U.S. EPA (2006)
WHO	--	--	WHO (2000)

The U.S. EPA has derived an inhalation RfC of 400 $\mu g/m^3$ for increased kidney weights in female rats and adrenal weights in male and female rats (U.S. EPA 2006). This RfC is based on a NOAEL of 2,438 mg/m^3 for kidney effects in rats following inhalation exposure to isopropylbenzene for 6 hours per day, 5 days per week for 13 weeks. The NOAEL was adjusted for intermittent exposure (6/24 x 5/7) to a concentration of 435 mg/m^3. A $NOAEL_{HEC}$ was calculated assuming a default value of 1.0 since b:a lambda values are unknown for the experimental animal species (a) and humans (h) (U.S. EPA 2006). An uncertainty factor of 1,000 was applied to the $NOAEL_{HEC}$ to account for subchronic-to-chronic extrapolation (10-fold), intra-species variability (10-fold), interspecies extrapolation (3-fold), and for database deficiencies (3-fold). A 3-fold uncertainty factor for interspecies variability was considered appropriate by the U.S. EPA since the HEC adjustment addresses the pharmacokinetic component of the extrapolation factor, leaving the pharmacodynamic area of uncertainty. This RfC of 400 $\mu g/m^3$ was used in the chronic inhalation effects assessment of isopropylbenzene.

No chronic oral exposure limit was required for the assessment of isopropylbenzene since it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multi-media exposure model.

23A.2.27 Methylene Chloride

23A.2.27.1 Acute Exposure Limit

Table 23A-62: Summary of Acute Inhalation Exposure Limits for Methylene Chloride

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	2,080	24-hour	ATSDR (2005a)
OEHHA	14,000	1-hour	OEHHA (2000)
OMOE	660 and 5,300 (interim) 220	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	3,000	24-hour	WHO (2000)

The OMOE (2005a) provides ½-hour and 24-hour standards for methylene chloride. However, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of methylene chloride.

The ATSDR has developed an acute inhalation MRL for methylene chloride of 0.6 ppm (2,080 µg/m^3) based on a LOAEL of 60 ppm for neurological effects (ATSDR 2000b, 2005a). In a randomized blind clinical chamber experiment, six to 20 volunteers were exposed to either filtered air or to concentrations of 300, 500, or 800 ppm of methylene chloride vapours. Subjects were exposed for 3 to 4 hours and tested at 45-minute intervals with standard neurobehavioural tests that measure critical flicker fusion frequency, auditory vigilance performance and psychomotor performance. Decreased critical flicker fusion frequency and auditory vigilance performance were identified at 300 ppm. This LOAEL was duration-adjusted to account for a 24-hour exposure scenario using the PBPK model, resulting in a $LOAEL_{ADJ}$ of 60 ppm. A cumulative uncertainty factor of 100 was applied to the LOAEL to account for using a LOAEL (10-fold) and for human variability (10-fold). This MRL of 2,080 µg/m^3 was used as a 24-hour exposure limit in the acute effects assessment of methylene chloride.

23A.2.27.2 Chronic Exposure Limit(s)

Table 23A-63: Summary of Chronic Inhalation Exposure Limits for Methylene Chloride

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	435 448 to 2,850	RsC RsC	Health Canada (2004b) CEPA (1993)
ATSDR	1,000	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	20	RsC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

Health Canada's RsC of 435 µg/m^3 is based on its inhalation unit risk of 2.3 x 10^{-5} per mg/m^3 (Health Canada 2004b). Although Health Canada does not provide the specific derivation of this inhalation unit risk, documentation of a range of tumorigenic concentrations that induced a 5% increase in the incidence of tumours (TC_{05}) was provided in CEPA (1993). Based on multi-stage modelling, a TC_{05} of 326 mg/m^3 for pulmonary adenomas and carcinomas (combined) in female mice and a TC_{05} of 3,574 mg/m^3 for hepatic adenomas and carcinomas (combined) in male mice were estimated (CEPA 1993). The TC_{05} of 326 mg/m^3 is equivalent to an RsC of 65 µg/m^3 and the TC_{05} of 3,574 mg/m^3 is equivalent to an RsC of 715 µg/m^3. Available data on methylene chloride is consistent with the hypothesis that variations in carcinogenic potential in different species are related to difference in the rates of metabolism. Therefore, PBPK modified TC_{05} values were developed, resulting in a TC_{05} of 2,238 mg/m^3 for pulmonary adenomas and carcinomas (combined) in female mice and a TC_{05} of 14,248 mg/m^3 for hepatic adenomas and carcinomas (combined) in male mice (CEPA 1993). The TC_{05} of 2,230 mg/m^3 is equivalent to an RsC of 448 µg/m^3 and the TC_{05} of 14,248 mg/m^3 is equivalent to an RsC of 2,850 µg/m^3.

The U.S. EPA (2006) recommends an inhalation unit risk of 4.7 x 10-4 per mg/m^3, which translates to an RsC of 20 µg/m^3 (in association with a one in 100,000 excess cancer risk). This value is considerably lower than Health Canada's RsC of 435 µg/m^3. The U.S. EPA unit risk is

based on the results of the same NTP inhalation study that Health Canada used to identify an increased frequency of combined adenomas and carcinomas in female mice exposed to methylene chloride. The U.S. EPA unit risk also incorporated information on the pharmacokinetics of methylene chloride.

Although the Health Canada and U.S. EPA unit risks are based on the same inhalation study, apparent differences in the interpretation of the results has led to two distinct unit risk values. In the absence of information about the validity of either of the agencies' interpretations of the data, the current assessment adopted the more stringent of the two inhalation unit risks, which is the U.S. EPA RsC of 20 µg/m^3.

A chronic oral exposure limit was not required for assessing methylene chloride, because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multimedia exposure model.

23A.2.28 n-Hexane

23A.2.28.1 Acute Exposure Limit

Table 23A-64: Summary of Acute Inhalation Exposure Limits for n-Hexane

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	n-hexane mixture:		
	7,500	½-hour	OMOE (2005a)
	2,500	24-hour	OMOE (2005a)
	n-hexane and n-hexane		
	isomers only:		
	22,500	½-hour	OMOE (2005a)
	7,500	24-hour	OMOE (2005a)
WHO	-	-	WHO (2000)

Because the OMOE 24-hour standard of 7,500 µg/m^3 for n-hexane and n-hexane isomers is higher then the 24-hour standard of 2,500 µg/m^3 for the n-hexane mixture, which was used in the acute effects assessment of the aliphatic C5-C8 group that includes n-hexane, n-hexane was not included in the acute effects assessment as an individual COPC. Instead, n-hexane was assessed on an acute-basis as a constituent of the C5-C8 aliphatic group.

23A.2.28.2 Chronic Exposure Limit(s)

Table 23A-65: Summary of Chronic Inhalation Exposure Limits for n-Hexane

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	21,000	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	700	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA developed a chronic RfC of 700 $\mu g/m^3$ for neurotoxicity (U.S. EPA 2006). This RfC is based on a benchmark concentration level (BMCL) of 430 mg/m^3 for peripheral neuropathy (decreased mean cell volume at 12 weeks) in a rat subchronic inhalation study. The BMCL was adjusted from intermittent to continuous exposure (12 hours/24 hours × 7 days/7 days) to a concentration of 215 mg/m^3. The human equivalent BMCL ($BMCL_{HEC}$) was calculated for an extrarespiratory effect of a category 3 gas. The blood:gas (air) partition coefficient ($H_{b/g}$) value for n-hexane in humans (H) is 0.8, whereas a value of 2.29 has been reported in rats (A) (U.S. EPA 2006). According to the RfC methodology, where the ratio of animal to human blood:air partition coefficients $[(H_{b/g})_A/(H_{b/g})_H]$ is greater than one, a value of one is used for the ratio by default. Thus, the $BMCL_{HEC}$ is equal to 215 mg/m^3. An uncertainty factor of 300 was applied to the $BMCL_{HEC}$ to account for intra-species variation (10-fold), interspecies variation (3-fold), extrapolation to chronic exposure from data in a less-than lifetime study (3-fold) and database deficiencies (3-fold).

Application of a full uncertainty factor of 10 for interspecies variation depends on two areas of uncertainty (i.e., toxicokinetic and toxicodynamic uncertainties). In this assessment, the toxicokinetic component is mostly addressed by the determination of a HEC (U.S. EPA 2006). The toxicodynamic uncertainty is also accounted for to a certain degree by the use of the applied dosimetry method. Thus a partial uncertainty factor of 3 was applied.

A subchronic (16 weeks) study was used for the derivation of the RfC. However, 16 weeks is half of the time required for a newly synthesized neurofilament protein to be transported from the neuronal cell body to the axon terminal in the longest axons of the CNS and the peripheral nervous system of an adult rat (Griffin et al., 1984). Since the lifetime of neurofilaments (target of toxicity of n-hexane) is shorter than the lifetime of an adult rat, extrapolation from subchronic to chronic exposure is not necessary and an uncertainty factor of 3 was applied.

The database for n-hexane lacks a developmental neurotoxicity study and a multigeneration reproductive and developmental toxicity study following inhalation exposure to pure n-hexane alone. On this basis, an uncertainty factor of 3 was applied.

This chronic RfC of 700 $\mu g/m^3$ was used in the chronic inhalation effects assessment of n-hexane alone.

A chronic oral exposure limit was not required for the assessment of n-hexane, because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multi-media exposure model.

23A.2.29 Naphthalene

23A.2.29.1 Acute Exposure Limit

Table 23A-66: Summary of Acute Inhalation Exposure Limits for Naphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	-	-	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	-	-	OEHHA (2000)
OMOE	36 22.5	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The OMOE (2005a) has developed a ½-hour POI of 36 $\mu g/m^3$ and an AAQC of 22.5 $\mu g/m^3$ for a 24-hour averaging period for naphthalene. The ½-hour POI is based on odour perception. Although the 24-hour criterion is based on health consideration, the specific basis of its derivation remains unknown. Consequently, the toxicity search was expanded to include intermediate MRLs provided by the ATSDR and occupational exposure values established by the ACGIH and the U.S. DOE for naphthalene.

The ACGIH (1991, 2006b) recommends a short-term exposure limit (STEL) of 15 ppm (79 mg/m^3) based on ocular irritation as a result of occupational naphthalene exposure. The STEL equates to a 15-minute air concentration that should not be exceeded at any time during a work day. The 15-minute STEL can be adjusted to an equivalent 1-hour concentration using the following equation:

$$\text{Equivalent 1-hour concentration} = \frac{\text{15-minute concentration}}{(\text{60 minutes}/\text{15 minutes})^{0.2}}$$

The exponent for the 15-minute multiplier (0.2) used for this assessment is based on neutral atmospheric conditions (OMOE 1996; Duffee et al. 1991). Based on the above conversion factor, the STEL is then adjusted to a concentration of 60 mg/m^3. A cumulative uncertainty factor of 100 was applied to the duration-adjusted STEL to account for intra-species variability (10-fold) and the apparent use of a LOAEL (10-fold). Thus, a 1-hour limit of 600 $\mu g/m^3$ was adopted as the short-term exposure limit for this assessment.

Because this 1-hour limit of 600 $\mu g/m^3$ was also adopted for the short-term assessment of the aromatic C9-C16 group (which includes naphthalene), naphthalene was not included in the acute effects assessment as an individual COPC. Instead, it was assessed on an acute-basis as a constituent of the C5-C8 aliphatic group.

23A.2.29.2 Chronic Exposure Limit(s)

Table 23A-67: Summary of Chronic Inhalation Exposure Limits for Naphthalene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	3.7	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	3	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The U.S. EPA has derived a chronic inhalation RfC for naphthalene of 3 $\mu g/m^3$ (U.S. EPA 2006). This RfC was estimated from a chronic inhalation mouse study that reported the LOAEL of 9.3 mg/m^3 based on nasal effects including hyperplasia and metaplasia in respiratory and olfactory epithelium (NTP 1992). The U.S. EPA incorporated an uncertainty factor of 3,000 to account for interspecies differences (10-fold), sensitive human individuals in the population (10-fold), to extrapolate from a NOAEL to a LOAEL (10-fold), and for database uncertainties (3-fold). Database uncertainties included the lack of a 2-generation reproductive toxicity study and chronic inhalation data for other animal species.

A chronic oral exposure limit was not required for the assessment of naphthalene, as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multi-media exposure model.

23A.2.30 Nitrogen Dioxide

23A.2.30.1 Acute Exposure Limit

The exposure limits used for the acute effects assessment of NO_2 were based on AENV's AAQOs (AENV 2005). These include a 1-hour objective of 400 $\mu g/m^3$ and a 24-hour objective of 200 $\mu g/m^3$. These AAQOs were adopted from the Health Canada's NAAQOs for NO_2. The NAAQOs are developed in 3 tiers: maximum desirable, acceptable and tolerable objectives. The Alberta objectives are based on the maximum acceptable levels, as maximum desirable NAAQOs (i.e., the lowest objectives) have not been developed for NO_2 on an acute-basis. These NAAQOs are health-based, and rely on controlled studies of the most sensitive population (i.e., asthmatics) to NO_2.

Using the above objectives and guidelines, the acute assessment for NO_2 was completed on a 1-hour and 24-hour basis.

23A.2.30.2 Chronic Exposure Limit(s)

The chronic exposure limit used for the assessment of NO_2 concentrations in air was based on AENV's AAQO of 60 $\mu g/m^3$ (AENV 2005). This guideline was adopted from Health Canada's NAAQO for NO_2 based on an annual averaging time. The NAAQOs are developed in 3 tiers: maximum desirable, acceptable and tolerable objectives. The maximum desirable level (i.e., the lowest objective) was adopted as the annual objective in Alberta. This objective is health-based and relies on controlled studies of the most sensitive population (i.e., asthmatics) to NO_2.

Nitrogen dioxide was assessed only for the inhalation route of exposure as the principal health effects are strictly related to inhalation.

23A.2.31 Particulate Matter

23A.2.31.1 Consideration of Potential Health Effects Associated with Particulate Matter

Particulate matter (PM) is the generic term applied to a broad class of chemically and physically diverse substances that exist as discrete particles (liquid droplets or solids) over a range of sizes. Particles less than 2.5 micrometers (<2.5 µm) are called "fine" particles (i.e., $PM_{2.5}$), while those larger than 2.5 µm but smaller than 10 µm are known as "coarse" particles (i.e., $PM_{2.5-10}$). When inhaled, these particles can reach the deepest regions of the lungs (U.S. EPA 2006b).

A significant amount of research has been, and is being conducted on the health effects associated with both fine and coarse PM in the ambient air. Short-term exposure to ambient PM in numerous urban areas has been associated with a range of health outcomes including:

- premature death in people with heart and lung disease
- non-fatal heart attacks
- respiratory and cardiovascular hospitalizations
- lung function changes
- adverse respiratory symptoms (e.g., cough, wheeze)
- aggravated asthma
- irregular heartbeats (U.S. EPA 2004b)

Long-term exposure to fine particles ($PM_{2.5}$) has been associated in some studies with cardiovascular and lung cancer mortality, effects on lung function and increases in respiratory symptoms (Brauer et al. 2002; Gauderman et al. 2004; Krewski et al. 2003; 2005a,b; Pope et al. 2002, 2004a,b). These associations do not appear to be explainable by other factors (e.g., weather and other compounds) and after careful review of the evidence, most scientists agree that these seem to be causal in nature (Samet et al. 2000 [reanalyzed in HEI 2003]; CEPA 2000b; U.S. EPA 2004a,b). This presents a difficult problem because PM is ubiquitous in the environment and sources are both natural and anthropogenic. Populations identified as being more sensitive to the adverse health effects of PM include individuals with existing respiratory or cardiovascular disease, the elderly, children and asthmatics (U.S. EPA 2004a,b).

Existing epidemiological studies on large populations have been unable to identify a threshold concentration below which ambient PM has no effect on health. It is likely that thresholds for specific responses exist for specific individuals, but these may vary markedly in the general population resulting in such a wide range in susceptibility that the identification of an explicit threshold for the general population may be impossible (WHO 2003). The U.S. EPA has noted that a convincing mathematical demonstration of a clear threshold in the population studies available is both complex and difficult to verify. They concluded that available evidence does not support or refute the existence of thresholds for the effects of PM on mortality across the range of concentrations in the studies (U.S. EPA 2004b).

The health impacts from exposure to PM are generally small in terms of measurable or relative risk. For example, the magnitude of the effect of PM exposure is much smaller than the effects of tobacco smoke (HEI 2001). However, because exposure to PM is widespread, the public health impact of increased air pollution (and in turn PM) can be significant. A recent large study of hospital admissions in 204 counties across the U.S. found a 10 $\mu g/m^3$ same day increase in $PM_{2.5}$ was associated with 0.5 to 2 % increased hospital admissions for cardiovascular and respiratory diseases by region (Dominici et al. 2006). Variation in risk across regions was found.

For example, positive associations with cardiovascular hospital admissions were found only in the Eastern region of the U.S. By contrast, relative risk estimates for respiratory tract infections were larger in the Western region (Dominici et al. 2006).

The emphasis of PM research has been shifting in recent years to address the many unanswered questions about how particles cause the health effects observed in epidemiological studies. Primary among these are questions related to a) the biological mechanisms responsible for the effects observed and; b) the types and sources of particles most likely causing the effects observed. At present, PM standards are based solely on size fraction (e.g., PM_{10}, $PM_{2.5}$, $PM_{2.5-10}$) but future standards could target the particle components or characteristics that are most toxic.

The primary biological mechanisms thought to underlie the reported health effects from ambient PM include oxidative stress and pulmonary or systemic inflammation (NRC 2004). Clinical and toxicological studies suggest that PM exposure is associated with increased airway hyperactivity, oxidative stress, inflammation, arrhythmias, atherosclerosis, heart rate variability, blood pressure and changes in blood characteristics (e.g., levels of C-reactive protein, fibrinogen, blood viscosity). This provides the important biological plausibility required to explain the morbidity and mortality observed in susceptible individuals in epidemiological studies. However, uncertainty remains in the degree to which toxicological findings from in vitro systems and high dose animal studies apply to real world human exposures, which are often orders of magnitude lower (NRC 2004). The National Research Council (NRC) states that: The findings from the clinical, animal and in vitro experimental work have often not addressed dose-response relationships, which may provide critical insights into the relevance of the experimental findings for interpreting epidemiological research (NRC 2004). Many studies also used a non-physiologic route of exposure such as intratracheal instillation, which the U.S. EPA (2004b) notes can result in very high individual cellular concentrations, requiring much caution in the extrapolation of findings.

Determining the characteristics of PM that are associated with adverse health effects is challenging. PM in ambient air is a complex mixture that varies in size and chemical composition, as well as varying spatially and temporally. Different types of particles may cause different effects with different time courses, and perhaps only in susceptible individuals. The interaction between PM and gaseous co-pollutants adds additional complexity because in ambient air pollution, a number of pollutants tend to co-occur and have strong inter-relationships with each other (e.g., PM, SO_2, NO_2, CO, and O_3) as well as different levels of measurement error (Peel et al. 2005; U.S. EPA 2004b). As a result it is difficult to attribute the effects of air pollution as a mixture to any one of these particular pollutants. A pollutant that exhibits a relatively strong association in a multi-pollutant model may be acting as a surrogate for an unmeasured or poorly measured pollutant (Metzger et al. 2004). Several investigators have noted that the effects observed in their studies are likely due to the mixture of air pollutants and not just one component (Chen et al. 2004; Goldberg et al. 2006).

Considerable research effort has gone into understanding the PM sources, components and size fractions likely to be responsible for the health effects observed in epidemiology studies. Characteristics that have been found to contribute to toxicity include: metal content, presence of polycyclic aromatic hydrocarbons and other organic components, endotoxin content and small (less than 2.5 µm) and extremely small (less than 0.1 µm) size (CAFÉ 2004).

Several studies using factor analyses indicate that combustion particles in the fine fraction but not fine crustal particles are associated with increased mortality (Laden et al. 2000; Schwartz et al. 1999; Mar et al. 2000; Tsai et al. 2000; Ozkaynak et al. 1996; Janssen et al. 2002). Crustal particles (also referred to as geological particles) are products of the natural abrasion of the

earth's crust and are mainly mechanically generated from agriculture, mining, construction, road dust and related sources. Particles associated with motor vehicle emissions stand out clearly as a source category associated with mortality in the factor analyses studies, but associations with an oil combustion factor, a regional sulphate factor and a source category related to vegetative burning have also been identified. Regional sulphate is highly correlated with $PM_{2.5}$, however, so it may be acting as a surrogate for $PM_{2.5}$ (U.S. EPA 2004b).

A number of studies have reported significant associations between adverse health effects and either traffic density or close proximity to major roads, including total and cardiopulmonary mortality, heart attacks, and adverse respiratory health effects (Brauer et al. 2002; Finkelstein et al. 2004; Hoek et al. 2002; Kim et al. 2004; Lipfert et al. 2006; Tonne et al. 2006; Venn et al. 2001). For example, in Hamilton, Ontario, living within 100 metres of a freeway or 50 metres of a major urban road was associated with increased all cause mortality (RR= 1.18; 1.02-1.38) (Finkelstein et al. 2004). The mortality rate advancement associated with residence near a major road was 2.5 years in this study, which is similar to that associated with chronic respiratory and pulmonary diseases and diabetes. In a study of 70,000 male U.S. veterans, Lipfert et al. (2006) reported that county-level traffic density was a better predictor of mortality than with ambient $PM_{2.5}$ levels. In multi-pollutant models including traffic density, the association with $PM_{2.5}$ was reduced and lost statistical significance (Lipfert et al. 2006). Another study reported that time spent in traffic (e.g., cars, public transport, bicycles) two hours prior was much more strongly associated with induction of nonfatal myocardial infarctions (MIs) than any of the air pollutants measured at a central monitoring site (Peters et al. 2005).

Future epidemiological studies and studies currently in progress should provide important information on the relative role of various PM size fractions and components in adverse health effects. A collection of studies in Atlanta is using extensive air quality data, including detailed PM composition and size fraction information from a monitoring station operated by the Aerosol Research and Inhalation Epidemiology Study (ARIES). Parameters measured include several gases and many PM components, including total metals, water-soluble metals, organic carbon (OC) and elemental carbon (EC), sulphates, nitrates, several speciated hydrocarbons, and polar volatile organic compounds (VOCs) (Metzger et al. 2004; Peel et al. 2005). Time series studies using ARIES data that examined associations with emergency department visits suggest the strongest and most consistent associations are with traffic related pollutants such as NO_2, CO, $PM_{2.5}$, OC, EC and oxygenated carbons (Metzger et al. 2004; Peel et al. 2005). Consistent associations with sulphates were not demonstrated.

A recent time-series analysis of PM in California indicated that ambient concentrations of several constituents of $PM_{2.5}$ were associated with daily mortality, specifically EC, OC, nitrates, copper, potassium, titanium and zinc (Ostro et al. 2006). Many of these constituents were associated with higher relative risks than $PM_{2.5}$ mass. The authors noted that their results support the hypothesis that pollution from motor vehicles and other sources of combustion may be of particular concern (Ostro et al. 2006).

Seagrave et al. (2006) examined the lung toxicity of ambient PM from various U.S. sites with different contributing sources and reported on the relationship between composition and effects. Summer and winter samples from each site were collected for toxicity testing, chemical analysis and source apportionment. After instillation into rat lungs, general toxicity, acute cytotoxicity and inflammation were assessed. The results support the concept that $PM_{2.5}$ composition affects its toxicity (Seagrave et al. 2006). Source apportionment suggested that the most potent samples were those with the largest contributions from diesel and gasoline exhaust. Wood burning was only weakly correlated with toxicity end points, while sulphate (SO_4^{2-}), secondary organic aerosols, meat cooking and vegetation burning were not correlated with the biological responses.

Untangling the relationships among components of mixtures of PM requires a sophisticated integration of air quality and health research and a systematic study of PM components (Samet et al. 2005). The Health Effects Institute (HEI) has noted that a systematic approach to these topics will generate more specific PM standards, and ones that target the types and inventories of particles most likely to contribute to health effects. Such a research initiative may lead to the identification of critical PM sources, enabling industry-specific guidance for control of those specific PM components that have been attributed with the greatest fraction of risk to health (HEI 2005).

23A.2.31.2 Exposure Limit for Particulate Matter

The Scientific Assessment Document (Part 1) of The National Ambient Air Quality Objectives for Particulate Matter prepared by the Canadian Environmental Protection Act and Federal Provincial Advisory Committee (CEPA/FPAC) Working Group on Air Quality Objectives and Guidelines concluded that both the mortality and hospitalization studies support the identification of 15 µg/m^3 averaged over 24 hours as the reference level for $PM_{2.5}$ (CEPA/FPAC 1999). The reference level was considered an estimate of the lowest ambient particulate matter level at which statistically significant increases in health responses can be detected based on data available up to 1996. It was derived based on the average 24-hour concentrations measured in the cities where these effects were found. The CEPA/FPAC Working Group states that reference levels should not be interpreted as thresholds of effects, or levels at which impacts do not occur. They are defined under Canada's National Ambient Air Quality Objectives as levels above which there are demonstrated effects on human health and/or the environment (CEPA/FPAC 1999).

A Canada-Wide Standard (CWS) of 30 µg/m^3 $PM_{2.5}$ averaged over 24 hours was developed by the CCME under the auspices of the Canadian Environmental Protection Agency (CEPA) (CCME 2000b). Under this standard, the government is committed to reduce levels of $PM_{2.5}$ significantly by 2010. Achievement of this standard is based on the 24-hour 98th percentile of the ambient measurement annually, measured over three consecutive years. The CWS is considered to be an important step towards the long-term goal of reducing the health risks of $PM_{2.5}$. It represents a balance between achieving the best health and environmental protection possible, and the feasibility and costs of reducing pollutant emissions that contribute to $PM_{2.5}$ in ambient air.

The California Air Resources Board (CARB) has identified an air quality annual average standard for $PM_{2.5}$ of 12 µg/m^3 (CARB 2002a,b). This recommended arithmetic mean value was "based on a growing body of epidemiological and toxicological studies showing significant toxicity (resulting in mortality and morbidity) related to exposure to fine particles". Similar to the CEPA/FPAC reference level, the value was derived mainly based on the average 24-hour concentrations in cities where statistically significant increases in health responses were detected. The CARB Staff report recommendation was adopted by the State of California as an ambient air quality standard in June of 2002.

In 1997, the U.S. EPA first set National Ambient Air Quality Standards (NAAQS) for fine particles. Two primary $PM_{2.5}$ standards were set: an annual standard of 15 µg/m^3 to protect against health effects caused by exposures ranging from days to years, and a 24-hour standard of 65 µg/m^3 to provide additional protection on days with high peak $PM_{2.5}$ concentrations. In September 2006, the U.S. EPA issued a new suite of standards to better protect public health from particle pollution. The revised NAAQS for $PM_{2.5}$ reduced the 24-hour standard from 65 to 35 µg/m^3 and retained the annual standard of 15 µg/m^3 (U.S. EPA 2006b). The 24-hour standard is based on the 98th percentile annual measurement, averaged over 3 years, while the

annual standard is met when the 3-year average of the annual average $PM_{2.5}$ concentration is less than or equal to 15 µg/m^3. The U.S. EPA also retained the existing 24-hour NAAQS for PM_{10} of 150 µg/m^3 and revoked the annual PM_{10} standard of 50 µg/m^3.

The final NAAQSs were selected by the U.S. EPA after completing an extensive review of thousands of scientific studies on the impact of fine and course particles on public health. The criteria document (i.e., the review) and the staff paper containing the U.S. EPA's recommendations on the range of alternative standards that should be considered, received extensive review by representatives of the scientific community, industry and public interest groups as well as the Clean Air Scientific Advisory Committee (CASAC) – a group of independent scientific and technical experts established by Congress (U.S. EPA 2006b).

It is worth noting that the final annual standard for $PM_{2.5}$ selected by the U.S. EPA does not reflect the advice of the CASAC PM panel, who recommended a 24-hour standard in the range of 30-35 µg/m^3 and an annual standard in the range of 13-14 µg/m^3 (CASAC 2006). They noted that clear and convincing scientific evidence as well as the U.S. EPA's own risk analyses (U.S. EPA 2005) indicated health risks at the current annual standard of 15 µg/m^3. Risk analyses indicated that uncertainties increase rapidly below an annual level of 13 µg/m^3 and that was the basis for CASAC's recommendation of 13 µg/m^3 as the lower bound for the annual $PM_{2.5}$ standard. The provisions do not require U.S. EPA standards to be set at a zero risk level but rather at a level that avoids unacceptable risks to public health. However, previously the U.S. EPA has accepted CASAC's advice with respect to NAAQS decisions (CASAC 2006).

The WHO (2005) suggests that PM guidelines cannot ensure the complete protection against adverse health effects because thresholds have not been identified and it is unlikely that any PM guideline will provide adequate protection for every individual against all possible adverse effects. Instead, guidelines need to achieve the lowest concentrations possible considering local constraints, capabilities and public health priorities.

With respect to air quality guidelines for $PM_{2.5}$, the WHO recommends an annual average of 10 µg/m^3 and a daily 99th percentile of 25 µg/m^3 for the protection of public health. The WHO (2005) suggests the annual average should take precedence over the daily guideline because at low levels there is less concern for episodic excursions. The annual average guideline is based on long-term exposure studies using the American Cancer Society (ACS) data (Pope et al. 2002) and Harvard Six-Cities data (Dockery et al. 1993). The studies reported a robust association between PM exposure and mortality. Historical mean $PM_{2.5}$ concentrations across cities in these two studies were 18 and 20 µg/m^3, respectively but average concentrations in individual cities were as low 11 µg/m^3 over the period of study. An annual mean guideline concentration of 10 µg/m^3 was therefore noted to be below the mean for most likely effects (WHO 2005). However, both the WHO (2005) and the U.S. EPA (2005) note that statistical uncertainties in the risk estimates become apparent at concentrations of about 13 µg/m^3, below which confidence bounds significantly widen, indicating the possibility of an effects threshold. In their staff paper, the U.S. EPA (2005) noted that an annual standard of 12 µg/m^3 would be precautionary, but a standard set below the range of 12-15 µg/m^3 would be highly precautionary, "giving little weight to the remaining uncertainties in the broader body of evidence, including other long-term exposure studies that provide far more inconsistent results".

It is apparent that the health protection afforded by the reference level for $PM_{2.5}$ of 15 µg/m^3 that was established by the CEPA/FPAC in 1999 should be considered generally equivalent to the intended or effective health protection of the Ambient Air Standard of California (12 µg/m^3), the annual NAAQ standard retained by the U.S. EPA (15 µg/m^3) or the new WHO annual guideline of 10 µg/m^3 $PM_{2.5}$.

The short-term value represented by the CWS of 30 µg/m^3 is analogous to the new 24-hour NAAQS identified by U.S. EPA of 35 µg/m^3, which was determined to better protect the public from the health effects associated with short-term fine particle exposures. The CWS is within the range set by the WHO annual guideline for $PM_{2.5}$ of 10 µg/m^3 and the U.S. EPA NAAQS of 35 µg/m^3. CARB refrained from setting a 24-hour standard in 2002, and has deferred a decision on this matter (CARB 2002b).

For the current assessment, predicted 24-hour $PM_{2.5}$ concentrations are compared to the CWS of 30 µg/m^3, which falls within the range of recent standards recommended by the WHO and the U.S. EPA. Predicted annual average concentrations were compared against the CARB annual standard of 12 µg/m^3, which also falls within the range of standards recommended by the WHO and the U.S. EPA. The choice of standards in the middle of the range of available guidelines or standards respects both the need to be conservative and the uncertainty which still remains regarding the types of PM that are most toxic and the existence of a threshold for PM-associated adverse effects.

Taken together, these health-based limits should offer an acceptable level of protection to the area residents.

23A.2.32 Propylene Oxide Group

Surrogate: Propylene oxide

23A.2.32.1 Acute Exposure Limit

Table 23A-68: Summary of Acute Inhalation Exposure Limits for Propylene Oxide

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	480	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	3,100	1-hour	OEHHA (2000)
OMOE	4.5 and 450 (interim) 1.5	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

On an acute basis, propylene oxide is a primary irritant of the eyes and of the upper and lower respiratory tracts.

The OMOE (2005a) provides ½-hour and 24-hour standards for propylene oxide. However, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of propylene oxide.

The AENV (2005) developed an AAQO of 480 µg/m^3 based on a 1-hour averaging period. Alberta's AAQO was adopted from the Oklahoma Department of Environmental Quality, which established its 24-hour averaging-time maximum acceptable ambient concentration by dividing the TLV–TWA of the ACGIH (ACGIH 2006b) (an 8-hour time-weighted average occupational exposure limit of 48,000 µg/m^3) by an uncertainty factor of 100. The basis of the 100-fold uncertainty factor is unknown. The ACGIH TWA is based on evidence that suggests that no genetic damage or excess cancer risk could be detected in workers exposed to propylene oxide concentrations no greater than 48,000 µg/m^3. However, ACGIH recently revised its TLV–TWA

for propylene oxide to a concentration of 4,800 µg/m^3. As a result, this AAQO was not used in the acute effects assessment for propylene oxide.

The OEHHA (2000) provides a 1-hour REL of 3,100 µg/m^3 that is protective against mild adverse effects. In an inhalation chamber 10 mice (5 per sex) were exposed to 387 or 859 ppm of propylene oxide for 4 hours. A LOAEL of 387 ppm was identified based on dyspea, which was observed in all exposed groups. In this case, the dyspea reflects nasal irritation, which is considered to be a mild effect. The OEHHA (2000) extrapolated the 4-hour concentration to a 1-hour concentration of 774 ppm based on the equation that follows.

$$387^2 \text{ ppm} \times 4 \text{ hours} = C^2 \times 1 \text{ hour}$$

A cumulative uncertainty factor of 600 was applied to the duration adjusted LOAEL to account for the use of a LOAEL (6-fold), interspecies variation (10-fold) and intra-species variation (10-fold). The result is a 1-hour REL of 1.3 ppm (3,100 µg/m^3), which was used in the acute effects assessment of propylene oxide.

23A.2.32.2 Chronic Exposure Limit(s)

Table 23A-69: Summary of Chronic Inhalation Exposure Limits for Propylene Oxide

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	3.7	RfC	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	30 3	RfC RsC	U.S. EPA (2006) U.S. EPA (2006)
WHO	-	-	WHO (2000)

The IARC (1994) classifies propylene oxide as being possibly carcinogenic to humans (Group 2B) based on sufficient evidence in experimental animals. Therefore, the U.S. EPA chronic RsC of 3 µg/m^3 based on nasal cavity hemangioma or hemangiosarcoma in male mice was used (U.S. EPA 2006). The RsC was derived from an inhalation unit risk of 3.7 x 10^{-6} per µg/m^3 and is associated with a risk level of one in 100,000.

A chronic oral exposure limit was not required for assessing propylene oxide, as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multimedia exposure model.

23A.2.33 Styrene

23A.2.33.1 Acute Exposure Limit

Table 23A-70: Summary of Acute Inhalation Exposure Limits for Styrene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	215	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	21,000	1-hour	OEHHA (2000)
OMOE	830 690 275	½-hour 1-hour 24-hour	OMOE (2005a) OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The AENV provides a 1-hour AAQO of 215 $\mu g/m^3$ that was adopted from the Texas Natural Resource Conservation Commission effects screening level for odour perception (AENV 2005). The Texas Natural Resource Conservation Commission has since updated its effects screening level for styrene to a concentration of 110 $\mu g/m^3$ based on odour perception (TCEQ 2003). These odour-based limits were not used in the acute effects assessment.

The OMOE (2005a) provides ½-hour, 1-hour and 24-hour standards for propylene oxide. However, no scientific basis is provided for these standards. As a result, the study team is unable to comment on the scientific merit of these limits and did not use them in the short-term assessment of styrene.

Instead, the acute exposure limit of 21,000 $\mu g/m^3$, based on OEHHA's 1-hour REL was used to assess the potential short-term health effects of styrene (OEHHA 1999h, 2000). This acute REL was derived from a NOAEL of 99 ppm (210,000 $\mu g/m^3$) for eye and throat irritation in three human subjects exposed for 20 minutes via inhalation. A safety factor of 10 was applied by the OEHHA to account for increased susceptibility of sensitive human individuals. The result is a 1-hour exposure limit of 21,000 $\mu g/m^3$ that is considered to be protective against mild adverse effects (OEHHA 1999h).

23A.2.33.2 Chronic Exposure Limit(s)

Table 23A-71: Summary of Chronic Inhalation Exposure Limits for Styrene

Regulatory Agency	Value ($\mu g/m^3$)	Type	Reference
Health Canada	92	RfC	Health Canada (2004b)
ATSDR	260	RfC	ATSDR (2005a)
RIVM	900	RfC	RIVM (2001)
U.S. EPA	1,000	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The Health Canada tolerable concentration of 92 µg/m^3 for styrene is based on observed effects on body weight changes and manifestations of neurotoxicity in Wistar rats (Health Canada 2004b). However, as the ATSDR, RIVM and U.S. EPA chronic inhalation exposure limits are based on an occupational study (Mutti et al. 1984), the Health Canada tolerable concentration was not chosen as the chronic exposure limit for the current assessment.

The ATSDR (2005a, 1992) provides a chronic inhalation MRL of 0.06 ppm (260 mg/m^3) based on decreased verbal learning skills. A LOAEL of 25 ppm was identified in 50 workers occupationally exposed to styrene for a mean of 8.6 years (Mutti et al. 1984). The ATSDR (1992) adjusted the LOAEL for intermittent exposure (8 hours/24 hours x 5 days/7days) to a concentration of 6 ppm. An uncertainty factor of 100 was applied to the duration-adjusted LOAEL to account for intra-species variation (10-fold) and use of a LOAEL (10-fold).

The RIVM (2001) has developed a TCA of 900 µg/m^3 based on the same occupational study as the ATSDR (1992). However, the RIVM identifies a NOAEC of 25 ppm (107 mg/m^3) for CNS effects in workers. Following the same methodology as the ATSDR, the RIVM adjusted the NOAEC for intermittent exposure (8 hours/24 hours x 5 days/7days) to a concentration of 6 ppm (26 mg/m^3). An uncertainty factor of 30 was applied to the duration-adjusted NOAEC to account for intra-species variation (10-fold) and extrapolation of a marginal affect to a NOAEC (3-fold).

A chronic inhalation RfC of 1,000 µg/m^3 was developed by U.S. EPA (2006) based the same occupational study as the ATSDR (1992) and RIVM (2001). A NOAEL of 25 ppm (106 mg/m^3) for CNS effects was reported by the U.S. EPA (2006). The NOAEL exposure level is based on a back extrapolation from worker urinary concentration of styrene metabolites reported in the principal study and was adjusted to the lower 95% confidence limit listed in Guillemin et al. (1982), which was 88% [25 ppm x 0.88 = 22 ppm (94 mg/m^3)]. The adjusted NOAEL was converted from an 8-hour time-weighted average occupational exposure to continuous exposure using the following calculation:

$$NOAEL_{HEC} = NOAEL \times \frac{MV_{ho}}{MV_h} \times \frac{Exp_{ho}}{Exp_h}$$

Where:

$NOAEL_{HEC}$ = no-observable-adverse-effects level in the human population from continuous exposure to styrene (mg/m^3)

NOAEL = no-observable-adverse-effects level for discontinuous exposure in an occupational setting (94 mg/m^3)

MV_{ho} = amount of air used by a worker during an 8-hour work period (10 m^3/d)

MV_h = amount of air used by an individual in the general population during a day (20 m^3/d)

Exp_{ho} = days per week a worker is exposed (5 days)

Exp_h = days per week an individual in the general population is exposed (7 days)

An uncertainty factor of 30 was applied to the $NOAEL_{HEC}$ of 34 mg/m^3 to account for database inadequacy (3-fold), intra-species variability (3-fold), and for lack of information on chronic studies (3-fold).

The U.S. EPA RfC was selected for use in the chronic inhalation effects assessment for styrene because it uses the preferred approach extrapolating between intermittent occupational exposure and continuous exposure.

A chronic oral exposure limit was not required for assessing styrene, as it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multimedia exposure model.

23A.2.34 Sulphur Dioxide

23A.2.34.1 Acute Exposure Limit

The acute exposure limits used for the assessment of SO_2 concentrations in air were based primarily on AENV's AAQOs (AENV 2005). These include a 1-hour objective of 450 µg/m^3 and a 24-hour objective of 150 µg/m^3. These AAQOs were adopted from the Health Canada NAAQOs, which recommends maximum desirable, acceptable and tolerable objectives for SO_2. The Alberta objectives are based on the maximum desirable levels (i.e., the lowest objective). These guidelines are health-based and rely on controlled studies of the most sensitive population (i.e., asthmatics) to air pollutants such as SO_2.

Sulphur dioxide also was assessed using a 10-minute air quality guideline of 500 µg/m^3 developed by the WHO (2000). This guideline is based on changes in lung function in asthmatics (WHO 2000).

Using the above objectives and guidelines, the acute assessment for SO_2 was completed on a 10-minute, 1-hour and 24-hour basis.

23A.2.34.2 Chronic Exposure Limit(s)

The chronic exposure limit used for the assessment of SO_2 concentrations in air was based on AENV's annual ambient air quality objective for SO_2 of 30 µg/m^3 (AENV 2005). This AAQO was adopted from the Health Canada annual NAAQO, which includes maximum desirable, acceptable and tolerable objectives for SO_2. The Alberta objectives are based on the maximum desirable levels (i.e., the lowest objective). This guideline is health-based and relies on controlled studies of the most sensitive population (i.e., asthmatics) to air pollutants such as SO_2.

Sulphur dioxide was assessed only on an inhalation exposure basis because potential health effects relate directly to inhalation exposure.

23A.2.35 Sulphuric Acid

23A.2.35.1 Acute Exposure Limit

Table 23A-72: Summary of Acute Inhalation Exposure Limits for Sulphuric Acid

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	10	1-hour	AENV (2005)
ATSDR	-	-	ATSDR (2005a)
OEHHA	120	1-hour	OEHHA (2000)
OMOE	100 120	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The AENV (2005) provides a 1-hour AAQO of 10 μg/m^3 that was adopted from the Texas Natural Resource Conservation Commission Reg II, but no specific basis is provided. In addition, the OMOE (2005a) does not provide supporting documentation for its ½-hour POI of 100 μg/m^3 and a 24-hour AAQC of 120 μg/m^3. Given that these objectives and criteria do not have adequate supporting documentation and thus the study team was unable to comment on the scientific merit of these limits, they were not used in the acute effects assessment.

The OEHHA (2000) provides an acute REL of 120 μg/m^3 for sulphuric acid based on small changes in airway function in 17 human asthmatics. A NOAEL of 450 μg/m^3 was reported following 16 minutes of exposure. The OEHHA extrapolated a 1-hour concentration of 120 μg/m^3 based on the equation that follows.

$$450^1 \text{ ppm} \times 16 \text{ minutes} = C^1 \times 60 \text{ minutes}$$

There were no uncertainty factors applied by the OEHHA (2000). The result is an acute exposure limit of 120 μg/m^3, which was used as the 1-hour limit for the acute effects assessment.

23A.2.35.2 Chronic Exposure Limit

Table 23A-73: Summary of Chronic Inhalation Exposure Limits for Sulphuric Acid

Regulatory Agency	Value (μg/m^3)	Type	Reference
Health Canada	-	-	Health Canada (2004b,c)
ATSDR	-	-	ATSDR (2005a)
RIVM	-	-	RIVM (2001)
U.S. EPA	-	-	U.S. EPA (2006)
WHO	-	-	WHO (2000)
OEHHA	1	RfC	OEHHA (2005)

A chronic inhalation criterion or guideline is not provided by any of the above regulatory agencies for sulphuric acid. Consequently, the toxicity search was expanded to include the OEHHA (2005). The OEHHA provides a chronic REL of 1 μg/m^3 based on significant increases in bronchial epithelial hyperplasia and bronchial thickening in cynomolgus monkeys. The monkeys were separated into exposure groups (5 males and 4 females) and exposed continuously via inhalation to 0, 380, 480, 2,400 or 4,800 μg/m^3 for 78 weeks. A LOAEL of 380 μg/m^3 was reported. An uncertainty factor of 300 was applied to the LOAEL to account for use of a LOAEL (3-fold; slight effects), subchronic to chronic exposure (3-fold), interspecies variation (3-fold; non-human primate) and intra-species variability (10-fold). This REL was used in the chronic assessment of sulphuric acid.

A chronic oral exposure limit was not required for the assessment of sulphuric acid since it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multi-media exposure model.

23A.2.36 Toluene

23A.2.36.1 Acute Exposure Limit

Table 23A-74: Summary of Acute Inhalation Exposure Limits for Toluene

Regulatory Agency	Value ($\mu g/m^3$)	Averaging Time	Reference
AENV	1,880 400	1-hour 24-hour	AENV (2005) AENV (2005)
ATSDR	3,800	24-hour	ATSDR (2000)
OEHHA	37,000	1-hour	OEHHA (2000)
OMOE	2,000	½-hour, 24-hour	OMOE (2005a)
WHO	260	1-week	WHO (2000)

The AENV (2005) provides a 1-hour AAQO of 1,880 $\mu g/m^3$, which was adopted from the Texas Natural Resource Conservation Commission. The Texas value was based on the ACGIH TLV-TWA of 50 ppm (188 mg/m^3) (ACGIH 1991, 2006b). The AENV (2005) adjusted the TLV-TWA by applying a 100-fold uncertainty factor (note: the basis of the 100 fold uncertainty factor is unknown). The 24-hour AAQO was adopted from the Michigan Department of Environmental Quality and the Washington Department of Ecology (AENV 2005). These regulatory agencies based their 24-hour guidelines on the U.S. EPA chronic inhalation RfC of 400 $\mu g/m^3$ (U.S. EPA 1998). The U.S. EPA RfC has since been revised to an inhalation RfC of 5,000 $\mu g/m^3$ for neurological effects. Because this 24-hour AAQO was based on a chronic inhalation exposure limit that has recently been raised by more than a factor of 10, this objective was not used in the acute effects assessment.

The OMOE (2005a) has developed a ½-hour standard and 24-hour AAQC of 2,000 $\mu g/m^3$ for toluene. These limits are based on odour perception and thus were not used in the short-term assessment.

The WHO (2000) provides a guideline of 260 $\mu g/m^3$ based on a 1-week averaging time. A LOAEL of 332 mg/m^3 (88 ppm) was identified for CNS effects from occupational studies. The LOAEL was adjusted for continuous exposure (8 hour/24 hour x 5 days/7 days) to a concentration of 79 mg/m^3. The duration-adjusted LOAEL was divided by an uncertainty factor of 300 to account for intra-species variation (10 fold), for use of a LOAEL (10-fold) and the given effects on the developing CNS (3-fold). This guideline was not used in the short-term assessment of toluene as the ATSDR (2000) and OEHHA (2000) both provide acute exposure limits based on a NOAEL.

The ATSDR (2000a, 2005a) has derived an acute MRL 1 ppm (3,800 $\mu g/m^3$) for neurological effects. A NOAEL of 40 ppm (150 mg/m^3) was reported based on a study by Andersen et al. (1983), wherein 16 healthy young subjects with no previous exposure to organic solvents were exposed to toluene for 6 hours per day on 4 consecutive days. The NOAEL was adjusted for intermittent exposure (8 hour/24 hours x 5 days/7 days). A 10-fold uncertainty factor was applied to the duration-adjusted NOAEL to account for intra-species variation.

The OEHHA (2000) provides an acute REL of 37,000 $\mu g/m^3$ for toluene based on the same study NOAEL identified in the ATSDR assessment. The difference between the limit values of the OEHHA and the ATSDR arises from a different way of extrapolating a 6 hour exposure to an acute exposure duration. The ATSDR adjusts the 6-hour exposure to a 24-hour limit using

8 hours/24 hours x 5 days/7days, which is the typical approach for deriving a chronic limit from intermittent occupational exposure of 8 hours per day, 5 days per week. This adjustment is inappropriate when deriving a 24-hour limit form a 6 hour exposure.

In contrast, the OEHHA converts the 6-hour exposure duration to a 1-hour REL of 98 ppm (370 mg/m^3) based on the following calculation.

40^2 ppm x 6 hours	=	C^2 x 1 hour

An uncertainty factor of 10 was then applied by the OEHHA to the duration-adjusted NOAEL. This acute REL of 37,000 μg/m^3 was used as the 1-hour exposure limit in acute effects assessment for toluene.

23A.2.36.2 Chronic Exposure Limit(s)

Table 23A-75: Summary of Chronic Inhalation Exposure Limits for Toluene

Regulatory Agency	Value (μg/m^3)	Type	Reference
Health Canada	3,800	RfC	Health Canada (2004b)
ATSDR	300	RfC	ATSDR (2000)
RIVM	400	RfC	RIVM (2001)
U.S. EPA	5,000	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

The ATSDR (2000) chronic inhalation MRL of 0.08 ppm (300 μg/m^3) was based on colour vision impairment in workers exposed to toluene. Three groups of Croatian workers were examined through interviews, medical examinations, and colour vision testing (Zavalic et al. 1998). A LOAEL of 35 ppm (130 mg/m^3) was determined for alcohol- and age-adjusted colour vision impairment. The LOAEL was adjusted for intermittent exposure (8 hours/24 hours x 5 days/7 days) to a concentration of 8 ppm (30 mg/m^3). An uncertainty factor of 100 was applied to the duration-adjusted LOAEL to account for use of a LOAEL (10-fold) and intra-species variation (10-fold). This MRL was not used as the chronic exposure limit for toluene because it was developed from a LOAEL and thus required the use of a 10-fold uncertainty factor acknowledging the uncertainty associated with use of a LOAEL instead of a NOAEL. Thus, the RfCs developed by Health Canada and the U.S. EPA from NOAELs were given preference.

The RIVM has also developed a TCA of 400 μg/m^3 for toluene (RIVM 2001). This TCA was adopted from the U.S. EPA RfC of 400 μg/m^3, which was revised in 2005 to a value of 5,000 μg/m^3 (U.S. EPA 2006). As a result, this TCA was not used in the chronic inhalation effects assessment for toluene.

Health Canada bases its chronic tolerable concentration of 3,800 μg/m^3 on the same (see the ATSDR acute MRL) lowest reported NOAEL of 150 mg/m^3 (40 ppm) for neurological effects and respiratory irritation in human volunteers (Andersen et al. 1983; CEPA 1992). The study NOAEL was adjusted from 6-hour daily dosing to continuous exposure and an uncertainty factor of 10 was applied to account for intra-species variation.

The U.S. EPA has derived an inhalation RfC based upon the findings of 10 human studies, each of which examined the neurological effects in occupationally exposed workers (U.S. EPA 2006). These studies were all more recent than the Andersen et al. 1983 study used in the Health

Canada assessment and included the study used as the basis of the ATSDR assessment. The analysis of the multiple studies resulted in an average NOAEL of 34 ppm (128 mg/m^3). This NOAEL was adjusted for the differences in breathing rates between workers and members of the public (i.e., 10/20 m^3/d) and the reduced weekly exposure time (i.e., 5 days/7 days). The U.S. EPA also applied an uncertainty factor of 10 to account for human variation. The U.S. EPA RfC of 5,000 µg/m^3 represents the most recent analysis of the available scientific literature, and therefore was used in the current assessment.

A chronic oral exposure limit was not required for the assessment of toluene since it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006) and thus was not incorporated into the multi-media exposure model.

23A.2.37 Xylenes

23A.2.37.1 Acute Exposure Limit

Table 23A-76: Summary of Acute Inhalation Exposure Limits for Xylenes

Regulatory Agency	Value (µg/m^3)	Averaging Time	Reference
AENV	2,300 700	1-hour 24-hour	AENV (2005) AENV (2005)
ATSDR	8,700	2-hour	ATSDR (2005a)
OEHHA	22,000	1-hour	OEHHA (2000)
OMOE	2,200 730	½-hour 24-hour	OMOE (2005a) OMOE (2005a)
WHO	-	-	WHO (2000)

The AENV (2005) adopted the OMOE's ½-hour POI of 2,300 µg/m^3 as its 1-hour AAQO. However, this POI was based on odour perception and has since been updated (OMOE 2005d). The AENV (2005) also provides a 24-hour AAQO of 700 µg/m^3. This guideline was not used in the acute effects assessment because it was taken from the chronic REL provided by the OEHHA (2005).

The OMOE (2005a, 2005d) currently provides a 24-hour limit of 730 µg/m^3 based on adverse neurological effects. A LOAEL of 62 mg/m^3 was established for headaches, eye and nasal irritation, and light headedness (floating sensation) in approximately 300 workers, 175 of whom were occupationally exposed for an average of seven years. The LOAEL was adjusted by the OMOE to account for discontinuous exposure (10 m^3/20 m^3 × 5 days/7 days) to a concentration of 22.1 mg/m^3. It should be noted that the scientific merit for the discontinuous exposure adjustment is questionable, considering that the OMOE standard is intended to be protective of short-term exposures and that the study subjects were exposed to xylene for seven years, on average. Regardless, the OMOE applied an uncertainty factor of 30 to the adjusted LOAEL to account for intra-species variability (10-fold) and use of a LOAEL (3-fold).

The ATSDR recently reviewed the short-term toxicity of xylenes (ATSDR 2005a,b). Based on a study by Ernstgard et al. (2002), 50 ppm (200 mg/m^3) was designated as a LOAEL for slight respiratory effects (e.g.., reduced forced vital capacity, increased discomfort in throat and airways in women, and breathing difficulties in both sexes) and subjective symptoms of neurotoxicity (e.g.., headache, dizziness, feelings of intoxication). Fifty-six healthy volunteers

(28 per sex) between the ages of 20 and 49 years were exposed to 50 ppm m-xylene, clean air (controls) or 150 ppm 2-propanol in a dynamic chamber for 2 hours. Each subject received 3 treatments separated by intervals of 2 weeks. The LOAEL was considered minimal because the magnitude of the changes was small. The ATSDR applied an uncertainty factor of 30 for use of a (minimal) LOAEL (3-fold) and human variability (10-fold), resulting in an acute MRL of 2 ppm (8,700 µg/m^3). This 2-hour MRL of 8,700 µg/m^3 was conservatively adopted as the 1-hour exposure limit used in the acute effects assessment.

23A.2.37.2 Chronic Exposure Limit(s)

Table 23A-77: Summary of Chronic Inhalation Exposure Limits for Xylenes

Regulatory Agency	Value (µg/m^3)	Type	Reference
Health Canada	180	RfC	Health Canada (2004b)
ATSDR	650	RfC	ATSDR (2005a)
RIVM	870	RfC	RIVM (2001)
U.S. EPA	100	RfC	U.S. EPA (2006)
WHO	-	-	WHO (2000)

Although Health Canada (2004b) recommends a tolerable concentration of 180 µg/m^3 for xylenes, the specific basis is unknown. Therefore, the chronic inhalation RfC derived by the U.S. EPA (2006) of 100 µg/m^3 was used in the chronic effects assessment. The RfC was derived from a NOAEL of 217 mg/m^3 for impaired motor coordination from a subchronic inhalation study in male rats (Korsak et al. 1994). The NOAEL was adjusted from intermittent to continuous exposure by the U.S. EPA, resulting in an adjusted NOAEL of 39 mg/m^3. A safety factor of 300 was applied by the U.S. EPA to the adjusted NOAEL to account for laboratory animal-to-human interspecies differences (3-fold), intra-species uncertainty to account for human variability and sensitive populations (10-fold), extrapolation from subchronic to chronic duration (3-fold), and uncertainties in the database (3-fold).

A chronic oral exposure limit was not required for the xylene assessment because it did not exceed any of the persistence and bioaccumulation parameters established by Environment Canada (2006), and thus was not incorporated into the multi-media exposure model.

23A.3 Chemical Mixtures

Possible additive interactions were identified for those COPCs known to cause respiratory effects, liver and kidney effects, reproductive and developmental effects, neurological effects and cancer (Table 23A-78). The inclusion of a COPC in the chemical mixture was based upon the endpoint of the exposure limit used in the current HHRA.

Table 23A-78: Potential Additive Interactions among the COPCs

Exposure Duration	Potential Health Effect	Toxicant Designation	COPCs
Acute inhalation	Respiratory effects	Respiratory irritants[1]	2-Methylnaphthalene, acetaldehyde, aliphatic aldehyde group, aliphatic ketone group, ammonia, dichlorobenzenes, formaldehyde, hydrogen sulphide, isopropylbenzene, nitrogen dioxide, propylene oxide group, sulphur dioxide, styrene, sulphuric acid, xylenes
	Neurological effects	CNS depressants	Aliphatic C5-C8 group, aliphatic alcohol group, carbon disulphide group, isopropylbenzene, methylene chloride, toluene, xylenes
	Reproductive and developmental effects	Reproductive and developmental toxicants	Carbon disulphide group, ethylbenzene
Chronic inhalation	Respiratory effects	Respiratory irritants[1]	2-Methylnaphthalene, acrolein, aliphatic aldehyde group, ammonia, dichlorobenzenes, hydrogen sulphide, naphthalene, nitrogen dioxide, sulphur dioxide, sulphuric acid
	Liver and kidney effects	Hepato- and nephro-toxicants	2-Chloronaphthalene, acenaphthene group, aliphatic C17-C34 group, aromatic C9-C16 group, aromatic C17-C34 group, benzaldehyde, isopropylbenzene
	Neurological effects	CNS depressants	Aliphatic C5-C8 group, aliphatic C9-C16 group, carbon disulphide group, n-hexane, styrene, toluene, xylenes
	Developmental effects	Developmental toxicants	Aliphatic alcohol group, aliphatic ketone group, cyclohexane, ethylbenzene
	Cancer	Carcinogens	1,3-Butadiene, acetaldehyde, benzene, benzo(a)pyrene (IPM and WMM) group, formaldehyde, methylene chloride, propylene oxide group
Chronic ingestion	Liver and kidney effects	Hepato- and nephro- toxicants	Aliphatic C9-C16 group, aliphatic C17-C34 group, aromatic C9-C16 group, aromatic C17-C34 group

NOTE:

The respiratory irritant mixture includes nasal irritants.

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