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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

Acrolein

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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

Acrolein

Environment Canada
Health Canada

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List of Acronyms and Abbreviations

BCF	bioconcentration factor
BMC	benchmark concentration
BMC_{05}	the concentration associated with a 5% increase in the benchmark endpoint
$BMCL_{05}$	the lower 95% confidence limit for the BMC_{05}
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
CEPA 1999	*Canadian Environmental Protection Act, 1999*
CFC	chlorofluorocarbon
CHO	Chinese hamster ovary
CTV	Critical Toxicity Value
EC_{50}	median effective concentration
EEV	Estimated Exposure Value
ENEV	Estimated No-Effects Value
GWP	Global Warming Potential
K_{oc}	organic carbon/water partition coefficient
K_{ow}	octanol/water partition coefficient
kg-bw	kilogram body weight
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	Lowest-Observed-Adverse-Effect Level
LOEC	Lowest-Observed-Effect Concentration
LOEL	Lowest-Observed-Effect Level
NAPS	National Air Pollution Surveillance
NOAEL	No-Observed-Adverse-Effect Level
NOEC	No-Observed-Effect Concentration
NOEL	No-Observed-Effect Level
ODP	Ozone Depletion Potential
POCP	Photochemical Ozone Creation Potential
PSL	Priority Substances List
TC	Tolerable Concentration

SYNOPSIS

Acrolein is not commercially produced in Canada. It is imported from the United States for use mainly as an aquatic herbicide in irrigation canals and as a microbiocide in produced water during oil explorations. These uses are regulated under the *Pest Control Products Act* and Regulations. An estimated minimum of 218 tonnes of acrolein is released yearly to the atmosphere from anthropogenic sources involving the combustion of organic matter (i.e., predominantly as a component of vehicle exhaust) or the forest industry. Unquantified amounts are also released from natural sources and the photooxidation of organic pollutants in air. No releases of "non-pesticidal" acrolein to water, sediments or soils in Canada have been identified.

Acrolein is unlikely to be transported over long distances because of its high reactivity and estimated short half-lives in air and water. It is also unlikely to partition from these compartments to soil or sediments. Acrolein is rapidly metabolized by organisms and does not bioaccumulate. The highest environmental concentrations of acrolein not directly released during its application as a pesticide in Canada have been measured in air from urban areas. With the exception of samples taken in the vicinity of pesticidal application, acrolein has not been detected in water, sediment or soil in Canada.

Acute and chronic data on toxicity are available for aquatic organisms and laboratory animals. Only acute data were identified for terrestrial crop plants. Terrestrial organisms appear less sensitive to acrolein than aquatic organisms. Known concentrations of acrolein in the Canadian atmosphere are less than the threshold for adverse effects estimated for terrestrial organisms. Exposure of other organisms to non-pesticidal acrolein is considered unlikely, since no sources or detectable concentrations of acrolein have been identified in other compartments. Acrolein is not involved in stratospheric ozone depletion and is not an important contributor to climate change or photochemical smog formation.

Based upon studies conducted primarily with laboratory animals, adverse health effects associated with exposure to acrolein are mostly confined to the tissue of first contact (i.e., the respiratory and gastrointestinal tracts after inhalation and ingestion, respectively) and are concentration related. Hence, for comparison with Tolerable Concentrations for both inhalation and ingestion, exposures via these routes have been assessed separately. Tolerable Concentrations are the concentrations to which it is believed that a person may be exposed continuously without deleterious effect.

Available information is considered insufficient to characterize exposure of Canadians to acrolein via ingestion. However, the range of concentrations measured in food in other countries (although highly dependent upon such factors as method of cooking) is within the range of a provisional Tolerable Concentration for ingestion that is protective for site-of-contact effects.

Probabilistic estimates of the distribution of time-weighted 24-hour concentrations of acrolein in air indicate that between 5% and 10% of the general population would be expected to be exposed to at least 5 $\mu g/m^3$. This is greater than the Tolerable Concentration for inhalation derived on the basis of site-of-contact effects in animal species.

Based on the information available, it is concluded that acrolein is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or that constitute or may constitute a danger to the environment on which life depends. It is concluded that acrolein is entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health. Therefore, acrolein is considered to be "toxic" as defined in Section 64 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

Indoor air is an important source of exposure, although the relative contribution of various sources therein is unknown. Better characterization of the significance of sources in indoor air and investigation of the potential to reduce emissions or exposure are desirable.

While for the general population the contribution of ambient air to overall exposure to inhaled acrolein is expected to be small compared with the contribution from indoor air, ambient air may be an important source of exposure via inhalation for populations residing in the vicinity of locations heavily impacted by vehicular exhaust. Additional characterization of the contribution of motor vehicle exhaust to air in Canada and investigation of the potential to reduce emissions from this source are also recommended.

In view of the sensitivity of some aquatic organisms, it is also recommended that the use of acrolein to control aquatic weeds be reviewed by appropriate authorities under the *Pest Control Products Act* in light of this assessment and other relevant considerations.

1.0 INTRODUCTION

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) requires the federal Ministers of the Environment and of Health to prepare and publish a Priority Substances List (PSL) that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" or are capable of becoming "toxic" as defined in Section 64 of the Act, which states:

> ...a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that
> (a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;
> (b) constitute or may constitute a danger to the environment on which life depends; or
> (c) constitute or may constitute a danger in Canada to human life or health.

Substances that are assessed as "toxic" as defined in Section 64 may be placed on Schedule I of the Act and considered for possible risk management measures, such as regulations, guidelines, pollution prevention plans or codes of practice to control any aspect of their life cycle, from the research and development stage through manufacture, use, storage, transport and ultimate disposal.

Based on initial screening of readily accessible information, the rationale for assessing acrolein provided by the Ministers' Expert Advisory Panel on the Second Priority Substances List (Ministers' Expert Advisory Panel, 1995) was as follows:

> Exposure to acrolein appears to be widespread in Canada. This substance has been detected in indoor and outdoor air, food and cigarette smoke. It is expected to be present in the effluents in manufacturing processes that use it as an intermediate in the production of other substances. Photooxidation of diesel and gasoline exhaust are other sources. Low levels of exposure have produced toxicological effects in animals and humans. Data indicate that acrolein is genotoxic and causes reproductive and developmental effects in animals. Information on this substance has been gathered, reviewed and evaluated by an international group of experts. An assessment of acrolein in the Canadian environment and of the concentrations that cause adverse effects is required to evaluate its potential impact on human health.

Descriptions of the approaches to assessment of the effects of Priority Substances on the environment and human health are available in published companion documents. The document entitled "Environmental Assessments of Priority Substances under the *Canadian Environmental Protection Act*. Guidance Manual Version 1.0 — March 1997" (Environment Canada, 1997a) provides guidance for conducting environmental assessments of Priority Substances in Canada. This document may be purchased from:

> Environmental Protection Publications
> Environmental Technology Advancement Directorate
> Environment Canada
> Ottawa, Ontario
> K1A 0H3

It is also available on the Internet at www.ec.gc.ca/cceb1/eng/psap.htm under the heading "Technical Guidance Manual." It should be noted that the approach outlined therein has evolved to incorporate recent developments in risk assessment methodology and which will be addressed in future releases of the guidance manual for environmental assessments of Priority Substances.

The approach to assessment of effects on human health is outlined in the following publication of the Environmental Health

Directorate of Health Canada: "*Canadian Environmental Protection Act* — Human Health Risk Assessment for Priority Substances" (Health Canada, 1994), copies of which are available from:

Environmental Health Centre
Room 104
Health Canada
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

or on the Environmental Health Directorate publications web site (www.hc-sc.gc.ca/ehp/ehd/catalogue/bch.htm). The approach is also described in an article published in the *Journal of Environmental Science and Health — Environmental Carcinogenesis & Ecotoxicology Reviews* (Meek *et al.*, 1994). It should be noted that the approach outlined therein has evolved to incorporate recent developments in risk assessment methodology, which are described on the Environmental Substances Division web site (www.hc-sc.gc.ca/ehp/ehd/bch/env_contaminants/psap/psap.htm) and which will be addressed in future releases of the approach paper for the assessment of effects on human health.

The search strategies employed in the identification of data relevant to assessment of potential effects on the environment (prior to May 1998) and human health (prior to October 1998) are presented in Appendix A. Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether acrolein is "toxic" under CEPA 1999 have been critically evaluated by staff of Environment Canada (entry and environmental exposure and effects) and Health Canada (human exposure and effects on human health).

Sections of this Assessment Report and the supporting documentation (Environment Canada, 1998) related to the environmental assessment of acrolein were prepared by the following members of the Environmental Resource Group at Environment Canada:

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J. Wittwer, Environment Canada

Environmental sections of the Assessment Report and the supporting documentation (Environment Canada, 1998) were also reviewed by internal reviewers at Environment Canada — namely, D. Campbell, L. Graham, D. Halliburton and K. Lloyd — as well as by external reviewers: C. Jacobs (Degussa AG, Germany), R. Parent (Consultox Ltd.), G. Rawn (Fisheries and Oceans Canada), S. Semeniuk (E.B. Eddy Forest Products Ltd.), N. Tolson (Pest Management Regulatory Agency) and J. van Koten (The Netherlands' National Institute of Public Health and the Environment).

The health-related sections of this Assessment Report and supporting documentation were prepared by the following staff of Health Canada:

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Sections of the Assessment Report and supporting documentation on genotoxicity were reviewed by D. Blakey of the Environmental and Occupational

Toxicology Division of Health Canada. Sections of the supporting documentation pertaining to human health were reviewed externally by R. Parent (Consultox Ltd.) and W.F. Mayr and S. Jacobi (both from Degussa AG), primarily to address adequacy of coverage. Accuracy of reporting, adequacy of coverage and defensibility of conclusions with respect to hazard characterization and dose–response analyses were considered in written review by staff of the Information Department of BIBRA International and at a panel meeting of the following members, convened by Toxicology Excellence for Risk Assessment (TERA) on November 16, 1998, in Cincinnati, Ohio:

M. Aardema, Procter & Gamble
J. Christopher, California Environmental Protection Agency
M. Dourson, TERA
M. Friedman, private consultant
M. Gargas, ChemRisk Division of McLaren/Hart
H. Heck, The Chemical Industry Institute of Toxicology (written comments)
G. Leikauf, University of Cincinnati
M. Moore, U.S. Environmental Protection Agency
R. Tardiff, The Sapphire Group, Inc.
V. Vu, U.S. Environmental Protection Agency
V. Walker, New York State Department of Health

The health-related sections of the Assessment Report were reviewed and approved by the Health Protection Branch Risk Management meeting of Health Canada.

The entire Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

A draft of the Assessment Report was made available for a 60-day public comment period (May 1 to June 29, 1999) (Environment Canada and Health Canada, 1999). Following consideration of comments received, the Assessment Report was revised as appropriate. A summary of the comments and their responses is available on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

The text of the Assessment Report has been structured to address environmental effects initially (relevant to determination of "toxic" under Paragraphs 64(a) and (b)), followed by effects on human health (relevant to determination of "toxic" under Paragraph 64(c)).

Copies of this Assessment Report are available upon request from:

Inquiry Centre
Environment Canada
Main Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

Unpublished supporting documentation, which presents additional information, is available upon request from:

Commercial Chemicals Evaluation Branch
Environment Canada
14th Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or

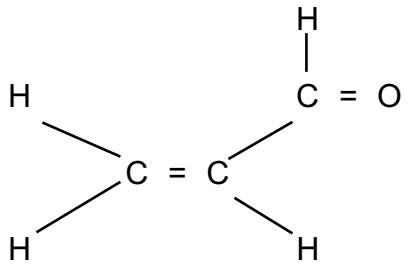
Environmental Health Centre
Room 104
Health Canada
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

2.0 Summary of Information Critical to Assessment of "Toxic" under CEPA 1999

2.1 Identity and physical/chemical properties

Acrolein is also known as acrylaldehyde, allyl aldehyde, acrylic aldehyde, propenal, prop-2-enal and prop-2-en-1-al. Its Chemical Abstracts Service (CAS) number is 107-02-8. Acrolein's chemical structure is shown in Figure 1.

Figure 1 Chemical structure of acrolein



The molecular formula of acrolein is $CHOCHCH_2$, and its molecular weight is 56.06. At room temperature, acrolein is a clear, colourless liquid with an intensively acrid odour. The ranges of values reported for its properties are given in Table 1.

The conversion factor for airborne acrolein used throughout this report is 1 ppm = 2.29 mg/m^3. For aqueous media (e.g., drinking water), 1 ppm = 1 mg/L.

2.2 Entry characterization

2.2.1 Production, uses and importation

Acrolein is not commercially produced in Canada. It is imported from the United States for use mainly as a pesticide (Agriculture Canada and Environment Canada, 1993). Two restricted-use pesticides registered under the Canadian *Pest Control Products Act* contain 92% acrolein as the active ingredient. These are used for the control of submersed and floating aquatic weeds in Alberta and Saskatchewan irrigation canals and for the control of slime, bacteria and mould in produced water during oil explorations (BPCI,

Table 1 Physical and chemical properties of acrolein

Property	Range[1]
melting point (°C)	–88 to –86.9
boiling point (°C, at 101.3 kPa)	52.1 to 53.5
relative density (g/cm^3, at 20°C)	0.8377 to 0.8430
vapour pressure (kPa, at 20°C)	29.3 to 36.5
water solubility (g/L, at 20°C)	206 to 270
Henry's law constant (Pa·m^3/mol, 20°C)	0.446 to 19.6
Henry's law constant (dimensionless, 25°C)	7.8 to 180
log K_{ow}	–1.1 to 1.02
log K_{oc}	–0.219 to 2.43

[1] Includes experimental and calculated values listed in Irwin (1987, 1988), ATSDR (1990), Eisler (1994), Mackay *et al.* (1995), BUA (1996), U.S. EPA (1996) and EU (1998).

1994, 1997). The use of acrolein as a pesticide is not considered in this assessment, since it is regulated under the *Pest Control Products Act* and Regulations.

The main "non-pesticidal" use of acrolein in Canada is as the active ingredient (92%) in a product used by oil companies to scavenge hydrogen sulphide (H_2S) from produced fluids in petroleum operations. This product can also solubilize ferrous sulphide (FeS) deposits that obstruct wells, tanks and barrels (BPCI, 1991). Small quantities of acrolein have also been used for laboratory purposes (Environment Canada, 1996a).

Small amounts (2 kg) of acrolein were present in hazardous wastes imported into Canada for treatment or disposal between 1994 and 1997 (Environment Canada, 1994; Wittwer, 1998). Acrolein has also been identified as an impurity (1%) in acetaldehyde imports (Environment Canada, 1997b).

2.2.2 Sources and releases

2.2.2.1 Natural sources

Acrolein is released into the environment as a product of fermentation and ripening processes. It has been identified as a volatile component of essential oils extracted from the wood of oak trees (Slooff *et al.*, 1994). It is also emitted by forest fires as a product of the incomplete combustion of organic matter. There are no quantitative data available on the total natural production of acrolein.

2.2.2.2 Anthropogenic sources

Sources and estimated releases of acrolein to the atmosphere are presented in Table 2. The principal anthropogenic source of acrolein emissions into the Canadian environment is estimated to be activities involving the combustion of organic matter. As a product of the incomplete combustion of organic matter, acrolein is released by waste incinerators, furnaces, fireplaces, power plants, agricultural burns and the cooking of food. The main combustion source is considered to be gas and diesel motor vehicle emissions. Few data are available for aircraft, railway engines, ships and other off-road vehicles, but releases from these sources could exceed those of road vehicles (see Table 2). Data on the total production of acrolein from combustion processes in Canada are limited, and there is a great deal of uncertainty concerning estimated releases.

Acrolein is formed by the reaction and photodecomposition of other airborne pollutants, such as 1,3-butadiene and allyl chloride (Maldotti *et al.*, 1980; Edney *et al.*, 1986a,b). Forest product manufacturing processes that release volatile organic compounds are known to emit appreciable amounts of acrolein to air (Environment Canada, 1997b). One Canadian company reported the formation of acrolein as a contaminant at 0.4% in the production of vinyl acetate. In this case, acrolein and other impurities are separated and processed for recovery or disposal (Environment Canada, 1997b). Data on non-combustion sources of acrolein are limited; as a result, the estimated releases presented in Table 2 are highly uncertain.

In 1985, acrolein was detected (detection limit 5 µg/L) in liquid effluents from two organic chemical manufacturing plants that discharged into the St. Clair River at Sarnia, Ontario, at estimated loadings of 3.9 and 0.45 kg/day (King and Sherbin, 1986). However, in an industrial survey conducted under CEPA Section 16, companies in this sector indicated in their responses that they were not involved in the production, import, use, release or monitoring of acrolein during the 1995–96 survey period (Environment Canada, 1997b).

No sources of acrolein releases to Canadian waters, sediments or soils have been identified other than the application of acrolein-based pesticides. During use as the hydrogen sulphide scavenger, acrolein is assumed to be fully consumed. During its application in petroleum operations, the acrolein reacts with

TABLE 2 Sources and estimated releases of acrolein to air in Canada

Sources	Estimated releases (kg/year)
Natural sources: fermentation, forest fires	Unknown
Road motor vehicles	209 000–2 730 000[1]
Off-road motor vehicles,[2] including aircraft	Unknown, could be greater than road vehicle release
Oriented-strand board (OSB) industry	3208–25 664[3]
Pulp and paper (kraft) mills	3747–18 735[4]
Waste incineration	2435[5]
Coal-based electric power generation plants	467–17 504[6]
Other combustion sources[7]	Unknown
Atmospheric production from other pollutants	Unknown
By-product of vinyl acetate production	Negligible[8]

[1] Based on emissions test data from BUA (1996), Graham (1996), Howes (1989a,b) and IPCS (1996), multiplied by the estimated 1995 mileage for on-road motor vehicles in Canada (Environment Canada, 1993). This estimate also considers that about 90% of light-duty gas vehicles in Canada have catalytic converters, which reduce emissions (King, 1998).

[2] These include aircraft, railway and marine vehicles, other off-road motor vehicles, and gas-powered lawnmowers and snowblowers, most of which are expected to have greater emission rates than on-road vehicles because of a lack of pollution control features (Graham, 1998).

[3] The lower estimate corresponds to the total emissions of acrolein in 1995 reported by two OSB companies responding to the CEPA Section 16 Industrial Survey (Environment Canada, 1997b) and one OSB company reporting to the Accelerated Reduction/Elimination of Toxics (ARET) program (ARET Secretariat, 1998). The larger value is the total emission estimated for all 24 such plants in Canada (Halliburton, 1998), assuming an average emission rate of 1070 kg/year per mill.

[4] The lower estimate corresponds to the total emissions of acrolein in 1995 reported in response to the CEPA Section 16 Industrial Survey by nine Canadian pulp and paper (kraft) mills (Environment Canada, 1997b). The larger value is the total emission estimated for all 45 such kraft mills in Canada (Halliburton, 1998), assuming an average emission rate of 416 kg/year per mill.

[5] Based on the estimated emission rate of acrolein from one municipal incinerator in Ontario (Novamann International, 1997), the nameplate capacity of Canadian hazardous waste incinerators and the amount of municipal, hazardous and biomedical waste incinerated in Canada in 1996.

[6] Based on U.S. emission rates (Lipari *et al.*, 1984; Sverdrup *et al.*, 1994), high heating value of fuel and Canadian coal consumption in 1995 (Rose, 1998).

[7] Includes prescribed burning, wood-burning furnaces and fireplaces, natural gas furnaces, other electric power generation plants and other industries (e.g., smelters).

[8] The unintentional production of 2700 kg of acrolein was reported in 1995 by one vinyl acetate producer in the CEPA Section 16 Industrial Survey. Related releases of acrolein are estimated to be negligible, because it is reported that impurities such as acrolein are separated and processed for recovery or disposal (Environment Canada, 1997b).

sulphides in oil–water mixtures to form a non-hazardous, water-soluble product, which is then re-injected into deep wells (BPCI, 1991). The acrolein used is considered to be completely reacted (Viti, 1998). Releases are therefore expected to be negligible.

Negligible quantities (approximately 2 kg) of acrolein were released to the environment as a result of a single spill to land during the period 1983–1997 (Transport Canada, 1997). No other data were found on releases of acrolein to Canadian soils.

2.3 Exposure characterization

2.3.1 Environmental fate

As a highly reactive substance, acrolein does not tend to persist in the environment, and its intercompartmental movement is small.

2.3.1.1 Air

Acrolein emitted to air reacts primarily with photochemically generated hydroxyl radicals (·OH) in the troposphere (Ghilarducci and Tjeerdema, 1995). Minor fate processes include direct photolysis, reaction with nitrate radicals ($\cdot NO_3$) and reaction with ozone (O_3) (Atkinson *et al.*, 1987; Haag *et al.*, 1988a; Howard, 1989; BUA, 1996). The occurrence of acrolein in rainwater indicates that it may be removed by wet deposition (Grosjean and Wright, 1983). The atmospheric half-life of acrolein, based on hydroxyl radical reaction rate constants, is calculated to be between 3.4 and 33.7 hours (Atkinson, 1985; Edney *et al.*, 1986b; Haag *et al.*, 1988a; Howard, 1989; Howard *et al.*, 1991; BUA, 1996). The overall reactivity-based half-life of acrolein in air, as estimated by Mackay *et al.* (1995), is less than 10 hours. These short estimated half-lives do not make acrolein a candidate for long-range atmospheric transport.

2.3.1.2 Water

The significant fate processes of acrolein in surface water are reversible hydration, biodegradation by acclimatized microorganisms and volatilization (Bowmer and Higgins, 1976; Tabak *et al.*, 1981; Irwin, 1987; Haag *et al.*, 1988b; Howard, 1989; ATSDR, 1990; Springborn Laboratories, 1993). In groundwater, anaerobic biodegradation and hydrolysis are expected to occur (Chou and Spanggord, 1990a). The overall reactivity-based half-life of acrolein in surface water is estimated to be between 30 and 100 hours (Mackay *et al.*, 1995). In groundwater, half-lives of 336–1344 hours (14–56 days) are estimated based on aerobic degradation (Howard *et al.*, 1991). Observed dissipation half-lives of acrolein applied as a herbicide in irrigation canals range from 7.3 to 10.2 hours (Jacobson and Gresham, 1991a,b,c; Nordone *et al.*, 1996a). The relatively short observed half-lives of acrolein in surface waters do not make long-range aquatic transport likely.

2.3.1.3 Sediment

In sediment–water systems, acrolein undergoes hydrolysis, self-oxidation and biodegradation. Experimental half-lives of 7.6 hours and 10 days were determined for aerobic and anaerobic conditions, respectively (Smith *et al.*, 1995). An overall reactivity-based half-life is estimated by Mackay *et al.* (1995) to be between 100 and 300 hours. Because of its low organic carbon/water partition coefficient (K_{oc}) and high water solubility, acrolein is not expected to significantly adsorb to suspended solids or sediments, nor are these suspended solids or sediments expected to significantly absorb acrolein from water (Irwin, 1988; Howard, 1989).

2.3.1.4 Soil

In the terrestrial environment, acrolein undergoes biodegradation, hydrolysis, volatilization and irreversible sorption to soil (Irwin, 1988; Howard, 1989; Chou and Spanggord, 1990b). These processes are expected to significantly decrease the high infiltration rate of acrolein estimated

from its low experimental K_{oc} (Irwin, 1988). The overall reactivity-based half-life of acrolein in soil is estimated to be between 30 and 100 hours (Mackay *et al.*, 1995).

2.3.1.5 Biota

Based on the high water solubility, low octanol/water partition coefficient (K_{ow}) and high reactivity of acrolein, uptake by organisms is predicted to be low. A bioconcentration factor (BCF) of 344 and a half-life of greater than 7 days were reported for acrolein in bluegill (*Lepomis macrochirus*) following exposure to a mean concentration of 13 mg acrolein/L for a 28-day period (Barrows *et al.*, 1980). However, these values may be overestimates, as the total ^{14}C measured in the fish may have included acrolein metabolites. A lower BCF of 0.6 was estimated using the linear regression equation of Veith *et al.* (1980) and a log K_{ow} of –0.01 for acrolein. Acrolein was not detected in the tissues of fish and shellfish sampled one day after a second exposure to [^{14}C]acrolein in water (0.02 and 0.1 mg/L for the first and second exposures, respectively) over a one-week period. The presence of metabolites indicates that these species were able to rapidly metabolize acrolein and its residues (Nordone *et al.*, 1998). These results, and the low reported BCFs, suggest that acrolein does not bioaccumulate or bioconcentrate significantly in aquatic organisms (Howard, 1989; ATSDR, 1990; DFO, 1995; Nordone *et al.*, 1996b). Absorption of acrolein by terrestrial plants is poor (WSSA, 1983).

2.3.1.6 Environmental partitioning

Fugacity modelling was conducted to characterize key reaction, intercompartment and advection (movement out of a system) pathways for acrolein and its overall distribution in the environment. A steady-state, non-equilibrium model (Level III fugacity model) was run using the methods developed by Mackay (1991) and Mackay and Paterson (1991). Assumptions, input parameters and results are presented in Mackay *et al.* (1995) and summarized here. Values for input parameters were as follows: molecular weight, 56.06 g/mol; melting point, -86.95°C; water solubility, 208 g/L; vapour pressure, 36.5 kPa; log K_{ow}, –0.01; Henry's law constant, 9.8 Pa·m^3/mol; half-life in air, 5 hours; half-life in water, 55 hours; half-life in soil, 55 hours; half-life in sediments, 170 hours. Modelling was based on an assumed default emission rate of 1000 kg/hour into a region of 100 000 km^2, which includes a surface water area (20 m deep) of 10 000 km^2. The height of the atmosphere was set at 1000 m. Sediments and soils were assumed to have an organic carbon content of 4% and 2% and a depth of 1 cm and 10 cm, respectively. The estimated percent distribution predicted by this model is not affected by the assumed emission rate.

Modelling indicates that acrolein behaves differently depending on the medium to which it is released. Generally, when acrolein is continuously discharged into a specific medium, most of it can be expected to be found in that medium. For example, if discharged into air, almost all of it will exist in the atmosphere, with very small amounts in soil and water. The same applies for discharge to water and soil (Mackay *et al.*, 1995). These predicted distributions suggest that acrolein does not tend to partition from one compartment to another. It could also be possible that when acrolein does partition to another compartment, its persistence in that second compartment is so short that little is found there.

2.3.2 Environmental concentrations

2.3.2.1 Ambient air

Available sampling and analytical methodologies are sufficiently sensitive to detect the presence of acrolein in many samples of ambient (outdoor) air. In urban areas in Canada, mean concentrations of acrolein in 4- or 24-hour samples are generally less than 0.2 µg/m^3. Acrolein was detected (detection limit 0.05 µg/m^3) in 1597 (or 57%) of 2816 24-hour samples collected between 1989 and 1996 under the National Air Pollution Surveillance (NAPS) program from rural, suburban and urban locations (n = 15) in five

provinces (Environment Canada, 1996b; Dann, 1998). The mean concentration in all samples was 0.18 μg/m³. Levels ranged from below the detection limit of 0.05 μg/m³ up to 2.47 μg/m³ for seven urban sites in Quebec (Montréal), Ontario (Ottawa, Windsor and Toronto) and British Columbia (Vancouver). Concentrations ranged up to 1.85 μg/m³ for two suburban sites (Saint John, New Brunswick; Montréal, Quebec) and up to 0.33 μg/m³ for two rural sites considered to be affected by urban areas (L'Assomption, Quebec; Simcoe, Ontario). The highest mean concentration of acrolein in air measured weekly over any three consecutive months during the NAPS monitoring between 1989 and 1996 was 1.58 μg/m³. This value was obtained for an urban site in Montréal, Quebec, during the period of June–August 1994 (Environment Canada, 1996b).

Concentrations of acrolein in ambient air corresponding to the 90th, 95th and 99th percentiles of the NAPS dataset are 0.4 μg/m³, 0.6 μg/m³ and 1.1 μg/m³, respectively. Based on these data, there is some evidence that concentrations of acrolein in ambient air in Canada have been increasing at urban and suburban sites.

Acrolein was less frequently detected in ambient air collected at rural sites in Canada. Mean concentrations at four rural sites considered to be regionally representative (Kejimkujik Park, Nova Scotia; Mount Sutton, Quebec; St. Anicet, Quebec; Egbert, Ontario) generally did not exceed 0.1 μg/m³; maximum concentrations were less than 0.5 μg/m³ in 24-hour samples (Environment Canada, 1996b; Dann, 1998). Concentrations of acrolein in urban and rural areas of Canada are similar to, but generally less than, those found in the United States and in other countries.

In a study conducted in Windsor, Ontario, from February to April 1992, acrolein was detected (detection limit 0.05 μg/m³) in 24 (or 83%) of 29 samples of ambient air at concentrations ranging up to 0.5 μg/m³, with an overall mean concentration of 0.16 μg/m³ (OMEE, 1994a; Bell, 1995). However, acrolein was not detected (detection limit 0.05 μg/m³) in any of 11 samples of ambient air collected during 1993 from residential and industrial areas of Hamilton, Ontario (Bell, 1996, 1997).

No data on concentrations of acrolein in the air near point sources in Canada were identified. The maximum ground-level airborne concentration of acrolein at a municipal waste incinerator in Ontario was estimated at 0.04 μg/m³, based on results of air dispersion modelling using stack emission rates for acrolein/acetone measured in 1997 (Novamann International, 1997).

2.3.2.2 Indoor air

In general, concentrations of acrolein in indoor air are about 2- to 20-fold higher than outdoor levels, although few potential sources of this compound in indoor locations have been identified. Acrolein was detected (detection limit 0.05 μg/m³) in all 29 indoor air samples collected from homes in Windsor, Ontario, between 1991 and 1992 (Bell *et al.*, 1994; Bell, 1995). The mean concentration of acrolein in these samples (3.0 μg/m³) was considerably higher than the mean ambient concentration (0.16 μg/m³; n = 29), with individual values in indoor air ranging from 0.4 to 8.1 μg/m³. Acrolein was detected (detection limit 0.05 μg/m³) in 3 of 11 samples of indoor air collected in 1993 from homes in residential and commercial areas of Hamilton, Ontario (Bell, 1996, 1997). The mean concentration was 1.1 μg/m³, with individual values ranging from <0.05 to 5.4 μg/m³; acrolein was not detected (detection limit 0.05 μg/m³) in any of the 11 corresponding samples of ambient air.

There was a general trend of increasing concentrations of acrolein in the indoor air of these homes with increasing concentrations of acetaldehyde and/or formaldehyde. The average concentrations of acrolein in the indoor air of Windsor and Hamilton homes with and without environmental tobacco smoke — i.e., 3.0 μg/m³

and 2.2 µg/m^3, respectively — provide some support for the hypothesis that cigarette smoking is a source of acrolein in indoor air. However, the difference in average concentrations in indoor air (i.e., for "smoking" versus "non-smoking" homes) is not statistically significant, as a result of the small sample sizes (n = 29 and n = 11) and high variances of the data sets.

Acrolein was detected (detection limit 0.43 µg/m^3) in 3 of 35 samples of indoor air collected in 1997 from randomly selected homes in the Greater Toronto Area at concentrations of 16, 22 and 23 µg/m^3 (Conor Pacific Environmental, 1998). It was not detected (detection limit 0.43 µg/m^3) in any of the 35 samples of outdoor air from these locations. Acrolein was not detected (detection limit 0.43 µg/m^3) in an additional 15 samples of indoor air collected from randomly selected homes in Nova Scotia (n = 6) or Alberta (n = 15), nor was it detected in the outdoor air at these locations (Conor Pacific Environmental, 1998).

Similar concentrations of acrolein have been measured in indoor air in residential and non-residential locations in other countries (Badré *et al.*, 1978; Weber *et al.*, 1979; Highsmith *et al.*, 1988; Löfroth *et al.*, 1989; CARB, 1991; Sheldon *et al.*, 1992; Lindstrom *et al.*, 1995; Williams *et al.*, 1996). Data from other countries are almost exclusively restricted to environments where there is an active combustion source (e.g., cigarettes, woodstoves and fireplaces, cooking).

2.3.2.3 Drinking water

Available quantitative data concerning the levels of acrolein in drinking water in Canada were limited to two investigations in which acrolein was not detected in raw or treated water supplies.

In monitoring studies conducted between July 1982 and May 1983, acrolein was below the limit of detection (i.e., <0.1 µg/L) in samples (n = 42) of treated drinking water collected at 10 municipalities in Ontario (Otson, 1987). In an extensive survey of municipal drinking water supplies at 150 locations in the four Atlantic provinces conducted between May 1985 and October 1988, acrolein was not detected (detection limit 1.0–2.5 µg/L) in an unspecified number of samples of raw or treated drinking water (Environment Canada, 1989a,b,c,d).

In studies conducted in the United States, acrolein was not detected (detection limit 3.5 µg/L) in an unspecified number of samples of raw and finished drinking water from three treatment plants surveyed between May and July 1988 (Glaze *et al.*, 1989). In other studies, acrolein was detected (detection limit not reported) in only 2 of 798 samples of well or surface water collected from unspecified locations throughout the United States between 1980 and 1982; the median concentration of acrolein in these samples was <14 µg/L (Staples *et al.*, 1985).

2.3.2.4 Surface water

Acrolein was not detected (detection limit 0.1 µg/L) in 42 raw water samples collected from potable water treatment plants in the Great Lakes region during 1982 and 1983 (Otson, 1987). In 1985, acrolein was detected at concentrations of 6.9 and 7.8 µg/L (detection limit 5 µg/L) in liquid effluents from two organic chemical manufacturing plants that discharged into the St. Clair River at Sarnia, Ontario (King and Sherbin, 1986). During 1989 and 1990, however, acrolein was not found (detection limit 4 µg/L) in the intake water or effluent of these or 24 other organic chemical manufacturing plants in Ontario (OMEE, 1993). Other data on concentrations of (non-pesticidal) acrolein in Canadian and U.S. surface waters are discussed in Section 2.3.2.3.

2.3.2.5 Sediment and soil

Adequate data on concentrations of acrolein in sediments and soils in Canada were not identified.

2.3.2.6 Biota

Adequate data on concentrations of acrolein in biota in Canada were not identified.

2.3.2.7 Food

Information concerning the concentrations of acrolein in foods consumed in Canada were not identified, although acrolein is believed to be a common component of foodstuffs (U.S. EPA, 1980). Indeed, available data are limited to a small number of foodstuffs from countries other than Canada. No regulations exist in Canada for its use in foods (Feeley, 1996). Data concerning the concentrations of acrolein in mothers' (breast) milk or infant formula preparations were not identified.

Acrolein is produced during the cooking or processing of fat-containing foods (Beauchamp *et al.*, 1985; Hirayama *et al.*, 1989; Lane and Smathers, 1991). Concentrations of acrolein ranged from 11.9 to 38.1 µg/g (mean 28.5 µg/g) in samples of five varieties of cooking oil heated to 80°C and aerated for 20 hours (Hirayama *et al.*, 1991). Acrolein was detected in the emissions from four varieties of heated cooking oils in China (Shields *et al.*, 1995) at concentrations ranging from 49 µg/L (peanut oil) to 392 µg/L (rapeseed oil). Lane and Smathers (1991) indicate that in addition to the production of acrolein from the frying medium, some ingredients common to commercial batter and breading systems may indirectly lead to the production of acrolein in fried foods.

Acrolein may be generated during the ripening of fruit (Kallio and Linko, 1973; Hayase *et al.*, 1984) and some types of cheese (e.g., Egyptian Domiati, 290–1024 µg/g; Collin *et al.*, 1993). Feron *et al.* (1991) measured concentrations of acrolein ranging from <0.01 to 0.05 µg/g in fruit and found a maximum concentration of 0.59 µg/g in vegetables; however, information concerning the location(s) and date(s) of sample acquisition and the number(s) of samples analysed was not presented. Acrolein has been detected (but not quantified) in cheese, caviar and lamb (Feron *et al.*, 1991), souring salted pork (Cantoni *et al.*, 1969), raw and cooked poultry (Hrdlicka and Kuca, 1965; Grey and Shrimpton, 1967), cocoa beans and chocolate liquor (Boyd *et al.*, 1965) and molasses (Hrdlicka and Janicek, 1968).

Acrolein may be produced as an unwanted by-product during alcoholic fermentation or during the storage and maturation of alcoholic products (Feron *et al.*, 1991), although available quantitative data are extremely limited. A maximum concentration of 3.8 µg/g was reported for red wine (Feron *et al.*, 1991). Mean concentrations of acrolein in samples of fresh (n = 3) and aged (n = 3) lager from the United Kingdom were 1.6 µg/L and 5.0 µg/L, respectively (Greenhoff and Wheeler, 1981), while acrolein was detected in only trace amounts (<10 µg/L) in an unspecified number of samples of Canadian apple wine purchased at a retail outlet in Ontario (Subden *et al.*, 1986). Acrolein has also been detected in non-alcoholic beverages (i.e., coffee and tea), although quantitative data were not presented (Feron *et al.*, 1991).

Acrolein is also produced as a thermal degradation product of cellophane and polystyrene thermoplastics used to package foods (Robles, 1968; Zitting and Heinonen, 1980); however, no data are available to indicate the migration of acrolein to the packaged food items.

Therefore, with the exception of data on heated vegetable oil (Hirayama *et al.*, 1991), the ripening of Egyptian Domiati cheese (Collin *et al.*, 1993) and the reported concentration of 3.8 µg/g for red wine (Feron *et al.*, 1991), there are no reports of concentrations of acrolein greater than 1 µg/g in any food items from other countries.

2.4 Effects characterization

2.4.1 Ecotoxicology

The toxicity of acrolein to aquatic organisms has been extensively studied, while a smaller data set exists on the toxicity of acrolein to terrestrial organisms. A brief summary of effects is presented below, with an emphasis on the most

sensitive endpoints for aquatic and terrestrial organisms.

2.4.1.1 Aquatic organisms

Acrolein is acutely toxic to aquatic organisms. Its toxicity in the aquatic environment has been extensively studied as a result of its use as an aquatic herbicide in irrigation canals.

The frog tadpole, *Xenopus laevis*, is the most sensitive aquatic species tested, with a 96-hour LC_{50} of 7 µg/L (Holcombe *et al.*, 1987). Short-term LC_{50}s for freshwater fish range from 14 to 250 µg/L. For marine fish, LC_{50}s of 56–240 µg/L have been reported (Holcombe *et al.*, 1987; Eisler, 1994; EU, 1998). Invertebrates have a range of sensitivity to acrolein similar to that of fish (U.S. EPA, 1978; Eisler, 1994). The water flea, *Daphnia magna*, is the most sensitive invertebrate, with a 48-hour LC_{50} ranging from 22 to 93 µg/L (EU, 1998). Microbes and bacteria are also sensitive to acrolein. Under closed static conditions, a 2-hour growth EC_{50} of 20 µg/L was observed for the bacterium, *Proteus vulgaris* (Eisler, 1994).

According to many field trials on the efficiency of acrolein as a pesticide, most submerged aquatic weeds and algae are sensitive (BPCI, 1994). The most sensitive species identified is the alga, *Scenedesmus subspicatus*, which has a 72-hour EC_{50} (biomass) of 26 µg/L and a No-Observed-Effect Concentration (NOEC) of 10 µg/L (EU, 1998). When acrolein is used to clear unwanted vegetation from irrigation canals, its effective dose range is 1–15 mg/L over an exposure period of 0.25–8 hours (BPCI, 1997). Most terrestrial crop plants can tolerate irrigation water containing 25 mg acrolein/L without damage (Ferguson *et al.*, 1961).

Few chronic studies are available for aquatic organisms. Acrolein was toxic to the fathead minnow (*Pimephales promelas*) following a 60-day exposure to 21.8 µg/L (Macek *et al.*, 1976). The survival of the F_1 fathead minnow was significantly reduced at 42 µg/L; the No-Observed-Effect Level (NOEL) for F_1 survival was estimated to be 11 µg/L. In a 64-day exposure of the zooplankton, *D. magna*, 100% mortality occurred in the F_2 generation at 42.7 µg/L. The NOEC for survival was estimated to be 16.9 µg/L (Macek *et al.*, 1976). In another study, a subchronic 14-day NOEC of 1800 mg/L was derived for the mollusc, *Dreissena polymorpha* (EU, 1998).

In many of the aquatic studies, the exposure solutions were periodically replenished via static renewal. In other cases, the organisms were exposed in a flow-through design to a continually renewed solution of acrolein. Dose–response relationships were frequently based on nominal concentrations of acrolein because of the ready volatilization and degradation of acrolein in aqueous solutions. The actual concentrations to which the organisms were exposed, particularly in the case of static renewal bioassays, may have been lower than reported. As a result, many of the existing data may underestimate the toxicity of acrolein to aquatic organisms.

2.4.1.2 Terrestrial organisms

The data on toxicity relevant for terrestrial wildlife are limited to studies on laboratory mammals and a few acute studies on crop plants. Data indicate that terrestrial organisms are less sensitive than aquatic organisms to acute exposure to acrolein (Eisler, 1994).

There have been no tests on wild terrestrial animals; effects on laboratory animals are presented in Section 2.4.3. Chickens, *Gallus* sp., suffered tracheal damage when exposed to concentrations of 113–454 mg acrolein/m^3 for up to 27 days (Denine *et al.*, 1971). With oral exposure to acrolein, the LD_{50} for mallards (*Anas platyrhynchos*) is 9.1 mg/kg-bw, and treatment levels as low as 3.3 mg/kg-bw produce signs of intoxication, such as regurgitation, ataxia, imbalance and withdrawal (Hudson *et al.*, 1984). The four-hour LC_{50} for the fruitfly, *Drosophila melanogaster*, which is the only invertebrate

tested, exceeded 4606 mg/L following exposure to an aqueous solution of acrolein on a petri dish (Comendador *et al.*, 1989).

The data on toxicity of acrolein in air to terrestrial plants are limited to three acute studies on crop plants. Smog-like leaf damage was observed for seven species exposed to concentrations of acrolein ranging from 233 to 4700 µg/m^3 (Haagen-Smit *et al.*, 1952; Darley *et al.*, 1960; Masaru *et al.*, 1976). The most sensitive plant tested was alfalfa (*Medicago sativa*), which developed speckled surface necrosis (percentage effect not given) after a nine-hour exposure to 233 µg acrolein/m^3, the lowest concentration tested in a study by Haagen-Smit *et al.* (1952). This concentration corresponded to a NOEC for the four other species of crop plants tested in that study (sugar beet, *Beta* sp.; endive, *Cichorium endivia*; spinach, *Spinacia oleracea*; oats, *Avena* sp.). The method of exposure involved the vaporization of liquid acrolein continuously injected into a fumigation chamber (Haagen-Smit *et al.*, 1952). In another study of the lily seed, *Lilium longiflorum*, there was a complete inhibition of pollen tube elongation following a five-hour exposure to 910 µg acrolein/m^3 (Masaru *et al.*, 1976). Pinto beans, *Phaseolus* sp., exposed to 4700 µg acrolein/m^3 in air for 1.2 hours exhibited 10% surface damage (Darley *et al.*, 1960).

2.4.2 Abiotic atmospheric effects

Worst-case calculations were made to determine if acrolein has the potential to contribute to the depletion of stratospheric ozone, ground-level ozone formation or climate change (Bunce, 1996).

The Ozone Depletion Potential (ODP) was calculated to be 0, since acrolein does not contain chlorine or bromine atoms.

The Photochemical Ozone Creation Potential (POCP) was estimated to be 116 (relative to the value of an equal mass of the reference compound ethene, which has a POCP of 100), based on the following formula:

$$POCP = (k_{acrolein}/k_{ethene}) \times (M_{ethene}/M_{acrolein}) \times 100$$

where:

- $k_{acrolein}$ is the rate constant for the reaction of acrolein with OH radicals (1.96×10^{-11} cm^3/mol per second),
- k_{ethene} is the rate constant for the reaction of ethene with OH radicals (8.5×10^{-12} cm^3/mol per second),
- M_{ethene} is the molecular weight of ethene (28.1 g/mol), and
- $M_{acrolein}$ is the molecular weight of acrolein (56.1 g/mol).

The Global Warming Potential (GWP) was calculated to be 8.2×10^{-5} (relative to the reference compound CFC-11, which has a GWP of 1), based on the following formula:

$$GWP = (t_{acrolein}/t_{CFC\text{-}11}) \times (M_{CFC\text{-}11}/M_{acrolein}) \times (S_{acrolein}/S_{CFC\text{-}11})$$

where:

- $t_{acrolein}$ is the lifetime of acrolein (2.0×10^{-3} years),
- t_{CFC-11} is the lifetime of CFC-11 (60 years),
- M_{CFC-11} is the molecular weight of CFC-11 (137.5 g/mol),
- $M_{acrolein}$ is the molecular weight of acrolein (56.1 g/mol),
- $S_{acrolein}$ is the infrared absorption strength of acrolein (2389/cm^2 per atmosphere, default), and
- S_{CFC-11} is the infrared absorption strength of CFC-11 (2389/cm^2 per atmosphere).

These figures suggest that the potential contribution of acrolein to stratospheric ozone depletion and climate change is negligible, and that its potential contribution to ground-level ozone formation is substantial. The magnitude of these effects would depend on the concentration of acrolein in the atmosphere, and concentrations of acrolein in air in Canada are very small. Acrolein's contribution to ozone formation is therefore considered negligible compared with those of other more abundant smog-forming substances, such as the reference compound ethene (Bunce, 1996).

2.4.3 Experimental animals and in vitro

2.4.3.1 Acute toxicity

Acrolein is highly acutely toxic, with LC_{50}s for four- or six-hour inhalation exposures of rats, mice and hamsters ranging from 8 to 66 ppm (18 to 151 mg/m^3) and LD_{50}s for oral administration to rats, mice and rabbits ranging from 7 to 46 mg/kg-bw. Signs of acute toxicity include irritation of the respiratory and gastrointestinal tracts and central nervous system depression.

Increased respiratory flow resistance and tidal volume and decreased respiratory rate have been observed in guinea pigs exposed by inhalation to 17 ppm (39 mg/m^3) acrolein for one hour (Davis *et al.*, 1967) or to 0.3 or 0.4 ppm (0.7 or 0.9 mg/m^3) acrolein for two hours (Murphy *et al.*, 1963; Leikauf, 1992). Reductions in pulmonary resistance, pulmonary compliance, tidal volume and respiratory rate have been observed among male Swiss mice exposed via tracheal cannula to acrolein vapour at 300 or 600 mg/m^3 for five minutes (Watanabe and Aviado, 1974).

In rats, exposure (nose-only) to 0.25 or 0.67 ppm (0.57 or 1.53 mg/m^3) acrolein for six hours produced a significant ($p < 0.01$) reduction in glutathione reductase activity in the nasal respiratory epithelium; no histopathological effects within the nasal cavity were observed (Cassee *et al.*, 1996). Histopathological effects in the bronchi and/or trachea (including exfoliation, edema, inflammation, vascular congestion and hemorrhagic necrosis) have been observed in Syrian golden hamsters (Kilburn and McKenzie, 1978), guinea pigs (Dahlgren *et al.*, 1972; Leikauf, 1992) and New Zealand white rabbits (Beeley *et al.*, 1986) exposed acutely to acrolein vapour at concentrations ranging from 0.91 (2.08 mg/m^3) to 489 ppm (1120 mg/m^3).

Increased mortality was observed among male F344 rats administered a single intragastric dose of 25 mg acrolein/kg-bw (in saline) (Sakata *et al.*, 1989). Other effects included degenerative changes in the liver (eosinophilic degeneration with micro vesicular steatosis), forestomach and glandular stomach (severe inflammation, hemorrhagic gastritis, multi-focal ulceration, fibrin deposition, focal hemorrhage, edema and polymorphonuclear leukocyte infiltration); however, no histopathological changes were observed in the bladder, lungs, kidneys or spleen.

2.4.3.2 Irritation and sensitization

Acrolein has been found to be irritating to the skin of rabbits (Albin, 1964; BSC, 1980a) and the eyes of laboratory animals (Albin, 1964; BSC, 1980b; BUA, 1994). A guinea pig maximization test revealed a lack of sensitizing effect of acrolein (Susten and Breitenstein, 1990).

2.4.3.3 Short-term and subchronic toxicity

2.4.3.3.1 Inhalation

Among the studies examining histopathological effects, exposure (nose-only) of male Wistar rats (number exposed not specified) to 0.25 or 0.67 ppm (0.57 or 1.53 mg/m^3) acrolein vapour for six hours per day for three days produced concentration-related histopathological changes (including disarrangement, necrosis, thickening, desquamation and basal cell hyperplasia) in the nasal respiratory/transitional epithelium, but not in the olfactory epithelium (Cassee *et al.*, 1996). **[Lowest-Observed-Adverse-Effect Level (LOAEL) = 0.25 ppm (0.57 mg/m^3)]**

In studies with female rats from Dahl selected lines (one susceptible and one resistant to salt-induced hypertension) exposed via inhalation (whole body) to 0.4, 1.4 or 4.0 ppm (0.9, 3.2 or 9.2 mg/m^3) acrolein vapour for six hours per day, five days per week, for up to 62 days, slight proliferative histopathological changes were observed in the lungs (including epithelial hyperplasia, squamous metaplasia and peripheral lymphoid aggregates) of both strains at 0.4 and 1.4 ppm (0.9 and 3.2 mg/m^3). Severe histopathological lesions were observed in the lungs (necrosis, edema, hemorrhage) and trachea

(squamous metaplasia) at 4.0 ppm (9.2 mg/m^3) acrolein. No microscopic changes were observed in the nasal turbinates, brain, heart, liver, kidneys or spleen in either strain seven days following the last exposure to acrolein (Kutzman *et al.*, 1984). **[LOAEL = 0.4 ppm (0.9 mg/m^3)]** However, histopathological changes in the nasal cavity but not the lungs of rats were reported in a more recent study (Leach *et al.*, 1987) in which male Sprague-Dawley rats were exposed (whole body) to 0.17, 1.07 or 2.98 ppm (0.39, 2.45 or 6.82 mg/m^3) acrolein vapour for six hours per day, five days per week, for three weeks. **[Systemic and site-of-contact effects at 2.98 ppm (6.82 mg/m^3)]**

Following repeated exposure (whole body) of F344 rats (n = 24 per sex) to 0.4, 1.4 or 4.0 ppm (0.9, 3.2 or 9.2 mg/m^3) acrolein vapour for six hours per day, five days per week, for up to 62 days, no adverse effects were observed at 0.4 ppm (0.9 mg/m^3), while animals exposed to 1.4 ppm (3.2 mg/m^3) acrolein exhibited biochemical (i.e., increased collagen) and histopathological changes in the lungs compared with unexposed controls. Effects observed following exposure to 4.0 ppm (9.2 mg/m^3) acrolein included increased mortality in males and histopathological changes in the trachea and lungs. Other systemic effects and histopathology in the nasal cavities were not presented in these reports (Kutzman *et al.*, 1985; Costa *et al.*, 1986); however, in an original report of this study (Kutzman, 1981), fluctuations in the incidence of submucosal lymphoid aggregates within the nasal turbinate were noted. In animals exposed to 0, 0.4, 1.4 or 4.0 ppm (0, 0.9, 3.2 or 9.2 mg/m^3) acrolein, the incidence of submucosal lymphoid aggregates within the nasal turbinate was 1/8, 3/8, 2/7 and 3/5, respectively. **[NOEL = 0.4 ppm (0.9 mg/m^3); LOAEL = 1.4 ppm (3.2 mg/m^3)]**

Repeated inhalation exposure (whole body) of Sprague-Dawley rats, Princeton or Hartley guinea pigs, male squirrel monkeys and very small groups of male beagle dogs to 0.7 or 3.7 ppm (1.6 or 8.5 mg/m^3) acrolein vapour for eight hours per day, five days per week, for six weeks produced histopathological inflammatory changes and mild emphysema in the lungs of all species (most notably in dogs and monkeys) at 0.7 ppm (1.6 mg/m^3) (Lyon *et al.*, 1970). Exposure to 3.7 ppm (8.5 mg/m^3) acrolein produced mortality in monkeys, clinical signs of toxicity in dogs and monkeys, significantly ($p < 0.005$) reduced body weights in rats and exposure-related histopathological effects in the trachea (squamous metaplasia and basal cell hyperplasia) of dogs and monkeys and in the lungs (necrotizing bronchitis, bronchiolitis with squamous metaplasia) of monkeys. **[LOAEL (rats, guinea pigs, dogs, monkeys) = 0.7 ppm (1.6 mg/m^3)]**

Identified data concerning the subchronic toxicity of inhaled acrolein are limited to two studies in which survival, growth, urinary and hematological parameters, serum biochemistry and histopathology were examined in several species (Lyon *et al.*, 1970; Feron *et al.*, 1978). In one study, Wistar rats, Dutch rabbits and Syrian golden hamsters were exposed to 0.4, 1.4 or 4.9 ppm (0.9, 3.2 or 11.2 mg/m^3) acrolein vapour for six hours per day, five days per week, for 13 weeks (Feron *et al.*, 1978). In rats, the frequency and severity of histopathological effects within the nasal cavity were concentration dependent; exposure to 4.9 ppm (11.2 mg/m^3) acrolein increased mortality, as well as producing moderate to severe histopathological changes in the nasal cavities, larynx, trachea, bronchi and lungs. In hamsters, exposure to 1.4 ppm (3.2 mg/m^3) acrolein produced slight inflammatory changes in the nasal cavities, while exposure to 4.9 ppm (11.2 mg/m^3) acrolein produced slight to severe histopathological changes in the nasal cavities, larynx and trachea. In rabbits, slight to moderate histopathological changes in the nasal cavities, trachea, bronchi and lungs were observed only in animals exposed to 4.9 ppm (11.2 mg/m^3) acrolein (Feron *et al.*, 1978). **[Lowest-Observed-Effect Level (LOEL) (rats) = 0.4 ppm (0.9 mg/m^3); NOEL (hamsters) = 0.4 ppm (0.9 mg/m^3); NOEL (rabbits) = 1.4 ppm (3.2 mg/m^3)]**

The continuous inhalation of 0.22, 1.0 or 1.8 ppm (0.50, 2.3 or 4.1 mg/m^3) acrolein by groups of Sprague-Dawley rats (n = 15 per sex), Princeton or Hartley guinea pigs (n = 15 per sex), male beagle dogs (n = 2–4) and male squirrel monkeys (n = 9–17) for 90 days produced exposure-related histopathological lesions in dogs (lungs, spleen and thyroid) at the lowest concentration tested, 0.22 ppm (0.50 mg/m^3). Histopathological changes in the lung, trachea, liver and/or kidney (in all species) were observed at higher concentrations; however, effects in the nasal cavity were not assessed (Lyon *et al.*, 1970). **[LOAEL (dogs) = 0.22 ppm (0.50 mg/m^3); NOEL (rats, guinea pigs) = 0.22 ppm (0.50 mg/m^3); NOEL (monkeys) = 1.0 ppm (2.3 mg/m^3)]**

2.4.3.3.2 Ingestion

Uncertainty concerning the doses administered and lack of clear exposure-related effects on survival, behaviour, body weight, organ weights, hematological parameters or stomach histopathology limit the usefulness, in the characterization of effects, of early short-term and subchronic toxicological studies in which rats were administered drinking water containing acrolein (Newell, 1958). In a study in which only a limited number of endpoints were assessed, the oral administration (by gavage) of 4.6–9.0 mg acrolein/kg-bw per day (at concentrations ranging from 0.46 to 0.90 mg/mL) for 14 consecutive days to male and female CD-1 mice had no dose-related effect upon mortality or weight gain, although there was a clear increase in the occurrence of white thickening of the gastric mucosa in the high-dose groups (BSC, 1983).

In a 13-week study, acrolein was administered by oral gavage in a 5% aqueous solution of methylcellulose to Fischer 344 rats at concentrations of 0.15, 0.25, 0.5, 1.0 or 2.0 mg/mL (0.75, 1.25, 2.5, 5.0 or 10.0 mg/kg-bw per day) and to B6C3F$_1$ mice at concentrations of 0.125, 0.25, 0.5, 1.0 or 2.0 mg/mL (1.25, 2.5, 5.0, 10.0 or 20.0 mg/kg-bw per day) (NTP, 1998). In a preliminary report of the results, concentration-related increases in the incidence of histopathological lesions in the stomach (including hemorrhage, necrosis and inflammation of the glandular stomach and forestomach and squamous epithelial hyperplasia of the forestomach) were observed in rats receiving ≥0.25 mg acrolein/mL and in mice receiving ≥0.125 mg acrolein/mL; however, the incidence and statistical significance of these lesions were not available. Systemic effects in rats (increased liver weights) and mice (increased liver and kidney weights) were observed at doses ≥2.5 mg acrolein/kg-bw per day (NTP, 1998). **[NOEL (rats) = 0.75 mg/kg-bw per day (0.15 mg/mL); LOAEL (mice) = 1.25 mg/kg-bw per day (0.125 mg/mL)]**

2.4.3.3.3 Dermal exposure

Erythema, edema, histopathological changes in the skin (hyperkeratosis, acanthosis, parakeratosis) as well as an increased incidence of interstitial nephritis and pulmonary interstitial pneumonia have been observed in male and female New Zealand white rabbits exposed dermally to acrolein (7, 21 or 63 mg/kg-bw; concentrations of 3.5, 10.5 and 31.5 mg/mL) for six hours per day, five days per week, for three weeks (BSC, 1982a).

2.4.3.4 Chronic toxicity and carcinogenicity

Identified data concerning the chronic toxicity/carcinogenicity of acrolein following the inhalation exposure of laboratory species are restricted to the results of two limited studies. In one study in which groups of Syrian golden hamsters (18 animals per sex) were exposed (whole body) to 0 or 4.0 ppm (0 or 9.2 mg/m^3) acrolein vapour for seven hours per day, five days per week, for 52 weeks (Feron and Kruysse, 1977), followed by a 29-week recovery period, exposure to acrolein produced variable (statistically significant) reductions in body weight among males ($p < 0.01$ to $p < 0.05$) and females ($p < 0.001$ to $p < 0.05$), an increase

($p < 0.05$) in relative lung weights and a reduction ($p < 0.05$) in relative liver weights in females, as well as slight to moderate histopathological effects in the anterior portion of the nasal cavity. No exposure-related tumours were observed among animals exposed to acrolein; however, this study is limited by the relatively short exposure period, small group sizes and single exposure concentration. **[Effects at 4.0 ppm (9.2 mg/m^3); single exposure concentration]**

Limited exposure (one hour per day) of small numbers (n = 20) of female Sprague-Dawley rats to a single concentration (8 ppm; 18 mg/m^3) of acrolein for up to 18 months had no apparent adverse effects on body weight, lung weight or histopathology in major tissues and organs (including nasal fossae, larynx, trachea and lungs) (LeBouffant *et al.*, 1980). **[No effects at 8 ppm (18 mg/m^3); single exposure level]**

Available data concerning the chronic toxicity/carcinogenicity of acrolein following oral exposure include three bioassays in which a wide range of endpoints was examined in Sprague-Dawley rats (Parent *et al.*, 1992a), CD-1 mice (Parent *et al.*, 1991) and beagle dogs (Parent *et al.*, 1992b) and an earlier study in male F344 rats, in which only mortality and histopathology in selected tissues were examined (Lijinsky and Reuber, 1987).

The only exposure-related effects noted in a study in which Sprague-Dawley rats were administered (by oral gavage) 0.05, 0.5 or 2.5 mg acrolein/kg-bw per day (solutions were prepared fresh daily in deionized water at concentrations of 0.005, 0.05 and 0.25 mg/mL) for up to 102 weeks were limited to an unspecified reduction ($p < 0.05$) in serum creatinine phosphokinase levels among both sexes at all levels of exposure and a (dose-related) increase in mortality among males ($p = 0.003$) at 0.5 and 2.5 mg acrolein/kg-bw per day during the first year only and in females ($p < 0.001$) at 0.5 and 2.5 mg/kg-bw per day throughout the entire exposure period, the cause of which was not specified (Parent *et al.*, 1992a). Exposure-related histopathological effects were not observed; examinations were conducted on all major tissues and organs (including esophagus, stomach and intestines) from animals in the control and high-dose groups and in animals found dead or sacrificed moribund, although only the stomachs of some animals sacrificed after 13 weeks were examined histopathologically. After the first year of the study, survival in the mid- and high-dose male rats was reduced, compared with the controls; however, survival appeared to be higher among males exposed to acrolein (at all dose levels) during the second year of exposure than in controls. No statistical evaluation of this apparent increase in survival in the acrolein-exposed male rats was presented. Although histopathological effects in the stomach were not observed in rats exposed to acrolein in this investigation, such changes have been noted in other adequate long-term (subchronic) oral studies conducted with Fischer 344 rats (NTP, 1998), in which the time-point of histopathological analysis was similar to one of those included in this study by Parent *et al.* (1992a). **[NOEL = 0.05 mg/kg-bw per day (0.005 mg/mL); LOAEL = 0.5 mg/kg-bw per day (0.05 mg/mL)]**

Similarly, no apparent dose-related effects on clinical or hematological parameters, organ weight, gross pathology or histopathology were observed when CD-1 mice were administered (by oral gavage) 0.5, 2.0 or 4.5 mg acrolein/kg-bw per day (solutions were prepared fresh daily in deionized water at concentrations of 0.05, 0.20 and 0.45 mg/mL) for 18 months (Parent *et al.*, 1991). Administration of 4.5 mg acrolein/kg-bw per day produced effects in male mice only, which included a significant ($p \leq 0.05$) reduction in growth (approximately 5%) and a significant ($p \leq 0.05$) increase in mortality throughout the entire study period, the cause of which was not specified. Notably, survival was higher in the low- and mid-dose males throughout the entire exposure period than in unexposed controls; no statistical evaluation of this apparent increase in survival in treated male mice was presented. Once again, although there was an absence of histopathological effects in the stomachs of mice

exposed to acrolein in this study, such changes have been observed in other adequate long-term (subchronic) oral studies (NTP, 1998) conducted with $B6C3F_1$ mice. **[NOEL (females) = 4.5 mg/kg-bw per day (0.45 mg/mL); NOEL (males) = 2.0 mg/kg-bw per day (0.2 mg/mL); LOAEL (males) = 4.5 mg/kg-bw per day (0.45 mg/mL)]**

In studies of small groups (n = 20) of male F344 rats receiving drinking water containing 0, 100, 250 or 625 mg acrolein/L (0, 14, 36 or 89 mg/kg-bw per day) [1] for five days per week for up to 124 weeks or male and female rats receiving drinking water containing 0 or 625 mg acrolein/L (0 or 89 mg/kg-bw per day) for up to 104 weeks, exposure to acrolein had no significant effect on mortality in either sex or on histopathology (including the forestomach, peritoneum and colon) in male rats (Lijinsky and Reuber, 1987). Female rats receiving drinking water containing 625 mg acrolein/L (89 mg/kg-bw per day) had a marginal increase in the incidence of adrenal cortical adenomas (5/20, $p = 0.091$) and in the combined incidence of adrenal cortical adenomas and "hyperplastic nodules" (7/20, $p = 0.022$) compared with unexposed controls (Lijinsky and Reuber, 1987). However, no additional details were provided. There was no indication in the Lijinsky and Reuber (1987) study that precautions had been taken to prevent the likely volatilization of acrolein, and therefore the doses that the animals received were likely considerably less than the nominal doses indicated above. Indeed, the highest dose at which non-neoplastic effects were not observed is considerably greater than reported LD_{50}s.

There were no increases in diethylnitrosamine-induced respiratory tract tumours in hamsters exposed simultaneously to acrolein, and there was only limited evidence of an enhancing effect on carcinogenesis induced by benzo[a]pyrene (Feron and Kruysse, 1977).

Non-neoplastic effects in dogs administered up to 2.0 mg acrolein/kg-bw per day, seven days a week for up to 53 weeks, were limited to transient (dose-dependent) vomiting at all levels of exposure, which decreased over time (suggesting that animals developed tolerance to acrolein), and (persistent) significant ($p < 0.05$) alterations in serum biochemical parameters (including reduced total protein [up to 17%], albumin [up to 19%] and calcium [up to 7%]) in animals at the highest dose (Parent *et al.*, 1992b). **[Non-neoplastic effects, No-Observed-Adverse-Effect Level (NOAEL) = 2.0 mg/kg-bw per day]**

2.4.3.5 Genotoxicity

Acrolein induces gene mutations in both bacteria (Hemminiki *et al.*, 1980; Lijinsky and Andrews, 1980; Hales, 1982; Lutz *et al.*, 1982; Haworth *et al.*, 1983; Marnett *et al.*, 1985; Foiles *et al.*, 1989; Parent *et al.*, 1996) and mammalian cells in culture (Smith *et al.*, 1990), as well as structural chromosomal aberrations in Chinese hamster ovary (CHO) cells (Au *et al.*, 1980) and sister chromatid exchanges in CHO cells (Au *et al.*, 1980; Galloway *et al.*, 1987) and cultured human lymphocytes (Wilmer *et al.*, 1986). The mechanism of acrolein genotoxicity appears to involve the induction of DNA damage. Acrolein binds to DNA, forms DNA–protein cross-links (Grafstrom *et al.*, 1988) and induces DNA single strand breaks in human fibroblasts (Dupbukt *et al.*, 1993) and bronchial epithelial cells (Grafstrom *et al.*, 1988). In human fibroblasts, acrolein induces mutations at the HPRT locus in DNA repair-deficient cells from xeroderma pigmentosum patients but not in normal cells (Curren *et al.*, 1988), supporting DNA damage as the primary mechanism for acrolein-induced mutagenesis. The results of *in vitro* studies suggest that intracellular glutathione (or other free sulphydryl groups) may protect against the DNA-damaging effects of acrolein (Eisenbrand *et al.*, 1995).

[1] Calculated based on the average amount of water consumed (0.05 L/day) by rats weighing 350 g (Health Canada, 1994; Meek *et al.*, 1994).

Although the results of *in vitro* studies indicate that acrolein can react directly with DNA and proteins to form stable adducts, an increased formation of DNA–protein cross-links was not observed in the nasal mucosa of male F344 rats exposed *in vivo* (by inhalation) to 2 ppm (5 mg/m^3) acrolein for six hours (Lam *et al.*, 1985).

Although less relevant to the assessment of genotoxicity at the site of initial contact (i.e., where critical effects occur), *in vivo* studies of the genotoxicity of acrolein at systemic sites are not extensive. In a dominant lethal study in male ICR/Ha Swiss mice, acrolein (administered by intraperitoneal injection) at doses up to 2.2 mg/kg-bw had no effect upon the numbers of pregnancies, implants or fetal deaths (Epstein *et al.*, 1972). Increases in the frequency of chromosomal aberrations were not observed in studies in which F344 rats were exposed (by inhalation) to concentrations up to 4.0 ppm (9.2 mg/m^3) acrolein six hours per day, five days per week, for 62 days (Kutzman, 1981) or in which Sprague-Dawley rats were administered (by intraperitoneal injection) single doses of up to 4.1 mg acrolein/kg-bw (BSC, 1982b).

2.4.3.6 Reproductive and developmental toxicity

Identified *in vivo* studies (using physiologically relevant routes of exposure) on the developmental/reproductive toxicity of acrolein conducted by oral gavage include a two-generation reproduction study in rats (Parent *et al.*, 1992c) and developmental toxicity studies in rabbits (Parent *et al.*, 1993), rats (BSC, 1982c,d) and mice (BSC, 1982c,d), while studies in which animals were exposed via inhalation are limited to the results of a single-generation reproduction study in rats (Bouley *et al.*, 1976). On the basis of these investigations, adverse effects have been confined primarily to the parental generation, limited mostly to the site of first contact.

In the most extensive reproductive bioassay identified, reproductive function was assessed in two generations of rats administered acrolein by gastric intubation (Parent *et al.*, 1992c). Sprague-Dawley rats (F_0) were administered (by gavage) 1.0, 3.0 or 6.0 mg acrolein/kg-bw per day (solutions prepared daily in deionized water at concentrations of 0.2, 0.6 and 1.2 mg/mL). A statistically significant ($p < 0.01$) reduction in body weight in F_0 males and females and gastric lesions (i.e., erosion of the glandular mucosa and hyperplasia/hyperkeratosis of the forestomach) in F_0 and F_1 females were also observed in animals receiving 3.0 mg acrolein/kg-bw per day (0.6 mg/mL).

2.4.3.7 Neurological effects and effects on the immune system

Limited data on neurotoxicity indicate a lack of morphological changes in the tracheal or pulmonary nerves of rats exposed by inhalation to up to 249 ppm (570 mg/m^3) acrolein for 10 minutes (Springall *et al.*, 1990), no histopathological changes in the nerve cells of the nasal olfactory epithelium of mice exposed by inhalation to 1.7 ppm (3.9 mg/m^3) acrolein for six hours per day for five days (Buckley *et al.*, 1984) and no behavioural effects in rats exposed by inhalation to up to 4.0 ppm (9 mg/m^3) acrolein for six hours per day, five days per week, for up to 62 days (Kutzman *et al.*, 1984).

The direct effects of acrolein on the immune system (including host resistance, pulmonary bacterial clearance, antibody responsiveness, lymphocyte blastogenesis and respiratory damage) have been investigated in *in vivo* studies conducted with rats (Bouley *et al.*, 1976; Sherwood *et al.*, 1986; Leach *et al.*, 1987) and mice (Jakab, 1977; Astry and Jakab, 1983; Aranyi *et al.*, 1986) exposed via inhalation. Immunological effects (i.e., reduced pulmonary bacterial clearance) have been observed in mice exposed to concentrations of acrolein as low as 0.1 ppm (0.23 mg/m^3) (Aranyi *et al.*, 1986), although effects have been transient in long-term studies.

2.4.3.8 Toxicokinetics and mechanism of action

Small amounts of acrolein are produced endogenously during the normal intermediary catabolism of various amino acids and polyamines (Alarcon, 1970, 1972, 1976) and during the peroxidation of membrane lipids (Nath *et al.*, 1997). Consistent with effects being restricted primarily to the initial site of contact following inhalation (i.e., the respiratory tract), available data indicate that the greatest proportion of exogenous inhaled acrolein is retained at the site of exposure, becoming rapidly and irreversibly bound to free protein and non-protein sulphydryl groups (most notably glutathione). Based upon kinetic studies in dogs, rats and ferrets (Egle, 1972; Ben-Jebria *et al.*, 1995; Morris, 1996), the absorption of inhaled acrolein into the systemic circulation is not extensive. Based on the metabolites most frequently identified in the urine of exposed animals (although incompletely characterized), the predominant pathway for the metabolism of acrolein appears to involve conjugation with glutathione and subsequent conversion to N-acetylcysteine compounds.

Many of the toxicological effects of acrolein may be due to the saturation of protective cellular mechanisms (most notably glutathione) and subsequent reaction with critical sulphydryl groups in proteins and peptides (Gurtoo *et al.*, 1981; Marinello *et al.*, 1984). In rats, inhalation of acrolein at levels ranging from 0.1 to 17 ppm (0.2 to 39 mg/m^3) produces a concentration-dependent reduction in non-protein sulphydryl groups in the respiratory tract, but not in the liver (McNulty *et al.*, 1984; Lam *et al.*, 1985; Heck *et al.*, 1986; Walk and Haussmann, 1989). Some studies have revealed that pre-treatment with compounds containing free sulphydryl groups (e.g., cysteine) is protective against the acute lethality of acrolein (Sprince *et al.*, 1979; Gurtoo *et al.*, 1981). Although there have been some suggestions that the toxic effects of acrolein may be mediated, at least in part, through mechanisms involving acrolein–glutathione conjugates (Mitchell and Petersen, 1989; Horvath *et al.*, 1992; Ramu *et al.*, 1996), available data remain inconclusive.

The nature of responses associated with exposure to acrolein is qualitatively similar to that of other aldehydes. Acrolein is, however, the most irritating of these compounds. The pattern of observed irritancy of acrolein at the site of contact and the results of *in vitro* studies indicating that it can react directly with DNA and proteins to form stable adducts are findings similar to those for other aldehydes (such as formaldehyde) that have been carcinogenic to the respiratory system in sensitive inhalation bioassays. Although the exact mechanism is unknown, induction of tumours by these aldehydes (notably formaldehyde) is considered to be a function of both regenerative proliferative response and DNA–protein cross-linking at the site of contact.

The limited available data indicate, however, that the pattern of DNA–protein cross-linking and proliferative response induced by acrolein differs from that of acetaldehyde and formaldehyde. For acetaldehyde, at the concentrations at which tumours are observed (750 ppm; 1350 mg/m^3), there are increases in DNA–protein cross-links in the respiratory and olfactory mucosa of rats but no increase in proliferation (Cassee *et al.*, 1996). For formaldehyde, at the lower concentrations at which tumours are observed (6 ppm; 7 mg/m^3), there are increases in DNA–protein cross-links and proliferation in the nasal respiratory (but not olfactory) epithelium (Casanova *et al.*, 1994).

Moreover, available data are inadequate to assess whether acrolein has the ability to induce tumours or interact directly with DNA at the site of contact following inhalation. While there was no increase in DNA–protein cross-links in the nasal mucosa of Wistar rats acutely exposed (by inhalation) to a single concentration of 2 ppm (5 mg/m^3) acrolein alone, acrolein enhanced the formation of formaldehyde-induced DNA–protein cross-links (Lam *et al.*, 1986). It is possible that the lack of observation of

DNA–protein cross-links at the site of exposure at the single dose administered in studies conducted to date (Lam *et al.*, 1985) might be attributable to preferential binding to sulphydryl-containing nucleophiles (such as glutathione). Moreover, it appears that the cytotoxicity of acrolein at low concentrations associated with the saturation of protective mechanisms (namely glutathione) may be the crucial determinant in the toxicity of this compound at the site of exposure.

Increases in cell proliferation have been observed in the nasal respiratory epithelium (but not olfactory epithelium) of Wistar rats following single (Roemer *et al.*, 1993) or repeated exposure (Cassee *et al.*, 1996) (by inhalation) to relatively low concentrations (0.2 ppm [0.5 mg/m^3] or greater) of acrolein, although data in this regard are also not completely consistent.

2.4.4 Humans

Acrolein is an upper respiratory tract and eye irritant in humans. The threshold concentration for the perception of acrolein vapour may be as low as 0.07 mg/m^3 (Sinkuvene, 1970), while the odour recognition threshold may be as low as 0.48 mg/m^3 (Leonardos *et al.*, 1969). Sensory ocular irritation has been observed at concentrations reportedly as low as 0.13 mg acrolein/m^3 (calculated value) (Darley *et al.*, 1960), while nasal (sensory) irritation has been reported following exposure to concentrations as low as 0.34 mg/m^3 (Weber-Tschopp *et al.*, 1977). Reduced respiratory rate was observed in male volunteers exposed to concentrations as low as 0.69 mg acrolein/m^3 for 40 minutes (Weber-Tschopp *et al.*, 1977). Inhalation of concentrations as low as 0.6 mg acrolein/m^3 may cause respiratory effects, including coughing, nasal irritation, chest pain and difficulty breathing (Kirk *et al.*, 1991). Most individuals cannot tolerate exposure to concentrations of acrolein in air of 5 mg/m^3 or higher for more than two minutes, while exposure to concentrations above 20 mg/m^3 may be lethal (Einhorn, 1975; Kirk *et al.*, 1991).

Effects including weakness, nausea, vomiting, diarrhea, severe respiratory and ocular irritation, shortness of breath, bronchitis, pulmonary edema, unconsciousness and death have been observed upon accidental exposure (by inhalation or ingestion) to acrolein. Direct dermal or ocular contact with liquid acrolein can produce severe skin or eye injury, including necrosis, edema, erythema, dermatitis and follicular pharyngitis (ITII, 1975; Beauchamp *et al.*, 1985; Kirk *et al.*, 1991; Bronstein and Sullivan, 1992; Rorison and McPherson, 1992). Effects following the ingestion or inhalation of acrolein have been consistently observed at the site of contact (i.e., stomach or respiratory tract) (Champeux *et al.*, 1966; Gosselin *et al.*, 1979; Schielke, 1987; Mahut *et al.*, 1996).

In patch tests conducted with volunteers, no dermal irritation was observed following exposure to 0.01% or 0.1% acrolein; however, positive reactions (i.e., severe edema with bullae and erythema) were observed in 6/48 individuals exposed to 1.0% acrolein, while more severe effects (including bullae, necrosis, inflammatory cell infiltration and papillary edema) were observed in 8/8 subjects exposed to 10% acrolein (Lacroix *et al.*, 1976).

The only identified epidemiological study (Bittersohl, 1975) is considered inadequate to assess the carcinogenicity of acrolein in humans, since it entailed only qualitative observations; there was no quantitative analysis by tumour site with a comparison population, standardizing for age and sex. Moreover, workers were exposed concomitantly to several other compounds.

3.0 ASSESSMENT OF "TOXIC" UNDER CEPA 1999

3.1 CEPA 1999 64(a): Environment

The environmental risk assessment of a PSL substance is based on the procedures outlined in Environment Canada (1997a). Environmental assessment endpoints (e.g., adverse reproductive effects on sensitive fish species in a community) are selected based on analysis of exposure pathways and subsequent identification of sensitive receptors. For each endpoint, a conservative Estimated Exposure Value (EEV) is selected and an Estimated No-Effects Value (ENEV) is determined by dividing a Critical Toxicity Value (CTV) by an application factor. A conservative (or hyperconservative) quotient (EEV/ENEV) is calculated for each of the assessment endpoints in order to determine whether there is potential ecological risk in Canada (summarized for acrolein in Table 3). If these quotients are less than one, it can be concluded that the substance poses no significant risk to the environment, and the risk assessment is completed. If, however, the quotient is greater than one for a particular assessment endpoint, then the risk assessment for that endpoint proceeds to an analysis where more realistic assumptions are used and the probability and magnitude of effects are considered. This latter approach involves a more thorough consideration of sources of variability and uncertainty in the risk analysis.

3.1.1 Assessment endpoints

Acrolein is released from natural and anthropogenic sources in Canada. Acrolein from non-pesticidal sources is released predominantly to air. The largest source appears to be exhaust from diesel and gasoline motor vehicles. Since acrolein is not persistent in air, environmental effects are expected to be greatest in urban areas where traffic volume is high and continuous. This is supported by monitoring data on concentrations of acrolein in ambient air in Canada.

Based on its physical/chemical properties, acrolein is unlikely to partition out of air when released into that medium. Because of the lack of non-pesticidal sources and the degradation of acrolein in water, sediment and soil, these compartments do not appear to be of concern. This is supported by air monitoring data in Canada and the lack of detectable concentrations of acrolein in water, sediment and soil. Acrolein does not bioaccumulate in organisms. Therefore, the assessment of acrolein will focus on terrestrial organisms exposed to air in urban areas.

Selected assessment endpoints for terrestrial biota are reductions in the growth, survival or reproduction of terrestrial plants and animals due to exposure to acrolein. Small animals, such as deer mice or songbirds, are likely to have the highest exposure because of their rapid respiration rate and high metabolism.

TABLE 3 Summary of the hyperconservative environmental risk analysis

Exposure scenario	EEV ($\mu g/m^3$)	CTV ($\mu g/m^3$)	Application factor	ENEV ($\mu g/m^3$)	Quotient
Acute / Plant	2.47	233	10	23	0.11
Acute / Animals	2.47	570	10	57	0.04
Chronic / Plant	1.58	233	100	2.33	0.68
Chronic / Animals	1.58	570	10	57	0.03

The most sensitive measurement endpoint identified for terrestrial plants is the acute effect of acrolein on the survival of the alfalfa plant. This endpoint will be used for both acute and chronic exposure scenarios because of the lack of chronic toxicity data on plants. The most sensitive measurement endpoint identified for terrestrial animals is the short-term effect of acrolein on rats exposed via inhalation, which will be used for both acute and chronic exposure scenarios.

3.1.2 Environmental risk characterization

3.1.2.1 Acute exposure of terrestrial plants and animals

The highest concentration of acrolein reported for ambient air in seven urban sites between 1989 and 1996 is 2.47 µg/m^3. This value was obtained for a 24-hour urban sample collected in Montréal, Quebec, on July 31, 1994. It will be used as the EEV in the hyperconservative analysis of acute exposure scenarios for terrestrial plants and animals.

3.1.2.1.1 Terrestrial plants

For acute exposure of terrestrial plants to acrolein in air, the CTV is 233 µg/m^3, based on a nine-hour exposure concentration causing speckled surface necrosis in the alfalfa plant (Haagen-Smit *et al.*, 1952). This value was selected from a data set composed of three acute toxicity studies conducted on seven species of crop plants representing monocots and dicots at two life stages.

For a hyperconservative analysis, the ENEV for terrestrial plants is derived by dividing the CTV by a factor of 10. This factor accounts for the uncertainty surrounding the conversion of a Lowest-Observed-Effect Concentration (LOEC) to a long-term no-effects value, the extrapolation from laboratory to field conditions and interspecies and intraspecies variations in sensitivity. As a result, the ENEV is 23 µg/m^3.

The hyperconservative quotient is calculated by dividing the EEV of 2.47 µg/m^3 by the plant ENEV as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{2.47\ \mu g/m^3}{23\ \mu g/m^3}$$

$$= 0.11$$

Since the hyperconservative quotient is less than one, it is unlikely that acrolein emissions cause acute adverse effects on terrestrial plants in Canada.

3.1.2.1.2 Terrestrial animals

For acute exposure of terrestrial animals to acrolein in air, the CTV is 570 µg/m^3, based on the LOAEL for exposure of the rat via inhalation for six hours per day for three days (Cassee *et al.*, 1996). The exposure caused an increase in cell proliferation and histopathological changes in the nasal respiratory epithelium. Since non-neoplastic effects in the respiratory tract of experimental animals are considered critical, this study represents the most sensitive inhalation study reported (see Section 3.3.3.1). This CTV was selected as the lowest short-term effects concentration from a large data set composed of more than 10 studies conducted on six species of laboratory mammals and one species of domestic fowl.

For the hyperconservative analysis, the ENEV is derived by dividing the CTV by a factor of 10. This factor accounts for the uncertainty surrounding the conversion of a LOAEL to a no-effects value, the extrapolation from laboratory to field conditions and interspecies and intraspecies variations in sensitivity. As a result, the ENEV is 57 µg/m^3.

The hyperconservative quotient is calculated by dividing the EEV of 2.47 µg/m³ by the ENEV as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{2.47\ \mu g/m^3}{57\ \mu g/m^3}$$

$$= 0.04$$

Since the hyperconservative quotient is less than one, it is unlikely that acrolein emissions cause acute adverse effects on terrestrial animals in Canada.

3.1.2.2 Chronic exposure of terrestrial plants and animals

The highest mean concentration of acrolein in air measured weekly over any three consecutive months during the monitoring of 15 Canadian sites between 1989 and 1996 is 1.58 µg/m³. This value was obtained for an urban site in Montréal, Quebec, during the period of June–August 1994 (Environment Canada, 1996b). This value will be used as the EEV in the hyperconservative analysis of chronic exposure scenarios for terrestrial plants and animals. A three-month mean was selected for the chronic EEV because it corresponds to an appropriate long-term exposure period relative to the lifespan of test organisms.

3.1.2.2.1 Terrestrial plants

For chronic exposure of terrestrial plants to acrolein in air, the CTV is 233 µg/m³, based on a nine-hour exposure concentration causing speckled surface necrosis in the alfalfa plant (Haagen-Smit *et al.*, 1952). This value was selected from a data set composed of three acute toxicity studies conducted on seven species of crop plants representing monocots and dicots at two life stages.

For a hyperconservative analysis, the ENEV is derived by dividing the CTV by a factor of 100. This factor accounts for the uncertainty surrounding the conversion of an acute LOEC to a long-term no-effects value, the extrapolation from laboratory to field conditions and interspecies and intraspecies variations in sensitivity. As a result, the ENEV is 2.33 µg/m³.

The hyperconservative quotient is calculated by dividing the EEV of 1.58 µg/m³ by the plant ENEV as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{1.58\ \mu g/m^3}{2.33\ \mu g/m^3}$$

$$= 0.68$$

Since the hyperconservative quotient is less than one, it is unlikely that acrolein emissions will cause adverse effects on populations of terrestrial plants in Canada.

3.1.2.2.2 Terrestrial animals

For chronic exposure of terrestrial animals to acrolein in air, the Cassee *et al.* (1996) study used for acute exposure will be used to derive an ENEV. In this assessment, the respiratory tract is considered to be the most sensitive site in mammals for acrolein, as indicated in the study by Cassee *et al.* (1996). Therefore, the CTV is 570 µg/m³, based on the LOAEL for exposure of the rat via inhalation for six hours per day for three days. This CTV value for the rat is selected from a large data set composed of more than 10 studies conducted on six species of laboratory animals.

For a hyperconservative analysis, the ENEV is derived by dividing the CTV by a factor of 10. This factor accounts for the uncertainty surrounding the extrapolation from a LOAEL to a no-effects value, the extrapolation from laboratory to field conditions and interspecies and

intraspecies variations in sensitivity. The concentration of acrolein at the site of contact is the critical effect concentration and not the total cumulative dose, which would only be observed over a longer exposure period. Therefore, the Cassee *et al.* (1996) short-term study can be used to derive an ENEV for chronic exposure without incorporation of an additional application factor to account for the "less than chronic" exposure period. The choice of application factor is consistent with other environmental risk assessments in protecting against population-level effects. The resulting ENEV is 57 $\mu g/m^3$.

The hyperconservative quotient is calculated by dividing the EEV of 1.58 $\mu g/m^3$ by the ENEV as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{1.58\ \mu g/m^3}{57\ \mu g/m^3}$$

$$= 0.03$$

Since the hyperconservative quotient is less than one, it is unlikely that acrolein emissions will cause adverse effects on populations of terrestrial animals in Canada.

3.1.2.3 Discussion of uncertainty

There are a number of sources of uncertainty in this environmental risk assessment. Regarding environmental exposure, there could be concentrations of acrolein in Canada that are higher than those identified and used in this assessment. While no or limited data were found for Canadian soil, sediments and waters, significant concentrations of acrolein in these compartments are not expected because of the lack of non-pesticidal sources identified for these media and the unlikely partitioning of acrolein to these compartments from air. No data were found on acrolein concentrations in air near industrial point sources such as pulp and paper kraft mills and power plants. However, the measurements used in this assessment are considered acceptable because they were selected from an extensive set of recent air monitoring data that includes Montréal, Toronto and Vancouver. Large urban centres such as these are expected to have the highest acrolein emissions as a result of concentrated and continuous vehicle emissions and other sources.

Regarding effects of acrolein on terrestrial organisms, uncertainty inevitably surrounds the extrapolation from available toxicity data to potential ecosystem effects. While the toxicity data set for plants includes monocot and dicot species, it does not contain data on coniferous species, which are often particularly sensitive to air pollution. Also, the extent to which surface necrosis of the alfalfa plant translates into long-term ecological damage is not known. The toxicity data set for animals, composed of studies on herbivores and carnivores, is more extensive. However, no data were found for small bird species such as songbirds, which are considered to be more sensitive than small mammals (Brownlee, 1997). It is also not known to what extent the physiological effects observed in the rat are representative of long-term ecological damage. To counter these uncertainties, appropriate application factors were used in the environmental risk analysis to derive ENEVs.

Despite a few data gaps regarding the environmental concentrations and effects of acrolein, the data available at this time are considered adequate for drawing a conclusion on the environmental risk of acrolein in Canada.

3.2 CEPA 1999 64(b): Environment upon which life depends

Acrolein does not deplete stratospheric ozone, and its potential for contributing to climate change is negligible. Acrolein's potential for photochemical ozone creation (smog) is substantial, but the low quantities of acrolein in the atmosphere are unlikely to make its contribution significant relative to that of other smog-forming substances.

3.3 CEPA 1999 64(c): Human health

3.3.1 Estimated population exposure

Since adverse health effects of acrolein are primarily confined to the tissue of first contact (i.e., the respiratory and gastrointestinal tracts after inhalation and ingestion, respectively) and are concentration related, exposures via inhalation and ingestion have been assessed separately.

Available information is considered insufficient to characterize exposure of Canadians to acrolein via ingestion, since data on levels in food are limited to a small number of foodstuffs from countries other than Canada. While concentrations of acrolein as high as 0.1% by weight have been determined on rare occasions in some items from other countries, the remainder contained less than 40 µg acrolein/g and, in most cases, less than 1 µg/g. Acrolein has not been detected in two surveys of drinking water supplies in Ontario and the Atlantic provinces (detection limits <0.1 and 1–2.5 µg/L, respectively).

Available data are sufficient to serve as a basis for development of probabilistic estimates of 24-hour time-weighted average concentrations of acrolein in the air to which the general population in Canada is exposed. The estimates were developed using simple random sampling with Crystal Ball™ Version 4.0c (Decisioneering, Inc., 1996), multiple simulations of 10 000 trials and the data on concentrations in ambient and indoor air outlined in Table 4.

The general population is considered to be exposed to acrolein in air for a full 24 hours per day. When indoors, it is assumed that the general population is exposed to concentrations of acrolein similar to those in the indoor air of their homes, as there are insufficient data concerning concentrations in other indoor environments.

A mean time spent outdoors of three hours per day is assumed based on point estimates of time spent indoors and outdoors (EHD, 1997). The distribution of the time spent outdoors is arbitrarily assumed to be normal in shape with an arithmetic standard deviation of one hour.

Based on the assumptions underlying this scenario, between 5% and 10% of the population would be expected to be exposed to a 24-hour time-weighted average concentration of acrolein of at least 5 µg/m^3 (Table 4).

Based on limited available data on concentrations of acrolein in mainstream smoke of Canadian cigarettes (Rickert *et al.*, 1980), smokers would be directly exposed to considerably higher concentrations of acrolein.

3.3.2 Hazard characterization

3.3.2.1 Effects in humans

Data relevant to the assessment of the potential adverse effects of exposure to acrolein in humans are limited primarily to irritation. Based on early clinical studies of small numbers of volunteers exposed for short periods, ocular and nasal sensory irritation have been reported at concentrations as low as 0.13 mg acrolein/m^3 (Darley *et al.*, 1960) and 0.34 mg acrolein/m^3 (Weber-Tschopp *et al.*, 1977), respectively, while reduced respiratory rate has been observed at concentrations as low as 0.69 mg/m^3 (Weber-Tschopp *et al.*, 1977). The single identified epidemiological study (Bittersohl, 1975) is inadequate to serve as a basis for assessment of the carcinogenicity of acrolein.

Because of the limited nature of data in humans, hazard characterization and dose–response analysis for acrolein are based primarily on studies in animals.

3.3.2.2 Effects in experimental animals

Acrolein is highly acutely toxic, inducing irritation of the respiratory and gastrointestinal tracts and central nervous system depression at relatively low levels. Acrolein is also irritating to the skin following dermal exposure. Based on a single identified study, acrolein has not induced sensitization.

TABLE 4 Estimation of human exposure to acrolein

Statistical parameters of distributions of time-weighted average concentrations[1,2,3]	Probabilistic estimates from:	
	Simulation No. 1[4]	Simulation No. 2[5]
25th percentile	0.7 µg/m³	0.2 µg/m³
median	1.7 µg/m³	0.6 µg/m³
mean	2.3 µg/m³	1.3 µg/m³
75th percentile	3.6 µg/m³	1.7 µg/m³
90th percentile	5.3 µg/m³	3.7 µg/m³
95th percentile	5.9 µg/m³	5.0 µg/m³
95e percentile	5.9 µg/m³	5.0 µg/m³

[1] Distributions of 24-hour time-weighted average concentrations of acrolein were estimated from distributions of concentrations of acrolein in outdoor air and indoor air, using an assumed normal distribution of time per day spent outdoors (i.e., arithmetic mean of 21 hours per day and standard deviation of 1).

[2] Concentrations of acrolein in outdoor air were represented by the distribution of 24-hour concentrations from the NAPS program. Acrolein was detected (detection limit 0.05 µg/m³) in 57% of 2816 samples collected between 1989 and 1996 at 15 rural, suburban and urban sites in New Brunswick, Nova Scotia, Quebec, Ontario and British Columbia (Dann, 1998).

[3] Concentrations of acrolein in indoor air were represented by limited data of the Windsor Air Quality Study and subsequent sampling in Hamilton, Ontario (Bell, 1995, 1996, 1997; OMEE, 1994a,b). Acrolein was detected (detection limit 0.05 µg/m³) in 80% of 40 homes sampled in Windsor and Hamilton between 1991 and 1993.

[4] The distribution of concentrations of acrolein in indoor air used for Simulation No. 1 was the frequency histogram of concentrations in the 40 homes sampled in Windsor and Hamilton, Ontario.

[5] The geometric mean of the data set of concentrations in the 40 homes sampled in Windsor and Hamilton was 0.94 µg/m³ (geometric standard deviation, 7.07). A lognormal distribution with this geometric mean and standard deviation, truncated at 8.1 µg/m³ (i.e., the maximum concentration of acrolein measured in the indoor air of homes in the Windsor Air Quality Study), was used to represent the concentrations in indoor air in Simulation No. 2.

The effects of acrolein have been most extensively investigated following exposure by inhalation. Acrolein is cytotoxic; in short- and long-term inhalation studies conducted in several species (rats, mice, guinea pigs, hamsters, monkeys and dogs), at lowest concentrations, effects (degenerative histopathological lesions) have occurred consistently at the site of entry (i.e., the respiratory tract). Effects in other organs have also sometimes been observed, although inconsistently. This is consistent with the results of toxicokinetic studies in rodents and dogs, in which there has been a high degree of retention of inhaled acrolein at the site of contact.

In primarily early, repeated-exposure inhalation studies, in which examination of the respiratory tract was often not complete, species-related differences in sensitivity to acrolein have been observed, with adverse effects on the respiratory tract of dogs and rats at lowest concentrations (Lyon *et al.*, 1970; Feron *et al.*, 1978; Cassee *et al.*, 1996). With some exceptions, and although histopathological examination was, in some cases, restricted to one area of the respiratory tract, the pattern of lesions among species is generally similar to that observed for other aldehydes, with effects in rats at lower concentrations primarily confined to the nasal

cavity but affecting the more distal airways at higher concentrations, whereas effects in hamsters and guinea pigs are observed primarily in the bronchi and/or trachea.

Based on short-term, subchronic and chronic studies in a range of species, consistent with observations for inhalation, non-neoplastic histopathological effects (i.e., gastric lesions) have been observed at the portal of entry in rodents following repeated ingestion of acrolein (Newell, 1958; BSC, 1983; NTP, 1998); in other studies, effects including mortality, the cause of which is uncertain (in rats and mice), reduced body weight gain (in mice) and alterations in serum biochemical parameters (in rats and dogs) have also been observed (Parent *et al.*, 1991, 1992a,b). Ulcerative gastric lesions have also been observed in rats and rabbits following repeated oral administration of acrolein in developmental/reproductive toxicity studies (Parent *et al.*, 1992c, 1993).

Following dermal exposure, in a single identified study, acrolein was irritating to the skin and induced histopathological changes in the kidney and lung of rabbits (BSC, 1982a).

Available data are inadequate to serve as a basis for assessment of the carcinogenicity of acrolein following inhalation. Tumours have not been observed in the two relevant identified studies in rats and Syrian golden hamsters. However, these investigations were limited by small group sizes, limited exposure periods and single dose levels (Feron and Kruysse, 1977; LeBouffant *et al.*, 1980).

Available data concerning the chronic toxicity/carcinogenicity of acrolein following oral exposure include three bioassays in which a wide range of endpoints was examined following administration in Sprague-Dawley rats (Parent *et al.*, 1992a), CD-1 mice (Parent *et al.*, 1991) and beagle dogs (Parent *et al.*, 1992b) and an earlier study in male F344 rats in which only mortality and histopathology in selected tissues were examined (Lijinsky and Reuber, 1987). In the more extensive of these studies, there have been no increases in the incidence of tumours of any type, although mortality, the cause of which is unclear, was increased in rats and mice (Parent *et al.*, 1991, 1992a).

Reproductive/developmental studies include a one-generation reproductive study in rats exposed by inhalation; for ingestion, there is a two-generation reproductive study in rats and developmental toxicity studies in rabbits, rats and mice, all conducted by oral gavage. In these studies, effects have been confined generally to those at the site of contact in the parental generation.

Based on the limited number of investigations identified to date, neurological and immunological effects have been observed at concentrations that are similar to those that have induced respiratory tract damage.

Acrolein is mutagenic *in vitro*, inducing gene mutations in both bacteria and mammalian cells in culture, as well as structural chromosomal aberrations in CHO cells and sister chromatid exchanges in CHO cells and cultured human lymphocytes. Acrolein binds to DNA, forms DNA–protein cross-links and induces DNA single strand breaks in human fibroblasts and bronchial epithelial cells. In human fibroblasts, acrolein induces mutations at the HPRT locus in DNA repair-deficient cells from xeroderma pigmentosum patients but not in normal cells, supporting DNA damage as the primary mechanism for acrolein-induced mutagenesis.

In the single relevant study identified, there was no increase in DNA–protein cross-links in the nasal mucosa of Wistar rats exposed by inhalation to a single concentration of acrolein (Lam *et al.*, 1986). Although less relevant to the assessment of genotoxicity at the site of initial contact (i.e., where critical effects occur), *in vivo*

studies of the genotoxicity of acrolein at systemic sites are not extensive, and results have been negative (Epstein *et al.*, 1972; Kutzman, 1981; BSC, 1982b).

Available data are considered inadequate to assess whether acrolein has the ability to induce tumours or interact directly with DNA at the site of contact following inhalation. In view of the inadequacy of the identified inhalation carcinogenicity bioassays conducted to date, the documented genotoxicity of acrolein *in vitro* and the paucity of data on genotoxicity at the site of contact *in vivo*, further studies are desirable.

3.3.3 Dose–response analyses

3.3.3.1 Inhalation

In inhalation studies conducted in several species, the respiratory tract has consistently been affected at lowest concentrations, with similar effects noted in the critical studies, although with some species variation in sensitivity and principal site. In identified short-term investigations, degenerative changes (including disarrangement, necrosis, thickening, desquamation and hyperplasia) were observed in the nasal respiratory epithelium of rats exposed (by inhalation) to 0.25 ppm (0.57 mg/m^3) acrolein (Cassee *et al.*, 1996), while degenerative changes in the nasal olfactory epithelium, trachea, bronchi and/or lungs (in rats, mice, guinea pigs, dogs and monkeys) were noted at higher concentrations (i.e., ≥0.4 ppm or ≥0.9 mg/m^3) (Lyon *et al.*, 1970; Buckley *et al.*, 1984; Kutzman *et al.*, 1984, 1985; Leach *et al.*, 1987). In subchronic inhalation studies in several species (rats, rabbits, hamsters, guinea pigs, dogs and monkeys), dogs were most sensitive, with histopathological changes in the lungs, spleen and thyroid observed at 0.22 ppm (0.50 mg/m^3), considered to be the LOAEL, while in rats exposed to 1.4 ppm (3.2 mg/m^3), there were moderate histopathological changes in the nasal cavities and a significant reduction in growth (Lyon *et al.*, 1970; Feron *et al.*, 1978). Exposure–response has not been well characterized in the two identified limited chronic inhalation studies, in both of which rodents were exposed to a single concentration of acrolein (Feron and Kruysse, 1977; LeBouffant *et al.*, 1980). In these investigations, non-neoplastic lesions in the nasal cavities of hamsters were observed at 4.0 ppm (9.2 mg/m^3).

Since non-neoplastic effects in the respiratory tract of experimental animals are considered critical, a Tolerable Concentration (TC) for acrolein has been derived on the basis of a benchmark concentration (BMC) in rats, one of the most sensitive species, divided by an uncertainty factor. Despite differences in the anatomy and physiology of the respiratory tract in experimental animals and humans, respiratory tract defence mechanisms are similar. In addition, the limited available data indicate that there is sensory irritation (nasal and ocular) in humans exposed to low concentrations of acrolein vapour. Thus, it is reasonable to assume that the response of the human respiratory tract mucosa to acrolein will be qualitatively similar to that of experimental species.

There are two short-term inhalation studies in rats for which information was sufficient to derive BMCs[2] — namely, those of Cassee *et al.* (1996) and Kutzman *et al.* (1985). Effects were observed at lowest levels by Cassee *et al.* (1996); moreover, this was one of the few studies in which histopathological effects in both the upper and lower respiratory tract were examined. However, the number of administered concentrations was limited to two in addition to controls in this study; moreover, the number of animals examined in each of the exposed groups was small (5–6 in exposed and 19 in control). Therefore, TCs have been developed on the basis of both a BMC and effect level in the most

[2] All attempts were made to access original data to serve as the basis for BMCs for critical studies.

TABLE 5 Critical data and benchmark concentrations for acrolein

Lesion[1]	Incidence (at 0, 0.57, 1.53 mg/m^3)	BMC_{05} (mg/m^3)	$BMCL_{05}$ (mg/m^3)	χ^2	df	p-value
Disarrangement, necrosis, thickening and desquamation of the respiratory/ transitional epithelium	0/19, 1/5, 3/6	0.141	0.0564	0	0	1
Basal cell hyperplasia and/or increased mitotic figures in the respiratory/transitional epithelium	0/19, 0/5, 4/6	0.678	0.132	0	0	1

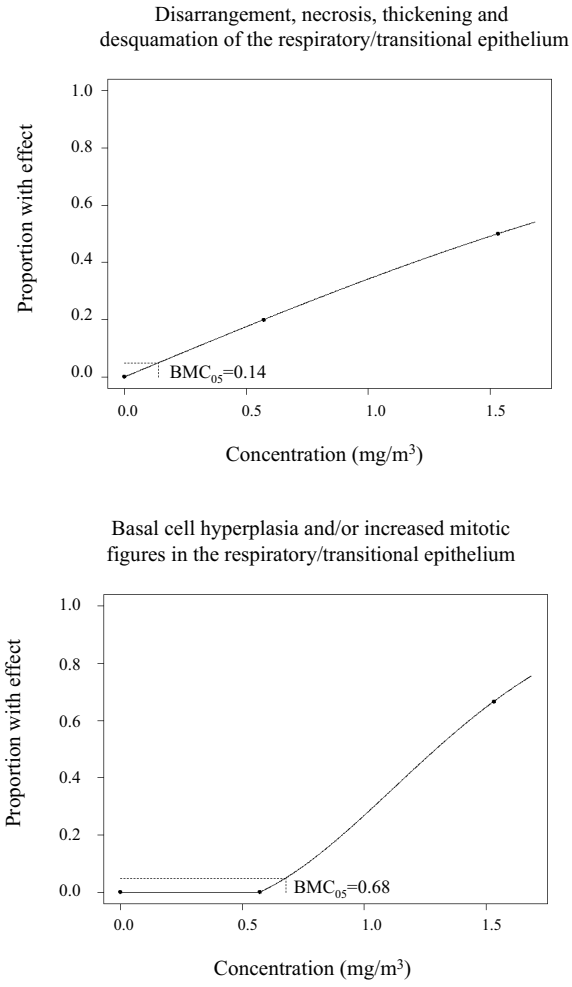
[1] Moderate and severe histopathological changes in nasal cavity of rats exposed (six hours per day) for three days (Cassee *et al.*, 1996).

sensitive investigation (i.e., Cassee *et al.*, 1996). The BMC from the Cassee *et al.* (1996) study is compared with a BMC reported by Kutzman *et al.* (1985), who used three administered concentrations and controls in their investigation. The TCs are compared with that which might be derived based on a LOAEL in dogs (Lyon *et al.*, 1970), another sensitive species for which available information is insufficient to develop a BMC.

For many types of effects, studies of short duration are not preferred as the basis for development of TCs. However, the investigation by Cassee *et al.* (1996) is the most sensitive of the inhalation studies in which the incidence of histopathological changes in the respiratory tract of experimental species has been reported. Although the data were derived from a short-term study, the type of degenerative changes observed in the nasal epithelium of male Wistar rats in this study was not dissimilar to those observed in longer-term bioassays conducted at similar concentrations in the same strain of rats (Feron *et al.*, 1978) and in hamsters (Feron and Kruysse, 1977). Thus, BMCs for non-neoplastic effects have been calculated for degeneration in the nasal respiratory epithelium of male Wistar rats exposed (by inhalation) to acrolein for three days, based on data from the critical study for characterization of concentration–response discussed above (Cassee *et al.*, 1996). The critical data are presented in Table 5. Analyses were limited to "moderate to severe" changes for those endpoints for which data were considered adequate to characterize exposure–response[3] — i.e., lesions where there were adequate data on incidence for two concentrations and controls: namely, "basal cell hyperplasia and/or increased mitotic figures in the respiratory/transitional epithelium" and "disarrangement, necrosis, thickening and desquamation of the respiratory/ transitional epithelium." On this basis, the BMC_{05} (the concentration associated with a 5% increase in the incidence of lesions in the nasal respiratory epithelium) for male Wistar rats for the most sensitive of these endpoints, modelled using THRESH (Howe, 1995), is 0.14 mg/m^3 (for moderate to severe disarrangement, necrosis, thickening and desquamation); the lower 95% confidence limit for this value ($BMCL_{05}$) is 0.06 mg/m^3 (Figure 2). For comparative purposes, the lowest BMC_{05} for lesions in the nasal turbinates reported by Kutzman (1981) and

[3] Where there was downturning or levelling at 100% of the dose–response curve, data were considered inadequate.

FIGURE 2 Benchmark concentrations[1] for acrolein



[1] Not adjusted for continuous exposure.

Kutzman *et al.* (1985) was 0.33 ppm (0.76 mg/m^3) ($BMCL_{05}$ = 0.12 ppm [0.27 mg/m^3]).

A TC has been developed on the basis of the BMC_{05} for non-neoplastic lesions in the nasal respiratory epithelium of rats as follows:

$$TC = \frac{0.14 \text{ mg/m}^3}{100} \times \frac{6}{24}$$

$$= 0.00035 \text{ mg/m}^3$$

$$= 0.4 \text{ µg/m}^3$$

where:

- 0.14 mg/m^3 is the concentration estimated to be associated with a 5% increase in disarrangement, necrosis, thickening, desquamation and hyperplasia in the nasal respiratory epithelium of rats exposed (by inhalation) to acrolein for three days (Cassee *et al.*, 1996); the lower 95% confidence limit was not utilized because of the instability in the data attributable primarily to small group sizes,
- 6/24 is the adjustment of intermittent (six hours per day) to continuous exposure. There are no data that provide direct evidence as to whether such an adjustment is suitable for acrolein, although it is likely that lesions would be more severe with continuous exposure, and
- 100 is the uncertainty factor (×10 for interspecies variation, ×10 for intraspecies variation). Available data are inadequate to further address toxicokinetic and toxicodynamic aspects of components of uncertainty with data-derived values. Also, consistent with data on respiratory irritation induced by other aldehydes and no indication for acrolein that severity of the critical effects increases with duration of exposure, an additional uncertainty factor to address the use of a short-term study as the basis for the TC is considered inappropriate. No additional quantitative element has been included to address limitations of the database, such as the lack of an adequate carcinogenesis bioassay via the inhalation route. While further studies of the potential relative roles of cytotoxicity, cell proliferation and DNA–protein cross-links observed *in vitro* are desirable, chronic studies via ingestion are available. Moreover, the TC is considered to be conservative in view of the fact that reductions in glutathione content have been observed in another strain of rats at concentrations less than the levels at which adverse effects have been observed in the study deemed critical here (McNulty *et al.*, 1984; Cassee *et al.*, 1996).

A TC has also been derived on the basis of the observed LOAEL in this study, as follows:

$$TC = \frac{0.57\ mg/m^3}{1000}$$

$$= 0.00057\ mg/m^3$$

$$= 0.6\ \mu g/m^3$$

where:

- 0.57 mg/m^3 is the LOAEL for disarrangement, necrosis, thickening, desquamation and hyperplasia in the nasal respiratory epithelium of rats exposed (by inhalation) to acrolein for three days (Cassee *et al.*, 1996), and
- 1000 is the uncertainty factor (×10 for interspecies variation, ×10 for intraspecies variation, ×10 for use of a LOAEL instead of a NOAEL and adjustment for intermittent to continuous exposure). Available data are inadequate to further address toxicokinetic and toxicodynamic aspects of components of uncertainty with data-derived values. Also, consistent with data on respiratory irritation induced by other aldehydes and no indication for acrolein that severity of the critical effects increases with duration of exposure, an additional uncertainty factor to address the use of a short-term study as the basis for the TC is considered inappropriate. No additional quantitative element has been included to address limitations of the database, such as the lack of an adequate carcinogenesis bioassay via the inhalation route. While further studies of the potential relative roles of cytotoxicity, cell proliferation and DNA–protein cross-links observed *in vitro* are desirable, chronic studies via ingestion are available. Moreover, the TC is considered to be conservative in view of the fact that reductions in glutathione content have been observed in another strain of rats at concentrations less than the levels at which adverse effects have been observed in the study deemed critical here (McNulty *et al.*, 1984; Cassee *et al.*, 1996). There are no data that provide direct evidence as to whether adjustment of intermittent (six hours per day) to continuous exposure is suitable for acrolein, although it is likely that lesions would be more severe with continuous exposure.

This TC is also considered to be protective based on a LOAEL of 0.22 ppm (0.50 mg/m^3) for non-neoplastic lesions in the lung (emphysema, congestion and focal vacuolation), thyroid (hyperplasia) and spleen (focal subcapsular hemorrhage) of dogs in the subchronic inhalation study by Lyon *et al.* (1970). Based on the application of an uncertainty factor of 1000 (×10 for interspecies variation, ×10 for intraspecies variation, ×10 for use of a LOAEL rather than a NOEL), the resulting value (i.e., 0.5 µg/m^3) is between 0.4 and 0.6 µg/m^3.

On the basis of limited available data in human studies, the TCs derived above (0.4–0.6 µg/m^3) are two or three orders of magnitude lower than the thresholds for odour perception (i.e., 70 µg/m^3) (Sinkuvene, 1970) and sensory irritation (i.e., 130 µg/m^3) (Darley *et al.*, 1960), respectively. Quantitative data on respiratory (versus sensory) irritation in humans are inadequate to draw conclusions concerning exposure–response.

3.3.3.2 Ingestion

Owing to uncertainties about the doses received by the animals exposed in drinking water, early studies are not informative in characterization of dose–response for effects of acrolein following ingestion (Newell, 1958; Lijinsky and Reuber, 1987), and results of the remaining studies are not consistent with respect to the nature of the effects observed at lowest doses or concentrations. In subchronic studies in rats and mice administered acrolein by gavage in solutions of methylcellulose (NTP, 1998), lesions in the stomach (including hyperplasia, necrosis, inflammation and hemorrhage) were observed at doses as low as 1.25 mg acrolein/kg-bw per day (administered concentrations of 0.25 mg/mL in rats and

0.125 mg/mL in mice). In mice exposed to higher concentrations by gavage in drinking water for 14 days, based on examination of a limited range of endpoints, effects were limited to thickening of the squamous portion of the gastric mucosa at 5.8 mg/kg-bw per day and above (administered concentration, 0.58 mg/mL) (BSC, 1983). In contrast, in chronic studies in which acrolein was administered by gavage in water to rats and mice at doses up to 2.5 mg/kg-bw per day (administered concentration, 0.25 mg/mL) and 4.5 mg/kg bw per day (administered concentration, 0.45 mg/mL), respectively, observed effects were limited to increased mortality, the cause of which was unclear (Parent *et al.*, 1991, 1992a); in a reproductive study in rats by the same investigators (Parent *et al.*, 1992c), however, lesions in the stomach were observed at lowest doses (3.0 mg/kg-bw per day; administered concentration, 0.6 mg/mL). In chronic studies in which dogs were administered gelatin capsules containing acrolein (Parent *et al.*, 1992b), alterations in serum biochemical parameters and (transient) clinical signs of toxicity were observed at 2.0 mg acrolein/kg-bw per day (considered to be the NOAEL). The reasons for these variations in results are unclear but have been suggested to be due to the variations in vehicles or, potentially, the development of tolerance in longer-term investigations. Available data are inconsistent with the latter hypothesis, however, in that lesions in the stomach were not noted at the 90-day interim sacrifice in the chronic study in rats (Parent *et al.*, 1992a); without systematic investigation of the progression of lesions, available data are inadequate to draw any conclusions in this regard.

Based on available data, it seems likely that effects at the site of contact following ingestion of acrolein will be limiting; moreover, the most sensitive study in rats and mice (NTP, 1998) is most informative in characterization of dose– and concentration–response in this regard. While effects were noted at administered concentrations of 0.25 mg/mL (rats) and 0.125 mg/mL (mice), there were no adverse effects in rats at 0.15 mg/mL (NTP, 1998). This latter value corresponded to a dose on a body weight basis of 0.75 mg/kg-bw per day. Since the effects at the site of contact are more likely related to administered concentration than dose, a TC based on administered concentration is derived here and the corresponding dose on a body weight basis presented for comparison.

A provisional[4] TC has been developed on the basis of the NOEL for non-neoplastic lesions in the gastrointestinal tract of rats as follows:

$$TC = \frac{0.15 \text{ mg/mL}}{100}$$

$$= 0.0015 \text{ mg/mL}$$

$$= 1.5 \text{ µg/L (corresponding to } 7.5 \text{ µg/kg-bw per day)}$$

where:

- 0.15 mg/mL is the NOEL for effects on the gastrointestinal tract (hyperplasia, necrosis, inflammation and hemorrhage) in rats exposed for 13 weeks to acrolein by gavage in a 5% solution of methylcellulose (NTP, 1998). Although it was considered that the dog (Parent *et al.*, 1992b) might be a more appropriate model for humans, due to its lack of forestomach, or that the TC could be based on the higher effect level in the glandular stomach of rats, in view of the nature of the effect, which relates to reactivity of the compound at the site of first contact, the more conservative effect level utilized here was selected, and
- 100 is the uncertainty factor (×10 for interspecies variation, ×10 for intraspecies variation). In view of the fact that there appears to be no indication that severity of the critical effects increases with duration of exposure, an additional uncertainty factor to address the use of a subchronic study as the basis for the TC is considered inappropriate.

[4] This value is considered provisional because it is based on preliminary results of the 13-week NTP (1998) study.

This TC is considered to be conservative in view of the fact that the critical concentration is based on a study in which administration was by gavage in a 5% solution of methylcellulose.

3.3.4 Human health risk characterization

Individuals in Canada appear to be exposed routinely to concentrations of airborne acrolein that are higher than the TC (for inhalation) of 0.4–0.6 µg/m^3. Indeed, mean, median and the 95th percentiles for distributions of 24-hour time-weighted average concentrations of acrolein in Canada exceed these values by up to 10-fold.

In addition, although available information is considered insufficient to characterize exposure of Canadians to acrolein in food, the range of concentrations in food measured in other countries (although dependent upon such factors as method of cooking) is within the range of the provisional TC for ingestion (1 µg/g versus 1.5 µg/mL, assuming a density of 1 g/mL).

3.3.5 Uncertainties and degree of confidence in human health risk characterization

Uncertainty associated with data on concentrations of acrolein in outdoor air from the 14 NAPS sites is judged to be low, since the analytical and sampling methodologies are among the best available for determining low concentrations of acrolein in air, all of the samples were analysed by a single specialized laboratory, the effects of diurnal variations are minimized by the 24-hour sampling duration, the data set is large (n = 2816) and reasonably current (i.e., 1989–1996), the concentrations of acrolein measured are consistent with concentrations reported for outdoor air in other Canadian and international studies, and the ratios of the concentrations of acrolein to concentrations of acetaldehyde and to concentrations of formaldehyde (both of which were also measured in these samples) are similar to ratios of concentrations in data from other studies. However, some uncertainty is expected, since the locations of the 14 NAPS sites were not determined by a random sampling scheme, at some sites the air is sampled at elevations higher than the breathing zone, and there is a relatively high proportion (i.e., 43%) among the 2816 samples in which acrolein was "not detected" (i.e., <0.05 µg/m^3). The greatest source of uncertainty in the estimates of exposure in air is attributable to lack of information concerning geographical population distribution in relation to the NAPS monitoring sites. However, samples from Canada's three major urban centres (i.e., Montréal, Toronto and Vancouver) account for 49% of the NAPS samples, and samples from three other cities (i.e., Saint John, Ottawa and Windsor) account for another 39%.

Uncertainty associated with data on concentrations of acrolein in indoor air from two studies in Canada is judged to be moderate, since the analytical and sampling methodologies are among the best available for determining low concentrations of acrolein in air, all of the samples were analysed by a single specialized laboratory, the sampling and analytical methodologies were the same as those employed for measuring the outdoor (ambient) acrolein concentrations in the NAPS data set, the effects of diurnal variations are minimized by the 24-hour sampling duration, the studies are reasonably current (i.e., 1991–1993), there were relatively few samples in which acrolein was not detected (i.e., 8 [or 20%] among the 40 samples), the concentrations of acrolein measured are consistent with limited data reported for residential indoor air in other studies, especially the more recent efforts, and the ratios of the concentrations of acrolein to concentrations of acetaldehyde and to concentrations of formaldehyde (both of which were also measured in these samples) are similar to ratios of concentrations in data from other studies. However, some uncertainty is introduced because this is a very small data set, the homes sampled were not selected by a random sampling scheme and often involved volunteers, homes in Windsor and Hamilton may not be representative of all homes in Canada, and indoor locations

other than home (e.g., work sites, public places, vehicle cabins) are not included.

Uncertainty concerning the time spent indoors by Canadians is judged to be low, since the estimate is based on the most current Canadian data, a random sampling scheme was used to obtain the time–activity data, and analysis of the data involved population weighting; however, the same mean time spent outdoors is assumed for Canadians of all age groups and in all regions of the country, a normal distribution is assumed for the hours per day spent outdoors, and the variance of the assumed normal distribution is also assumed (i.e., standard deviation of 1).

There is a high degree of uncertainty concerning the acrolein content of food currently consumed by Canadians. Data on concentrations in this medium are restricted to a very small number of food samples collected in other countries. Indeed, this information is considered inadequate for characterization of exposure of the general population in Canada except in a rather crude bounding sense. Monitored concentrations from these other countries seem high and are likely related to such factors as method of cooking, in view of the physical/chemical properties of the compound. Acrolein is not expected to partition into the fatty compartments of foods, and fugacity modelling does not predict significant bioconcentration.

There is a high degree of certainty that consumption of drinking water does not contribute significantly to the daily intake of acrolein by Canadians, based on sensitive measurements of Canadian water from numerous sources.

The degree of confidence in the database on toxicity that serves as the basis for the development of the TCs for inhalation and ingestion is moderate, although there is a relatively high degree of certainty that critical effects are those that occur at the site of entry. There are few relevant studies in humans, restricted primarily to early investigations of subjective reports of sensory irritation, and none in which histopathological changes in the upper respiratory tract have been examined following exposure to acrolein for comparison with the results of studies in animals. Confidence in the notion of the possible development of tolerance to the effects of acrolein following repeated exposure is low, owing to the lack of reliable data. The derived TCs for inhalation are highly conservative, compared with the limited data from studies in humans, where signs of nasal and ocular sensory irritation have been observed at levels as low as 130 µg acrolein/m^3. The carcinogenicity of inhaled acrolein has not been adequately investigated and warrants further study, although it is possible, based primarily on data for other aldehydes, that concentrations developed to protect against irritant effects at the site of contact may also be protective for possible carcinogenicity.

The degree of confidence in the provisional TC for ingestion will be increased by confirmation in more detailed reports of the preliminary results of the 13-week NTP (1998) study.

3.4 Conclusions

CEPA 1999 64(a): Based on available data, acrolein is not entering the environment in a quantity or concentration or under conditions that are having or that may have an immediate or long-term harmful effect on the environment or its biological diversity. Therefore, acrolein is not considered to be “toxic” as defined in Paragraph 64(a) of CEPA 1999.

CEPA 1999 64(b): Based on available data, acrolein is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the

environment on which life depends. Therefore, acrolein is not considered to be "toxic" as defined in Paragraph 64(b) of CEPA 1999.

CEPA 1999 64(c): Based on available data, acrolein is entering the environment in a quantity or concentrations or under conditions that constitute or may constitute a danger in Canada to human life or health. Therefore, acrolein is considered to be "toxic" as defined in Paragraph 64(c) of CEPA 1999.

Overall conclusion: Based on critical assessment of relevant information, acrolein is considered to be "toxic" as defined in Section 64 of CEPA 1999.

3.5 Considerations for follow-up (further action)

Since acrolein is considered to be "toxic" as defined in Section 64 of CEPA 1999, it is recommended that, as a matter of some priority, options to reduce exposure be investigated.

The inhalation of acrolein in indoor air is expected to be an important source of exposure for the general population. Concentrations of acrolein in indoor air are highly variable and depend largely on individual activities and circumstances, including the use of consumer products (e.g., cigarettes), combustion appliances, cooking and the infiltration of vehicle exhaust from attached garages. While data are inadequate to determine the relative contribution of each of these sources to the concentration of acrolein in indoor air — an area that deserves prioritization for further investigation — the highest concentrations of acrolein in indoor air have generally been detected in indoor environments contaminated with environmental tobacco smoke.

For the general population, the contribution of ambient air to overall exposure to inhaled acrolein is expected to be small compared with the contribution from indoor air (and cigarette smoking). However, for populations residing in the vicinity of industrial point sources or in locations heavily impacted by vehicular exhaust, ambient air may be an important source of exposure to acrolein via inhalation. Based upon the available data (see Table 2), motor vehicle exhaust may be the principal anthropogenic source of acrolein released into the air in Canada, although the relative contribution of off-road motor vehicles is unknown.

Although pesticidal uses are not the focus of this assessment, the low concentrations that kill sensitive aquatic organisms (such as the LC_{50} of 7 µg/L in the frog tadpole) in relation to concentrations applied (1–15 µg/L) to effectively control aquatic weeds in irrigation canals are noted. It is recommended, therefore, that the use of acrolein to control aquatic weeds be reviewed by appropriate authorities under the *Pest Control Products Act*, in light of this assessment and other relevant considerations.

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APPENDIX A SEARCH STRATEGIES EMPLOYED FOR IDENTIFICATION OF RELEVANT DATA

Environmental assessment

Data relevant to the assessment of whether acrolein is "toxic" to the environment under CEPA were identified from existing review documents, published reference texts and on-line searches conducted between January and May 1996 of the following databases: Aqualine (Water Research Centre, Buckinghamshire, 1990–1996), ASFA (Aquatic Sciences and Fisheries Abstracts, Cambridge Scientific Abstracts; 1996), BIOSIS (Biosciences Information Services; 1990–1996), CAB (Commonwealth Agriculture Bureaux; 1990–1996), CESARS (Chemical Evaluation Search and Retrieval System, Ontario Ministry of the Environment and Michigan Department of Natural Resources; 1996), Chemical Abstracts (Chemical Abstracts Service, Columbus, Ohio; 1990–1996), CHRIS (Chemical Hazard Release Information System; 1964–1985), Current Contents (Institute for Scientific Information; 1990–1992, 1996), ELIAS (Environmental Library Integrated Automated System, Environment Canada library; January 1996), Enviroline (R.R. Bowker Publishing Co.; November 1995 – May 1996), Environmental Abstracts (1975 – February 1996), Environmental Bibliography (Environmental Studies Institute, International Academy at Santa Barbara; 1990–1996), GEOREF (Geo Reference Information System, American Geological Institute; 1990–1996), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine; 1990–1996), Life Sciences (Cambridge Scientific Abstracts; 1990–1996), NTIS (National Technical Information Service, U.S. Department of Commerce; 1990–1996), Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1996), POLTOX (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1995), RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health; 1996), Toxline (U.S. National Library of Medicine; 1990–1996), TRI93 (Toxic Chemical Release Inventory, U.S. Environmental Protection Agency, Office of Toxic Substances; 1993), USEPA-ASTER (Assessment Tools for the Evaluation of Risk, U.S. Environmental Protection Agency; up to December 21, 1994), WASTEINFO (Waste Management Information Bureau of the American Energy Agency; 1973 – September 1995), Water Resources Abstracts (U.S. Geological Survey, U.S. Department of the Interior; 1990–1996).

A survey of Canadian industry was carried out under authority of Section 16 of CEPA (Environment Canada, 1997c). Companies were required to provide information on uses, releases, environmental concentrations, effects or other data on acrolein that were available to them if they met the trigger quantity of 50 kg acrolein per year. Reveal Alert was used to maintain an ongoing record of the current scientific literature pertaining to the potential environmental effects of acrolein. Data obtained after May 1998 were not considered in this assessment unless they were critical data received during the 60-day public review of the report (May 1 to June 29, 1999).

Health assessment

Data relevant to the assessment of the potential risks of acrolein to human health were identified through evaluation of existing review documents of the U.S. Environmental Protection Agency (U.S. EPA, 1987), the Agency for Toxic Substances and Disease Registry (ATSDR, 1990), the International Programme on Chemical Safety (IPCS, 1992) and the International Agency for

Research on Cancer (IARC, 1979, 1985, 1987, 1995). A survey of Canadian industries was conducted under Section 16 of CEPA, in which companies were required to supply information concerning the use, release, environmental levels and toxicological effects of acrolein (Environment Canada, 1997c). To identify additional relevant exposure and toxicological data, literature searches on acrolein were conducted using the strategy of searching by its name or CAS registry number in the following databases: Canadian Research Index, CCRIS (Chemical Carcinogenesis Research Information System, U.S. National Cancer Institute), Dialog, EMIC (Environmental Mutagen Information Center database, Oak Ridge National Laboratory), GENE-TOX (Genetic Toxicology, U.S. Environmental Protection Agency), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine), IRIS (Integrated Risk Information System, U.S. Environmental Protection Agency) and RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health). Its name, registry number and major synonyms were searched in the Toxline (U.S. National Library of Medicine; 1985–1998) and Medline (U.S. National Library of Medicine; 1989–1998) databases. The CAS registry number was searched in the Toxnet (1985–1997) database. The EMBASE database (on-line version of Excerpta Medica; 1985–1997) was searched using the name, registry number and major synonyms.

Data relevant to the assessment of whether acrolein is "toxic" to human health obtained after October 1998 have not been included.