



**HEALTH-BASED GUIDANCE VALUES
FOR SUBSTANCES ON
THE SECOND PRIORITY SUBSTANCES LIST**

Our mission is to help the people of Canada
maintain and improve their health.

Health Canada

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Minister of Health

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pour les substances figurant sur la deuxième liste des
substances d'intérêt prioritaire*

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Preface

The guidance values presented within this booklet are intended to form, in part, the basis for development of reference points against which the quality of various environmental media can be judged. They were developed on the basis of information reviewed for assessments conducted for substances on the second Priority Substances List (PSL2) under the *Canadian Environmental Protection Act, 1999* (CEPA 1999). Tolerable Concentrations (TCs) provide a health-based goal against which levels of various pollutants in indoor or ambient air can be compared. Similarly, Tumorigenic Concentration_{05S} (TC_{05S}) divided by a suitable margin also provide a benchmark against which the quality of ambient or indoor air can be judged with respect to potential carcinogenicity. Tolerable Intakes (TIs) and Tumorigenic Dose_{05S} (TD_{05S}) (the latter divided by a suitable margin) provide a reference against which amounts of contaminants ingested in, for example, drinking water or food can be compared.

The PSL2 assessments on which the guidance values presented herein are based were externally peer reviewed by identified experts. Following external review, they were approved by the Environment Canada/Health Canada CEPA Management Committee. A draft of this booklet was circulated for information and comment within Health Canada and externally reviewed by Dr. V.C. Armstrong, consultant.

These guidance values are derived solely from assessment of toxicological and epidemiological data for the ingestion and inhalation routes of exposure and take into consideration potential effects on human health only. Although dermal contact may, in some cases, also contribute significantly to total exposure to environmental contaminants, this route has not been addressed herein, due principally to limitations of the available data that serve as a basis for development of health-based guidance in this area.

It should also be emphasized that the guidance values presented herein do not take into account any considerations related to risk management, such as feasibility of attainment or costs of measurement and control. Moreover, potential for exposure by ingestion via more than one medium (e.g., drinking water and food) needs to be considered in the development of media-specific values from the TIs and TD_{05S} presented herein. A detailed discussion of the allocation of TIs or TD_{05S} as a basis for development of media-specific guidance values is included in IPCS (1994).

Every effort has been made to present information in this booklet as accurately as possible without unduly delaying its publication. However, should errors be noted or should readers wish to comment on the suitability of derived values included herein, relevant information should be submitted to the Existing Substances Division for consideration at:

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1. Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) authorizes the Ministers of the Environment and Health to investigate a wide variety of substances that may contaminate the environment and cause adverse effects on the environment and/or on human health. Under the Act, assessments were completed in 2000 for the 25 environmental contaminants (or groups thereof) on the second Priority Substances List (PSL2).

Based on the assessments conducted for PSL2 substances, health-based Tolerable Intakes/Concentrations (TIs/TCs) and Tumorigenic Dose_{05S}/Concentration_{05S} (TD_{05S}/TC_{05S}) have been developed and are presented herein.

Information on the classification of the weight of evidence of carcinogenicity, the nature of the critical effects, the critical study and the size of the uncertainty factor incorporated for non-neoplastic effects for each substance is included in the respective Assessment Report, available on request from:

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Synopses of the Assessment Reports are currently available on-line at <http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl2.htm>, whereas the full Assessment Reports will soon be available on the Internet at <http://www.ec.gc.ca/substances/ese/eng/psap/final/main.cfm>. A detailed description of the approach to human health risk assessment for Priority Substances is included in Health Canada (1994), available on-line at <http://www.hc-sc.gc.ca/hecs-sesc/exsd/pdf/approach.pdf>.

Guidance values developed herein are based on lifetime exposure, and short-term excursions above these values do not necessarily imply that exposure constitutes an undue risk to health. The amount by which and period for which TCs/TIs can be exceeded without posing a health risk must be considered on a case-by-case basis, taking into account the nature of the effects of the specific substance.

For carcinogenic effects for which the weight of evidence indicates that the mode of action involves direct interaction with genetic material, it is assumed that there is some probability of harm to human health at any level of exposure and that continuing efforts should be made, therefore, to reduce exposure to such compounds by the greatest extent possible. However, incremental risks associated with exposure to low levels of such substances (i.e., TD_{05S}/TC_{05S} divided by a suitable margin) may be sufficiently small so as to be essentially negligible compared with other risks encountered in society.

Presentation of the guidance values herein should not be regarded as implying that the quality of various media may be degraded to specified levels. Indeed, continuous efforts should be made to ensure that the media through which humans are exposed are of the highest possible quality.

Information on uncertainties in the data that served as the basis for the development of TIs/TCs and TD_{05S}/TC_{05S} is presented in the relevant tables. This information is relevant to the characterization of the degree of confidence in and flexibility in application of derived guidance values.

2. Explanation of Terms

Different approaches were adopted for assessments of those chemicals for which the weight of evidence indicated that the critical effect (cancer) is mediated through direct interaction with genetic material, resulting in a probability of harm at all levels of exposure, and those for which there is assumed to be a threshold (i.e., a level of exposure below which there is considered to be no risk). For substances for which the critical effect is considered to have a threshold, TIs or TCs have been developed by dividing effect levels observed in studies in exposed populations or animal species by uncertainty factors.

For carcinogenic effects for which the weight of evidence indicates that the mode of action involves direct interaction with genetic material, potency is generally expressed as the concentration (TC_{05}) or dose (TD_{05}) that induces a 5% increase in the incidence of, or deaths due to, tumours considered to be associated with exposure, observed in epidemiological studies in human populations or bioassays in experimental animals.

Wherever data are sufficient, based on understanding of mode of action, relevant toxicokinetic or toxicodynamic information is incorporated in lieu of default values into TIs/TCs or quantitative estimates of potency to address interspecies differences or human variability.

For those substances for which values for both carcinogenic and non-carcinogenic effects are presented, it is recommended that the more conservative of the TD_{05S}/TC_{05S} divided by a suitable margin or TIs/TCs be adopted, in part, as the basis for development of reference points against which the quality of various media can be judged.

In general, depending upon the sources and physical/chemical properties of a substance, exposure via one of the routes addressed herein (i.e., inhalation and ingestion) for specific chemical substances will predominate. Where, for specific substances, there is potential for significant intake via both ingestion and inhalation, however, it is important that this be taken into account in the development of media-specific values (i.e., exposure via inhalation and ingestion should, in total, not exceed the TI/TC or TD₀₅/TC₀₅ divided by a suitable margin; see examples in IPCS, 1994). As a basis for consideration of relevant media, proportions of total exposure contributed via each medium based on estimates of human exposure to the PSL2 substances are presented in Section 3.3.

2.1 Tolerable Intake (TI)

TIs (Section 3.1), expressed on a body weight basis (e.g., mg/kg-bw per day), are the total intakes by ingestion to which it is believed that a person can be exposed daily over a lifetime without deleterious effect. Absolute values per day for various age groups can be developed by multiplying the TI by the average body weight of the age group under consideration. It should be noted, however, that exceedance of such calculated intakes by a particular age group for a small proportion of the life span does not necessarily imply that exposure constitutes an undue risk to health. In assessments for Priority Substances under CEPA 1999, mean body weights of various age groups were considered to be as follows (EHD, 1998):

Age	Body weight (kg)
0–6 months	7.5
7 months – 4 years	15.5
5–11 years	31
12–19 years	59.4
20–59 years	70.9
60+ years	72

2.2 Tolerable Concentration (TC)

TCs (Section 3.1) (often expressed in mg/m³) are concentrations (generally airborne) to which it is believed that a person can be exposed continuously over a lifetime without deleterious effect.

2.3 Tumorigenic Dose₀₅ (TD₀₅)

For Existing Substances under CEPA 1999, tumorigenic potencies for carcinogens acting through direct interaction with genetic material are estimated in the range of the experimental

data in animal species or epidemiological studies and expressed generally as the TD₀₅ (Section 3.2). The TD₀₅ is the total intake (often expressed in mg/kg-bw per day) associated with a 5% increase in the incidence of, or mortality due to, tumours, scaled, where appropriate, to reflect adequate quantitative data on interspecies variations in toxicokinetics or toxicodynamics.

This measure of dose–response is considerably more accurate than estimates of risk predicted based on extrapolation over many orders of magnitude from experimental studies in animals to the much lower levels of contaminants to which the general population is likely to be exposed, generally in the absence of information on mode of action. In view of these considerable uncertainties, these risks are not specified in absolute terms of predicted incidence or numbers of excess deaths per unit of the population.

Since it is assumed, for carcinogens acting through direct interaction with genetic material, that there is some probability of harm to human health at any level of exposure, continuing efforts should be made to reduce exposure to such compounds to the greatest extent possible. However, incremental risks associated with exposure to low levels of such substances may be sufficiently small so as to be essentially negligible compared with other risks encountered in society. As examples, therefore, values based on division of the TD₀₅ by margins of 5000 and 50 000 are presented in Section 3.2. These values afford protection similar to that associated with the range of low-dose risk estimates generally considered by various agencies to be “essentially negligible” (i.e., 10⁻⁵ to 10⁻⁶).

It should not be inferred that Health Canada deems any of these values as “acceptable” from a societal viewpoint. As indicated above, the department encourages *reduction, to the extent possible, of exposure of the general public* to compounds that are carcinogenic with likely mode of action involving direct interaction with genetic material.

As is the case for TIs, absolute values per day for various age groups can be developed by multiplying the TI by the average body weight of the age group under consideration, although exceedance of these absolute values by a particular age group (constituting a small proportion of the life span) does not necessarily imply that exposure constitutes an undue risk to health.

2.4 Tumorigenic Concentration₀₅ (TC₀₅)

The TC₀₅ (Section 3.2) is the concentration, generally in air (expressed, for example, in mg/m³), associated with a 5% increase in the incidence of, or mortality due to, tumours. As for the TD₀₅ values described above, as examples, values based on division of the TC₀₅ by margins of 5000 and 50 000 are presented in Section 3.2. These afford protection similar to that associated with the range for low-dose risk estimates generally considered by various agencies to be “essentially negligible” (i.e., 10⁻⁵ to 10⁻⁶).

Again, Health Canada does not deem any of these values as “acceptable” from a societal viewpoint, but rather, as indicated above, encourages *reduction, to the extent possible, of exposure of the general public* to compounds that are carcinogenic with likely mode of action involving direct interaction with genetic material.

3. Summary of Values

Guidance values for PSL2 substances based upon non-carcinogenic and carcinogenic effects are given in Sections 3.1 and 3.2, respectively. Estimates of exposure to PSL2 substances are provided in Section 3.3.

Health-based Guidance Values for Substances on the Second Priority Substances List

3.1 Tolerable Concentrations/Intakes for Priority Substances

Substance [CAS ¹ No.]	Cut-off date for literature review	Guidance values based upon non-carcinogenic effects		Basis of TI/TC	Uncertainties/degree of confidence
		TI (oral)	TC (inhalation)		
Acetaldehyde [75-07-0]	April 1998		390 µg/m ³	Based upon the 95% lower confidence limit (LCL) of a benchmark concentration (BMC) associated with a 5% increase in non-neoplastic lesions (BMCL ₀₅) in nasal olfactory epithelium of male Wistar rats exposed for 4 weeks (Appelman et al., 1982, 1986)	The degree of confidence in the database on toxicity (animals) that serves as the basis for the development of the TC for inhalation is moderate, although there is a relatively high degree of confidence that critical effects occur at the initial site of exposure.
Acrolein [107-02-8]	October 1998	1.5 µg/mL drinking water (provisional) ²	0.4 µg/m ³	TI and TC based, respectively, upon: - preliminary results of a 13-week gavage study in rats (NTP, 1998a); effects in the gastrointestinal tract included hyperplasia, necrosis, inflammation and hemorrhage - BMC associated with a 5% increase (BMC ₀₅) in disarrangement, necrosis, thickening, desquamation and hyperplasia in nasal respiratory epithelium of rats exposed by inhalation for 3 days (Cassee <i>et al.</i> , 1996)	The degree of confidence in the database on toxicity (animals) that serves as the basis for the development of the TC for inhalation and TI for ingestion is moderate, although there is a relatively high degree of certainty that critical effects are those that occur at the site of entry.
2-Butoxyethanol [111-76-2]	October 1999		11 mg/m ³	Based upon the lower end of the range of BMCs for hematological effects in a chronic inhalation study in rats (NTP, 1998b)	There is a moderate degree of certainty that hematotoxicity is the principal critical endpoint for 2-butoxyethanol based on studies in animals.
Butylbenzylphthalate [85-68-7]	April 1998	1.3 mg/kg-bw per day		Based upon the 95% LCL for a benchmark dose (BMD) associated with a 5% increase in the incidence of pancreatic lesions (BMDL ₀₅) in male rats in a subchronic dietary assay (Hammond <i>et al.</i> , 1987)	The degree of confidence in the database on toxicity (animals) that serves as the basis for development of the TI is moderate to high. Although available data do not support the conclusion that butylbenzylphthalate is estrogenic, the potential for other endocrine-

¹ Chemical Abstracts Service.

² This value is considered provisional because it is based upon preliminary results of the 13-week NTP (1998a) study. Note that incorrect units were used in Environment Canada and Health Canada (2000b).

Health-based Guidance Values for Substances on the Second Priority Substances List

Substance [CAS ¹ No.]	Cut-off date for literature review	Guidance values based upon non-carcinogenic effects		Basis of TI/TC	Uncertainties/degree of confidence
		TI (oral)	TC (inhalation)		
					mediated effects cannot be precluded at this time. Compounds such as phthalates are likely early candidates for consideration of endocrine disruption once more sensitive frameworks for testing and assessment are developed.
Carbon disulfide [75-15-0]	August 1999		100 µg/m ³	Based upon the BMCL ₀₅ estimated for a 5% adverse response for peroneal motor nerve conduction velocity (original data obtained for the assessment) from the cross-sectional study of U.S. viscose rayon workers with long-term exposure to carbon disulfide reported by Johnson <i>et al.</i> (1983)	The degree of confidence in the available data regarding the effects of exposure to carbon disulfide is moderate. There is a good degree of confidence in the results of the critical epidemiological study that served as the basis for exposure–response analysis.
Chloroform [67-66-3]	October 1999	37 mg/L drinking water 95% LCL = 12 mg/L	9.8 mg/m ³ 95% LCL = 3.4 mg/m ³	Determined by physiologically based pharmacokinetic (PBPK) modelling of data on hepatic fatty cysts in dogs in a chronic study (Heywood <i>et al.</i> , 1979); lifetime exposure to either medium is predicted to result in a 5% increase in fatty cysts	The degree of confidence that critical effects in animal species are well characterized in the available database is high.
N,N-Dimethylformamide [68-12-2]	June 2000		0.1 mg/m ³	Based upon Lowest-Observed-Adverse-Effect Level (LOAEL) of 21 mg/m ³ for increases in serum hepatic enzymes in exposed workers (Cirila <i>et al.</i> , 1984; Fiorito <i>et al.</i> , 1997)	There is a high degree of confidence based on studies in both humans and experimental animals that the liver is the target organ for toxicity of N,N-dimethylformamide. Exposure–response analysis was based upon epidemiological data.
Ethylene glycol [107-21-1]	January 2000	0.05 mg/kg-bw per day ³		Based upon BMD ₀₅ for tubular damage in the kidney of male rats in the study (16 weeks) in which exposure–response was best characterized (Gaunt <i>et al.</i> , 1974)	The degree of confidence in the database on toxicity that serves as the basis for development of the TI is moderate. Critical data gaps related to progression of renal lesions in long-term studies were identified.

³ There is uncertainty associated with this TI, due to limitations of the available studies.

Health-based Guidance Values for Substances on the Second Priority Substances List

Substance [CAS ¹ No.]	Cut-off date for literature review	Guidance values based upon non-carcinogenic effects		Basis of TI/TC	Uncertainties/degree of confidence
		TI (oral)	TC (inhalation)		
Formaldehyde [50-00-0]	January 1999	2.6 mg/L of ingested products	≤0.12 mg/m ³	<p>Oral: Based upon the No-Observed-Effect Level (NOEL) for histopathological changes in the gastrointestinal tract in a 2-year drinking water assay in rats (Til <i>et al.</i>, 1989)</p> <p>Inhalation: Only a very small proportion of the population experiences symptoms of irritation following exposure to this concentration. This is less than the levels that reduce mucociliary clearance in the anterior portion of the nasal cavity in available clinical studies in human volunteers and induce histopathological effects in the nasal epithelium in cross-sectional studies of exposed workers. Additional investigation of preliminary indication of effects on pulmonary function in children in the residential environment associated with lower concentrations (48–72 µg/m³) (Krzyzanowski <i>et al.</i>, 1990) is warranted.</p>	The degree of confidence that critical effects are well characterized is high. The degree of confidence in the database that supports an obligatory role of regenerative proliferation in the induction of nasal tumours in rats is moderate to high. Dose–response is based on a biologically motivated case-specific model that incorporates considerable biological information.
Hexachlorobutadiene [87-68-3]	December 1996	0.34 µg/kg-bw per day		Based upon the BMDL ₀₅ for increase in renal tubular regeneration in mice administered hexachlorobutadiene for 13 weeks via the diet (Yang <i>et al.</i> , 1989; NTP, 1991)	The degree of confidence in the database on toxicity (animals) that serves as the basis for development of the TI is moderate to high.
Phenol [108-95-2]	September 1997	120 µg/kg-bw per day		Based upon a No-Observed-Adverse-Effect Level (NOAEL) of 12 mg/kg-bw per day (Lowest-Observed-Effect Level [LOEL] = 40 mg/kg-bw per day) for histopathological effects in kidneys in female rats in a 14-day gavage study (Berman <i>et al.</i> , 1995)	The degree of confidence in the database on toxicity (animals) that serves as the basis for development of the TI is low to moderate. The epidemiological data are inadequate. There are also no recent repeated-dose toxicity studies in animals in which a range of endpoints has been well characterized by current standards, with the exception of developmental toxicity. In addition, available data on reproductive effects are quite limited.

Health-based Guidance Values for Substances on the Second Priority Substances List

3.2 Tumorigenic Doses/Concentrations for Priority Substances

Substance [CAS No.]	Cut-off date for literature review	Estimate of carcinogenic potency		Comment (critical study)	Uncertainties	TD ₀₅ or TC ₀₅ divided by 5000 and 50 000
		TD ₀₅ (ingestion)	TC ₀₅ (inhalation, unless otherwise specified)			
Acetaldehyde [75-07-0]	April 1998		86 mg/m ³ 95% LCL = 28 mg/m ³	Increased incidence of nasal adenocarcinomas and squamous cell carcinomas (combined) in male Wistar rats exposed for up to 28 months (Woutersen <i>et al.</i> , 1986)	The greatest source of uncertainty in the health assessment is the relative lack of information concerning the potential roles of cytotoxicity, proliferation and induction of DNA-protein cross-links in the carcinogenicity of this compound at high concentrations and implications for dose-response for the general population.	TC ₀₅ : 0.0172 mg/m ³ ; 0.00172 mg/m ³
						95% LCL of TC ₀₅ : 0.0056 mg/m ³ ; 0.00056 mg/m ³
Acrylonitrile [107-13-1]	April 1998	2.3 mg/kg-bw per day 95% LCL = 1.4 mg/kg-bw per day	6 mg/m ³ 95% LCL = 4.5 mg/m ³	Human equivalent values, based upon quantitative estimates of potency derived on the basis of: (a) incidence of tumours in brain and/or spinal cord observed in a drinking water assay with rats (Bio/Dynamics Inc., 1980) (b) incidence of tumours in brain and/or spinal cord in an inhalation assay with rats (Quast <i>et al.</i> , 1980)	The degree of confidence in the database on toxicity of acrylonitrile is moderate. The databases on non-cancer toxicity and carcinogenicity of acrylonitrile in laboratory animals are limited.	TD ₀₅ : 0.00046 mg/kg-bw per day; 0.000046 mg/kg-bw per day
						95% LCL of TD ₀₅ : 0.00028 mg/kg-bw per day; 0.000028 mg/kg-bw per day
						TC ₀₅ : 0.0012 mg/m ³ ; 0.00012 mg/m ³

Health-based Guidance Values for Substances on the Second Priority Substances List

Substance [CAS No.]	Cut-off date for literature review	Estimate of carcinogenic potency		Comment (critical study)	Uncertainties	TD ₀₅ or TC ₀₅ divided by 5000 and 50 000
		TD ₀₅ (ingestion)	TC ₀₅ (inhalation, unless otherwise specified)			
						95% LCL of TC ₀₅ : 0.0009 mg/m ³ 0.00009 mg/m ³
1,3-Butadiene [106-99-0]	April 1998		TC ₀₁ ⁴ = 1.7 mg/m ³	Based upon an epidemiological study of the incidence of leukemias in 15 649 workers (Delzell <i>et al.</i> , 1995)	There is some degree of uncertainty that the epidemiological evidence for the association between butadiene and leukemia satisfies criteria for causality; however, there is a high degree of confidence that butadiene is likely to be carcinogenic in humans and induces tumours through direct interaction with genetic material. Estimates of carcinogenic potency are based on epidemiological data.	TC ₀₁ : 0.00034 mg/m ³ ; 0.000034 mg/m ³
Chloroform [67-66-3]	October 1999	3247 mg/L drinking water 95% LCL = 2363 mg/L drinking water	147 mg/m ³ 95% LCL = 74 mg/m ³	Determined by PBPK modelling of data on renal tumours in rats in a drinking water assay (Jorgenson <i>et al.</i> , 1985); lifetime exposure to either medium is predicted to result in a 5% increase in tumour risk	The degree of confidence that critical effects in animal species are well characterized in the available database is high. The degree of confidence in the database that supports an obligatory role of sustained cytotoxicity in the carcinogenicity in rats and mice of chloroform is high.	TD ₀₅ : 0.6494 mg/L drinking water 0.06494 mg/L drinking water 95% LCL of TD ₀₅ : 0.4726 mg/L drinking water 0.04726 mg/L drinking water TC ₀₅ : 0.0294 mg/m ³ ; 0.00294 mg/m ³

⁴ Estimates of potency for 1,3-butadiene were calculated on the basis of data from epidemiological studies. The TC₀₁ is the ambient level of exposure at which the excess risk is equal to 0.01 at 70 years.

Health-based Guidance Values for Substances on the Second Priority Substances List

Substance [CAS No.]	Cut-off date for literature review	Estimate of carcinogenic potency		Comment (critical study)	Uncertainties	TD ₀₅ or TC ₀₅ divided by 5000 and 50 000
		TD ₀₅ (ingestion)	TC ₀₅ (inhalation, unless otherwise specified)			
						95% LCL of TC ₀₅ : 0.0148 mg/m ³ ; 0.00148 mg/m ³
Ethylene oxide [75-21-8]	January 1999		2.2 mg/m ³ 95% LCL = 1.5 mg/m ³	Based upon the incidence of mononuclear leukemia in female F344 rats in a 2-year inhalation assay (Snellings <i>et al.</i> , 1984; Garman <i>et al.</i> , 1985; Garman and Snellings, 1986)	There is some uncertainty concerning the relevance to humans of mononuclear cell leukemias in F344 rats; however, potencies based on other tumours would be similar, and there is a high degree of confidence that ethylene oxide is likely to be carcinogenic in humans and induces tumours through direct interaction with genetic material.	TC ₀₅ : 0.00044 mg/m ³ ; 0.000044 mg/m ³
						95% LCL of TC ₀₅ : 0.0003 mg/m ³ ; 0.00003 mg/m ³
Formaldehyde [50-00-0]	January 1999		The predicted additional risk of upper respiratory tract cancer for non-smokers associated with 80 years of continuous exposure to 1.2 µg/m ³ is 2.3×10^{-10} ; risk at 120 µg/m ³ is 2.7×10^{-8}	Based upon the incidence of nasal squamous tumours in rats exposed for up to 24 months (Monticello <i>et al.</i> , 1996); calculated from a two-stage clonal growth model (CIIT, 1999)	The degree of confidence that critical effects are well characterized is high. The degree of confidence in the database that supports an obligatory role of regenerative proliferation in the induction of nasal tumours in rats is moderate to high, although the mechanisms of carcinogenicity of formaldehyde are unclear.	
N-Nitrosodimethylamine [62-75-9]	August 1999	34 µg/kg-bw per day 95% LCL = 18 µg/kg-bw per day		Based upon the incidence of hepatic biliary cystadenoma in female Colworth-Wistar rats in a drinking water assay (Brantom, 1983; Peto <i>et</i>	There is a high degree of certainty that NDMA induces tumours through direct interaction with DNA.	TD ₀₅ 0.0068 µg/kg-bw per day; 0.00068 µg/kg-bw per day

Health-based Guidance Values for Substances on the Second Priority Substances List

Substance [CAS No.]	Cut-off date for literature review	Estimate of carcinogenic potency		Comment (critical study)	Uncertainties	TD ₀₅ or TC ₀₅ divided by 5000 and 50 000
		TD ₀₅ (ingestion)	TC ₀₅ (inhalation, unless otherwise specified)			
		µg/kg-bw per day		water assay (Brantom, 1983; Peto <i>et al.</i> , 1991a,b)		95% LCL of TD ₀₅ : 0.0036 µg/kg-bw per day; 0.00036 µg/kg-bw per day

Health-based Guidance Values for Substances on the Second Priority Substances List

3.3 *Estimates of Exposure to PSL2 Substances*

Substance [CAS No.]	Cut-off date for literature review	Human exposure	Contribution to intake by individual medium
Acetaldehyde [75-07-0]	April 1998	Based upon probabilistic estimates of 24-hour time-weighted concentrations of acetaldehyde in air, median and 95th percentiles were 13.5 and 51.7 µg/m ³ , respectively (Environment Canada and Health Canada, 2000a).	Critical effects of exposure to exogenous acetaldehyde, based upon animal studies, occur at the site of first contact (i.e., the respiratory tract following inhalation and the gastrointestinal tract following ingestion). For this reason, effects of exposure by different routes are addressed separately. Point estimates of total daily intake by six age groups of the general population of Canada were developed, primarily to determine the relative contributions from various media to total exposure. For all six age groups of the general population, intake by ingestion was predominant. Quantitative data on concentrations of acetaldehyde in foods in Canada were not identified. The estimated intakes are based upon limited studies in which details concerning the number of samples analysed and the location and date of sample acquisition were generally not reported.
Acrolein [107-02-8]	October 1998	Probabilistic estimates of 24-hour time-weighted concentrations in air indicate that between 5 and 10% of the population are exposed to at least 5 µg/m ³ . Mean, median and 95th-percentile time-weighted average concentrations were 2.3, 1.7 and 5.9 µg/m ³ , respectively (Environment Canada and Health Canada, 2000b).	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. Inhalation: Acrolein was detected in ambient air in New Brunswick, Nova Scotia, Quebec, Ontario and British Columbia (Dann, 1998). For concentrations of acrolein in indoor air, data were limited to the Windsor Air Quality Study and subsequent sampling in Hamilton (OMEE, 1994a,b; Bell, 1995, 1996, 1997). Ingestion: Limited data on concentrations of acrolein in 26 food items from countries other than Canada were considered inadequate as a basis for estimation of the average daily intake. Nevertheless, crude estimates of intake of acrolein from ingestion of foods were generated for comparison with estimates of intake from inhalation and ingestion of drinking water. For non-smokers of all age groups, the ingestion of food can account for 80–90% of the estimated total daily intake from all routes of exposure. However, the crude estimates of intake from food were based upon limited studies of a small number of foodstuffs, none of which were of Canadian origin.
Acrylonitrile [107-13-1]	April 1998	Estimated daily intake of acrylonitrile by the general population ranges from 0.01 to 0.65 µg/kg-bw per day (Environment Canada and Health Canada, 2000h).	Although based upon limited information, indoor air is likely the principal medium of exposure to acrylonitrile, followed by ambient air. Intakes from food and drinking water are likely to be negligible in comparison. Exposures from ambient air may be substantially higher for populations in the vicinity of point sources.

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Substance [CAS No.]	Cut-off date for literature review	Human exposure	Contribution to intake by individual medium
1,3-Butadiene [106-99-0]	April 1998	Median and 95th-percentile values of 24-hour average concentrations of butadiene in air were 0.21 µg/m ³ and 1.0 µg/m ³ , respectively. For the proportion of the general population that is regularly exposed to higher concentrations of butadiene in urban areas (i.e., the “reasonable worst-case scenario”), the 50th- and 95th-percentile values of 24-hour average concentrations of butadiene are 0.40 µg/m ³ and 1.3 µg/m ³ , respectively (Dann, 1997a).	The principal source of environmental exposure to butadiene is air. Although few data were identified regarding levels in drinking water and food, intake of butadiene in these media is expected to be negligible in comparison with that in air because of its physical/chemical properties and environmental release patterns.
2-Butoxyethanol [111-76-2]	October 1999	The mean concentration in outdoor air reported in the multimedia exposure study was 8.4 µg/m ³ , with a maximum of 243 µg/m ³ . The mean concentration in indoor air reported in the multimedia exposure study was 27.5 µg/m ³ , with a maximum of 438 µg/m ³ (Conor Pacific Environmental Technologies Inc., 1998).	Available data on levels of 2-butoxyethanol in environmental media in Canada upon which estimates of population exposure may be based are limited to air and drinking water. Inhalation of indoor air represents the principal route of exposure, with outdoor air and dermal absorption of airborne 2-butoxyethanol contributing smaller amounts; exposure via drinking water is negligible in comparison. In addition, exposure through use of consumer products containing the substance is estimated as being considerable.
Butylbenzylphthalate [85-68-7]	April 1998	Estimated average daily intake ranges from 0.01 to 5.0 µg/kg-bw per day. Reasonable worst-case estimates of daily intake range from 0.27 to 145 µg/kg-bw per day (Environment Canada and Health Canada, 2000c).	Point estimates of average daily intake were calculated for six age groups in the Canadian population, based upon data on concentrations in ambient and indoor air, drinking water, food and soil. Food is overwhelmingly the principal source of exposure to butylbenzylphthalate.
Carbon disulfide [75-15-0]	August 1999	The mean airborne concentrations of carbon disulfide on which estimates of exposure of the general population were based are 0.63 µg/m ³ in indoor air and 0.30 µg/m ³ in outdoor air (Phillips, 1992); 24-hour time-weighted concentration for exposure of the general population was 0.58 µg/m ³ .	Point estimates of total daily intake by six age groups of the general population of Canada were developed, based upon a small number of surveys of ambient air conducted at a few locations in Canada and the United States and limited Canadian surveys in drinking water and soil. Indoor air is the principal source of exposure.
Chloroform [67-66-3]	October 1999	Deterministic estimates of average daily intake of chloroform by the general population range from 0.6 to 10.3 µg/kg-bw per day. Upper-bounding deterministic estimates of daily intake range from 40 to 148 µg/kg-bw per day. For the general population exposure scenario, the probabilistic 95th percentiles of the distribution of intakes from inhalation and	Estimates of daily intake, based upon the maximum reported concentrations of chloroform in indoor and outdoor air and in drinking water in Canada and the maximum reported concentrations in foods in Canada and/or the United States, were developed. The main pathways of exposure to chloroform for the general population in Canada are inhalation of indoor air and ingestion of tap water. The average daily intake from a single daily 10-minute shower can exceed the intake from all other exposure pathways. Midpoint and 95th-percentile estimates of concentrations of chloroform in indoor air were 2.28 µg/m ³ and 8.0

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Substance [CAS No.]	Cut-off date for literature review	Human exposure	Contribution to intake by individual medium
		ingestion of drinking water range from 4.9 to 12.9 µg/kg-bw per day. For the reasonable worst-case scenario, the probabilistic 95th percentiles of the distribution of intakes from inhalation and ingestion of drinking water range from 7.0 to 19.1 µg/kg-bw per day (Environment Canada and Health Canada, 2001a).	µg/m ³ , respectively.
N,N-Dimethylformamide [68-12-2]	June 2000	Worst-case estimate of airborne levels in the immediate vicinity of the largest emitter in Canada is 0.11 mg/m ³ (Environment Canada and Health Canada, 2001b), which is likely 10- to 100-fold greater than levels anticipated under most conditions. Based on lack of detection in the multimedia study, levels of N,N-dimethylformamide in indoor air of 50 homes were less than 3.4 µg/m ³ (Conor Pacific Environmental Technologies Inc., 1998).	Identified data on concentrations of dimethylformamide in environmental media in Canada were insufficient to allow estimates of population exposure to be developed. Concentrations in food in Canada or elsewhere were not identified. For water, either quantitative data on concentrations were unreliable or dimethylformamide was not detected. Levels of dimethylformamide in indoor air in 50 homes in Canada were below the limit of detection. Air in the vicinity of point sources appears to be the greatest potential source of exposure of the general population (Environment Canada, 1998, 1999).
Ethylene glycol [107-21-1]	January 2000		Data on levels of ethylene glycol in environmental media in Canada to serve as a basis for development of estimates of population exposure were identified only for areas near industrial point sources in Alberta. These data are limited to a few predicted concentrations in ambient air at ground level and to measured concentrations in soil. No data were identified concerning the presence or concentrations of ethylene glycol in drinking water in Canada or elsewhere (Environment Canada and Health Canada, 2000f).
Ethylene oxide [75-21-8]	January 1999	Concentration predicted for ambient air in southern Ontario was 0.0062 µg/m ³ . Censored mean concentrations in ambient air and indoor air were 0.34 µg/m ³ and 0.17 µg/m ³ , respectively. Predicted maximum average daily concentration in ambient air in the vicinity of Canadian hospitals was 2.12 µg/m ³ . Maximum concentrations in ambient and indoor air were 4.9 µg/m ³ and 4.0 µg/m ³ , respectively (Environment Canada and Health Canada, 1999).	Information on monitored levels of ethylene oxide in air, drinking water and foodstuffs in Canada is exceedingly limited, being restricted to detection in a few samples of ambient and indoor air in a small monitoring survey. It should be noted that ethylene oxide is generally transferred to air following release to other media and is not expected to accumulate in sediment or soil or bioaccumulate, as a result of its high water solubility and vapour pressure.
Formaldehyde [50-00-0]	January 1999	Probabilistic estimates of the median, mean and 95th-percentile 24-hour time-weighted average concentrations of formaldehyde in air range from 24 to	Critical effects associated with exposure to formaldehyde occur primarily at the site of first contact (i.e., the respiratory tract following inhalation and the gastrointestinal tract following ingestion) and are related to the concentration of formaldehyde in media to which

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Substance [CAS No.]	Cut-off date for literature review	Human exposure	Contribution to intake by individual medium
		<p>29 µg/m³, from 33 to 36 µg/m³ and from 80 to 94 µg/m³, respectively. Estimated median and 95th-percentile concentrations of formaldehyde in indoor air range from 28.7 to 29.8 µg/m³ and from 84.6 to 91.2 µg/m³, respectively (Environment Canada and Health Canada, 2001d).</p> <p>Estimated average concentration of formaldehyde in drinking water was 5 µg/L (Environment Canada and Health Canada, 2001d). The concentrations of formaldehyde in foods ranged from less than 0.03 to 14 mg/kg (Health Canada, 2000); however, the proportion of formaldehyde in foods that is bioavailable is unknown.</p>	<p>humans are exposed, rather than the total intake of the substance. The general population is exposed to low concentrations of formaldehyde in outdoor air (Dann, 1997b, 1999) and to generally higher concentrations in indoor air (Health Canada, 2000). Few data were available with which to characterize the range and distribution of concentrations of formaldehyde in either food or drinking water in Canada.</p>
Hexachlorobutadiene (HCBD) [87-68-3]	December 1996	Average total intakes of HCBD from air, food and drinking water range from 0.01 to 0.2 µg/kg-bw per day (Environment Canada and Health Canada, 2002).	HCBD has been detected in surface waters, sediments, aquatic organisms and, occasionally, air. Food is likely the principal source of exposure (Kotzias <i>et al.</i> , 1975; McConnell <i>et al.</i> , 1975; Goldbach <i>et al.</i> , 1976; Yip, 1976; Oliver and Nicol, 1982; Fox <i>et al.</i> , 1983; Oliver and Niimi, 1983; Clark <i>et al.</i> , 1984; Malins <i>et al.</i> , 1985), although ambient air may also contribute significant amounts in some areas.
N-Nitrosodimethylamine (NDMA) [62-75-9]	August 1999		It is not possible to develop defensible estimates of the current average daily intakes of NDMA for the general population, due to limitations of the available data. However, based upon the data, most of the daily intake can be attributed to consumption of food (Liteplo and Meek, 2001).
Phenol [108-95-2]	September 1997	Total intake of phenol for the general population is estimated to range from 0.06 to 0.71 µg/kg-bw per day.	<p>No adequate data concerning background concentrations of phenol in ambient air in Canada were identified. Intake from air is based upon the mean concentration of phenol in ambient air of 0.12 µg/m³ reported by Jones (1976) for an urban/suburban site in the United States. Intake from food was based upon concentrations of phenol reported in a market basket survey in Windsor, Ontario, in 1992 (ETL, 1992).</p> <p>Although based upon limited data, ingestion of food is likely the principal route of exposure to phenol for non-smokers of all age groups in populations removed from point sources. Exposure from ingestion of drinking water and soil appears to be negligible compared with that from food. Exposures from ambient air may be substantially higher for populations located in the vicinity of some point sources. The general population is also exposed periodically to phenol through the use of several consumer products (mouthwashes, throat</p>

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Substance [CAS No.]	Cut-off date for literature review	Human exposure	Contribution to intake by individual medium
			lozenges, antiseptic lotions). Based upon limited data, the contribution to total phenol exposure from use of consumer medical products may be greater than that from environmental exposures.

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