SCREENING HEALTH ASSESSMENT OF EXISTING SUBSTANCES UNDER THE *CANADIAN ENVIRONMENTAL PROTECTION ACT, 1999*

Background and Mandate

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) requires the federal Ministers of the Environment and of Health to identify and determine which existing substances already in the environment pose a risk to human health or to the environment. Existing substances are those included in an inventory known as the Domestic Substances List (DSL), published in 1994. The DSL is a compilation of about 23 000 substances used in, manufactured in or imported into Canada for commercial purposes between January 1, 1984, and December 31, 1986, at a quantity of greater than 100 kg per year; substances that are not listed on the DSL are considered as being new to Canada.[1] The DSL is periodically amended to add substances that have met the listing requirements under the New Substances Notification Regulations of CEPA 1999.

The identification of existing substances that may pose a risk to human health and subsequent assessment of those risks are undertaken within the Existing Substances Division (ExSD) of the Healthy Environments and Consumer Safety Branch of Health Canada. One of the ways in which health risks are evaluated is through a **screening health assessment.**

Objective of a Screening Health Assessment

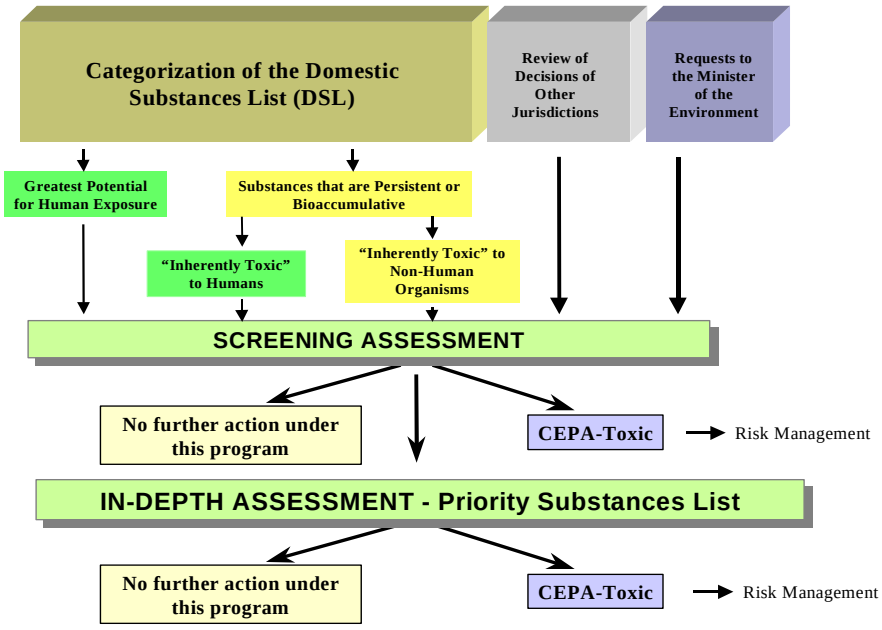
The objective of a screening health assessment[2] is to consider in a preliminary fashion whether or not a substance is likely to pose a risk to human health. It is part of an overall strategy designed to focus action on those compounds that pose the greatest risks to the health of Canadians. The focus of the screening health assessment is limited principally to the information that is considered most critical in assessment of human exposure to a substance and its health-related effects. It entails an initial look at this information only, thereby enabling a large number of existing substances to be evaluated more quickly and efficiently. If needed, some substances will undergo a more in-depth assessment of the risks to human health, but only after a screening assessment has been conducted.

Substance Identification for Screening Assessment

There are three principal ways in which substances may be identified for a screening assessment:

[1] Substances new to Canada after December 31, 1986, are assessed under the new substances provisions of CEPA 1999.

[2] Screening environmental assessments under CEPA 1999 are conducted by Environment Canada.



1. **Categorization of the DSL under Section 73 of CEPA 1999:** This involves the identification of:
    a) Substances on the DSL considered to pose to individuals in Canada the greatest potential for exposure; or
    b) Substances on the DSL that are persistent and/or bioaccumulative that are also deemed to be inherently toxic to humans or non-human organisms.

2. **Reviews of Decisions of Other Jurisdictions under Section 75 of CEPA 1999:** Decisions taken in other jurisdictions to prohibit or restrict substances for environmental or health reasons are reviewed by the Ministers to determine whether the substance in question could potentially represent a danger to human health or the environment in Canada. Depending upon that review, a screening assessment of the substance may be conducted.

3. **Public Requests under Section 76(3) of CEPA 1999:** The Act enables any person to write to the Minister of the Environment and request that a substance be added to the Priority Substances List (PSL). Substances so nominated for addition to the PSL would first typically undergo a screening assessment.

Outcome of a Screening Health Assessment

On the basis of a screening assessment, the Ministers of the Environment and of Health may recommend to take no further action in respect of the substance, to add the substance to the PSL for a more in-depth assessment of risks to human health or the environment or to recommend that the substance be added to the List of Toxic Substances in Schedule 1 of the Act, which may set the stage for taking actions to manage the risk.

These outcomes are dependent, in part, on determining in a screening assessment whether a substance is toxic or capable of becoming toxic as defined in Section 64 of CEPA 1999, 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

This definition of "toxic" under CEPA 1999 is a legal one that may be considered in the context of risk, since it embodies the concept that harm is a function of both the intrinsic toxicity (i.e., toxicity in the traditional sense) and the extent of exposure. However, substances with high intrinsic toxicity to human health (e.g., those that cause cancer through direct interaction with genetic material) are also considered "toxic" under CEPA 1999.

Process for Screening Health Assessments

In broad terms, the process for conducting screening health assessments is as follows:

1. **Substance Identification:** As noted above, there are three principal ways in which a substance may be identified for a screening health assessment. Screening assessments would also be conducted on any other substances for which preliminary assessment is desirable.

2. **Data/Information:** Information on effects and exposure is obtained from a wide variety of sources, such as web-based databases, surveys and previous reviews or assessments of substances conducted by national or international agencies. Information is identified from published and unpublished studies. Data gathering is robust, employing comprehensive search strategies, like those used for the assessment of Priority Substances (see http://www.hc-sc.gc.ca/hecs-sesc/exsd/psap.htm). Screening assessments take into account existing, up-to-date, peer-reviewed national and international risk assessment evaluations to the maximum extent possible.

3. **Preparation of the Draft Screening Health Assessment and Supporting Working Documentation:** Screening assessments of risks to human health focus directly on the most critical effects and conservative effect levels and upper-bounding estimates of exposure, after consideration of all relevant identified information. Documentation prepared as part of this process includes:

    - A **Screening Health Assessment Report**. This is a brief (e.g., typically 4–8 pages) summary of the information on identity, production and uses, sources and levels of human exposure and health effects. The report also outlines the objective of the screening assessment, the approach to decision-making and conclusions and transparently delineates the databases that serve as the basis for determination of the

critical effect levels and upper-bounding exposure estimates. An explicit summary is included in the text, and more detailed information that constitutes the basis for estimations of exposure and assessment of effects is presented in accompanying tables. A full reference list is included to ensure transparency of the identified database. The screening health assessment report is posted on the ExSD website.

- A **Supporting Working Document**. This unpublished document provides greater detail on the information used in the screening health assessment and decision-making process. It is available upon request from ExSD.

- A joint amalgamated brief (3–6 paragraphs) **scientific summary** of the Health Canada and Environment Canada screening assessments and the Ministers' proposed measure are published in the *Canada Gazette.*

4. **Internal Peer Review:** The draft screening health assessment report and supporting working documentation are reviewed at meetings involving senior ExSD technical staff to consider the critical issues and conclusion.

5. **External Peer Review:** The draft screening health assessment report and supporting working documentation are then reviewed externally, primarily to address adequacy of data coverage and defensibility of the conclusion.

6. **Public Comment:** The draft screening health assessment report (and proposed conclusion and Ministerial recommendation) are posted for public comment for a period of 60 days, as mandated under CEPA 1999. Feedback received from the public comment period is then taken into consideration in finalization of the conclusions and Ministerial recommendations. Summaries of the comments and responses thereto are also posted, upon revision of the draft screening health assessment.

Basis for Decision-Making in Screening Health Assessments

Decision-making for screening health assessments under CEPA 1999 is based on a "margin of exposure" approach. The "margin of exposure" is the magnitude of the ratio between the level (dose) at which the critical effect is observed in studies conducted in animals or, in some cases, humans and the upper-bound estimated (or measured) level of human exposure to a substance. Recommendations are based on the adequacy of this margin of exposure, taking into account confidence in the completeness of the identified databases on effects and exposure, within a screening context:

- Generally, margins greater than 1000 are adequate as a basis for recommending no further action for substances where the databases on exposure and effects are relatively complete.

- For margins less than 1000, limitations of and confidence in the exposure and effects databases are carefully considered and documented.

- In some cases, consideration of some more complex information, such as that on mode of action (i.e., the manner in which a substance induces toxic effects), and/or more refined estimates of exposure and/or assessment of critical effect levels may be required. However, in cases where an original comprehensive analysis of available data on mode of action and/or the generation of such data are warranted to more fully inform decision-making, the substance would be recommended for addition to the PSL for further in-depth assessment.

- In some cases, where the margins of exposure are less than 1000, but the uncertainty in the available databases on exposure and/or effects is significant, a conclusion of "suspected to be toxic" is proposed as a basis to solicit additional information to permit a more definitive conclusion to be reached.

- For substances with high intrinsic toxicity to human health (e.g., those that cause cancer through direct interaction with genetic material), with effects where there is some probability of harm at any level of exposure, the substance would be proposed "toxic" under Paragraph 64(c) of CEPA 1999 and recommended for addition to the List of Toxic Substances under the Act, and guidance would be provided concerning priority of analysis of options to reduce exposure. For substances with potentially high intrinsic toxicity to human health, but with significant uncertainty in the available database on effects, a conclusion of "suspected to be toxic" is proposed as a basis to solicit additional information to permit a more definitive conclusion to be reached.

The relative uncertainty of and degree of confidence in exposure and effects databases that serve as the basis for decision-making in the assessment of high intrinsic toxicity or the adequacy of margins of exposure are explicitly delineated and consistent across screening assessments. They are consistent with similar considerations made for the health risk assessment of Priority Substances under CEPA 1999 and include, for example, consideration of aspects such as:

- interspecies and intraspecies variation,
- nature of the critical effect,
- dose spacing in the critical study,
- steepness of the dose–response curve,
- extent of the database as the basis for characterization of hazard for all effects including that considered critical,
- degree of protection provided by the critical effect level, and
- whether or not estimates of exposure are based on, for example, environmental monitoring or modelled data or higher-confidence internal doses (e.g., levels in blood).

Cut-Off Date for the Review of Data

A cut-off date for consideration of relevant data is specified in all screening health assessment reports to ensure the full evaluation of identified information through several stages of internal and external review. This approach is consistent with international practice and is

designed to achieve transparency and defensibility of the process, while respecting the mandate under CEPA 1999 to complete assessments on large numbers of existing substances expeditiously. Information submitted after the cut-off date is considered primarily in the context of its implications for risk management (if appropriate) or in setting priorities for reassessment at a later date.

Comparison of Screening and Priority Substances List Health Assessments

The following table presents a comparison of some of the key differences and similarities between a screening health assessment and the assessment of health risks conducted for Priority Substances under CEPA 1999.

Issue	Screening Assessment	Priority Substances List Assessment
Concept	Initial assessment of whether a substance poses a risk to human health.	A critical and comprehensive analysis of the risks to human health.
Possible Outcomes	There could be no further action on the substance, it could be considered for risk management or it could be considered for more in-depth PSL risk assessment.	There could be no further action on the substance or it could be considered for risk management.
Information Gathering	Comprehensive information search strategies employed. Similar to that for PSL assessments. Greater reliance on other peer-reviewed assessments for identification and assessment of previously reviewed data.	Comprehensive information search strategies employed. The search strategies are noted in the PSL assessment reports.
Evaluation of Exposure	Focus on upper-bounding estimates of exposure, after consideration of all relevant identified information.	Detailed analysis (e.g., probabilistic) of exposure, after consideration of all relevant identified information.
Evaluation of Effects	Focus directly on health-related effects, which occur at lowest concentration or dose.	Detailed review of all relevant health-related data and full weight of evidence analysis for hazard characterization. This includes weighting of all relevant data, taking into account factors such as consistency, plausibility of observed effects, etc.
Hazard Characterization	Focus directly on the most conservative effect level associated with the critical health-related effect and/or identification	Weight of evidence approach with in-depth evaluation of mode of action (i.e., how a substance induces its toxic effects), toxicokinetics

Issue	Screening Assessment	Priority Substances List Assessment
	of substances with high intrinsic toxicity to human health.	(how the substance is absorbed and distributed within the body), metabolism and exposure–response (e.g., benchmark dose) relationships, where data permit.
Approach to Dose–Response Assessment	Margin of exposure approach — i.e., magnitude of the ratio between conservative effect level for effect considered critical and upper-bound estimated (or measured) level of human exposure.	Development of tolerable daily intakes/concentrations, employing default or compound-specific adjustment factors where data permit. Consideration/incorporation of physiologically based pharmacokinetic models or biologically motivated case-specific models, where data permit.
Confidence/ Uncertainties in the Assessment	- Deals principally with characterization of the extent of the available database that serves as basis for the delineation of the critical data on exposure and effects. - Specified in the screening assessment report and supporting working documentation.	- Deals with characterization of the extent of the available database that serves as basis for the delineation of the critical data on exposure and effects, but primarily with the characterization of specific aspects of dose–response. - Specified in the PSL assessment report.
Documentation Prepared	- Screening health assessment report (published).[3] - Supporting working documentation (unpublished). - Short amalgamated summary of health and environmental screening assessments published in the *Canada Gazette.*	- Amalgamated health and environmental risk evaluations published in a PSL assessment report. - Supporting documentation (unpublished) for the health components (exposure and effects) assessment. - Synopsis of amalgamated health and environmental assessments published in the *Canada Gazette.*
Delineation of Follow-up Actions	- When the recommendation is to add the substance to the PSL for more in-depth assessment, the additional work required is clearly delineated in the screening assessment report.	- When the recommendation is to consider the substance “toxic” under Paragraph 64(c) of CEPA 1999, the appropriate considerations for follow-up and guidance on the priority for the development of

[3] Screening environmental assessment report published separately.

Issue	Screening Assessment	Priority Substances List Assessment
	- When the recommendation is to consider the substance "toxic" under Paragraph 64(c) of CEPA 1999, the appropriate considerations for follow-up and guidance on the priority for the development of options to reduce exposure are clearly delineated in the screening health assessment report.	options to reduce exposure are clearly delineated in the PSL assessment report.
Scientific Review — Internal	Internal review meetings by senior ExSD technical staff to consider critical issues and the conclusion of the assessment.	Review by senior ExSD technical staff.
Scientific Review — External	External review by small number of experts primarily to address adequacy of data coverage and defensibility of the conclusion or to address specific questions on identified critical issues. All reviewers must have declared non–conflict of interest.	External review often by convened panels of experts for adequacy of data coverage, defensibility of selection of the critical data, dose–response analysis and exposure assessment. All reviewers must have declared non–conflict of interest.
Public Comment	Sixty-day public comment period mandated under CEPA 1999.	Sixty-day public comment period mandated under CEPA 1999.

DSL Pilot Phase

Health Canada and Environment Canada selected 123 substances from the DSL to be part of a pilot phase to assist in development of the process, procedure and criteria for decision-making for the screening assessment program under CEPA 1999. Health Canada selected 30 substances on the basis that they likely present to individuals in Canada the greatest potential for exposure. Environment Canada selected 93 substances considered to be persistent and/or bioaccumulative and inherently toxic to non-human organisms. Over the next few years, the screening assessments conducted will focus primarily on substances in the pilot phase.

Update

This document will be revised and updated as the approach to screening health assessment becomes more refined, based upon the additional operational experience gained in conducting such assessments on larger numbers of existing substances.