

New Substances

Risk assessment of micro-organisms under the *Canadian Environmental Protection Act, 1999*

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Environment Canada
and Health Canada

Environnement Canada
et Santé Canada

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Overview and objectives of presentation

- Describe types of micro-organisms assessed under *Canadian Environmental Protection Act, 1999*.
- Review the *EC/HC Risk Assessment Framework for Micro-organisms*.
 - Framework describes science-based considerations used to assess risks posed by micro-organisms to humans and the environment.
- Provide other relevant information.
 - For aspects not covered in oral presentation, summarize in annexes information regarding the joint EC/HC New Substances Program and process for assessing and controlling micro-organisms.



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Micro-organisms assessed under CEPA 1999

‘Existing’ micro-organisms

- Listed on the DSL.
- EC and HC is responsible for (i) gathering necessary information and (ii) conducting the risk assessment (no mandated timeline).

‘New’ micro-organisms

- Not listed on the DSL.
- Manufacturer or importer is responsible for notifying (i.e. provide necessary information) under one of four schedules of *New Substance Notification Regulations (Organisms)*
- EC and HC conducts risk assessment under mandated timelines.

Typical uses of micro-organisms assessed under CEPA 1999

- Micro-organism based production of enzymes and other bio-products, bioremediation, compost starters, septic tank treatments, pond cleaners, degreasers, drain cleaners (list not exhaustive).

Domestic Substances List (DSL): A compilation of (i) all reported substances that were in Canadian commerce between 1984 and 1986 (i.e. ‘grandfathered’ substances) or ii) were added to DSL after notification and assessment. As of April 2008, there are 44 microbial strains and 1 consortium on DSL, all added under (i).



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How are micro-organisms assessed under CEPA 1999?

Definition of 'CEPA toxic'

Under section 64 of CEPA 1999, a substance is considered 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.*

Paradigm for assessing risk

$$\text{Risk} \propto \text{Hazard} \times \text{Exposure}$$



If assessment determines 'CEPA toxic'
Control measures may be put in place



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Hazard Assessment: (i) Identification of factors that could potentially cause an adverse effect on the environment and human health and (ii) characterization of the severity of the adverse effect (quantitative and/or qualitative).

Hazards posed by: (i) micro-organism, (ii) its genetic material, and/or (iii) toxins.

Information for: (i) specific micro-organism and/or (ii) suitable surrogate.

Key information

Taxonomic identification key element of hazard assessment. Polyphasic methodology encouraged.

Strain history from original source until final product development.

Genetic modifications all directed or intentional changes (if any) (e.g. the source, nature and function of inserted genetic material, methods used to modify organism, stability of modifications).

Pathogenicity ability to cause disease to humans and/or other organisms.

Toxigenicity/toxicity ability to cause adverse effect(s) on humans and/or other organisms (e.g. due to production of toxin, secondary metabolites, and/or structural components).

Invasiveness ability to establish itself, persist, out-compete indigenous species, take over new environments and threaten biological diversity.

Other effects adverse ecological effects on habitats or biogeochemical cycles, etc.



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Exposure Assessment: (i) Identification of mechanisms by which humans, non-human species, and the environment come into contact with the substance (i.e. micro-organism, its genetic material, and/or its toxins) and (ii) characterization of the potential for exposure (quantitative and/or qualitative).

Key information

Potential for introduction Both intentional and unintentional release.

Release sites Single site, multiple defined sites, or essentially ubiquitous.

Release scenarios Into air, water, and/or soil; exposure to dead and/or live micro-organisms; quantity, duration, frequency and nature of releases (e.g. aerial spray, deep-well injection, terrestrial surface applications, wastes).

Use patterns Industrial, commercial, or domestic activities.

Target endpoints Biotic or abiotic entities that may be impacted (positively, negatively or neutrally) following exposure to substance.

Post-release biological and/or physical characteristics Persistence in the environment; potential for proliferation and dispersal of micro-organism or traits which have the potential to produce adverse effects.

Background levels of micro-organism, suitable surrogate, and/or hazardous 'aspect'.



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Risk characterization: estimate (quantitatively and/or qualitatively) magnitude of risk based on the assumption that hazard(s) (if any) will be realized due to exposure (if any).

Hazard Severity	Potential for Exposure			
	High	Medium	Low	Negligible
High	High	High	Medium	Low
Medium	High	Medium	Medium	Low
Low	Medium	Medium	Low	Negligible
Negligible	Negligible	Negligible	Negligible	Negligible

Annex 5: Description of criteria used to characterize **hazard severity**.

Annex 6: Description of criteria used to characterize **potential for exposure**.



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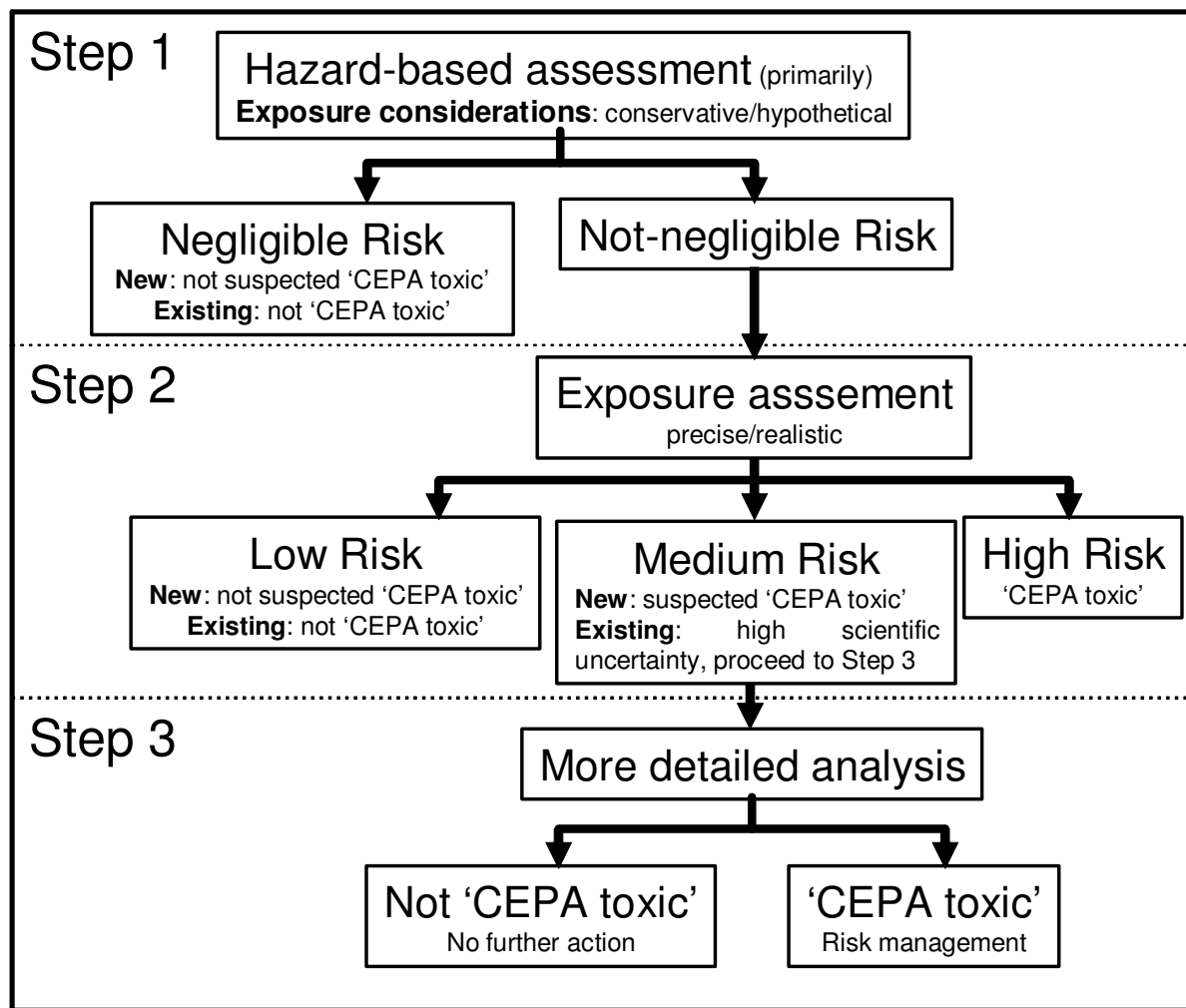
Risk characterization: estimate (quantitatively and/or qualitatively) magnitude of risk based on the assumption that hazard(s) (if any) will be realized due to exposure (if any).

Risk	Description	Control Measures
High	Serious effects that could be irreversible. Risks considered unacceptable	Substantial risk control measures would be imposed
Medium	Potential for risk to increase quickly, but under normal circumstances the risk is not of serious concern	Appropriate control measures to mitigate the risk would be necessary
Low	Insignificant negative effects	Rarely requires that control measures be imposed, except under specific circumstances
Negligible	Effectively no risk	No control measures would be imposed



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Overview of step-wise approach



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Questions?

To contact us, for further information, or to provide feedback New Substances Program

- General: www.ec.gc.ca/substances
- E-mail: NSN-Infoline@ec.gc.ca
- Phone: (800) 567-1999 (Toll Free in Canada)
(819) 953-7156 (Outside of Canada)
- Fax: (819) 953-7155
- Mailing: New Substances Division
Science and Technology Branch
Environment Canada
Place Vincent Massey, 14th Floor
Gatineau QC K1A 0H3

Regulation and assessment of micro-organisms and other relevant links

- General: http://www.ec.gc.ca/substances/nsb/eng/biotech_e.shtml
- Guidelines: http://www.ec.gc.ca/substances/nsb/eng/bio_guidance_e.shtml
- Advisory Notes: http://www.ec.gc.ca/substances/nsb/eng/bio_advisory_e.shtml
- Assessment of 'existing' micro-organisms: http://www.ec.gc.ca/substances/nsb/eng/bio_screening_e.shtml



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Annex 1: 'Existing' micro-organisms (i.e. on Domestic Substances List)

<i>Arthrobacter globiformis</i> (ATCC 8010)	<i>Escherichia hermannii</i> (ATCC 700368)
<i>Aspergillus awamori</i> (ATCC 22342)	<i>Micrococcus luteus</i> (ATCC 4698)
<i>Aspergillus niger</i> (ATCC 9642)	<i>Nitrobacter species</i> (16969-4)
<i>Aspergillus oryzae</i> (ATCC 11866)	<i>Nitrobacter winogradskyi</i> (ATCC 25391)
<i>Bacillus amyloliquefaciens strain</i> (13563-0)	<i>Nitrococcus species</i> (16972-7)
<i>Bacillus cereus</i> (ATCC 14579)	<i>Nitrosococcus species</i> (16971-6)
<i>Bacillus circulans</i> (ATCC 9500)	<i>Nitrosomonas europaea</i> (ATCC 25978)
<i>Bacillus licheniformis</i> (ATCC 12713)	<i>Nitrosomonas species</i> (16968-3)
<i>Bacillus licheniformis</i> (ATCC 55406)	<i>Pseudomonas aeruginosa</i> (ATCC 31480)
<i>Bacillus megaterium</i> (ATCC 14581)	<i>Pseudomonas aeruginosa</i> (ATCC 700370)
<i>Bacillus polymyxa</i> (ATCC 842)	<i>Pseudomonas aeruginosa</i> (ATCC 700371)
<i>Bacillus polymyxa</i> (ATCC 55407)	<i>Pseudomonas denitrificans</i> (ATCC 13867)
<i>Paenibacillus polymyxa strain</i> (13540-4)	<i>Pseudomonas fluorescens</i> (ATCC 13525)
<i>Bacillus species</i> (16970-5)	<i>Pseudomonas fluorescens</i> (ATCC 31483)
<i>Bacillus subtilis</i> (ATCC 6051)	<i>Pseudomonas putida</i> (ATCC 12633)
<i>Bacillus subtilis</i> (ATCC 6051A)	<i>Pseudomonas putida</i> (ATCC 31800)
<i>Bacillus subtilis</i> (ATCC 55405)	<i>Pseudomonas putida</i> (ATCC 700369)
<i>Bacillus subtilis strain</i> (11685-3)	<i>Pseudomonas stutzeri</i> (ATCC 17587)
<i>Bacillus thuringiensis</i> (ATCC 13367)	<i>Rhodopseudomonas palustris</i> (ATCC 17001)
<i>Candida utilis</i> (ATCC 9950)	<i>Saccharomyces cerevisiae</i> (Strain F53)
<i>Cellulomonas biazotea</i> (ATCC 486)	<i>Trichoderma reesei</i> (ATCC 74252)
<i>Chaetomium globosum</i> (ATCC 6205)	Complex microbial culture (13637-2)
<i>Enterobacter aerogenes</i> (ATCC 13048)	

•Current as of April, 2008.

- DSL for living organisms: http://www.ec.gc.ca/substances/nsb/eng/biolist_e.shtml
- Guidelines for Prioritization of Living Organisms on the DSL Prior to the Screening Assessment: http://www.ec.gc.ca/substances/nsb/eng/bio_guid_doc_fs_e.shtml



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Annex 2: Schedules for notification of 'new' living organisms

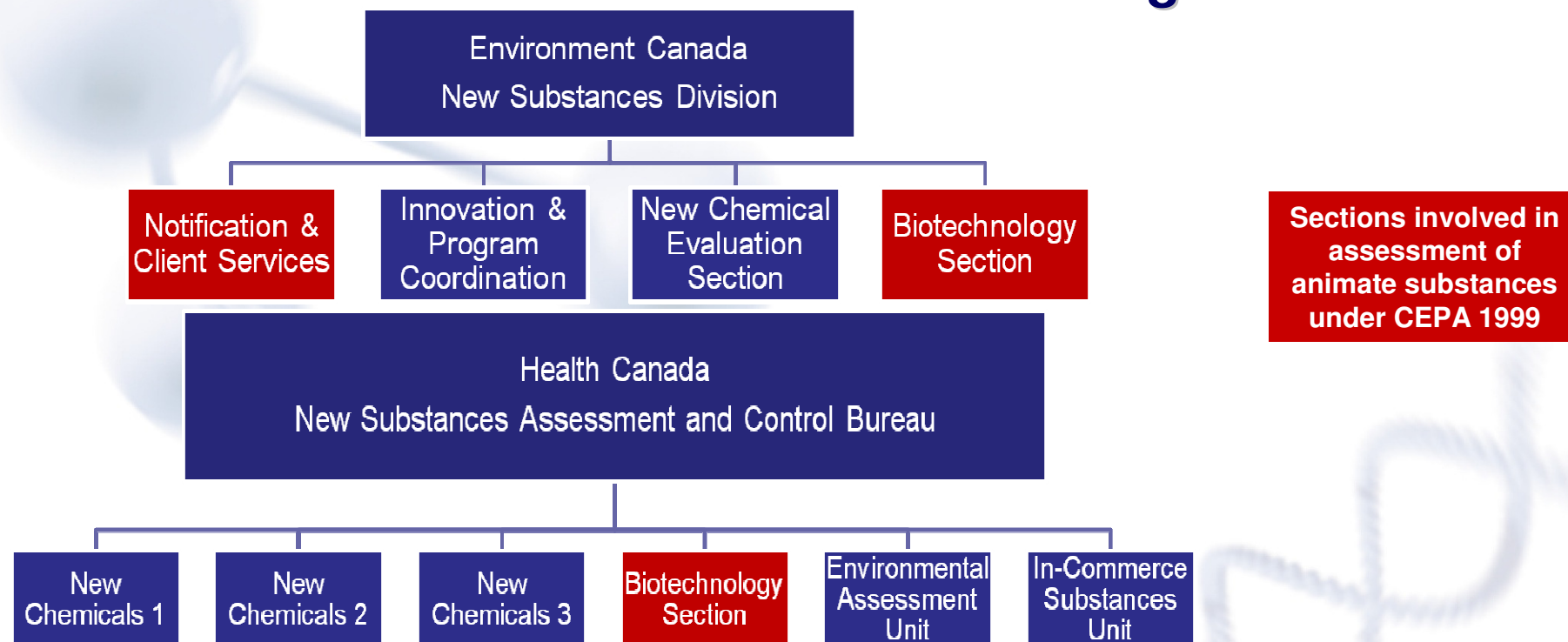
Schedule	Type of Organism	Description	Assessment Period (days)
1	Micro-organism	Introduction anywhere in Canada	120
2	Micro-organism	Contained facility OR export only	30
3	Micro-organism	Experimental field trials	90
4	Micro-organism	Introduction at the same site where isolated and manufactured	30
5	Other than micro-organism	All	120

A micro-organism is defined in subsection 1(1) of the NSNR (Organisms) as: “a microscopic organism that is: (a) classified in the Bacteria, the Archaea, the Protista, which includes protozoa and algae, or the Fungi, which includes yeasts; (b) a virus, virus-like particle, or sub-viral particle; c. a cultured cell of an organism not referred to in paragraphs (a) and (b), other than a cell used to propagate such organism; or (d) any culture other than a pure culture.” Includes a micro-organism as a pure culture as well as a complex unformulated natural combination of micro-organisms (i.e., a consortium).



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Annex 3: Organizational structure of joint Environment Canada/Health Canada New Substances Program

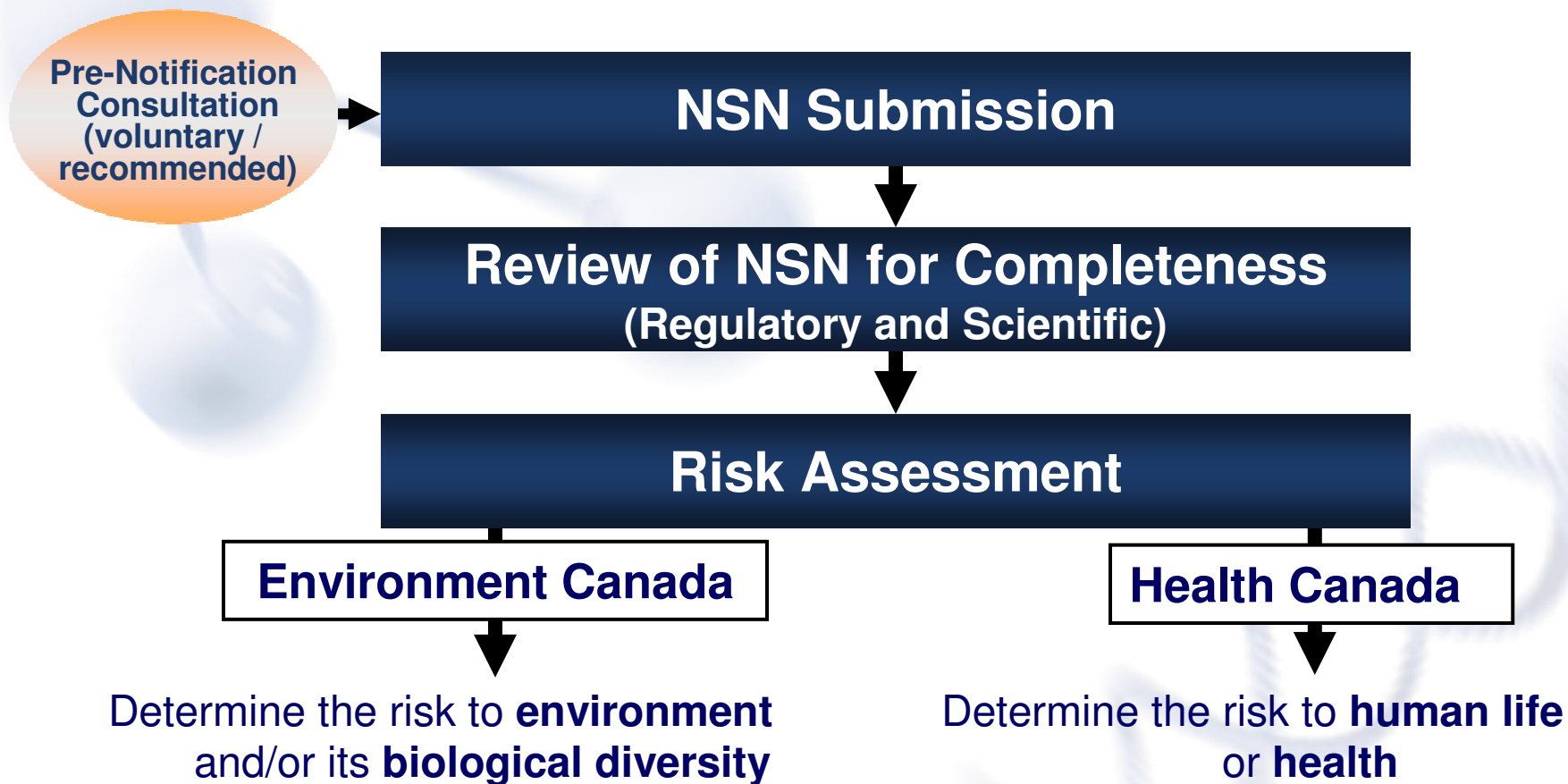


Substance: Under CEPA 1999, any distinguishable kind of organic or inorganic matter, whether inanimate (e.g. chemicals and polymers) or animate (living organisms that are (i) micro-organisms and (ii) organisms other than micro-organisms ['higher organisms']).



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Annex 4: New Substances Notification (NSN) Process



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Annex 5: Criteria used to characterize Hazard Severity

Hazard	Definition
Negligible	Hazard is null (effectively zero) on microbial, plant and/or animal populations, ecosystems, and/or humans
Low	Effects are mostly benign. Theoretical negative impacts are possible, but no predicted effect for microbial, plant and/or animal populations, ecosystems or healthy humans
Medium	Some adverse but reversible effects are possible to microbial, plant and/or animal populations or ecosystems (e.g. decrease in population, loss of community structure) or healthy humans
High	Irreversible adverse effects are possible (e.g. loss of biodiversity, loss of habitat, impacts on healthy humans)

NOTE: In the absence of quantitative information, hazard is categorised qualitatively, a convenient method for communicating the relative degree of predicted exposure to substance.



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Annex 6: Criteria used to characterize Potential for Exposure

Exposure	Criteria/Examples
Negligible	(i) use of contained facilities; (ii) very limited survival/ persistence of the micro-organisms or toxin; (iii) single 'point source' with little/no discharge (intentional or unintentional).
Low	Use in accordance with 'confinement procedures' such as: (i) genetic material is 'biological confined' so that not likely transferred to or persist in alternative hosts; (ii) low exposure duration (e.g. low survival/persistence); or (iii) the release into a localized environment with minimal exposure to susceptible human populations and/or endangered species.
Medium	(i) open release on an infrequent basis could impact areas larger than the local environment and/or in low quantities; (ii) the micro-organism may have a potential for survival, persistence and proliferation at a sub-chronic level; and/or (iii) there is a more regional release of the micro-organism (e.g. into part of an ecosystem).
High	(i) release quantities may be high and/or chronic, (ii) the survival and/or persistence is high, and/or (iii) the geographical area in which there is release extends beyond a region or single ecosystem (for example release into a large watershed or Pan-Canadian release)

NOTE: In the absence of quantitative information, likelihood of exposure is categorised qualitatively, a convenient method for communicating the relative degree of predicted exposure to substance.



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Annex 7: Outcomes of substance assessment under CEPA 1999

<p>‘New’ substance</p>	<p>Not Toxic</p> <p>↓</p> <ul style="list-style-type: none"> ▪ no further action 	<p>Not Toxic for the Proposed Activity</p> <p>↓</p> <ul style="list-style-type: none"> ▪ Significant New Activity Notice 	<p>Suspicion of Toxic or Capable of becoming Toxic</p> <p>↓</p> <ul style="list-style-type: none"> ▪ Manufacture or import with <u>condition</u>; or ▪ Prohibition; or ▪ Prohibition pending additional information
<p>‘Existing’ substance</p>	<p>No further action</p> <p>↓</p> <ul style="list-style-type: none"> ▪ If not ‘CEPA toxic’ ▪ If ‘CEPA toxic’ but actions being taken/about to be taken under other federal acts or by provincial, territorial or Aboriginal governments sufficient to manage risks effectively and in timely manner 	<p>Addition to List of Toxic Substances</p> <p>↓</p> <ul style="list-style-type: none"> ▪ If ‘CEPA toxic’ 	<p>Significant New Activity Notice</p> <p>↓</p> <ul style="list-style-type: none"> ▪ If suspicion that an alternative use of the living organism may result in the organism becoming toxic



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Annex 8: Considerations and limitations of science-based evaluations

Weight of evidence approach

- Following CEPA 1999, micro-organisms must be assessed by applying a weight of evidence (WOE) approach, which recommends the use of several component lines of evidence to reduce overall uncertainties in making decisions in all phases of an assessment. These lines of evidence are weighted based on the number of independent studies supporting a line of evidence and their inferential strength.

Scientific uncertainties

- Risk estimates always contain some level of uncertainty. Uncertainties result from the limited availability of scientific data, and difficulties applying study results to real situations: exposure or intake rates; long time delays between exposure and effect; the need to extrapolate data to predict the consequences of exposures; difficulties in determining appropriate mathematical models for extrapolation; and simultaneous exposures to a variety of different agents (making it difficult to determine the effects of a single agent). Judgments on these factors are made at each step in the risk assessment process, and small uncertainties are compounded.

The Precautionary Principle

- Environment Canada and Health Canada are mandated to apply the precautionary principle according to Section 76.1 and as justified in paragraph 2(1)(a) of CEPA 1999 which states: “*where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation*”.



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Annex 9: References

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