

New Substances Notification Regulations (NSNR)

Effective Date: October 2007

Revised: November 2008

Applicable Legislation:

Canadian Environmental Protection Act, 1999 (CEPA 1999)
New Substances Notification Regulations (Chemicals and Polymers)
New Substances Notification Regulations (Organisms)
Food and Drugs Act
Food and Drugs Regulations

- Intent:** to promote compliance with federally prescribed requirements for notifications concerning research, development and registration of new products of biotechnology;
- to publicize University requirements for physical containment, containment protocols and due diligence for new substances, and resources for compliance initiatives.
- Scope:** all University and contract research and development involving new substances.

Definitions

- living organism* in the context of NSNR, an animate product of biotechnology; includes microorganisms and organisms other than microorganisms (*i.e.*, macro-organisms) developed through the application of science and engineering, or are naturally occurring but where science and engineering is being applied in their use.
- manufacture* a term interpreted to mean produced, developed or grown (with respect to NSNR and CEPA 1999).
- microorganism* a microscopic living organism; any bacteria, mycoplasma, Chlamydia, rickettsia, protozoa, fungi,

algae, viruses, parts of these microorganisms, and any combination (consortia) thereof, and cultured cells of an organism.

<i>notification</i>	the submission of a prescribed information package to Environment Canada (or other federal authority) so that a new substance may be assessed for potential environmental or human health risks.
<i>organism</i>	any unicellular or multi-cellular biological entity capable of reproduction or replication including plants and animal vertebrates and invertebrates.
<i>release</i>	to discharge, spray, inject, inoculate, abandon, deposit, spill, leak, seep, pour, emit, empty, throw, dump, place, or exhaust.
<i>research and development organism</i>	a living organism that is undergoing systematic investigation or research by means of experimentation or analysis other than test marketing, the primary objective of which is to: (a) create or improve a product or process; (b) determine the technical viability or performance characteristics of a product or process, or (c) evaluate the organism prior to its commercialization through pilot plant trials, production trials, or customer plant trials so that technical specifications can be modified in response to the performance requirements of potential customers.
<i>substance</i>	any distinguishable kind of organic or inorganic matter, whether animate or inanimate, including living organisms that are microorganisms and organisms other than microorganisms (<i>i.e.</i> , plants, animal invertebrates and animal vertebrates); a "new" substance is a substance not listed on the Domestic Substances List (DSL).
<i>toxic</i>	refers to a substance that may have an immediate or long term harmful effect on the environment or its biodiversity, on the environment upon which life depends, or on human life or health.

toxicity the capacity of any substance to cause injury to humans, animals, plants or microorganisms.

Guidelines

Canadian Environmental Protection Act 1999 (CEPA)

The *Canadian Environmental Protection Act 1999 (CEPA)* is the primary legislation that ensures that all new substances, including living organisms, introduced into Canada via import or domestic manufacturing are assessed for their potential to harm human health, the environment and biodiversity. (The legislation may be perused at <http://laws.justice.gc.ca/en/C-15.31/index.html>.) The CEPA Environmental Registry (<http://www.ec.gc.ca/CEPARegistry>) encourages public involvement in environmental decision-making and facilitates access to documents, information and references.

The *toxicity* of a new substance is the key characteristic under regulatory scrutiny; *i.e.*, its capacity to cause injury to humans, animals, plants or to microorganisms. See the discussion about toxicity at http://www.ec.gc.ca/CEPARegistry/gene_info/fact_01.cfm).

CEPA includes a provision whereby new substances regulated by other "CEPA-equivalent" Acts, identified in Schedules 2 and 4, are exempt from CEPA notification requirements. (Schedule 2 identifies Acts concerning chemicals and polymers and Schedule 4 identifies Acts concerning animate products of biotechnology; each Act prescribes notification requirements and applies an evaluation process for toxicity and impact assessments.) The assignment of federal government regulatory authority over new substances is explained at http://www.ec.gc.ca/substances/nsb/eng/roadmap_e.shtml.

The federal departments that have responsibilities to evaluate submissions concerning new products of biotechnology include the

- Canadian Food Inspection Agency (CFIA);
- Environment Canada (EC);
- Fisheries and Oceans Canada (FOC);
- Health Canada (HC).

Persons wishing to conduct research, import, manufacture (*i.e.*, produce, develop or grow) or sell any new substance are advised to

contact the appropriate federal authority well in advance of the planned activity.

All new substances not regulated by “CEPA-equivalent” Acts fall under CEPA provisions; Part 5 covers new chemicals and polymers and Part 6 covers new substances that are animate products of biotechnology (organisms and microorganisms). The New Substances Division of Environment Canada is the primary contact for all notifiers (www.ec.gc.ca/substances). EC co-ordinates the involvements of other federal departments and agencies for specific aspects of risk assessments (e.g., health or safety impact).

The *New Substances Notification Regulations (NSNR)* pursuant to CEPA 1999 prescribes the obligations of notifiers (importers and manufacturers) to submit information for ‘life-cycle’ environmental protection assessments. General information about the new substances program is available at http://www.ec.gc.ca/substances/nsb/eng/home_e.shtml.

New Substances Notification Regulations

There are two explicit stand-alone NSNR regulations; one for inanimate new substances and one for animate new substances.

NSNR (Chemicals and Polymers) address inanimate products of biotechnology (i.e., new chemicals and polymers, and the inanimate products of microorganisms such as biochemicals and biopolymers). Guidance documents concerning prescribed notifications and testing are posted at http://www.ec.gc.ca/substances/nsb/eng/cp_guidance_e.shtml.

NSNR (Organisms) address living organisms that are

- microorganisms;
- organisms other than microorganisms such as plants, invertebrates and vertebrates;
- organisms developed through the application of science and engineering, i.e., genetically modified organisms (e.g., transgenics, clones, chimerics), and organisms derived from *in vitro* culture;
- naturally occurring organisms that are used in engineered processes such as fermentation, bioremediation, phyto-remediation, industrial enzyme and drug production;
- organisms that are also regulated under the *Food and Drugs Act*.

Guidance documents concerning notifications and testing for living organisms are posted at http://www.ec.gc.ca/substances/nsb/eng/bio_guidance_e.shtml.

Research and development organisms must not be removed from approved containment or confinement locations and may not be transferred to the possession of other parties without approval from Environment Canada.

Domestic Substances Lists (DSLs)

The DSLs are lists of federally approved 'existing' substances compiled under Section 66 of CEPA. DSL-listed substances were either in Canadian commerce between 1984 and 1986 or have been added subsequently after undergoing comprehensive CEPA toxicity risk assessments. DSL-listed substances may or may not have usage conditions or restrictions assigned. Substances in the lists associated with Significant New Activities (SNACs) are identified with an "S" flag; uses beyond those approved would require additional notifications and assessments. Any 'new' organisms that do not appear on Canada's Domestic Substances Lists (DSL) may be subject to NSNR; see http://www.ec.gc.ca/substances/nsb/eng/lists_e.shtml.

New substances in products regulated under the *Food and Drugs Act* (e.g., pharmaceuticals, biologics, natural health products, food additives, novel foods, medical devices, personal care products, cosmetics) must undergo safety assessments under F&DA and environmental assessments under NSN (i.e., until the F&DA is amended to include ecological assessments). Health Canada maintains an In Commerce List (ICL) of substances for which notification requirements do not apply at present; see http://www.hc-sc.gc.ca/ewh-semt/contaminants/person/impact/consultation/icl_lsc-eng.php.

Inanimate Substances Exempt from NSNR (Chemicals and Polymers)

Certain inanimate new substances (e.g., those assessed under other legislation, transient reaction intermediaries, impurities and contaminants related to the preparations of new substances, substances occurring in nature) are exempt from NSNR. See http://www.ec.gc.ca/substances/nsb/cpguide/eng/c3_e.html#s3_3.

Living Organisms Exempt from NSNR (Organisms)

Pursuant to Section 26 of CEPA 1999, there are a number of noteworthy exemptions to NSNR notification requirements:

- organisms regulated by other legislation pursuant to Schedule 4 of CEPA 1999 as noted above;
- existing organisms listed on the Domestic Substances Lists (DSL), http://www.ec.gc.ca/substances/nsb/eng/lists_e.shtml, unless the organisms are associated with Significant New Activities (SNACs) as identified with an "S" flag;
- impurities and contaminants in minimal concentrations in accordance with CEPA 1999 para. 106(6)(c);
- living organisms in transit through Canada;
- naturally occurring indigenous plants to which science and engineering has not been applied;
- naturally occurring indigenous animals (domesticated, livestock, zoo, aquaria) when produced through traditional breeding, artificial insemination, surrogate hosting or embryo splitting;
- research and development (R&D) organisms that meet the following criteria:
 - *microorganisms in a contained facility*
 - maximum import quantity less than 50 ml or 50 g;
 - maximum manufacture quantity less than 1000 L for Biosafety Level 1 or less than 250 L for Biosafety Level 2 to 4.
 - *organisms other than microorganisms*
 - imported or manufactured in a facility from which there is no release of the organism, the genetic material of the organism, or material from the organism involved in toxicity.

Note: The R&D notification exemption for *organisms other than microorganisms* in a contained facility will likely be removed by the summer of 2009. Environment Canada has served notice that its New Substances Division wishes to be informed about research and development activities with macroscopic organisms prior to formal health, safety and environmental assessments. The nature and extent of the information required for R&D activities would be dependent on the containment and confinement proposed and the risks of exposures. EC also intends to prepare consensus guidelines concerning recommended standards for containment and confinement of vertebrate macro-organisms. Consult the Director of Research Risk Management (ext. 52048) for up-to-date information.

Notification Requirements for Chemicals and Polymers

Environmental and human health assessments are conducted on new chemicals and polymers to determine whether they are toxic or capable of become toxic. Guidelines for notification and testing of new substances (chemicals and polymers) are outlined at

http://www.ec.gc.ca/substances/nsb/cpguide/eng/cpguide_e.html.

Notification information requirements and notification information packages are described in this document.

Substances subject to notification are specifically described at

http://www.ec.gc.ca/substances/nsb/cpguide/eng/c3_e.html#s3_4.

Assistance with chemical safety, containment and occupational health protection is available by contacting the University's Laboratory Safety Officer (ext. 56401) and/or the Director of Research Risk Management (ext. 52048).

Notification Requirements for Living Organisms

The information to be notified to Environment Canada is summarized in the Schedules to the NSNR (Organisms); see

<http://canadagazette.gc.ca/partII/2005/20050921/html/sor248-e.html>. Pre-notification consultations with EC are recommended;

telephone 1-800-567-1999. The applicant may request that confidential business information (CBI) in the notification submission be protected from public access.

Microorganisms are notifiable under Schedules 1 to 4. Schedule-specific assessment periods range from 30 to 120 days. Import or manufacture cannot begin until the assessment period has expired. Risk group classifications for biological agents and biosafety containment level precautions are required to identify appropriate laboratory facilities and operational protocols. However, these details convey no information about environmental risks.

Schedule 1 Notification – has a 120-day assessment period

- for microorganisms intended for use anywhere in Canada;
- for microorganisms intended for use in an industrial process;
- for microorganisms introduced into an ecozone where it is not indigenous;
- for microorganisms introduced into an ecozone where it is indigenous.

Schedule 2 Notification – has a 30-day assessment period

- for microorganisms imported into or manufactured in containment facility, or for export only.

Schedule 3 Notification – has a 90-day assessment period

- for microorganisms imported or manufactured for use in an experimental field study.

Schedule 4 – Notification has a 30-day assessment period

- for microorganisms introduced or used at the same site where isolated or manufactured.

Organisms other than microorganisms are notifiable under Schedule 5. The assessment period is 120 days. Again, import or manufacture cannot begin until the assessment period has expired.

Schedule 5 Notification – has a 120-day assessment period

- for plants, invertebrates, animal vertebrates;
- for aquatic organisms with novel traits;
- for R&D organisms that do not meet the exemption criteria (*e.g.*, where environmental releases are possible).

Guidance documents for notifications are available at

http://www.ec.gc.ca/substances/nsb/eng/bio_guidance_e.shtml. The nature and extent of the information that must be submitted to Environment Canada is dependent on the organism's characteristics, the proposed use, and anticipated concerns about potential exposures.

For Health Canada Guidelines concerning the notification of new substances developed under the *Food and Drugs Act* (*e.g.*, human biologics, novel foods and food additives), see <http://www.hc-sc.gc.ca/ewh-semt/contaminants/person/impact/notification-declaration/index-eng.php>.

Assessment Outcomes

- No suspicion of toxic, and posting to the DSL;
- No suspicion of toxic for the proposed use; posting of a SNAC notice;
- Suspicion of toxicity:
 - a request for more information;

- control measures are imposed regarding how the organism is imported, manufactured, used and/or disposed.

Post-Notification Responsibilities of Importers and/or Manufacturers

- submitting notifications under the appropriate Schedule for an intended new use;
- submitting notifications prescribed by SNAc provisions;
- notifying EC of any errors in the original notification;
- notifying EC about new information concerning toxicity.

Containment Standards for Research and Development

Microorganisms

Containment standards for microorganisms in research and development settings are recommended in the following documents:

Laboratory Biosafety Guidelines, Health Canada, 3rd Edition, 2004
<http://www.phac-aspc.gc.ca/ols-bsl/lbg-ldmbl/index.html>. Further information and performance checklists are found at <http://www.phac-aspc.gc.ca/ols-bsl/containment/index.html>.

The Risk Group classifications for human pathogens and containment information are available from the Public Health Agency of Canada (613-957-1799). Dynamic organism lists are posted at http://www.phac-aspc.gc.ca/ols-bsl/pathogen/organism_e.html.

The Animal and Plant Health Directorate (APHD) of CFIA maintains a database of animal pathogens and emerging animal pathogens. For more information and guidance on containment required, the APHD must be contacted at 613-952-8000.

The U.S. National Institutes of Health (NIH) *Guidelines on Recombinant DNA and Gene Transfer* describe containment levels for biological organisms via special laboratory design, containment equipment, and laboratory safety protocols. Appendix B classifies human etiologic agents into risk groups on the basis of hazard, and Appendix G describes biosafety level-specific physical containment and

prudent microbiological practices. The document is available at <http://www4.od.nih.gov/oba/RAC/guidelines/guidelines.html>.

For assistance with containment design for microorganisms, contact the University's Biological Safety Officer at extension 53190.

Organisms other than microorganisms

The CFIA Office of Biohazard Containment and Safety (BCS), <http://www.inspection.gc.ca/english/sci/bio/bioe.shtml>, sets biocontainment standards for animal and zoonotic pathogens. Minimum design, physical and operational requirements for laboratories and animal containment facilities are specified in the CFIA document *Containment Standards for Veterinary Facilities*, 2005, at <http://www.inspection.gc.ca/english/sci/lab/convet/convete.shtml>.

The NIH *Guidelines on Recombinant DNA and Gene Transfer*, Appendix Q, also describes containment and confinement practices for research involving whole animals that are transgenic, or that involve viable recombinant DNA-modified microorganisms tested on whole animals (<http://www4.od.nih.gov/oba/RAC/guidelines/guidelines.html>).

The University's standards for containment of plants with novel traits (PNTs) are outlined in the Research Guidelines document titled *Agricultural Biotechnology – Plants with Novel Traits (PNTs)*, http://www.uoguelph.ca/research/forms_policies_procedures/biotechnology.shtml

A CFIA document concerning *Containment Standards for Facilities Handling Plant Pests* (draft September, 2006) may be relevant; see <http://www.inspection.gc.ca/english/sci/bio/plaveg/placone.shtml>. Information about Canada's plant protection program is found at <http://www.inspection.gc.ca/english/plaveg/plavege.shtml>.

University standards for containment and confinement of experimental laboratory and agricultural animals are described in the Research Guidelines document titled *Agricultural Biotechnology – Biotechnology-Derived Animals*. See the web-page http://www.uoguelph.ca/research/forms_policies_procedures/biotechnology.shtml.

The University's Biosafety Officer, (extension 53190), the Director of Research Management (extension 52048), Animal Facility Managers should be consulted about the human, animal and environmental risk

assessments that must be undertaken, and about physical containment needed for BD/GE animals and recombinant organisms. CFIA has produced helpful checklists for facility assessment purposes: <http://www.inspection.gc.ca/english/sci/bio/anima/inspect/formindexe.shtml>.

CEPA Compliance and Enforcement

Environment Canada promotes compliance with CEPA via communications to the public, consultations with stakeholders, and publication of information. Environmental audits are voluntary internal evaluations undertaken to verify compliance. External EC enforcement is achieved via inspection activities, investigations of suspected violations, and via measures that compel compliance either extra-judicially (*e.g.*, orders or directives) or through court actions (*e.g.*, injunctions or prosecutions).

Explanations about compliance and enforcement of CEPA are found at www.ec.gc.ca/CEPAREgistry/documents/policies/candepolicy/toc.cfm.

Importation of Animal, Plant and Human Pathogens

Permits are required from CFIA in order to import animal pathogens into Canada. Instructions in this regard are found at <http://www.inspection.gc.ca/english/sci/bio/anima/animae.shtml#2>. A *Facility Certification for the Importation of Animal Pathogens* form (<http://www.inspection.gc.ca/english/for/pdf/c5083apaze.pdf>) must also be submitted to CFIA. Contact the University Biosafety Officer (ext. 52049), the Director of Animal Facilities Management (ext. 58856), the Director of Animal Care Services (ext. 54305), the Manager of Campus Animal Facilities (ext. 54304), and/or the Director of Research Risk Management (ext. 52048) for assistance with permit applications and required certifications.

For guidance concerning the importation of human pathogens, and the requisite permits from the Public Health Agency of Canada, see <http://www.phac-aspc.gc.ca/ols-bsl/pathogen/index.html>.

For guidance about the import of exotic plants, please see <http://www.inspection.gc.ca/english/plaveg/plavege.shtml>.

Transportation of Dangerous Goods

The Transport Dangerous Goods Directorate of Transport Canada (<http://www.tc.gc.ca/tdg/menu.htm>) is responsible for the national compliance program to regulate and enforce public safety in all transportation modes for dangerous goods. Details are at <http://www.tc.gc.ca/tdg/site.htm>. The *Transportation of Dangerous Goods Regulations* are at <http://www.tc.gc.ca/tdg/clear/menu.htm>.

Advice about procedures concerning the transport of specimens is available from the Biohazard and Safety Containment Unit at CFIA, <http://www.inspection.gc.ca/english/sci/bio/bioe.shtml>. Guidelines from the Office of Laboratory Security, Public Health Agency of Canada may also be helpful; see http://www.phac-aspc.gc.ca/dpg_e.html.

The International Air Transport Association (IATA) is another source of information; see <https://www.iataonline.com/>.

Assistance with dangerous goods compliance is available from Environmental Health and Safety, extension 56401.

Further Assistance

Contact the Director of Research Risk Management (ext. 52048) for advice and assistance with NSNR compliance.

References

Environment Canada (the "Green Lane")
www.ec.gc.ca

New Substances Website, Environment Canada
www.ec.gc.ca/substances

Regulatory Roadmap for New Substances in Canada
http://www.ec.gc.ca/substances/nsb/pdf/roadmap_e.pdf

Terrestrial Ecozones of Canada
<http://www.ec.gc.ca/soer-ree/English/vignettes/default.cfm>

Public Health Agency of Canada
www.phac-aspc.gc.ca

Canada's Laboratory Biosafety Guidelines

<http://www.phac-aspc.gc.ca/ols-bsl/lbg-lmbml/index.html>

CEPA 1999 Compliance and Enforcement Policy

www.ec.gc.ca/CEPAREgistry/documents/policies/candepolicy/toc.cfm

National Institutes of Health (NIH) *Guidelines on Recombinant DNA and Gene Transfer*, 2002

<http://www4.od.nih.gov/oba/RAC/guidelines/guidelines.html>

CFIA *Containment Standards for Veterinary Facilities*, up-dated 2005

<http://www.inspection.gc.ca/english/sci/lab/convet/convete.shtml>.

U.S. Centers for Disease Control (CDC · NIH), *Biosafety in Microbiological and Biomedical Laboratories*, 5th edition, 2007

<http://www.cdc.gov/OD/ohs/biosfty/bmb15/bmb15toc.htm>.