New Substances Notification (NSN) for Cell and Gene Therapy Organisms

CAPRA

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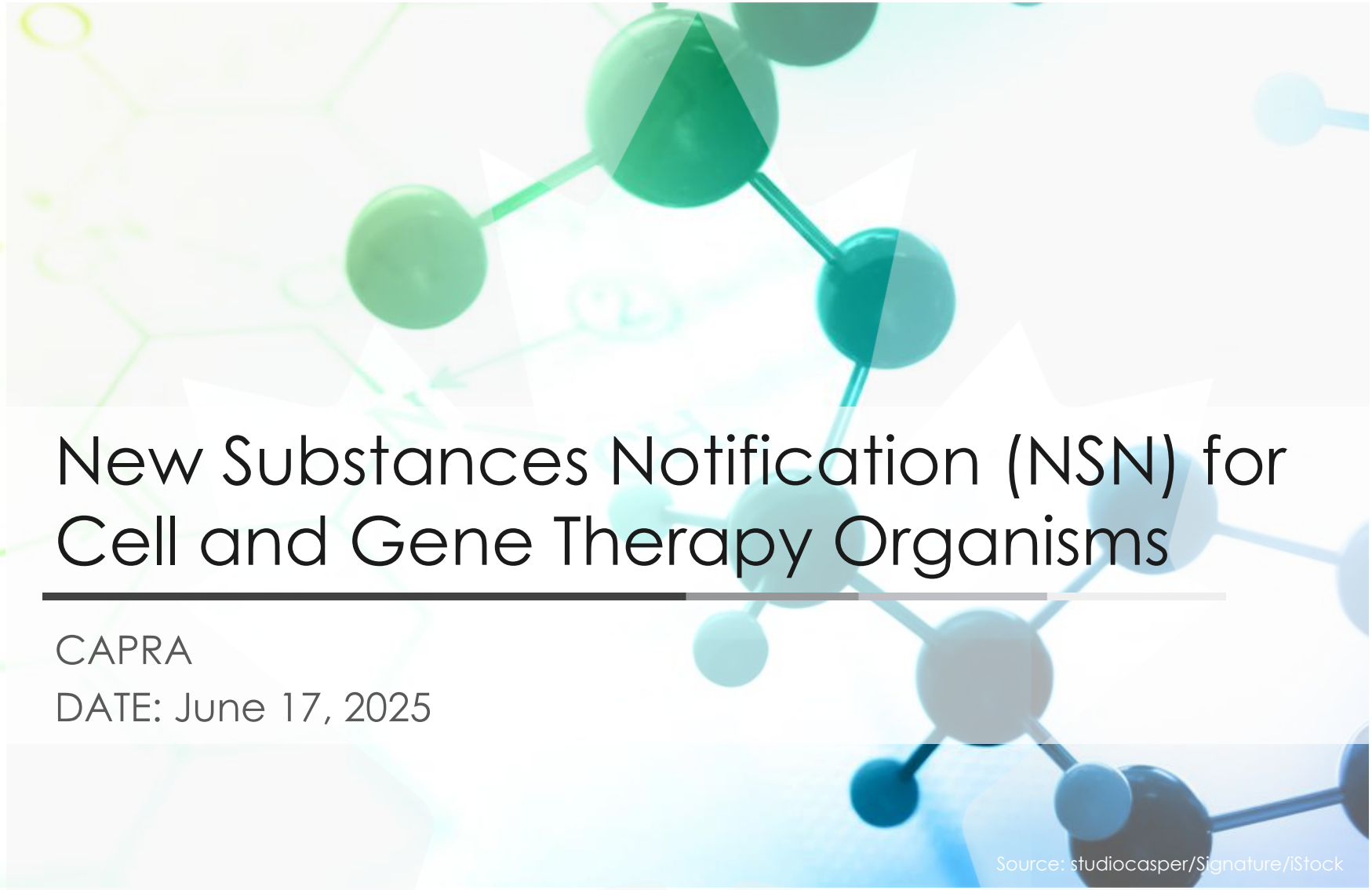

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***Catherine Sullivan Regulatory Affairs Specialist**, Regulatory Affairs Unit, Health Canada*

Canada

Overview

- In the first part of the presentation, we will go over the *Canadian Environmental Protection Act* and the *New Substances Notification Regulations* (NSNR)

- The second part of the presentation will focus on the *New Substances Notification Regulations (Organisms)* and cell and gene therapy organisms specifically

Legal and Regulatory Authority

- *Canadian Environmental Protection Act,1999* (CEPA)
  - Important part of Canada's federal environmental legislation aimed at preventing pollution and protecting the environment and human health
  - Defines 'substance'
  - Defines the criteria of section 64 of the Act (toxicity)
  - Establishes the Domestic Substances List

- There are 2 New Substances Notification Regulations:
  - *New Substances Notification Regulations (Chemicals and Polymers)*
  - *New Substances Notification Regulations (Organisms)*
  - Ensures that no new substance is introduced into the Canadian marketplace before an assessment of its potential risks has been completed

The Domestic Substances List

- Domestic Substances List (DSL):
  - If substance is not listed on the DSL, it is considered new to Canada and is subject to the NSNR

- All additions and deletions are published in the *Canada Gazette*
  - living organisms are listed by explicit biological name on the public list or by confidential number and masked name on the confidential list

Substance

- Defined in CEPA as:
  - Any distinguishable kind of organic or inorganic matter whether animate or inanimate

- Substances include living organisms:
  - Bacteria
  - viruses
  - Cells

- Definition of a living organism:
  - Living organism is a substance that is an animate product of biotechnology

- Substances used in biologic drugs, such as cell and gene therapy organisms, are captured in the definition of biotechnology as outlined in CEPA:
  - *the application of science and engineering in the direct or indirect use of living organisms or parts or products of living organisms in their natural or modified forms*.

Substances regulated under other Acts

Substances manufactured or imported for a use that is regulated under an Act or Regulation listed in Sch 2/4 of CEPA are not subject to the NSNR

Schedule 2 (Chemicals and Polymers)	Schedule 4 (Living Organisms)
Pest Control Products Act & Pest Control Products Regulations	Pest Control Products Act & Pest Control Products Regulations
Feeds Act & Feeds Regulations	Feeds Act & Feeds Regulations
Fertilizers Act & Fertilizers Regulations	Fertilizers Act & Fertilizers Regulations
	Seeds Act & Seeds Regulations
	Health of Animals Act & Health of Animals Regulations (veterinary biologics)

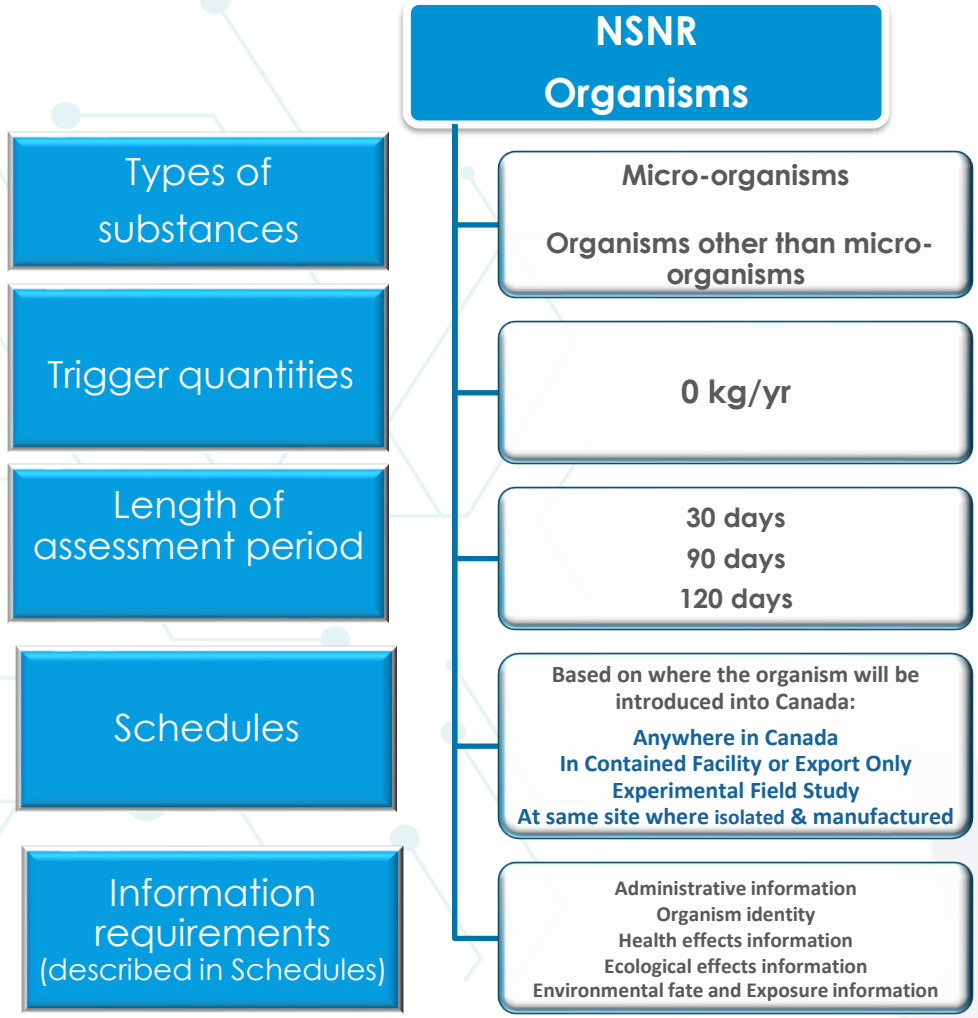
The *Food and Drugs Act* is not listed in Sch 2 or Sch 4; substances intended for use in products regulated under the F&DA (such as biologic drugs) are subject to the NSNR

Research and Development Exemption

- Is used only for R&D (as defined in NSNR (Organisms))
  -specific containment criteria and quantity restrictions

- Organisms used in drug clinical trials are not considered R&D if they are injected into patients – no longer considered contained.

New Substances Notification Regulations (Organisms) Overview



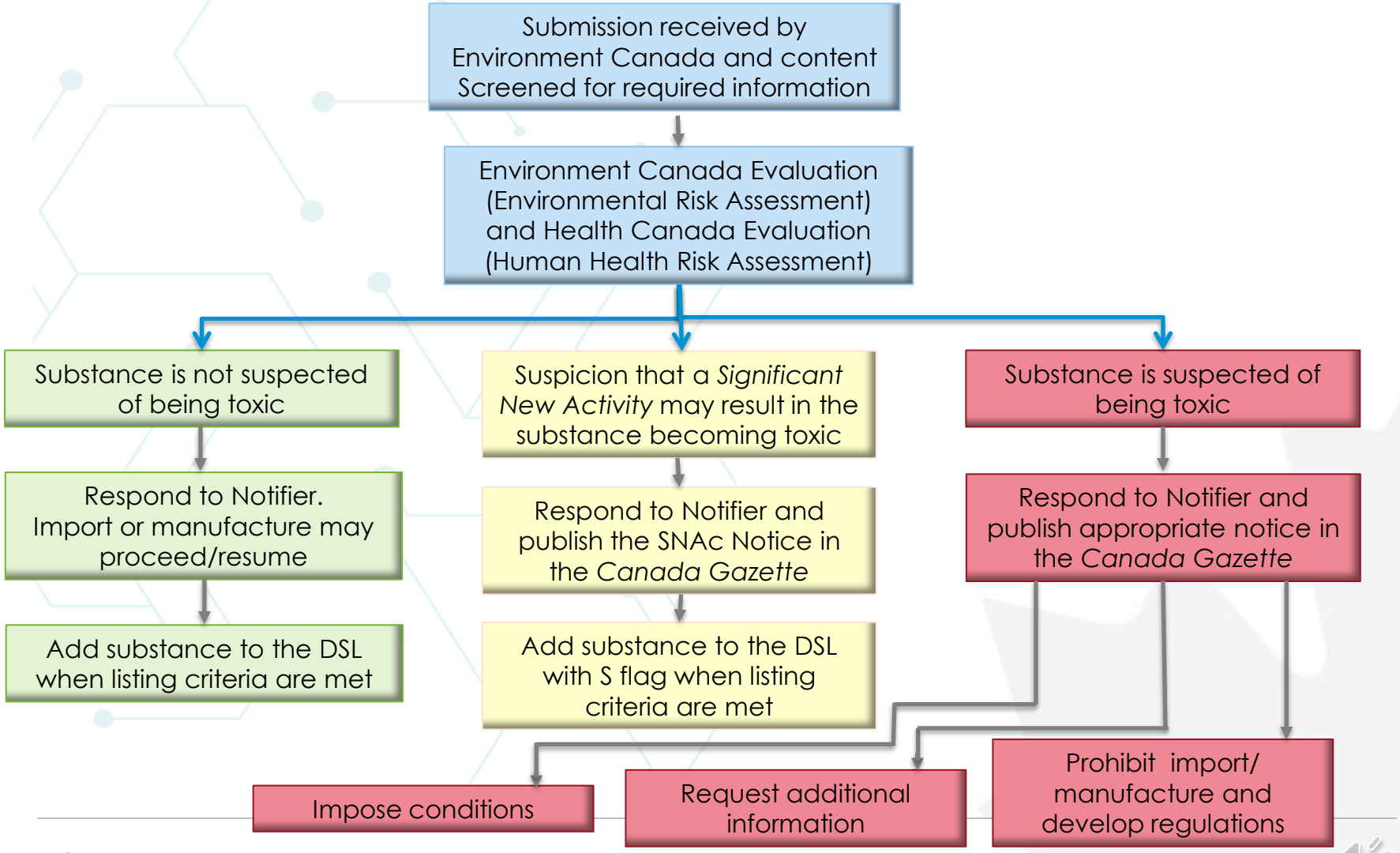
New Substances Notification (NSN)

- Manufacturer/Importer responsibility to submit prescribed information prior to manufacture or import beyond regulatory trigger quantities:
  - Cover letter
  - NSN reporting form
  - Attachments (including required test data and all other information required by the schedule)

- Government responsibility to assess information and take action when warranted within prescribed timeframes.

- Assistance preparing an NSN:
  - Pre-notification consultation
  - Guidance Document for the *New Substances Notification Regulations (Chemicals and Polymers)*: https://www.canada.ca/en/environment-climate-change/services/managing-pollution/evaluating-new-substances/chemicals-polymers/guidance.html
  - Guidelines for the Notification and Testing of New Substances: Organisms http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=22FC25C8-1

Notification Process and Assessment Outcomes



Assessment of Biologic Drugs

- Safety, quality and efficacy of biologic drugs are assessed under the *Food and Drugs Act* (F&DA) administered by the Biologics and Radiopharmaceutical Drugs Directorate (BRDD);

- Environmental and indirect human health assessment of new substances found in biologic drugs is conducted by the New Substances Program, which is jointly administered by ECCC and HC, under *Canadian Environmental Protection Act, 1999* (CEPA).

Supplementary Guidance for Cell and Gene Therapy Organisms

- *Supplementary Guidance Document for the Notification and Testing of New Substances: Organisms Used in Cell and Gene Therapy under Schedule 1 of the New Substances Notification Regulations (Organisms)*

- This supplementary guidance document is intended to complement *the Guidelines for the Notification and Testing of New Substances: Organisms.*

- The supplementary guidance is an interim measure intended to assist notifiers until a more permanent solution is adopted for cell/gene therapy substances

- The supplementary guidance addresses the technical requirements for 3 different types of cell and gene organisms:
  - human cells
  - replicating substances
  - non-replicating substances

Supplementary Guidance Continued

Human cell-based substances:

- cultured non-modified human cells, or
- genetically modified human cells that carry a non-replicative/replication incompetent vector or carry no vector at all.

Non-replicating substances:

- genetically modified to be incapable of replication except under specifically controlled conditions, such as non-replicative virus, non-replicative bacterium or non-replicative vector

Replicating substances:

- the capacity to divide or replicate in the human body and/or in the environment such as a replicative vector (including a human cell-based substance that contains a replicative vector), oncolytic virus or oncolytic bacterium.

Supplementary Guidance Continued

- Streamlined the notification process: notifiers can provide standardized statements for certain information requirements instead of literature searches

- For example:

  A description of the biological and ecological characteristics of the micro-organism, including its life cycle

  The following statement may be included to meet the information requirement if it is applicable:

  The notified substance is a human cell. As mentioned in subparagraph 1(f)(v), human cells require specific conditions to survive, grow and replicate which are not found outside the human body. A description of the life cycle outside of the human body is not available as it will not survive or replicate outside the human body.

- The guidance document provides standard statements for certain waiver requests

Cell and Gene Therapy

- Policy for cell/gene therapy organisms: 30-day assessment period instead of 120 days.
- Possible to cross reference information found in the CTA/NDS to satisfy information requirements in the NSN.
- Consolidated NSNs.

Review of the NSNR (Organisms): Proposed Approach for Regulatory modernization

- NSNR (Organisms) modernization is focussed on 3 themes:
  - Improving openness and transparency
  - Responding to advances in science and technology; and
  - Reducing regulatory inefficiencies

Objective: Facilitate access to innovative products of biotechnology, including biologic drugs subject to F&DA by streamlining the environmental assessment of living organisms used in biologic drugs.

Inspection & Enforcement

- Environment and Climate Change Canada enforcement officers may carry out inspections under CEPA

- If convicted, possible penalties are:
  - Fine and/or imprisonment

- Discussed in further detail in the Enforcement and Compliance Policy for the Canadian Environmental Protection Act:
  https://www.canada.ca/en/environment-climate-change/services/environmental-enforcement/publications/compliance-policy-canadian-protection-act.html

Key Messages

- Living organisms not on the DS Lintended for use in cell and gene therapy require the submission of a Schedule 1 anywhere in Canada NSN 120 days prior to import or manufacture
- The New Substances program has a policy of completing the assessment in 30 days rather than 120 days
- The supplementary guidance for cell and gene therapy organisms is specifically tailored for cell and gene therapy substances
- Pre-Notification Consultation (PNC) to help notifiers with their NSN package
- For assistance preparing a New Substances Notification:

Substances Management Information Line	substances@ec.gc.ca 1-800-567-1999
Environmental Assessment Unit	eau-uee@hc-sc.gc.ca 1-866-996-9913