Compliance under CEPA

- **What is New and What you need to know**

Michele Richardson Consulting
CAPRA Presentation
Oct 29, 2019

Meeting Objectives

Facilitate understanding of pharmaceutical industry responsibilities related to:

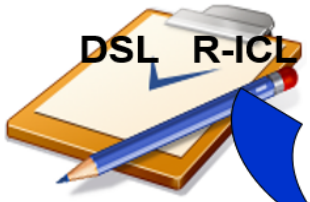
Canadian Environmental Protection Act (CEPA) compliance for new and existing substances in products regulated under the *Food and Drugs Act (F&DA)*

Learning Outcomes

- Describe *CEPA* and the *NSNR*, their relevance and respective requirements for the pharmaceutical sector.
- Explain how *CEPA* compliance impacts a company's chemical inventory management with respect to **new** and **existing** substances.
- What is NEW in this space?

The New Reality

Regulatory Decision Making has become significantly more complex



Industry Challenge (High Priorities, Batches 1-12)

Rapid Screening (low priorities)

DSARs, SARs and RM considerations (all priorities)

CMP3 Grouping initiatives: Fatty Acids and Derivatives, Furan Compounds, Epoxy Resins, Seven Hydrocarbon-based substances, Benzophenone, Talc

Ministerial Conditions

Revised-ICL Categorization and Prioritization

Nanotechnology Provisions (NSNR)

Microbeads

Plastics

Schedule 1 listing

NSNR Organisms

Proposal to Amend F&DR

CEPA 1999

DSL inventory update

Section 71 Notices

What are F&DA Substances?

In products regulated under F&DA:

- pharmaceuticals
- radiopharmaceuticals
- veterinary drugs
- biologics
- cosmetics
- food additives
- medical devices
- natural health products
- novel foods

CEPA 1999

Key Principles

- pollution prevention / sustainable development
- application of the precautionary principle
- protection of the environment and human health

Purpose of Parts 5 and 6

- Part 5: Controlling Toxic Substances
- Part 6: Animate Products of Biotechnology

To ensure that “new substances” are not introduced into Canada before an assessment to determine whether they are “toxic” or capable of becoming “toxic” has been made

.

Definition of a Substance

Substance

- Any distinguishable kind of organic or inorganic matter, whether animate or inanimate.
- Includes living organisms that are micro-organisms and organisms other than micro-organisms, and their metabolites

Exclusions from the definition of a substance

- Mixtures (can contain notifiable substances)
- Manufactured items

Definition of Toxic, CEPA 1999

Section 64 of the Act states that a substance is “toxic” if it is entering or may enter the environment in a quantity or concentration or under conditions that:

- have or may have an immediate or long-term harmful effect on the environment or its biological diversity; or
- constitute or may constitute a danger to the environment on which life depends; or
- constitute or may constitute a danger in Canada to human life or health.

Existing and New Substances

Substances listed on the Domestic Substances List (DSL) are considered **existing** substances.

Substances not listed on the DSL are considered new substances **(see Search engine).**
Note Search engine continuously updated and **NEW** updates should be seen in the next year.

All new substances are regulated by someone, somewhere in federal government (i.e. including other Acts/Regulations listed in CEPA Schedules 2 and 4). **Examples** – *Pest Control Products Act*, *Seeds Act*, *Feeds Act*, *Fertilizers Act*, *Health of Animals Act*.

- Note that the ***F&DA* was NOT listed** in Schedule 2 or 4.

Regulation of Substances under CEPA 1999

Substance (Chemical, Polymer, Living Organism,)

On the Domestic Substances List (DSL) (Existing)

- Were in commerce in Canada between 1984 – 1986 i.e. "grandfathered"

or

- Were added to DSL after a comprehensive assessment – for example, Schedule 1 (full release) under NSNR-O

New to Canada

- Assessed under NSNR prior to manufacture and/or import

Notification may be required

Inventory Lists

Domestic Substances List (DSL)

- Compilation of substances known to be in Canadian commerce between January 1, 1984, and December 31, 1986

Non-Domestic Substances List (NDSL)

- Inventory of substances assessed by the US Environmental Protection Agency (US EPA) by listing on the Toxic Substances Control Act (TSCA) Chemical Substances Inventory.
- Substances are added to the NDSL one year after being listed on the public TSCA Chemical Substances Inventory.
  - Update to list twice a year
  - Fewer information requirements

CEPA 1999 Impact to *Food and Drugs Act* (F&DA) substances

September 14, 2001

- Ingredients in products regulated under the *Food and Drugs Act (F&DA)* became subject to Canadian Environmental Protection Act, 1999 (CEPA 1999) and the *New Substances Notification Regulations* (Chemicals and Polymers) and (Organisms).

September 1, 2001

- Notice of Intent published in *Canada Gazette* Part I, for Health Canada's Environmental Impact Initiative (EII) to develop *Environmental Assessment Regulations* (EARs)

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Non-Statutory Inventory List for F&DA substances

In-Commerce List

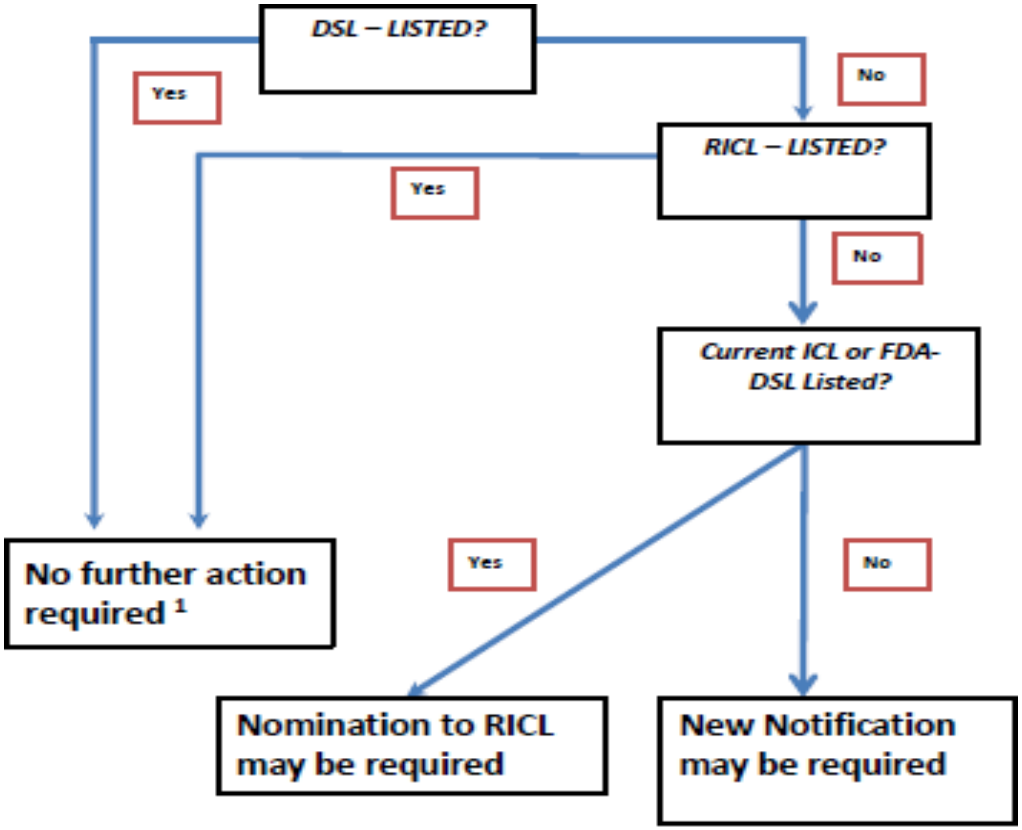
Compilation of substances from HC records known to be in Canadian commerce between January 1, 1987 and September 13, 2001.
Current ICL ~9,000 substances

Refinement of this list after nominations closed Feb 14, 2012.

Revised ICL (R-ICL) ~3,400 substances

- Current ICL substances whose identity was verified by HC prior to the nomination process, and
- Substances accepted for addition to the R-ICL by nomination process.
- Substances in F&DA product on R-ICL are NOT considered new.

Substances in F&DA Products Compliance Algorithm



[1] If on DSL and no risk management measures imposed i.e., SNAc then free to import/manufacture for any use.

Evolution of the Lists

DSL, NDSL and R-ICL are not static lists…..

- Substances can be added to each list through notification and/or nomination processes
- Substances on each list are being continuously reviewed for accuracy and potential for risk to human health and the environment.

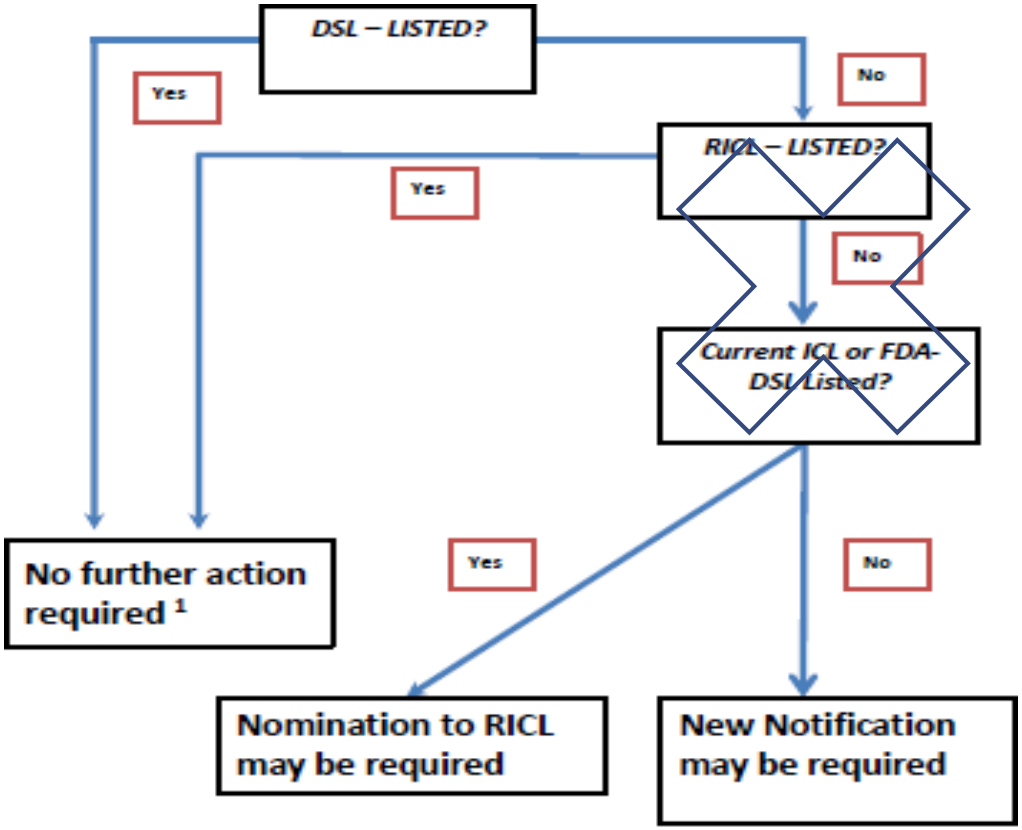
This status will change for the R-ICL very soon!!

R-ICL being closed

Closing of the nomination period

- The nomination process for the R-ICL ends on November 3, 2019, one year after publication of the Final Notice in the *Canada Gazette*, Part I.
- No further nominations will be accepted thereafter.
- See the Final Notice - Termination of the Revised In Commerce Substances List nomination process for further information.

Substances in F&DA Products Compliance Algorithm



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Environmental Assessment Regulations

Objective

- Ensure that new substances in products regulated under the *F&DA* are evaluated through a pre-market, comprehensive notification and assessment process for risks to the Canadian environment and indirect human health through environmental exposure.

Nearing end of construction….

Environmental Assessment Regulations

Regulations amending the Food and Drug Regulations for Environmental Risk Assessments of **Active Ingredients in Drugs**

Plan laid out in the Forward Regulatory Plan (FRP)

Why?

- To tailor environmental data requirements to the type of drug being assessed….at lower thresholds for Active ingredients in drugs.
- Specific data required to better understand the potential environmental and indirect human health effects of drugs.
- Aligning data requirements with other key regulatory agencies where possible (i.e., US FDA, EMA).
- Align notification and environmental risk assessment with drug approval process.

Regulations amending the Food and Drug Regulations

What is it?

- A proposal by HC to modernize the environmental risk assessment of drugs by creating a notification and assessment regime in the *Food and Drug Regulations*.
- Replaces the current environmental and indirect human health risk assessments for active ingredients used in drugs under the NSNR/NSNRO

When?

- Targeting publication of a regulatory proposal in *Canada Gazette, Part I* in Spring, 2020

Plan is on track….right around the corner.

Regulations amending the Food and Drug Regulations

Fall 2018

- ~ 2,000 stakeholders were asked for feedback on a cost-benefit analysis (CBA) survey.

April 2019

- Feedback informed policy positions which were presented to stakeholders during targeted consultations

July 2019

- ~ 200 stakeholders were asked for additional feedback through a follow-up CBA survey.

Spring 2020

- Publication of proposal in CGI and public comment period for ~70 days.

Regulations amending the Food and Drug Regulations

Impact

- Notification triggers at three stages:
  - Import/Fabricate stage
  - Clinical Trial stage (organisms only)
  - Market Authorization stage
- Canadian and international pharmaceutical industry will be impacted by increased notification and data requirements.
- Full extent of the impact assessed by Cost Benefit Analysis Survey responses - end of summer 2019.

Regulations amending the Food and Drug Regulations

1. Terminology Changes: 2018 ⟹ 2019 CBA survey

- Manufacture – changed to " fabricate" to align with the current language used in the Food and Drugs Act
- Animate/Inanimate Biologics – changed to "Organisms (living and non-living)"
- Additional explanation on distinction between Organism, biochemical/biopolymer

  Organisms (living and non-living) – live cells, live viruses and inactivated viruses.

  Biochemicals/biopolymers – chemicals/polymers produced by micro-organisms or proteins or nucleic acids derived from plant or animal (e.g. glycoproteins and enzymes).

Regulations amending the Food and Drug Regulations

2. Import/Fabrication Stage

Removal of scientific data requirements

Now only require annual import/fabricate quantities of:

- Active ingredient being imported;
- Drug in finished dosage form being imported; and/or
- Active ingredient being fabricated.

- Required to be submitted annually.
- Allows HC to track cumulative quantities across industry of active ingredients on the market and conduct cumulative risk assessment when quantities become a potential concern.

Regulations amending the Food and Drug Regulations

3. Market Authorization Stage
Basic Dataset
Name changed to "Screening Assessment Dataset"

- Removal of physical/chemical data requirements
- Removal of environmental risk assessment
- Used only to determine if the more comprehensive dataset is required

Environmental Fate and Effects Dataset
Name changed to "Risk Assessment Dataset"

- Used to conduct environmental risk assessment of the active ingredient

Regulations amending the Food and Drug Regulations

4. Other Changes

Creation of a List of Exemptions

Will include active ingredients:

- Listed on the Domestic Substances List (DSL) prior to promulgation of the proposed regulations;
- Listed on the Revised In-commerce List (R-ICL); and
- After they have had a full environmental risk assessment conducted and no risk was identified or that have met the criteria for a conditional exemption.

List will reduce:

- duplication of having to resubmit data for active ingredients already assessed, and
- number of generic products that would require data.

Regulations amending the Food and Drug Regulations

Next steps

***Canada Gazette* I – proposed Spring, 2020**
Public Comment period – 70? days
***Canada Gazette* II – TBD**
Coming into force TBD

New Substances Notification Regulations

Chemicals, Polymers and Organisms

Regulatory Compliance

To be compliant with *NSNR* and *CEPA*, all chemical, polymer, organism, food, cosmetic, natural health product and pharmaceutical substances should be:

- Inventoried on the DSL (Revised ICL option for food, cosmetic, natural health products or drugs); OR
- Eligible for exclusion from the provisions of the NSNR; OR
- Under the minimum volume threshold requiring notification; OR
- Notified through the submission of dossier.

NSNR Chemicals and Polymers

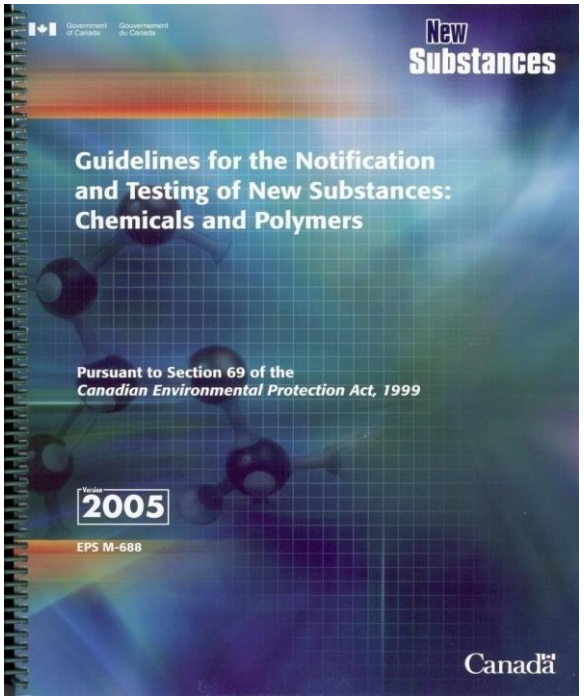
Graduated pre-market assessment process

- Based on increasing volumes of substance introduced into the market

Sets out ‘clear’ guidance as to when and how a substance should be notified to the government.

NEW Guidance expected to be published late 2019.

NEW NSN form includes questions on substitutes.



NSNR Chemicals and Polymers Schedules

Schedule	Description
1	R&D substances, contained site-limited intermediate substances, or contained export-only substances
2	Biochemicals and biopolymers
3	Polymers and biopolymers that are R&D substances, contained site-limited intermediate substances, or contained export-only substances
4	Other chemicals and biochemicals not on the NDSL (100 kg), or on the NDSL (1000 kg)
5	Other chemicals and biochemicals not on the NDSL (1000 kg), or on the NDSL (10000 kg)
6	Other chemicals and biochemicals not on the NDSL (10000 kg)
9	Reduced regulatory requirement for polymers and other polymers and biopolymers (1000 kg)
10	Other polymers and biopolymers on the NDSL or all of whose reactants are on the DSL or NDSL (10000kg)
11	Other polymers and biopolymers not on the NDSL (10000kg)

Overview of type of data/information NSNR Chemicals and Polymers

Country	Trigger Quantity	Data Requirements
Schedule 4	100 kg/year	• Use information • Identity information • Data on hand
Schedule 5	1000 kg/year	• Information from Schedule 4 • Phys-chem data • Ready biodegradation • One acute ecotoxicity test • Mammalian toxicity data • Exposure information
Schedule 6	10 000 kg/year	• Information from Schedules 4 and 5 • Additional phys-chem data • Two additional acute ecotoxicity tests • Additional mammalian toxicity • Skin sensitization / irritation tests • Additional exposure information

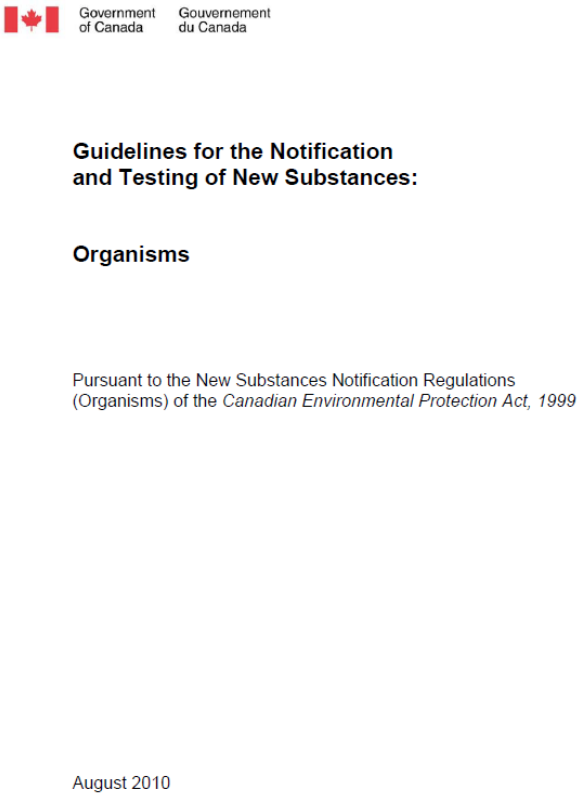
*Trigger quantities are higher for substances that are on the Non-Domestic Substances List (NDSL)
** For simplicity, only the most frequently notified NSNR Schedules are presented here. Other NSNR Schedules may apply to chemicals and polymers

Comparison Overview for Active ingredients -Chemicals and Polymers

	NSNR: C&P (Current)	Proposal (CBA)	Updated Proposal
Trigger Quantity	• 100 kg/year • 1000 kg/year • 10 000 kg/year	100 kg/year	0 kg/year
Notification Requirements	• Schedule 4 • Schedule 5 • Schedule 6	Schedule 4 + (includes phys-chem data)	Subset of Schedule 4 (substance identity information and annual kg quantities – submitted yearly)

- **Pros of the Updated Proposal**
  - Reduction in data requirements as import/fabrication volumes increase
  - Reduction in costs to industry of having to conduct data requirements (i.e. no higher Schedules as volumes increase)
- **Potential Concerns**
  - Increase in frequency in providing import/fabrication quantities (further consultation with industry and associations underway to fully characterize any benefits and costs)

NSNR Organisms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Guidelines for the Notification and Testing of New Substances:

Organisms

Pursuant to the New Substances Notification Regulations (Organisms) of the *Canadian Environmental Protection Act, 1999*

August 2010

Canada

Pre-market assessment process

Sets out 'clear' guidance as to whether subject to notification, when and how a substance should be notified to the government.

NEW Guidance expected to be published - date TBD.

NEW Guidance on Immunotherapy and Gene Therapy subset to be published – date TBD.

NEW NSNO form - date TBD

NSNR Organisms Schedules

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

Chart from HC presentation, Shearer 2015

Overview of type of data/information NSNR Organisms

Country	Trigger Quantity	Data Requirements

Schedule 1	0 kg/year	• Information on:
		  ○ Identity
		  ○ Manufacture/import
		  ○ Environmental introduction
		  ○ Environmental fate
		  ○ Human health effects
		  ○ Test procedures
		• Data on hand

** For simplicity, only the most frequently notified NSNR Schedules are presented here. Other NSNR Schedules may apply to organisms

Comparison Overview for Active ingredients - Organisms

	NSNR:O	Proposal (CBA)	Updated Proposal
Trigger Quantity	0 kg/year	0 kg/year	0 kg/year
Notification Requirements	Schedule 1	Subset of Schedule 1	Smaller subset of Schedule 1, annual kg quantities – submitted yearly

- **Pros of the Updated Proposal**
  - Reduction in data requirements
  - Reduction in costs to industry of having to conduct data requirements
- **Potential Concerns**
  - Increase in frequency in providing import/fabrication quantities (further consultation with industry and associations underway to fully characterize any benefits and costs)

NSN esubmission portal

Single Window Information Manager (SWIM) is a secure online system for environmental reporting.

The Chemicals Management Plan Reporting Dashboard

- Start, view and edit NSNs;
- Submit completed forms; and
- View or amend, when applicable recent submissions.
- Provides links to Guidance/indicates notification status.
- **NEW** updates in late 2019 (organisms, updated NSN form, etc.)

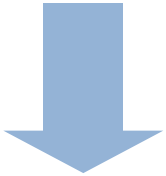
Existing Substances Management

Chemicals, Polymers and Organisms

Existing Substances Management

Chemicals Management Plan

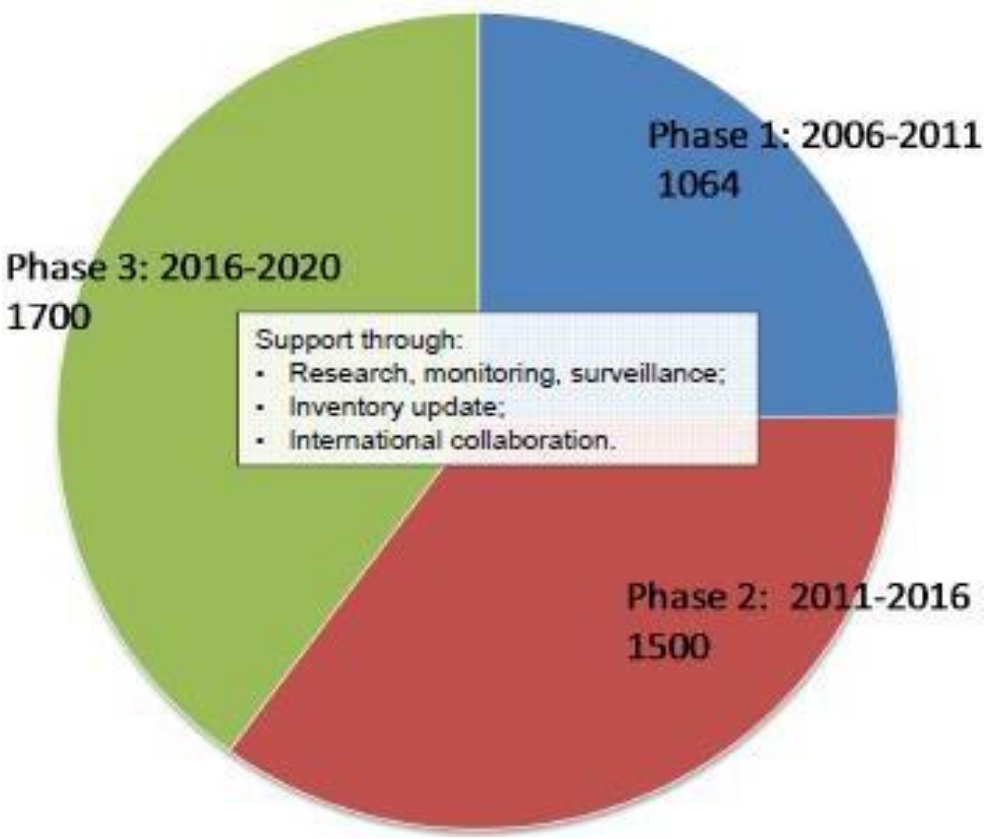
Categorization of Domestic Substances List



Chemicals Management Plan (CMP) for the screening of all substances categorized based on impact these substances may have on human or environmental health.

Timeline: to be completed by **2020**

Priorities under CMP

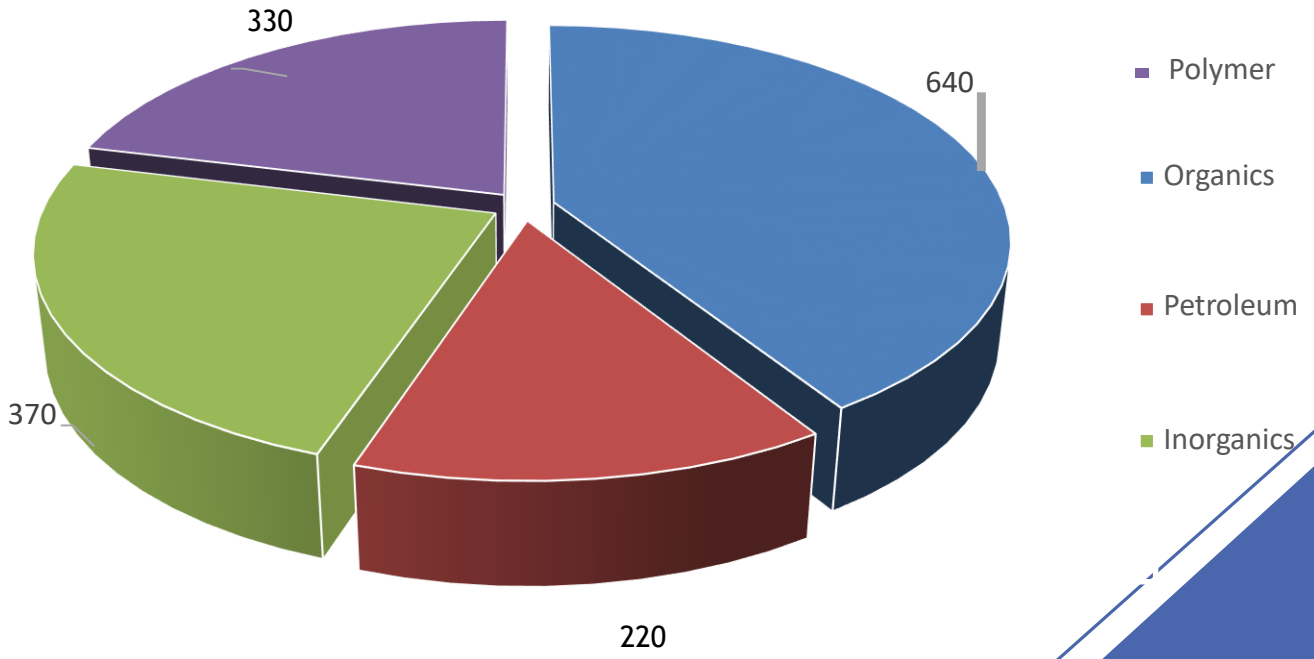


4,300 substances to be assessed by 2020

~19,000 substances identified as “not requiring further action at this time”

Priorities under CMP

Approximately 1,550 substances to be addressed in CMP3



Existing Substances Management

Post 2020?

- Work on the future of the Government of Canada chemicals management activities is being informed by the ENVI report from the House of Commons Standing Committee on Environment and Sustainable Development on the statutory review of the Canadian Environmental Protection Act, 1999 (CEPA 1999).
  - ~ 87 recommendations

- In June 2018, Government submitted a follow-up report to the Committee, and committed to further consider a number of recommendations related to chemicals as part of its engagement on the future of chemicals management, which could inform legislative reform.

Consultations are ongoing

RECAP

What's NEW

- R-ICL closes Nov 3, 2019
- *Regulations Amending the F&DR for Environmental Risk Assessments of Active Ingredients in Drugs* Spring 2020
- NSNR Chemicals and Polymers Guidance document and form December 2019
- NSNR Organisms Guidance document and form as well as specific Guidance for Gene Therapy and Immunotherapy 2020
- SWIM updates December 2019
- ENVI report actions 2020?
- CMP3 risk assessment summaries being published
- CMP post 2020 consultations ongoing including those for informed substitution

Acknowledgements

- CEPA Industry Coordinating Group [CEPA ICG]
- Environment and Climate Change Canada
- Health Canada

Thank you!

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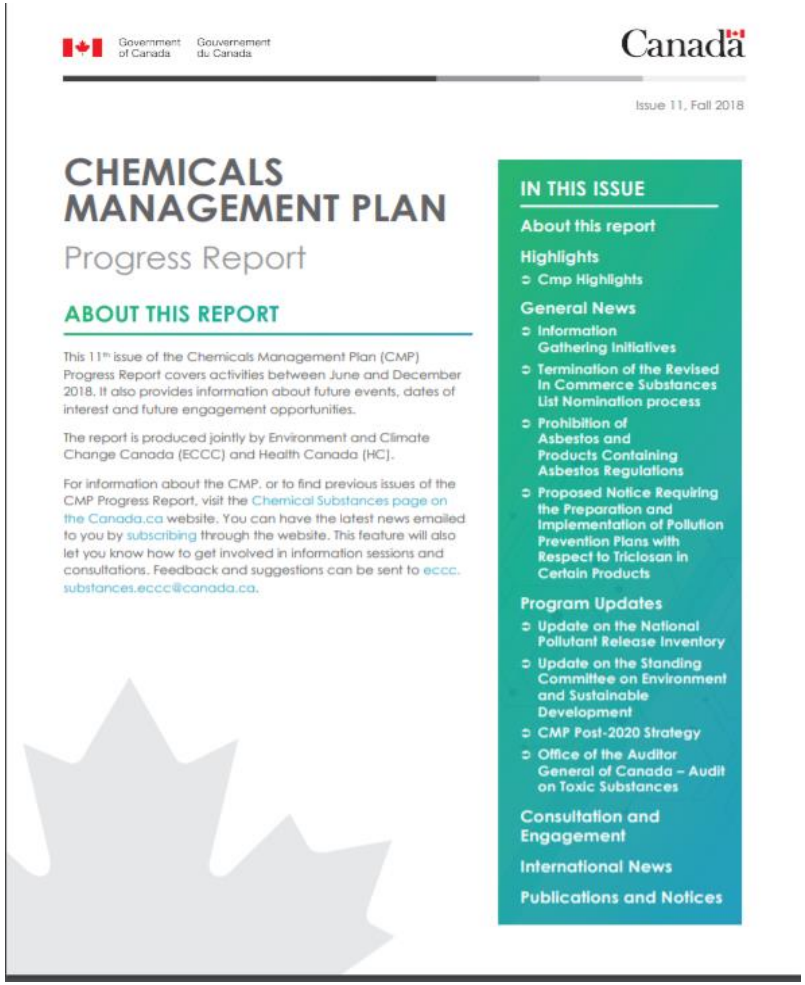
Chemicals Management Plan Progress Reports



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Issue 11, Fall 2018

CHEMICALS MANAGEMENT PLAN

Progress Report

ABOUT THIS REPORT

This 11th issue of the Chemicals Management Plan (CMP) Progress Report covers activities between June and December 2018. It also provides information about future events, dates of interest and future engagement opportunities.

The report is produced jointly by Environment and Climate Change Canada (ECCC) and Health Canada (HC).

For information about the CMP, or to find previous issues of the CMP Progress Report, visit the Chemical Substances page on the Canada.ca website. You can have the latest news emailed to you by subscribing through the website. This feature will also let you know how to get involved in information sessions and consultations. Feedback and suggestions can be sent to eccc.substances.eccc@canada.ca.

IN THIS ISSUE

Chemicals Management Plan March 2019 Report

CMP Highlights

General News

- Information Gathering Initiatives
- Termination of the Revised In Commerce Substances List Nomination process
- Prohibition of Asbestos and Products Containing Asbestos Regulations
- Proposed Notice Requiring the Preparation and Implementation of Pollution Prevention Plans with Respect to Triclosan in Certain Products