Agile Licensing for Drugs

CAPRA
2025 BIOLOGICS & BIOSIMILAR SYMPOSIUM

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Modernization plan enables Health Canada to regulate for the future

Modernizing clinical trial regulations

to encourage clinical trials by creating an environment that supports more innovative trials

Enabling Advanced Therapeutic Products

to ensure a flexible approach for innovative products that do not fit in the current system

Agile licensing for drugs

to advance agile licensing regulations that enhance safety while supporting innovation and economic growth

Agile licensing for medical devices

to ensure appropriate oversight while better enabling innovation

Supported by a modernized compliance and enforcement program

Agile Licensing builds on authorities introduced under Vanessa's Law in 2014 and contributes directly to the government's *Biomanufacturing and Life Sciences Strategy* that recognizes the importance of the regulatory system as an enabler of growth of Canada's domestic biomanufacturing sector.

Modernizing Regulations

Canada's Biomanufacturing and Life Sciences Strategy: Enabling innovation by ensuring world class regulation

Canada Gazette, Part I, Volume 155, Number 31: GOVERNMENT NOTICES (July 31, 2021)

Canada Gazette, Part I, Volume 156, Number 51: Regulations Amending Certain Regulations Made Under the Food and Drugs Act (Agile Licensing)- (Dec 17th 2022)

Consultation on proposed agile regulations and guidance for licensing drugs and medical devices- (December 17, 2022-April 26, 2023)

Regulations Amending Certain Regulations Made Under the Food and Drugs Act (Agile Licensing): SOR/2024-238
Canada Gazette, Part 2, Volume 158, Number 26: Index, Nov 29th 2024)

Agile Guidance Published at CGII

Related guidance documents and notices include:

- Guidance on the Food and Drug Regulations for public health emergency drugs

- Guidance document: Labelling of pharmaceutical drugs for human use

- Updates to the Quality (Chemistry and Manufacturing) Guidance: New Drug Submissions and Abbreviated New Drug Submissions

- Updates to the New agile regulatory provisions and updated guidance document for submitting risk management plans: Notice

-New terms and conditions for human and veterinary drugs: Notice – December 20, 2024

-Guidance on terms and conditions for class II to IV medical devices – December 18, 2024 published (will come into force January 1, 2026)

Coming into Force

Immediate Coming into Force (upon publication on Dec 18th 2024):

1. Amendments related to Public Health Emergency Drugs (including rolling reviews and terms and conditions for these drugs)
2. Information to support the examination of a drug submission
3. Disaggregated data
4. Labelling and manufacturer's standard

Delayed Coming into Force:

5. Modernizing requirements for biologic drugs – July 1, 2025
6. Terms and conditions for drugs – April 1, 2027
7. Risk Management Plans – April 1, 2027

1.Regulations for Public Health Emergency Drugs

- Extending COVID-19 modified requirements, including rolling reviews, to other public health emergency drugs Guidance on the Food and Drug Regulations for public health emergency drugs

The amendments to the *Regulations* enable:

- Timely access to safe, effective and high-quality PHEDs
- Modified requirements, for example, the option of a rolling review, draft labels and sufficient safety, quality and efficacy evidence
- The early importation and placement in Canadian facilities (pre-positioning) of a promising PHED for which a government contract for its procurement is in place, before that drug receives market authorization in Canada
- An agile approach for Drug Establishment Licences (DELs) that authorize regulated activities for PHEDs
- Terms and conditions (T&Cs), i.e., obligations placed on authorization holders, sponsors and importers

Scope and Application of a Public Health Emergency Drug

Given the lessons learned from the COVID-19 pandemic, Health Canada is now expanding the provisions in Part C, Divisions 1, 1A, 2 and 8 of the Regulations for activities related to a Public Health Emergency Drug (PHED), which is a drug that relates to a condition referred to on the List of Conditions that Threaten Public Health in Canada (List) that is incorporated by reference (IbR).

The Minister of Health may add a condition to the List only if the Minister has reasonable grounds to believe that:

(a) The condition presents, or is the result of, a significant risk to public health in Canada; and

(b) Immediate action is required to deal with the risk [C.08.001.2]

Overview of the CGII PHED Guidance

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› Applications and Submissions - Drug Products › Guidance documents on applications and submissions for drug products

Guidance on the Food and Drug Regulations for public health emergency drugs: Overview

Overview	Preparing a drug submission for a PHED	Drug establishment licences, good manufacturing practices
Post-market requirements	Pre-positioning a public health emergency drug	References, key contacts

Download in PDF format
(PDF format, 661 KB, 39 pages)

Organization: Health Canada

Date published: March 2025

Ongoing PHED Implementation

PHEDs (including terms and conditions and rolling review for these drugs) came into force upon CGII registration. Health Canada has repealed the definition, “designated COVID-19 drug” in the *Regulations* and has listed COVID-19, at the time of CGII registration, on the List.

- Provisions [as defined in subsection C.01.001(1) to the list under subsection C.08.001.2(2)] have been included to allow the Minister to add COVID-19 to the List provided they have reasonable grounds to believe that the addition is necessary to protect public health or safety.
- COVID-19 drug submissions which are variant specific and continue to have modified requirements and terms and conditions will apply as supplements or new drugs submissions for a PHED upon CGII publication.
- NOC, RMPs and T&Cs to remain active for authorized COVID-19 drugs.

The amendments to *the Fees in Respect of Drugs and Medical Devices Order* (Fees Order)

For PHEDs that use the rolling review option, may not be possible to complete within the set performance standards. As such, an exception from the requirement [paragraph 6(2)(c)] to remit fees if performance standards are not met for new drug submissions (NDSs) and supplemental new drug submissions (SNDs) for PHEDs that use rolling review option is required.

2. Information to support the examination of a drug submission

- 10 regulations are in the new Division 4. Two amendments related to the Division 4, include Division 8 (on-site evaluations), and Division 2 (storage). There is no change to current practice or expectations

Additional information or material for the review of drug submissions

- Division 8 is revised to reflect activities under current practice for review of drug submissions
- In line with current practice, C.08.003.1 is revised to clarify the Minister's authority to consider information or material that could be examined on a risk-based, case-by-case basis in reviewing a drug submission
- C.08.003.1 provides greater transparency for the current practices of potentially considering information or material obtained from sites (e.g., on-site evaluations (OSEs)), information filed under the FDA (e.g., Divisions 1, 5, and 8), and information from foreign regulatory partners in reviewing drug submissions

Storage

- Division 2 is revised to reflect activities under current practice for good manufacturing practices
- In line with current practice, C.02.012.1 is added to make explicit the implicit understanding that drugs must be prepared, stored, and transported in a manner that preserves their quality.

3. New Drug Submissions: Disaggregated Data

- Data to enable Health Canada's assessment of a drug's safety and effectiveness in different subgroups (*e.g.*, sex, age, race and ethnicity).
- HC proposed a regulatory amendment requiring manufacturers to submit human clinical data broken down into population subgroups for new and supplemental human drug submissions if the disaggregated data has already been submitted to the US FDA or the EMA
- Stakeholders expressed overall support for the proposed amendment and the Draft Guidance Document on the Collection and Analysis of Disaggregated Data in Clinical Trials was included as part of the CGI public consultation held from Dec 2022 to April 2023

Implementation & Next Steps:

- The requirements for disaggregated data came into force at CGII
- Guidance Document will be revised in 2025

4. Labelling and manufacturer's standard

- Removing industry irritants regarding drug labelling and manufacturer's standard. Updates were made to the following two guidance documents:
  - Guidance document: Labelling of pharmaceutical drugs for human use
  - Quality (Chemistry and Manufacturing) Guidance: New Drug Submissions and Abbreviated New Drug Submissions

Paragraphs C.01.004(1)(a)(iii) & (iv) of the *Food and Drug Regulations* were repealed, therefore making it no longer a requirement to list a standard on the product labels. There is no requirement for sponsors to update their labels to remove the standard. Rather, moving forward, sponsors will have the ability to decide if they would like to list the standard on the product labels. If they would like to update their labels, they would follow the processes set out in the relevant guidance documents.

As per Section C.01.011 (5) of the *Food and Drugs Regulations,* for Division 8 drugs (i.e. new drugs) other than those in Schedule C to the Act (Radiopharmaceuticals), where a manufacturer's standard is claimed, sponsors will have the option to propose limits that differ from the most stringent requirements for purity and potency of all the pharmacopoeial standards listed in Schedule B provided the limits are scientifically qualified.

-These limits will need to be provided in their submission and found acceptable to the Minister prior to the issuance of a Notice of Compliance. This amendment does not apply to Division 1 only drugs due to the regulatory structure outlined in Division 1, and the level of review that is conducted for these products.

5. Modernizing requirements for biologic drugs (Division 4)

Modernizing requirements for biologic drugs and removing outdated requirements

- Division 4 in Part C of the FDR dates from the 1950s and 1960s. The bulk of the 194 regulations in the current Division 4 are outdated, overly prescriptive, or unnecessarily product-specific.

- They will be replaced by 12 flexible and outcome-based regulations that support the flexible and outcome-based practices that currently and appropriately address biologic drugs.

- Expanding on the Notice published concurrently with the proposed regulations, BRDD is developing a Guidance document to accompany the new regulations when they come into force on July 1, 2025.

6. Terms and Conditions (T&Cs)

- Expanding terms and conditions to all drugs for improved post-market oversight

- Discretionary authority in Division 1 of the FDR that enables the Minister to impose or amend a T&C on the Drug Identification Number (DIN) of a human or veterinary drug (Division 1 and Division 8), at any time.
  - T&Cs **do not change the current threshold** for a drug to be authorized.

- T&Cs apply a lifecycle approach to Canadian authorized human and veterinary drugs (other than NHPs)
  - allow enhanced post-market oversight and monitoring of authorized therapeutic products
  - used when evolving science can inform decision making at all stages of a drug's lifecycle with the objective of continuously optimizing benefits while minimizing risks

- Overall objective: to ensure a drug maintains a favourable benefit-risk profile throughout its life cycle and that the safety, efficacy, or quality of a drug has not changed from when the market authorization was issued.

Use of Terms & Conditions for Drugs

- T&Cs are meant **to be used exceptionally** and when other regulatory mechanisms are not available to address the issues/concerns.

- Applying T&Cs is appropriate when:
  - information is being sought to verify if there is a change to the benefit-risk profile of a drug (e.g., uncertainty of the drug when used in a specific population)
  - the effectiveness of the drug needs to be confirmed (drugs with promising evidence of efficacy)
  - risks are to be managed through enhanced monitoring (can include to enforce elements of an RMP)
  - the quality of a drug requires monitoring

- T&Cs should **not** be imposed:
  - to address deficiencies in a drug submission or enable a submission to be filed with suboptimal data
  - to obtain additional information that would not result in a change to the benefit-risk profile of the drug
  - on a class of drugs for a general application requirement
  - to gather information to expand or add an indication to drug.

Next Steps – T&C Policy

- T&Cs authorities come into effect on April 1, 2027
- Two guidance documents are under development:
  1. Draft Guidance on terms and conditions for human and veterinary drugs
     - ➢ This guidance was posted for consultation at the same time as publication of the draft Agile Licensing Regulations (CGI) and has been revised based on comments received
  2. Draft Guidance: Notice of Compliance with Terms and Conditions (Promising Evidence) for human and veterinary drug submissions
     - ➢ New draft guidance that has not yet been posted for public consultation.

A Notice was posted at the time of the final Agile Licensing Regulations publication in CGII informing stakeholders that the two draft guidances will be posted for a 60-day consultation in the Spring 2025.

6. Risk Management Plans – Key Elements

- Risk Management Plans to better manage risks and uncertainties: [New agile regulatory provisions and updated guidance document for submitting risk management plans: Notice - Canada.ca]

Authority to require

- an RMP as part of a pre-market submission or application (including for SNDSs)
- an RMP in the post-market space
- an updated RMP (including for SNDSs) where warranted

Regulations also outline

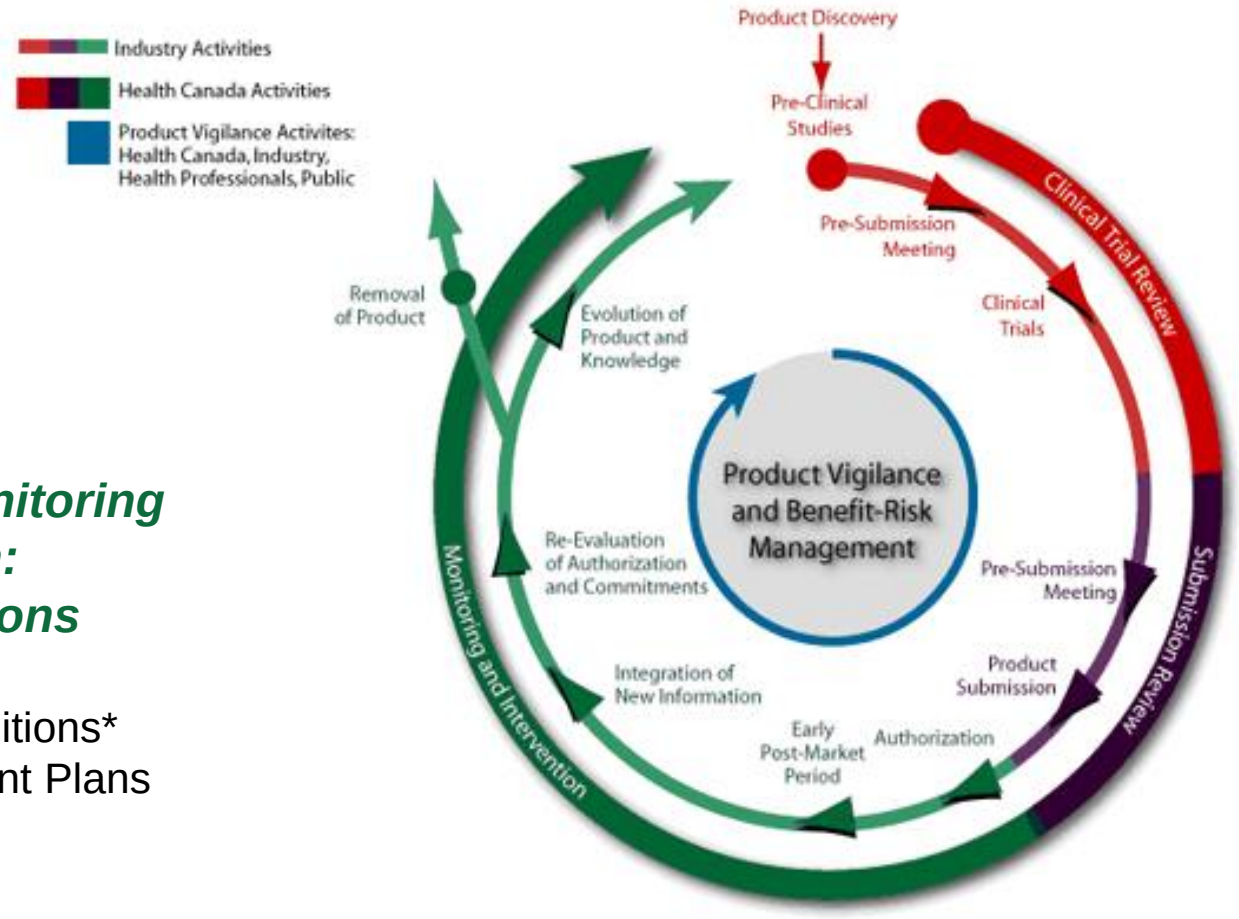
- triggers and thresholds to require an RMP
- purpose and content of an RMP, including that the RMP must
  - take into account Canadian context
  - include a summary in both English and French
- standing requirement to provide an updated RMP if risks, uncertainties or measures are significantly different from existing plan

RMP Guidance and Implementation Timelines

Updated Submitting risk management plans guidance document published on February 24, 2025

RMP Information Webinar for Industry to be held in Spring 2025

How Agile Licensing Components Fit in the Life-Cycle



Post-Market Monitoring and Intervention: the new regulations allow for

- Terms and Conditions*
- Risk Management Plans

Submission Review: the new regulations allow for

- Terms and Conditions*
- Risk Management Plans
- Analysis of Disaggregated Data
- Flexibilities for Public Health Emergencies
- Consideration of additional Information

➢ The new regulations also modernize the requirements for biologic drugs and provide greater flexibility in the application of drug standards and labelling throughout the life-cycle

* Terms and conditions apply to both drugs and devices, other components are focused on drugs only

Summary

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Questions?