Consultation: Proposed Enhancements to the Health Canada, CADTH, and INESSS Aligned Review Processes

1. PURPOSE

The *Aligned Reviews Between Health Canada and Health Technology Assessment Organizations* process was launched in June 2018 as part of Health Canada's Regulatory Review of Drugs and Devices (R2D2) initiative. This is a joint initiative between Health Canada, CADTH, and Institut national d'excellence en santé et en services sociaux (INESSS) that established a process to facilitate information sharing between Health Canada and the health technology assessment (HTA) agencies (CADTH and INESSS), coupled with the expansion of the window for filing HTA submissions on a pre-Notice of Compliance (NOC) basis from 90 to 180 calendar days in advance of market authorization. The aligned review process is currently optional for sponsors who are filing HTA submissions on a pre-NOC basis.

As described in the initial announcement regarding the aligned review process, Health Canada, CADTH, and INESSS committed to continuously monitoring the participation rates by sponsors, and adjusting the aligned review process as required to ensure that it provides benefits to all participants. Health Canada, CADTH, and INESSS have conducted an initial evaluation of the aligned review process and are seeking feedback on two proposals to enhance the processes for all stakeholders:

- a proposal to make participation in the information-sharing process mandatory for all HTA submissions that are filed on a pre-NOC basis (Section 3)
- a proposal for minor revisions to the consent letter to reduce the need for Health Canada to distribute information separately to CADTH and INESSS (Section 4).

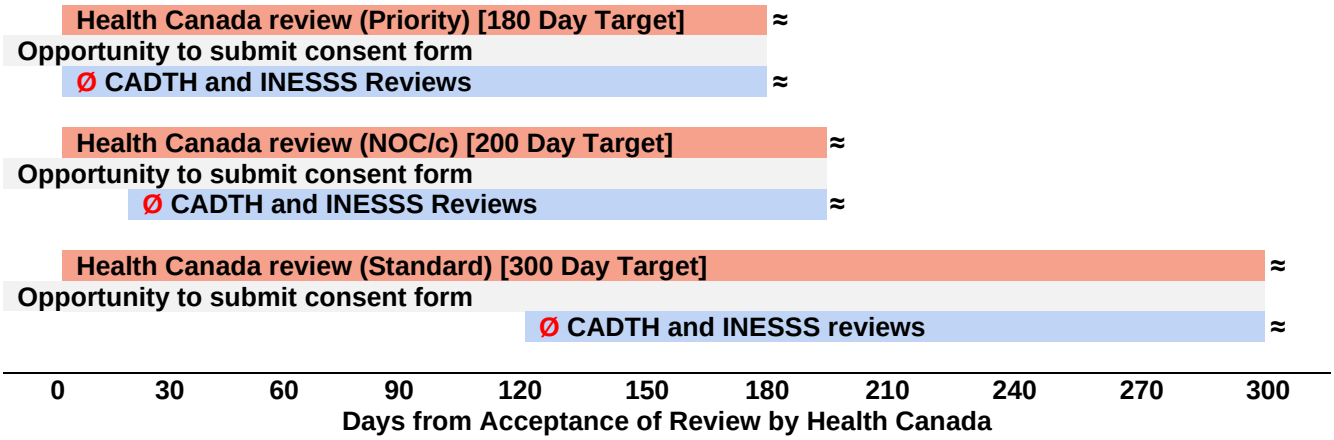
2. BACKGROUND ON ALIGNED REVIEWS

Participation in the aligned review process requires two elements: parallel review timelines between Health Canada and the HTA agencies (i.e., pre-NOC filing); and consenting to information sharing between Health Canada and the HTA agencies.

2.1 Parallel Review Timelines

As part of the aligned review process with Health Canada, CADTH and INESSS began accepting pre-NOC submissions up to 180 calendar days prior to the anticipated date of market authorization (Figure 1). This offered the potential for a substantial reduction in the interval between the issuance of a NOC and the HTA recommendations.

Figure 1: Examples of Parallel Review Timelines for Health Canada, CADTH, and INESSS



Ø = submission filing to health technology assessment agencies for optimal alignment; NOC/c = advanced consideration under the Notice of Compliance with Conditions policy; INESSS = Institut national d'excellence en santé et en services sociaux.

2.2 Consenting to Information Sharing

The information-sharing process was established to allow Health Canada to exchange information with CADTH and INESSS regarding drugs that are being reviewed on a pre-NOC basis. The information-sharing process helps ensure that the HTA agencies have advance notice of any issues that may have the potential to impact their review of the drug (e.g., changes to the indicated patient population), which would potentially avoid delays in the HTA review processes. Participation in the information-sharing process requires the sponsor to complete Health Canada's consent form, which authorizes sharing of information with CADTH and INESSS (e.g., distribution of Clarifaxes/Clarimails and Health Canada reports that may be relevant to the HTA review).

3. PROPOSAL FOR MANDATORY INFORMATION SHARING

3.1 Proposal and Rationale

Health Canada and the HTA agencies have continuously monitored participation rates by sponsors and the operational impact of the aligned review process. Participation rates have been sufficient to determine that the information-sharing process is beneficial for the HTA review processes in Canada. Information sharing has the potential to help reduce the interval between market authorization and HTA recommendations, as well as the following additional benefits:

- Permitting the HTA agencies to receive the Health Canada reviewer reports directly from Health Canada (rather than from sponsors after market authorization) allows the CADTH review to incorporate relevant findings into the reports before the sponsor comment period. This gives the sponsor the opportunity to review and provide clarification, if required, during the comment period.
- Information sharing can help ensure that the HTA agencies are fully aware of changes to the indication(s) for the drugs under review. This can help avoid delays in the review

process by allowing the HTA agencies to rapidly assess the impact of any revisions to the indication at an earlier point in the process.

- Sponsors that consent to information sharing and receive a Notice of Deficiency (NOD) or Notice of Non-Compliance (NON) may be permitted to remain in CADTH's review process (rather than mandatory withdrawal).

An important limitation of the current information-sharing process is that CADTH is currently forced to operate two parallel pre-NOC submission processes to accommodate the voluntary nature of the process (i.e., one process with information sharing and one without information sharing). This creates operational inefficiencies for CADTH and limits the ability of the agency to maximize the benefits of interacting with Health Canada and leverage opportunities to build upon the interpretations and appraisals conducted by Health Canada reviewers. As such, the agencies are seeking stakeholder feedback on an important procedural revision that would make participation in the information-sharing process mandatory for all submissions filed on a pre-NOC basis.

Key points regarding the proposed revisions to the pre-NOC submission process are as follows:

- There would be no changes to the timing for filing pre-NOC submissions (i.e., up to 180 calendar days prior to the anticipated date that market authorization will be issued).
- In order to be eligible to file a submission on a pre-NOC basis, all sponsors would be required to indicate that they have or will be providing Health Canada with the completed consent form.
- CADTH would require that the sponsor indicate that it has or will be providing Health Canada with consent in the following documents:
  - advance notification form
  - declaration form.
- INESSS would require that the sponsor indicate that it has or will be providing Health Canada with consent in the following document:
  - pre-notice documentation.
- Failure to provide the consent form or revoking authorization could result in a suspension of the HTA review or mandatory withdrawal from the pre-NOC submission process.
- In order to avoid disruption with any existing plans for filing submissions, CADTH will ensure that sponsors are provided with at least 12 weeks of notification prior to implementing any revisions to the pre-NOC filing procedures.

3.2 Key Messages Regarding Information Sharing

- Health Canada, CADTH, and INESSS make their best efforts to limit the sharing of information to that which is deemed relevant to the alignment of their reviews. For example, manufacturing process information would generally not be shared as it is typically not needed by the HTAs (as described in the existing submission requirements).

Sponsors are reminded that both CADTH and INESSS have well-defined processes and procedures regarding the disclosure of information related to the drug under review. Sponsors are given the opportunity to review and request the redaction of confidential information before any reports are posted by the HTA agencies.

- The aligned review process is respectful of independent processes, timelines, and decision-making by Health Canada and the HTA agencies. Participation in an aligned review does not affect Health Canada's labelling decisions, the outcome of the market authorization decision, or the recommendations issued by the HTA agencies. However, it does provide opportunities to avoid delays in the HTA processes for sponsors and helps ensure that CADTH and INESSS are able to conduct operations in the most efficient manner.
- Health Canada and the HTAs are committed to transparency. Information about which submissions are part of the aligned review process is currently disclosed on Health Canada's Submissions Under Review Lists, on INESSS website, and will be disclosed on CADTH's website.

4. PROPOSAL FOR REVISED CONSENT LETTER

4.1 Proposal and Rationale

Health Canada, CADTH, and INESSS are proposing revisions to the existing consent letter to enable the three agencies to share information more efficiently. Under the existing process, Health Canada is required to compile and distribute relevant documents to CADTH and INESSS separately. As these documents are sent via secure distribution mechanisms, the processes involved can be resource intensive for Health Canada. The proposed revision to the consent letter would allow both CADTH and INESSS to securely access relevant documents from Health Canada using CADTH's Collaborative Workspaces. This will introduce efficiencies by eliminating the need for Health Canada to complete multiple distributions of the same documents. The consent letter has also been revised to reflect the current list of authorized recipients for CADTH. The proposed changes to the consent letter are summarized in Section 4.2.

4.2 Proposed Revisions to Template

The proposed revisions to the consent letter are marked in red:

This letter authorizes the sharing of certain information set out below (including confidential business information as defined in section 2 of the Food and Drugs Act (R.S.C., 1985, c. F-27)) with respect to the drug submission for "[Submission type], [Brand name, common name, medicinal ingredient(s), control number [NUMBER] (if available)/E-identifier: eXXXXXX]" (the "Product") between Health Canada (HC), and the Canadian Agency for Drugs and Technologies in Health (CADTH), and l'Institut national d'excellence en santé et en services sociaux (INESSS) (hereinafter referred to as Health Technology Assessors [HTAs]). ~~*This letter does not serve to allow the sharing of this information between HTAs.*~~

Specifically, [name of manufacturer] authorizes meetings of HC and HTAs, and the sharing of information and documents (final and draft versions) related to the Product, including:

- *HC and HTA Review Reports*
- *HC Reports (including, but not limited to, Manager's Memos, Executive Summaries, and Priority Review request assessments (may be under separate control number))*
- *Draft Summary Basis of Decision*
- *Meeting Minutes (may be under a separate control number)*
- *Questions and responses related to the review of the Product*
- *Product Monograph*
- *Submission Status*

[Manufacturer Name] understands and acknowledges that once HC shares information (including confidential business information) with HTAs, the following HTAs may engage in further sharing of this information solely with the entities specified below, and solely in accordance with the published policies and any applicable legislation governing the treatment of confidential information by the HTAs:

CADTH

- ~~*Participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies*~~
- *Federal, Provincial, and Territorial governments, including their agencies and departments*
- ~~*P/T health authorities, including regional health authorities*~~
- *Pan-Canadian Pharmaceutical Alliance (pCPA) Office*
- *Canadian Association of Provincial Cancer Agencies*
- *Canadian Blood Services*
- *Institut national d'excellence en santé et en services sociaux (INESSS)*

INESSS

- *INESSS may include the above information in their evaluation of the product or in the notice and/or recommendation submitted to the Quebec Minister of Health and Social Services, being expressly understood by the Manufacturer that, according to its enabling act, INESSS shall publish the notices and recommendations it makes within 30 days after sending them to the Minister*
- *INESSS may share the above information with the Canadian Agency for Drugs and Technologies in Health (CADTH) and Pan-Canadian Pharmaceutical Alliance (pCPA) Office*

This authorization remains valid until such time as it is revoked by the Manufacturer, in writing to HC: [Director of the Office of Submissions and Intellectual Property, Resource Management and Operations Directorate, Health Canada].

It is understood and acknowledged by the Manufacturer that this authorization for the sharing of information or any subsequent revocation of this authorization does not operate to authorize or prevent HC from sharing information (including confidential business information) that HC is otherwise legally authorized to disclose.

It is confirmed that the wording of this consent letter has not been modified in any way by the Manufacturer from the Health Canada template, other than submission identification and contact information.

Duly executed by [print name], an authorized representative of [name of Manufacturer].

I [Name and Title of Senior Official of Manufacturer of Product], represent and warrant that I have the authority to give this consent on behalf of [name of Manufacturer].

[Signature]

5. SUBMITTING FEEDBACK

To provide comments on the proposal, please use the following Survey Monkey feedback templates:

- English
- French.

Feedback must be received by CADTH by 5:00 p.m. EDT on August 10, 2020. For feedback to be considered, you must identify yourself to CADTH. Only one response per organization will be considered. If you have any questions about the feedback process, please email CADTH.

6. NEXT STEPS

Following the consultation period, Health Canada, CADTH, and INESSS will carefully assess all stakeholder feedback before announcing any decisions regarding changes to the current processes. We thank you in advance for your interest.

If you have any questions about the feedback process, please email CADTH.