Health Canada Santé Canada

Draft Pause the Clock Proposal for Pre-market Submissions/Applications

Health Products and Food Branch
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Canada

Health Canada is responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

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Ébauche de proposition de temps de pause dans l'examen des demandes ou des présentations préalables à la mise en marché

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1. What is pause the clock?

Pause the clock (commonly referred to as "stop the clock") is a mechanism that allows for the review clock to be formally paused, under specified circumstances or points in time. It is proposed as part of the implementation of Health Canada's renewed cost recovery framework for drugs and medical devices[1]. Under the new framework, the new penalty model is intended to ensure each review is completed within the performance standard. This objective will not change. All individual submissions/applications that are not completed within the established performance standard will be rebated 25% of the fee. What is proposed with the pause the clock is to allow for flexibility to accommodate certain defined circumstances, such as a request from a sponsor for additional time to respond to a clarification request, and, as such, Health Canada is only accountable for the time it spends on a particular submission/application. While mechanisms exist that stop the review (user fee) clock [e.g. Notice of Deficiency, Notice of Noncompliance, Additional Information Requests (medical devices)], there are currently no mechanisms in place that enable Health Canada to pause and resume the review clock during the review of drugs and medical devices.

2. Scope and application

A pause the clock mechanism would be applicable to all pre-market human and veterinary drug submissions/applications and medical device applications that are subject to user fees. Refer to the Revised Fee Proposal for Drugs and Medical Devices for a complete list of applicable submissions/applications and their accompanying performance standards.

At this point in time, the proposal only applies once submissions/applications are accepted for review.

Out of scope of this particular project is the acceptance of unsolicited[2,3,4] additional data during the review process as this is not linked to a mechanism to pause the review clock.

The Regulatory Operations and Regions Branch is developing a separate pause the clock proposal specific to the Establishment Licensing process.

3. Proposed model

The proposed triggered pause the clock model consists of pausing the review clock during the review process only when pre-specified conditions (triggers) are met. The purpose of this consultation is to solicit feedback from industry on the proposed triggers.

[1] https://www.canada.ca/en/health-canada/services/drugs-health-products/funding-fees/cost-recovery-initiative.html
[2] Refer to the Guidance Document: Management of Drug Submissions/Applications for human drugs.
[3] Refer to the Guidance Document: *Management of Regulatory Submissions* for Veterinary Drugs.
[4] Refer to the Guidance Document: *Management of Application for Medical Device Licences and Investigational Testing Authorizations*

4. Proposed Principles

The following key principles will guide the implementation of a pause the clock mechanism:

A pause the clock mechanism is not intended to limit a regulator's ability to interact with and/or request clarification from sponsors at any time during a product's regulatory lifecycle.

A pause the clock is not intended to delay approvals.

- Within the proposed model, it is anticipated that clock pauses would be triggered only under defined circumstances; therefore would not routinely add to the total time to decision (alignment with the Regulatory Review of Drugs and Devices objectives related to access)
- In some circumstances, a pause could avoid the submission receiving a negative decision (i.e. a pause the clock could avoid the need for a submission/application to receive a Notice of Non-compliance, such as when the sponsor is unable to respond to a clarifax within 15 days)

A pause the clock mechanism would be one of many tools used to manage the review process.

Health Canada is committed to openness, transparency, and consistency regarding circumstances under which the clock would pause.

For drug submissions, a pause would not occur within 15% of the performance standard (for example, a pause would not occur within the last 45 days of a submission with a 300 day performance standard).

Health Canada is committed to continuously monitor, assess and report on how the pause the clock mechanism is being implemented and its effectiveness in achieving desired objectives.

5. Proposed triggers that would pause the clock

Human and veterinary drugs

A. Sponsor request for an extension to respond to a Request for Clarification (Clarifax) for human drugs or Minor Information Request (MIR) for veterinary drugs.

The review clock would pause when there is Health Canada approval of a sponsor's request for an extension to a clarification or Minor Information Request beyond the number of days that they have to respond in accordance with applicable guidance documents (e.g. *Management of Drug Submissions* for Human Drugs, *Management of Regulatory Submissions* for Veterinary Drugs, and the *Management of Disinfectant Drug Applications*). The sponsor would need to provide a written rationale for the extension. If Health Canada grants the extension, the review clock would pause and the sponsor would have additional time to respond to the request. The extension period would be mutually agreed upon by the sponsor and Health Canada. It is proposed that the extension cannot be less than 5 days or more than 90 days per clarifax/MIR.

As a pause would not occur within 15% of the performance standard, a request for an extension to a clarifax would not be accepted in the last 15% of the review.

The review clock would resume at the end of the agreed upon extension period assuming receipt of the requested information by the Office of Submissions and Intellectual Property (OSIP) for human drugs and by the Administrative Officer for veterinary drugs.

Listed below are some examples of when this trigger may be used:

- Request for re-analysis of data and the sponsor needs more time to respond
- There is a significant safety and/or efficacy issue identified within the submitted data packageand the sponsor requires more time to respond
- The sponsor needs more time to respond because of its own internal operational constraints (national or global office shut down)

B. Advice from an Expert Advisory Panel/Committee is sought by Health Canada

This trigger applies when Health Canada determines the need to use an expert advisory panel/committee. Where possible, the timing of this pause would be mutually agreed upon by both Health Canada and the sponsor. The clock would pause when Health Canada provides the sponsor with a letter confirming this pause with the draft questions for the expert advisory panel/committee included in the letter. The review clock and Health Canada's review would resume upon receipt of the recommendation(s) from the panel.

Medical devices

A. Combination products when medical device performance standards apply

This trigger would only apply when the combination product's principal mechanism of action is achieved by the medical device portion of the product (i.e. regulated as a medical device). The review clock would pause when the review of the device portion of the product results in a positive recommendation but the drug review is ongoing. Health Canada would provide the sponsor with a letter confirming this pause. The device review clock would resume upon completion of the drug review.

B. Linked medical device applications where different timelines apply

The review clock would pause when the review of one device application is complete except that the review of the additional device application it is linked to remains outstanding. Health Canada would provide the sponsor with a letter confirming this pause. The device review clock would resume upon completion of the linked device application. In this scenario, pause the clock would be implemented as a tool to formalize current practice.

Example: When a Class II License Application is completed (15 day performance standard) while the linked Class III or IV application (60 or 75 day performance standards, respectively) is not.

6. Consultation questions

Interested and affected stakeholders are asked to provide their feedback on this proposal within 60 days from date of publication. Health Canada is interested in stakeholder feedback on the following questions:

1. What are your thoughts on the proposed triggers listed? Please provide specific feedback on the proposed triggers.
2. Can you think of a situation in the review process beyond those mentioned where a trigger could be used? When would it be valuable from industry's point of view to be able to pause the clock? Please describe under what circumstances this would occur.

7. Next steps

All comments will be considered in the finalization of the pause the clock mechanism. Health Canada intends to publish a "What Was Heard" report summarizing all of the feedback submitted.

A pause the clock policy will be implemented in parallel with the new user fees for drugs and medical devices, by April 2019. Once implemented, Health Canada will monitor/track and report on the use of the pause the clock mechanism to determine its frequency of use and benefits to the management of the submission/application process.

The following guidance documents that are used by Health Canada and drug sponsors to navigate the submission/application process will be revised to reflect the pause the clock mechanism:

- *Guidance for Industry: Management of Drug Submissions* for human drugs
- *Guidance For Industry Management of Regulatory Submissions* for veterinary drugs
- *Management of Application for Medical Device Licences and Investigational Testing Authorizations* for medical devices
- *Guidance document - Management of Disinfectant Drug Applications* for disinfectants