CADTH

Procedures for CADTH Review of Nationally Procured Drug Products

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1 Purpose

This document outlines the procedures for the CADTH review of nationally procured drug products (e.g., those indicated for use in the treatment COVID-19 or monkeypox). This process is distinct from the CADTH reimbursement review process and is focussed on providing implementation advice to support Federal, Provincial, and Territorial governments. Any manufacturers with questions about this process should contact CADTH at requests@cadth.ca.

2 Eligibility

2.1 Drug Eligibility

Eligibility for review through the *Procedures for CADTH Review of Nationally Procured Drug Products* will be determined by CADTH in consultation with federal, provincial, and territorial governments. Manufacturers with eligible products will be contacted by CADTH.

2.2 Market Authorization Status

Reviews can be initiated prior to receiving market authorization from Health Canada or after receiving market authorization from Health Canada (i.e., pre-Notice of Compliance [NOC] and post-NOC, respectively).

2.3 Sponsor Eligibility

Pharmaceutical industry sponsors are typically the Drug Identification Number (or DIN) holders for the drug being filed for review with CADTH; however, it could be another manufacturer, supplier, or entity recruited by the manufacturer or the supplier.

2.4 Declining to Participate

If a manufacturer declines to participate in the review process (e.g., failure to provide the required documentation), CADTH may continue with the review based on publicly available information. The manufacturer may not have the opportunity to review and comment on the draft report prior to publication by CADTH.

3 Pre-submission Meetings

Pre-submission meetings will be offered in the same manner as described in section 4.1 of the *Procedures for CADTH Reimbursement Reviews.* Given the expedited review timelines for these reviews, CADTH may permit pre-submission meetings to be scheduled after the review has been initiated.

4 Required Documentation

Table 1: Required Documents for Review of Nationally Procured Drug Products

Section	Specific items and criteria
General information	Signed cover letter
	Draft and final product monograph
	Completed declaration letter template
Health Canada documentation	Table of Clarimails or Clarifaxes (as soon as available)
Efficacy, effectiveness, and safety information	Results for pivotal and supportive clinical studies
	Common Technical Document sections 2.5, 2.7.3, 2.7.4, and 5.2 (if applicable)
	Clinical study reports for pivotal and key studies (if applicable)
	Table of studies

4.1 General Information

4.1.1 Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the sponsor, providing the following information:

- a statement that the documentation is being filed for review through the *Procedures for CADTH Review of Nationally Procured Drug Products*
- the relevant indication(s) currently approved or under review by Health Canada
- target dates for completion of the Health Canada review (if known)
- the names and contact information (email and phone number) for the primary and backup contact(s).

4.1.2 Product Monograph

Table 2 summarizes the product monograph requirements for reviews conducted on a pre-NOC or post-NOC basis. Sponsors must immediately notify CADTH, up until the time that the final implementation advice report is issued, of any changes to the Health Canada–approved product monograph for the drug under review and provide a revised copy. Following the notification of changes to the product monograph, CADTH will assess the nature and extent of the changes and determine the timelines required for review and, if necessary, incorporate the changes into the review report(s). This could result in the review timelines being extended.

Table 2: Requirements for Filing Product Monograph With CADTH

NOC status	Requirements

Pre-NOC	• At the time of filing the initial documentation: a copy of the most recent draft product monograph showing the company, drug brand, and non-proprietary names that correspond to the anticipated NOC
	• As soon as available:
	  ○ a copy of the draft product monograph initially filed with CADTH showing, in tracked changes, all of the clinical and label review changes made up to the time of the product monograph being approved by Health Canada (if there are no changes to the draft product monograph initially filed with CADTH, other than the date on the product monograph, please include a placeholder document indicating this)
	  ○ a copy of the clean and dated product monograph approved by Health Canada.

Post-NOC	• A copy of the most current version of the Health Canada–approved product monograph

NOC = Notice of Compliance.

4.1.3 Declaration Letter

A letter from the holder of the NOC or NOC/c (or from the sponsor applying for an NOC, in the case of a review being conducted on a pre-NOC basis), using the declaration letter template in Appendix 2, printed on company letterhead, and signed by an appropriate senior official.

4.2 Health Canada Documentation

Table 3 summarizes the requirements for Clarimails/Clarifaxes for pre-NOC and post-NOC reviews.

Table 3: Requirements for Filing Clarimails/Clarifaxes With CADTH

NOC status	Requirements
Pre-NOC	• At time of filing initial documentation: a summary table of Clarimails/Clarifaxes relating to any clinical aspects of the Health Canada review of the drug (e.g., clinical studies or product monograph, not chemistry- and manufacturing-related topics) up to the time of filing with CADTH; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included • On an ongoing basis up to the point of the NOC or NOC/c being issued, the sponsor must provide CADTH with revised summary tables to reflect any additional Clarimails/Clarifaxes as aforementioned
Post-NOC	• A summary table of Clarimails/Clarifaxes relating to any clinical aspects of the Health Canada review of the drug (e.g., clinical studies or product monograph, *not* chemistry- and manufacturing-related topics) up to the point of the NOC or NOC/c being issued; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included.

NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

4.3 Efficacy, Effectiveness, and Safety Evidence

4.3.1 Results for Pivotal and Supportive Clinical Studies

Sponsors will be required to provide documentation with the results from the pivotal and supportive clinical studies that were submitted to Health Canada. CADTH's preference is for any unpublished data to be submitted in accordance with the CONSORT 2010 statement checklist, using clearly labelled sections (if available).

If the studies have been published, please provide copies of the publications, any supplemental appendices that are associated with published studies, and any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata). Should an unpublished study submitted become published during the review process, the sponsor must provide a copy of the published study to CADTH. Depending on the nature of the information, CADTH will determine the timelines required to review it and incorporate it into the report. The sponsor will be apprised of any revisions to the anticipated timelines for the review.

Please include a reference list in the folder with all the published and unpublished studies (including any errata).

4.3.2 Common Technical Document (if applicable)

If available, a copy of the common technical document sections listed here are required. If any of these sections of the common technical document were not a requirement for filing the regulatory submission with Health Canada, a placeholder document with a statement confirming this is required. The sections include the following:

- 2.5 Clinical Overview
- 2.7.3 Summary of Clinical Efficacy
- 2.7.4 Summary of Clinical Safety
- 5.2 Tabular Listing of All Clinical Studies.

4.3.3 Clinical Study Reports (if applicable)

If available, clinical study reports should be provided for the pivotal trials, as well as any other studies that address key clinical issues. The clinical study reports should be provided in full and include both the complete study protocol and analysis plan. If a clinical study report is unavailable to the sponsor, a placeholder document with a statement confirming this is required.

4.3.4 Table of Studies

A tabulated list of all published and unpublished clinical studies using the table of studies template must be provided. Any data (e.g., pre-planned analyses of primary outcome measures) for a planned or ongoing clinical study included in the "table of studies" requirement that becomes available during CADTH's review process must be provided as soon as possible to CADTH using Collaborative Workspaces. CADTH will assess the information upon receiving it and determine the timelines

required to review it and incorporate it into the review report(s). The sponsor will be apprised of any revisions to the anticipated timelines for the review.

5 Stakeholder Engagement

5.1 Sponsor Engagement

Once the request for implementation advice has been received, CADTH notifies the sponsor of the drug under review. The sponsor will have the opportunity to provide relevant information to CADTH regarding each of the implementation issues (see section 7.1). The input should be provided using the sponsor comments on implementation advice request template.

CADTH provides the sponsor with the opportunity to review and comment on the draft implementation advice report (see section 7.6); however, there is no formal reconsideration process for reviews of COVID-19 drugs.

During the review phase, CADTH may request, from the sponsor, any additional information and clarification required to complete the review. These requests will be provided in writing and CADTH encourages the sponsor to respond in a timely manner to avoid potential delays with the review timelines.

5.2 Patient and Clinical Group Engagement

Due to the need to expedite the review process, CADTH will not issue open calls for input or feedback from patient groups or clinician groups. Patient and clinician perspectives will be reflected in the panel deliberations.

5.3 Health Canada Information Sharing

Reviews of Nationally Procured Drug Products will be eligible for the information sharing process as described in section 4.2.3 of the *Procedures for CADTH Reimbursement Reviews.* To help avoid delays in the review process, CADTH strongly encourages manufacturers to participate in this process.

5.4 Federal, Provincial, and Territorial Governments

CADTH may consult and seek feedback from the federal, provincial, and territorial governments and their agencies.

6 Filing and Screening Procedure

By filing documentation with CADTH and participating in the review process, the sponsor consents to be bound by the terms and conditions specified in this document and all provisions regarding the withdrawal from the process. Consent to the terms and conditions contained herein cannot be revoked by the sponsor at any time during or after the CADTH's review processes.

6.1 Filing Documentation

A recommended format for filing documentation is provided in Appendix 1. Sponsors must be registered with CADTH Collaborative Workspaces before filing the required documents with CADTH. For detailed information on how to register, please consult CADTH Collaborative Workspaces Registration. Please ensure that both primary and secondary contacts, as well as any submitting consultants, are registered with Collaborative Workspaces. Requirements must be filed using Collaborative Workspaces.

6.2 Document Screening

There is no formal document screening process for nationally procured drug products drugs. CADTH will review the materials as they are received and may contact the sponsor for additional material or clarification, if required.

6.3 Finalized Information for Reviews Conducted on a Pre-NOC Basis

For reviews that are initiated on a pre-NOC basis, some requirements will be outstanding or not finalized at the time that the initial documentation is filed with CADTH (e.g., product monograph). The sponsor must provide all outstanding and/or finalized requirements to CADTH as soon as they are available. CADTH will assess finalized information upon receiving it. Depending on the nature and extent of changes to the information compared with what was originally filed, CADTH will determine the timelines required to review the information and incorporate it into the report. This could result in an extension of review timelines. The sponsor will be apprised of any revisions to the anticipated timelines.

7 Advice Procedure

7.1 Notification and Sponsor Input

Once the request for implementation advice has been received, CADTH notifies the sponsor of the drug under review. The sponsor will have 5 business days to provide written input to CADTH regarding the implementation issues. This input must be shared using the template provided by CADTH and must not contain any confidential information (all information included in the template will be considered disclosable by CADTH).

7.2 CADTH Review Team

The unique composition of each review team is established based on the nature of the review and in consideration of the proposed team members' qualifications, expertise, and compliance with the *CADTH Conflict of Interest Guidelines for Members of CADTH Committees and Expert Review Panels.* Except for the review manager(s), the names of the review team members, including members of clinical expert panels (if applicable), will not be disclosed to the sponsor.

7.3 Review of Clinical Evidence

CADTH will summarize and conduct an appraisal of the clinical evidence filed by the sponsor. Strengths and limitations with respect to both internal validity (i.e., how well the study was designed, conducted, and reported) and external validity (i.e., how well the results of the study could be applied to the target population in Canada) are documented. The CADTH clinical review and the implementation advice will be presented in a single report.

7.4 Implementation Advice Panel

CADTH will convene a panel of subject matter experts to address the relevant implementation questions. Whenever possible, CADTH will seek to obtain representation from across Canada. Potential panellists will be identified by CADTH. In accordance with the current policies used by CADTH, the identities of the panellists will remain confidential. CADTH will apply its current conflict of interest policy and all panellists will be required to provide completed conflict of interest declarations.

The attendance at clinical panel meetings will typically be limited to the panellists, key CADTH staff (i.e., review team members), and selected representatives from federal, provincial, and territorial governments and agencies. Representatives from the Institute national d'excellence en santés et en services sociaux (INESSS) and/or INESSS' expert committee members may also attend the panel meeting(s) at their discretion.

7.5 Panel Briefing Materials

Materials contained in the panel brief will typically include, but are not limited to, the following:

- CADTH evidence review
- draft or final product monograph for the drug under review
- key clinical studies (e.g., manuscripts and/or clinical study reports)
- sponsor input on the implementation issues
- sponsor-provided table of studies.

In addition to the materials in the committee brief, the committee has access to the complete package of requirements filed by the sponsor.

7.6 Draft Implementation Advice Report

7.6.1 Sponsor Comments

The draft implementation advice report is provided to the sponsor for review and comment. The sponsor will have 2 business days to provide their comments. This input must be provided using a template provided by CADTH and must not contain any confidential information (all information included will be considered disclosable by CADTH). CADTH may also obtain feedback from representatives of federal, provincial, and territorial governments and agencies. CADTH will review and discuss the feedback with the panellists and the guidance report will be revised, as required. There will be no further opportunities to formally comment on the implementation advice report prior to issuing the final report.

7.6.2 Redaction Requests

Before posting on the CADTH website, sponsors are responsible for identifying and requesting the redaction of any confidential information supplied by the sponsor that may have been included in the final implementation advice report. If the sponsor requests that confidential information be redacted from the final implementation advice report, CADTH will redact the confidential information in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines* described in the *Procedures for CADTH Reimbursement Reviews*. Pursuant to the *CADTH Reimbursement Review Confidentiality Guidelines,* CADTH will indicate that the sponsor requested that this information be kept confidential.

Sponsors are asked to identify any confidential information using the identification of confidential information template provided by CADTH. All requests for redactions must be accompanied by a clearly stated rationale. Sponsors must submit the completed form to CADTH via Collaborative Workspaces by the date and time specified by CADTH (typically 4:00 p.m. Eastern Time 5 business days after the draft implementation advice report was issued to the sponsor).

7.7 Final Implementation Advice Report

7.7.1 Posting Final Implementation Advice Report

The final report from this process will be posted on the CADTH website. Prior to posting, the sponsor will be requested to review and validate any redactions that were requested on the draft implementation advice report.

7.7.2 Validation of Redactions

The sponsor will have 1 business day to review and validate the redactions in the final implementation advice report. If the sponsor expresses disagreement regarding redactions, CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay the timeline for posting the final implementation advice report.

8 Temporary Suspension and Withdrawal

CADTH may temporarily suspend the review in accordance with section 10 of the *Procedures for CADTH Reimbursement Reviews*. If the sponsor voluntarily withdraws from the process, CADTH may continue with the review but will not use any information that has been filed by the sponsor in confidence. It may be noted on the CADTH website that the manufacturer voluntarily withdrew from the process.

Appendix 1: CADTH Requirements for Reviews of Nationally Procured Drug Products

Represents 1 folder • Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Signed Cover Letter
- 2 - Product Monograph
- 3 - Declaration Letter

2_Brand Name_Health Canada Documentation

- 1 - Table of Clarimails

3_Brand Name_Clinical Information

3.1_Results for Clinical Studies

- _Reference_List
- 1 - Trial Name_Year
- 2 - Trial Name_Year

3.2_Table of Studies

- Table of Studies

3.3_Common Technical Document **(if available)**

- 1 - Section 2.5
- 2 - Section 2.7.3
- 3 - Section 2.7.4
- 4 - Section 5.2

3.4_Clinical Study Reports **(if available)**

- 1 - Trial Name
- 2 - Trial Name

Appendix 2: Declaration Letter

[Sponsor's letterhead]

[Date]

CADTH (Canadian Agency for Drugs and Technologies in Health)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Reference: [Brand name/generic name]

Disclosure of all studies
This letter confirms that [name of sponsor] has disclosed all unpublished studies known to [name of sponsor], including those undertaken by other companies that distribute, market, and license this drug in Canada or in other countries and those undertaken by other groups or individuals, as of [insert date].
Authorizing unrestricted sharing of information
This letter acknowledges that CADTH may communicate, without restriction with respect to the product under review, with the authorized recipients in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines* described in the *Procedures for CADTH Reimbursement Reviews*. This includes, but is not limited to, the federal, provincial, and territorial government representatives (including their agencies and departments) and the pan-Canadian Pharmaceutical Alliance office.
Consenting to terms and conditions
This letter acknowledges that by filing documentation and participating in the CADTH review process, the sponsor consents to be bound by the terms and conditions specified in the *Procedures for CADTH Review of Nationally Procured Drug Products* and all provisions regarding withdrawal from the CADTH review process. Consent to the terms and conditions cannot be revoked by the sponsor at any time during or after the CADTH review.

[Signature]
[Name and Title of Senior Company Official of Sponsor]