CADTH

CADTH Common Drug Review Procedure and Submission Guidelines for Biosimilars

FEBRUARY 2018

CADTH

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Abbreviations

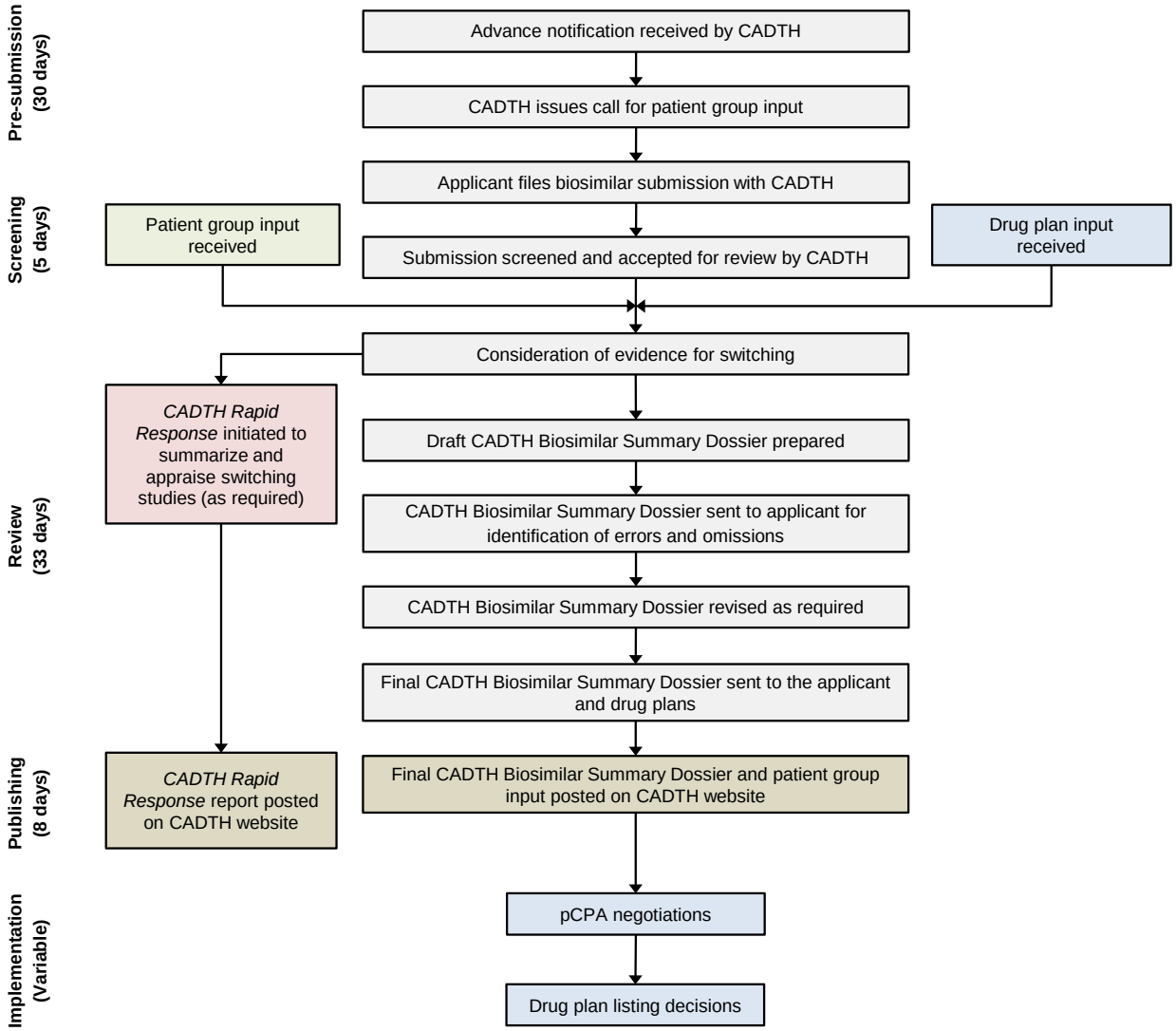
BIA	budget impact analysis
CDR	CADTH Common Drug Review
NOC	Notice of Compliance
NOC/c	Notice of Compliance With Conditions
pCPA	pan-Canadian Pharmaceutical Alliance

1. Foreword

1.1 About This Document

The purpose of the *CADTH Common Drug Review Procedure and Submission Guidelines for Biosimilars* is to provide an overview of the CADTH Common Drug Review (CDR) procedure and to provide guidance to applicants in the preparation of CDR submissions for biosimilars. This document must be read in conjunction with the Procedure for the CADTH Common Drug Review *(*August 2014*)* and any relevant issues of the CDR Update.

Figure 1: CADTH Common Drug Review Process for Biosimilars



pCPA = pan-Canadian Pharmaceutical Alliance.

2. CDR Procedure for a Biosimilar Submission

2.1 Eligible Submissions for Biosimilars

A biosimilar is a biologic drug that enters the Canadian market subsequent to a biologic already authorized in Canada or an authorized non-Canadian biologic drug from a jurisdiction that has an established relationship with Health Canada (i.e., a "reference product") with which it demonstrates a high degree of similarity.

Manufacturers for biosimilars that have been reviewed by CADTH and are subsequently issued new indications by Health Canada should contact CADTH (requests@cadth.ca) to determine if a CDR submission should be filed for the new indications. The decision to review additional indications for the same biosimilar will be made on a case-by-case basis by CADTH, in consultation with the CDR-participating drug plans.

2.2 Pre-submission Meetings

Pre-submission meetings are not offered for biosimilar CDR submissions. Manufacturers who have questions regarding a pending biosimilar submission should contact CADTH (requests@cadth.ca).

2.3 Advance Notification Process

2.3.1 Timing of Advance Notification

Applicants are required to provide CADTH with a minimum of 30 business days of advance notification for anticipated submissions. All applicants are encouraged to provide CADTH with as much notice as possible to facilitate resource planning, including clinical expert recruitment, and budgeting for the CDR program. CADTH encourages applicants to consider the threshold of 30 business days as the minimum amount of advance notification that is required to avoid a delay in processing the submission and not as the target or optimal amount of notification.

Applicants who provide notification of greater than 30 business days in advance of the anticipated date of filing are required to confirm the anticipated filing date 30 business days in advance (Table 1). Information regarding a pending CDR submission will be posted on the CADTH website at the time the call for patient input is issued (i.e., 20 business days before the anticipated filing date), to give patient groups as much notice as possible about a pending review.

Table 1: Advance Notification Process for CDR Submissions and Resubmissions

Advance Notification Process	Days Prior to Anticipated Filing Date
CADTH preferred advance notification	≥ 120 calendar days
Minimum mandatory advance notification	30 business days
Confirmation of anticipated filing date	30 business days[a]
Call for patient input issued	20 business days

[a] Required only if more than 30 business days of advance notice was provided.

Applicants are required to advise CADTH by email (requests@cadth.ca) of changes in the anticipated date of filing a submission as soon as possible. For changes to an anticipated filing date made before posting the pending CDR submission or resubmission on the CADTH website and issuing the call for patient input, the timelines will be adjusted based on the new anticipated filing date. For changes to an anticipated filing date made after the pending CDR submission has been posted on the CADTH website and the call for patient input has been issued, the call for patient input will remain open for a total of 35 business days. CADTH strongly discourages applicants from revising the anticipated filing date after the mandatory 30 business day notification has been provided.

The confirmed anticipated filing date is the basis for determining CADTH resourcing and timelines. Submissions received at CADTH earlier than the confirmed anticipated filing date will be held and considered received only on the anticipated filing date.

2.3.2 CADTH Advance Notification Form

All manufacturers are required to use the following advanced notification form:

- CADTH Common Drug Review Advance Notification Form

2.4 Disclosure of Information

CADTH is committed to providing an open and transparent drug review process for biosimilars.

a) All of the information included by the manufacturer in the biosimilar submission template is subject to (dissemination and) publication by CADTH.

b) All applicants filing a biosimilar submission with CADTH are required to acknowledge in writing their understanding that the information included in the biosimilar submission template is subject to (dissemination and) publication by CADTH.

c) CADTH does not accept confidential submitted prices in the CDR process.

d) The *CADTH Biosimilar Summary Dossier* is posted on the CADTH website for all completed biosimilar submissions.

e) There will be no opportunity for an applicant to request redaction of any information in the *CADTH Biosimilar Summary Dossier*.

2.5 Patient Group Input

Patient input provides patients' experiences with and perspectives on living with the medical condition; experiences with currently available treatments; and expectations for the drug under review.

2.5.1 Notifying Patient Groups About Calls for Patient Input

a) CADTH posts the drug to be reviewed along with the deadline date for receiving patient group input on the CADTH website and notifies all subscribed patient groups by email. Patient groups can subscribe to receive E-Alerts by using the "subscribe" option on the CADTH website. CADTH also tweets about calls for patient input to those who follow CADTH's Twitter accounts (English: @CADTH_ACMTS; French: @ACMTS_CADTH). Note: a copy of the Health Canada–approved product monograph is posted with the call for patient input for post-NOC submissions.

b) The call for patient input regarding a biosimilar submission is posted 20 business days in advance of the anticipated date of filing the application, as provided in the mandatory advance notification template. Patient groups have a total of 35 business days to submit patient input for biosimilar submissions.

2.5.2 Submitting Patient Input

a) Patient input is submitted to CADTH by patient groups. Individual patients or caregivers who wish to provide input are encouraged to work with a patient group that represents their condition and prepare a group submission to CDR. CADTH will accept patient input from individual patients and caregivers only when there is no patient advocacy group representing patients with a condition for which a drug under review is indicated. Individual patients and caregivers who wish to submit input for a drug review should first contact CADTH (requests@cadth.ca) to confirm the absence of a relevant patient group.

b) Patient groups are asked to use the biosimilar patient input template posted on the CADTH website. The template has questions and prompts to help guide patients to provide the information that will be most helpful to the pan-Canadian Pharmaceutical Alliance (pCPA) and drug plans.

c) Patient groups must submit their input by the posted deadline date for the information to be used by CADTH.

2.5.3 How Patient Group Input Is Used

a) For biosimilar submissions, CADTH collates and summarizes patient group input for consideration by the pCPA and the drug plans that participate in the CDR process.

b) The patient input summary is sent to each of the patient groups that provided input for their review and comments. Patient groups are asked to comment on whether the summary reflects the main issues and outcomes of importance to them and to ensure that no private information is included in the summary. A period of up to five business days is allotted for receipt of patient group comments regarding the summary document.

c) The patient group input summary is incorporated into its own section in the *CADTH Biosimilar Summary Dossier*.

d) All patient input submissions are kept on file and may be referred to in future CDR reviews of the same drug.

2.5.4 Posting Patient Group Input

a) The patient group input submissions are shared with the drug plans and posted on the CADTH website, although the name and contact details of the author are not shared.

b) The conflict of interest information will be included in the posted material.

c) CADTH takes reasonable precautions to remove any private information, such as names of individual patients, before posting the patient group input submissions in their entirety. However, it is the responsibility of the patient group to ensure that no private information is included in the input submitted.

d) The target time frame for posting patient group input on the CADTH website is at the same time the *CADTH Biosimilar Summary Dossier* is posted.

2.6 Application and Screening Procedure

2.6.1 Filing a Submission or Resubmission

a) The appropriate submission requirements filed must adhere to the content, format, and organization stipulated in section 3 and any applicable CDR Updates.

b) Applicants must be registered with CADTH Collaborative Workspaces before filing a submission or resubmission. Ensure both primary and secondary contacts and any submitting consultants working on a CDR application are registered with Collaborative Workspaces.

c) Submissions must be filed using Collaborative Workspaces. To file a submission the applicant must upload one copy of all category 1 requirements to the corresponding CDR review following the electronic file folder and file format specified below.

d) Submissions must be filed using Collaborative Workspaces during regular CADTH business hours (8:00 a.m. to 4:00 p.m. ET). If filed outside of CADTH business hours, the next business day will be considered the date of transmittal.

e) Applicants who experience difficulties filing a submission using Collaborative Workspaces should contact CADTH by email (requests@cadth.ca) for support or to arrange an alternative delivery method for the submission requirements; e.g., by email or mailing a USB flash drive.

f) Category 2 requirements may be filed at the same time as category 1 requirements, if available. When not provided at the same time as category 1 requirements, one copy of all category 2 requirements should be submitted to CADTH using Collaborative Workspaces within 20 business days of the submission being accepted for review. The final *CADTH Biosimilar Summary Dossier* will not be posted until all category 2 requirements have been received. CADTH does not screen category 2 requirements for completeness.

g) CADTH will provide copies of the category 1 and category 2 requirements to the drug plans.
Applicants are still required to provide copies of their CDR submission, including all drug plan–specific requirements, to the individual drug plans (i.e., CADTH does not provide the CDR category 1 and category 2 requirements on behalf of the applicant).

2.6.2 Screening of Biosimilar Submissions

The following provisions apply to all biosimilar submissions filed by manufacturers or drug plans.

a) The date of receipt is considered day zero for the purpose of calculating the five-day targeted time frame for initial screening of category 1 requirements. This targeted time frame is posted in the CDR project status reports section of the CADTH website.

b) If the filed category 1 requirements for a biosimilar submission are deficient or require revision in order to meet the requirements as outlined in the section 3, CADTH sends a notice to the applicant advising what information needs to be included or revised in order to meet the requirements. Rescreening of category 1 requirements is completed by CADTH as soon as possible after receipt, but may take up to five days.

c) When category 1 requirements for a biosimilar submission have been accepted for review, CADTH sends an accepted-for-review letter to the applicant.

2.6.3 Finalized Information for Submissions Filed on Pre-NOC Basis

For submissions filed on a pre-NOC basis, some requirements (e.g., product monograph) will be outstanding or not finalized at the time that an application is filed with CADTH. It is the responsibility of the applicant to provide such information as soon as it is available.

a) 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 it and incorporate it into the *CADTH Biosimilar Summary Dossier*. The applicant will be apprised of any revisions to the anticipated timelines for the review.

b) When a CDR submission has been filed on a pre-NOC basis, the applicant must provide all outstanding and/or finalized category 1 requirements as soon as they are available using Collaborative Workspaces. Once CADTH has notified the applicant that the finalized category 1 requirements have been accepted, the applicant must ensure that drug plans are provided with a copy of the finalized category 1 requirements.

2.6.4 Application Fees for Biosimilar Submissions

All biosimilar CDR submissions are subject to a schedule D application fee (Appendix 1 of the *Procedure for the CADTH Common Drug Review* [August 2014]). An invoice for the application fee owing will be sent once the review has been initiated by CADTH. Applicants who withdraw from the process at any time will not be entitled to a refund.

2.7 Time Frames and Tracking

CADTH posts CDR key targeted time frames and the status of the review on the CADTH website. Table 2 indicates the targeted time frames for key tasks within the CDR process. CADTH typically updates these reports every other week, as applicable.

Table 2: Target Time Frames for Biosimilar Submission

Phase	Milestones	Business Days Task (Cumulative)
Pre-submission	• Advance notification received	1 (–30)
	• Patient input posted	1 (–20)
Screening	• Receipt, screening, acceptance for review	5 (5)
Review	• Review initiated	1 (6)
	• Patient group input summarized by CADTH • Patient group input summary validated by patient group(s) • Draft *CADTH Biosimilar Summary Dossier* prepared	24 (30)
	• Preparation and distribution of *CADTH Biosimilar Summary Dossier* to the applicant for identification of errors and omissions	1 (31)
	• Applicant identifies errors and omissions • The *CADTH Biosimilar Summary Dossier* is revised as required based on the template completed by the applicant • Final draft of *CADTH Biosimilar Summary Dossier* prepared and sent to applicant and drug plans	7 (38)
Publishing	• *CADTH Biosimilar Summary Dossier* is prepared and posted on the CADTH website	6 (44)

2.8 CADTH Review of a Biosimilar CDR Submission

2.8.1 Review of a Biosimilar Submission Template

a) CADTH validates and comments on the information provided by the applicant in the Biosimilar Submission Template.

b) The review team includes its assessment of the submitted information and comments directly into the appropriate sections of the template, which then becomes the *CADTH Biosimilar Summary Dossier*. Only a single report combining both clinical and pharmacoeconomic information is prepared by CADTH for biosimilars.

c) CADTH may contact the applicant if additional information is required. Delays in providing such information may result in a temporary suspension of the review due to incomplete information to conduct an appraisal.

d) Depending on the volume or complexity of material to be reviewed, extension of the review time-frame deadlines may be required. The applicant will be notified of any extensions, and reasons for the extensions.

e) In the case of pre-NOC biosimilar submission, the applicant is required to provide an updated biosimilar submission template (using tracked changes) to CADTH using Collaborative Workspaces at the time the NOC or NOC/c is issued by Health Canada.

f) If an applicant submits new information for inclusion in an ongoing review (i.e., after category 1 requirements have been accepted and the review initiated), CADTH will determine the timelines required to review the new information and incorporate it into the summary dossier. The applicant would be apprised of any revisions to the anticipated timelines for the review.

2.8.2 Identification of Errors and Omissions

a) The draft summary dossier is sent to the applicant for the purposes of identifying errors and omissions.

b) In the case of a pre-NOC biosimilar submission, CADTH will not forward the draft summary dossier to the applicant until the NOC or NOC/c and an updated biosimilar submission template (using tracked changes) have been sent to CADTH. Upon receipt of an updated biosimilar submission template, CADTH will revise the draft summary dossier as required (typically within two business days) and then forward it to the applicant for the purposes of identifying errors and omissions.

c) The applicant has three business days following receipt of the draft summary dossier to review and identify errors and omissions using the template provided by CADTH.

d) The summary dossier is revised by CADTH, as required, on the basis of the applicant's completed template. This is typically completed within three business days.

2.8.3 Finalization of CADTH Biosimilar Summary Dossier

a) CADTH forwards the final version of the *CADTH Biosimilar Summary Dossier* to the applicant and drug plans.

b) The *CADTH Biosimilar Summary Dossier* is posted on the CADTH website for all completed biosimilar submissions. Posting will generally occur eight business days after the report has been sent to the applicant and the drug plans.

c) As all information included in the biosimilar submission template must be disclosable, there will be no opportunity for an applicant to request redaction of any information in the *CADTH Biosimilar Summary Dossier* before these documents are posted on the CADTH website.

2.8.4 Review of Evidence for Switching

a) CADTH may conduct a review of evidence for switching from the reference product or a biosimilar to the biosimilar under review.

b) CADTH reviews the information provided in 0 (i.e., table of studies and copies of studies investigating switching) and discusses with the CDR-participating drug plans to determine if a rapid response should be conducted.

c) These reviews will be conducted using the CADTH Rapid Response process and will be posted on the CADTH website.

d) The decision to conduct a rapid response is made on a case-by-case basis. Factors that may inform the decision to conduct a response will typically include the following:

- The volume and quality of the available evidence
- Reimbursement and switching policies for other biosimilar products for same reference drug and/or indications.

e) The applicant will be provided with written notification regarding CADTH's decision on whether or not a rapid response will be conducted. The applicant will not have the opportunity to provide materials or review the draft rapid response report.

f) CADTH will notify stakeholders that a rapid response is being conducted by posting the project name and number on the Projects in Progress portion of the CADTH website.

2.9 Withdrawal From the CDR Process

Applicants may withdraw from the CDR process at any time up to the time the *CADTH Biosimilar Summary Dossier* is posted on the CADTH website. The applicant must submit to CADTH a dated written request for withdrawal that has the following information:

- the name and signature of the applicant
- the reason that the request for withdrawal is being made.

Upon receipt of a request for withdrawal from an applicant, CADTH will withdraw the submission in accordance with *Procedure for the CADTH Common Drug Review* (August 2014). Submissions for biosimilars that have been previously withdrawn must be re-filed in accordance with the procedure and submission requirements described in this document.

2.10 Disposition of Submission Documents

The posting of the *CADTH Biosimilar Summary Dossier* signals the completion of the review for a biosimilar submission. CADTH then undertakes the steps detailed in the *Procedure for the CADTH Common Drug Review (*August 2014*)* section regarding the disposal and archiving of files associated with the review. CADTH also follows this procedure for a withdrawn submission.

3. Submission Guidelines for Biosimilars

3.1 Notice of Compliance Status at the Time of Filing

In accordance with the *Procedure for the CADTH Common Drug Review (August 2014)*, a CDR submission for a biosimilar can be made on either a pre-NOC or a post-NOC basis.

3.2 Organization of Submission Requirements

The submission requirements are grouped into category 1 and category 2, and additional information. To expedite the screening of submissions for completeness and to facilitate the efficient use of documents, applicants must organize the submission requirements as prescribed in the category 1 and category 2 requirements below and follow the electronic file folder format in Appendix 1. The submission checklists used by CADTH for screening category 1 and category 2 requirements can be found in Appendix 2. These checklists may assist applicants in ensuring that all requirements have been included in the submission.

Table 3: Submission Requirement Categories

Requirement Category	Function in the CDR Process	Due
Category 1	Used by CADTH for the review process.	At the time of filing the application.
Category 2	Used by the drug plans and are not considered as part of the CDR review process. CADTH provides secretariat support to the drug plans by ensuring that category 2 requirements have been filed.	≤ 20 business days from the date the submission was accepted for review.
Additional information	Additional information that CADTH may require for completion of the review.	As soon as possible following a request by CADTH, to avoid delays in the review process.

CDR = CADTH Common Drug Review.

3.3 Category 1 Requirements

The category 1 requirements for biosimilar submission are summarized in Table 4. Where specific submission requirements for a submission are filed on a pre-NOC versus post-NOC basis, they are delineated in the descriptions below.

Table 4: Category 1 Requirements for Biosimilar Submissions

Section	Specific Items and Criteria
General Information	• Completed application overview template
	• Signed cover letter
	• Product monograph
Submission Template	• Completed biosimilar submission template
Health Canada Documentation	• NOC, or • NOC/c and Letter of Undertaking, or • A placeholder document specifying the anticipated NOC date
Evidence for switching	• Table of studies • Copies of published studies investigating switching from the reference product or a biosimilar to the biosimilar under review
Pricing and Distribution	• Submitted price per smallest dispensable unit to four decimal places
	• Method of distribution
Declaration Letter	• Completed declaration letter template for a biosimilar o Authorizing unrestricted sharing of information o Commitment to honour the submitted price o Declaration that all known unpublished studies have been disclosed o Declaration that all information provided in the biosimilar submission template is disclosable

NOC = Notice of Compliance; NOC/c = Notice of Compliance With Conditions.

3.3.1 General Information

a) Application Overview Template

A completed Application Overview Template.

b) Signed Cover Letter

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

- A clear description of the submission being filed and confirmation that all of the requirements have been provided in the submission (e.g., all category 1 requirements for a biosimilar submission filed on a pre-NOC basis).
- The indication(s) to be reviewed through the CDR process.
- The issued or anticipated date of NOC or NOC/c (day, month and year) for the indication(s) to be reviewed
- The requested reimbursement criteria, if applicable.
- A statement confirming whether the submitted price is the anticipated or current marketed price.
- The names and contact information (email and phone number) for the primary and secondary contact(s) for the submission. The applicant may designate the consultant(s) preparing the submission as primary and/or backup contact(s). Any changes in contacts should be communicated to CADTH as soon as possible, by emailing requests@cadth.ca.

c) Product Monograph

Table 5 summarizes the product monograph requirements for submissions filed on a pre-NOC and post-NOC basis. Applicants must notify CADTH, up until the time that the *CADTH Biosimilar Summary Dossier* is posted, of any changes to the Health Canada–approved product monograph for the drug under review. Upon Health Canada approval of the revisions, applicants are required to notify CADTH immediately by email (requests@cadth.ca) of the specific changes and provide a copy of the revised product monograph. Following notification, CADTH will assess the nature and extent of the changes and determine the timelines required to review and, if necessary, incorporate the changes into the *CADTH Biosimilar Summary Dossier*. The applicant will be apprised of any revisions to the anticipated timeline for the review. Failure by the applicant to inform CADTH of any changes to the product monograph could result in temporary suspension of the review.

d) Declaration Letter

A letter from the holder of the NOC or NOC/c (or from the manufacturer applying for an NOC, in the case of a submission filed on a pre-NOC basis), using the Biosimilar Declaration Letter Template, printed on company letterhead and signed by an appropriate senior official. This letter serves the following purpose:

- Permits unrestricted sharing of information regarding the drug product under review through the CDR process, between CADTH and:
  - Federal, provincial, and territorial governments, including their agencies and departments
  - pan-Canadian Pharmaceutical Alliance (pCPA) office.
- Provides a signed commitment to honour the submitted price for all drug plans.
- Provides a signed declaration that all known unpublished clinical studies have been disclosed.
- Provides a signed declaration that all information provided in the biosimilar submission template is disclosable.

Table 5: Requirements for Filing Product Monograph With CADTH

NOC Status	Submission Requirements
Pre-NOC	• At the time of filing the submission: 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, sent by email to requests@cadth.ca: o 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. o 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; NOC/c = Notice of Compliance With Conditions.

3.3.2 Health Canada NOC

Table 6 summarizes the NOC requirements for submissions filed on a pre-NOC and post-NOC basis.

Table 6: Requirements for Filing Notice of Compliance with CADTH

NOC Status	Submission Requirements
Pre-NOC	• At the time of filing the submission: a placeholder document indicating the anticipated target date for receipt of an NOC or NOC/c for the indication(s) to be reviewed. • A copy of the granted NOC or NOC/c for the indication(s) under review by CADTH, dated and signed by Health Canada, must be sent by email to requests@cadth.ca as soon as it is available (i.e., on the day of, or next business day after, receipt from Health Canada). • If the drug receives an NOC/c for the indication(s) being reviewed by CADTH: a copy of the Letter of Undertaking that outlines the confirmatory studies intended to verify the clinical benefit, including an indication of time frames, must also be provided by email to requests@cadth.ca as soon as it is available.
Post-NOC	• A copy of the NOC or NOC/c granted, dated, and signed by Health Canada. The NOC or NOC/c must be for the indication(s) for which the drug is to be reviewed under the CDR process. • If the drug in the submission has received an NOC/c for the indication(s) to be reviewed, the applicant must provide a copy of the Letter of Undertaking that outlines the confirmatory studies intended to verify the drug's clinical benefit, including an indication of time frames.

NOC = Notice of Compliance; NOC/c = Notice of Compliance With Conditions.

3.3.3 Submission Template

- A completed Biosimilar Submission Template.
- In the case of a pre-NOC submission, the applicant must update the Biosimilar Submission Template to reflect any changes to the product monograph and send it to CADTH once the NOC has been issued by Health Canada.

3.3.4 Evidence for Switching

a) Table of Studies

A tabulated list of all published and unpublished clinical studies using the Table of Studies Template.

b) Copies of published studies

Copies of published studies that investigated any of the following:

- Switching from the reference product to the biosimilar under review
- Switching from a biosimilar to the biosimilar under review.

3.3.5 Pricing and Distribution Information

a) Submitted Price

- The submitted price for the drug, reported to four decimal places, as follows:
  - price per smallest dispensable unit for all dosage forms and strengths available in Canada
  - price for all packaging formats available in Canada.
- The submitted price is the price per smallest dispensable unit that is submitted to CADTH and that must not be exceeded for any of the drug plans following completion of the CDR review process. The submitted price will be disclosed in all applicable CADTH reports.
- Only one price (anticipated or current market price) to four decimal places per smallest dispensable unit is to be submitted per drug that is to be reviewed through the CDR process (i.e., only one price for all indications undergoing review by CADTH concurrently).
- The submitted price must be used in the pharmacoeconomic evaluation included in the biosimilar submission template and in the budget impact analyses (BIAs) (budget impact reports and the models used to produce the results).

b) Method of Distribution

Indicate within the pricing and distribution document the method of distribution to pharmacies (e.g., wholesale, direct, or other arrangements).

3.4 Category 2 Requirement

Category 2 requirements for biosimilar submissions are summarized in Table 7.

Table 7: Category 2 Requirements for Biosimilar Submissions

Section	Specific Items and Criteria
Budget impact analyses	Budget impact analysis reports
	Budget impact analysis models
	Copies of all supporting documentation used and/or cited in the budget impact analyses

a) Budget Impact Analyses and Supporting Documentation

The following information is required for all biosimilar submissions:

- Budget impact analyses (i.e., budget impact reports and the models used to product the results) for all of the following jurisdictions' drug plans, in accordance with their individual requirements: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and Non-Insured Health Benefits Program. When data specific to Prince Edward Island are unavailable, the BIA for Prince Edward Island is to be based on Nova Scotia data.
- Copies of all supporting documentation used and/or cited in the BIAs.
  - As specified in Appendix 2, the first file in the folder must be a reference list of the documents included in the folder.

The base unit price used in the budget impact analyses must be the same as the price submitted in the category 1 requirements and must be clearly identified in each budget impact analysis. Jurisdiction-specific markups or discounts can then be applied, if applicable.

Appendix 1: Electronic File Format for Biosimilar CDR Submissions

Instructions for Applicants

Please carefully review the following electronic file structure and naming convention before assembling the CDR submission or resubmission requirements. If you have any questions regarding the CDR application process, please email requests@cadth.ca with the complete details of your question(s).

Filing Category 1 and Category 2 Requirements:

- All materials must be submitted using the Collaborative Workspaces. To file a submission, applicants are to use the Submit and Contribute — Pharmaceutical Manufacturers function to upload the file and complete the online submission form.
- Files should be submitted as zipped (.zip) files. The maximum file size is approximately 1 GB. If there are several .zip files, the number of files should be noted in the additional comments box of the submission form (e.g., file 1 of 4). The root folder(s) should be clearly named with the brand or generic drug name and submission requirement (e.g., Brand Name - Category 1).
- An email notification will be sent to the applicant when the file has been submitted successfully.
- File names cannot exceed 64 characters or contain special characters; applicants are asked to use abbreviations as necessary.
- Documents must be provided in PDF or Microsoft Word format, unless otherwise indicated in the requirement descriptions. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.
- Documents must be organized and labelled according to the file structure and naming format provided in this appendix.
- If any extra supporting documents that do not have a designated folder are being submitted at the applicant's discretion (e.g., Clinical Study Reports), these should be appropriately named and filed in a logical location in the file structure.

Providing Additional Information During the Review:

- If CADTH requests additional information during the course of the review, applicants can provide the requested information to CADTH using Collaborative Workspaces.
- The documents must be provided in PDF or Microsoft Word format. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.
- File names cannot exceed 64 characters or contain special characters; applicants are asked to use abbreviations as necessary.

Submission Requirements for Biosimilars

The following folder and file structure reflects each of the CDR category 1 requirements for a biosimilar submission and the order in which they are to be provided as .zip files through the Collaborative Workspaces.

Represents one folder Represents one file (unlocked, searchable, and printable)

Brand Name – Category 1

- 1_Brand Name_General Information
  - 1 - Application Overview
  - 2 - Signed Cover Letter
  - 3 - Product Monograph
  - 4 - Declaration Letter
- 2_Brand Name_Health Canada Documentation
  - 1 - Health Canada NOC
  - 2 - Letter of Undertaking (Note: only if applicable)
- 3_Brand Name_Submission Template
  - 1 - Biosimilar Submission Template
- 4_Brand Name_Evidence for Switching
  - 1 – Table of Studies
  - 2 – Copies of Published Studies
- 5_Brand Name_Pricing and Distribution
  - 1 – Pricing and Distribution

Brand Name — Category 2

- 1_Brand Name BIAs
  - 1.1_BIAs
    - 1 - BIA Report BC
    - 2 - BIA Model BC
    - 3 - BIA Report AB
    - 4 - BIA Model AB
    - 5 - BIA Report SK
    - 6 - BIA Model SK
    - 7 - BIA Report MB
    - 8 - BIA Model MB
    - 9 - BIA Report ON
    - 10 - BIA Model ON
    - 11 - BIA Report NB
    - 12 - BIA Model NB
    - 13 - BIA Report NS
    - 14 - BIA Model NS
    - 15 - BIA Report PEI
    - 16 - BIA Model PEI
    - 17 - BIA Report NL
    - 18 - BIA Model NL
    - 19 - BIA Report NIHB
    - 20 - BIA Model NIHB
  - 1.2_BIA Supporting Documentation
    - _List of References
    - 1 - Name of document

Appendix 2: Checklists for CDR Biosimilar Submissions

Category 1 Requirements for a CDR Biosimilar Submission Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Overview	• Completed application overview template	☐
Signed Cover Letter	• Clear description of submission filed	☐
	• The indication(s) to be reviewed	☐
	• Anticipated date of NOC for indication(s) to be reviewed	☐
	• Requested reimbursement criteria	☐
	• Names and contact information for primary and backup contacts	☐
Product Monograph	**At the time of filing:**	
	• A copy of the most recent draft product monograph	☐
	After NOC or NOC/c is issued:	
	• Draft product monograph with tracked changes	☐
	• Clean and dated version of Health Canada–approved product monograph	☐
Declaration Letter	• Completed declaration letter template for a biosimilar ▪ Authorizing unrestricted sharing of information ▪ Commitment to honour the submitted price ▪ Declaration that all known unpublished studies have been disclosed ▪ Declaration that all information provided in the biosimilar submission template is disclosable	☐
Health Canada Documentation		
NOC	**At the time of filing:**	
	• A placeholder document specifying the anticipated NOC date for the indications(s) to be reviewed by CDR	☐
	After NOC or NOC/c is issued:	
	• Copy of NOC or NOC/c granted for the indication(s) under review	☐
	• Letter of Undertaking (only if NOC/c granted)	☐
Submission Template		
Submission Template	**At the time of filing:**	
	• Completed biosimilar submission template	☐
	After NOC or NOC/c is issued:	
	• Updated biosimilar submission template	☐
Evidence for Switching		
Table of Studies	• Completed table of studies	☐
Copies of published studies	• Copies of published studies that investigated any of the following: ▪ Switching from reference product to the biosimilar under review ▪ Switching from a biosimilar to the biosimilar under review	☐
Pricing and Distribution Information		
Price and Distribution Method	• Submitted unit pricing to four decimal places	☐
	• Method of distribution	☐

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance With Conditions.

Category 1 Requirements for a CDR Biosimilar Submission Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Overview	• Completed application overview template	☐
Signed Cover Letter	• Clear description of submission filed	☐
	• The indication(s) to be reviewed	☐
	• Date of NOC for indication(s) to be reviewed	☐
	• Requested reimbursement criteria	☐
	• Names and contact information for primary and backup contacts	☐
Product Monograph	• A copy of the most recent product monograph	☐
Declaration Letter	• Completed declaration letter template for a biosimilar o Authorizing unrestricted sharing of information o Commitment to honour the submitted price o Declaration that all known unpublished studies have been disclosed o Declaration that all information provided in the biosimilar submission template is disclosable	☐
Health Canada Documentation		
NOC	• Copy of NOC or NOC/c for the indication(s) under review	☐
	• Letter of Undertaking (only if NOC/c granted)	☐
Submission Template		
Submission Template	• Completed biosimilar submission template	☐
Evidence for Switching		
Table of Studies	• Completed table of studies	☐
Copies of published studies	• Copies of published studies that investigated any of the following: o Switching from reference product to the biosimilar under review o Switching from a biosimilar to the biosimilar under review	☐
Pricing and Distribution Information		
Price and Distribution Method	• Submitted unit pricing to four decimal places	☐
	• Method of distribution	☐

NOC = Notice of Compliance; NOC/c = Notice of Compliance With Conditions.

Category 2 Requirements for a CDR Biosimilar Submission

Requirement	Specific Items and Criteria	Included
Budget Impact Analyses (Reports and Models)	• BIA report British Columbia	☐
	• BIA model British Columbia	☐
	• BIA report Alberta	☐
	• BIA model Alberta	☐
	• BIA report Saskatchewan	☐
	• BIA model Saskatchewan	☐
	• BIA report Manitoba	☐
	• BIA model Manitoba	☐
	• BIA report Ontario	☐
	• BIA model Ontario	☐
	• BIA report New Brunswick	☐
	• BIA model New Brunswick	☐
	• BIA report Nova Scotia	☐
	• BIA model Nova Scotia	☐
	• BIA report Prince Edward Island	☐
	• BIA model Prince Edward Island	☐
	• BIA report Newfoundland and Labrador	☐
	• BIA model Newfoundland and Labrador	☐
	• BIA report Non-Insured Health Benefits	☐
	• BIA model Non-Insured Health Benefits	☐
Supporting BIA Documentation	• Reference list of all supporting documentation used and/or cited in BIAs	☐
	• Copies of all supporting documentation used and/or cited in BIAs	☐

BIA = budget impact analysis