

Procedure and Submission Guidelines for the CADTH Common Drug Review

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Record Of Updates

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CADTH Contact Information

Table 1: How and Where to Direct CDR–Related Inquiries or CDR Applications

Type of Inquiry or CDR Application	How and Where to Direct
General inquiries regarding the CDR procedure and process	<p>Email: requests@cadth.ca</p> <p>Fax: 613-226-5392</p> <p>Mail: Central Intake CADTH 600-865 Carling Avenue Ottawa, ON K1S 5S8</p>
Filing CDR submission or resubmission	Collaborative Workspaces
Inquiries regarding an active CDR review	By email to the designated submission coordinator contact provided in the category 1 accepted for review letter
Inquiries regarding CDR application fees	Email: accountsreceivable@cadth.ca

CDR = CADTH Common Drug Review.

Table 2: Delivery Times

Means of Delivery	When Considered to Have Been Delivered
By courier, registered mail, regular mail, in person	On the day of receipt by CADTH's reception desk during CADTH business hours (8: 00 a.m. to 4:00 p.m. Eastern time)
Email or fax	Between business hours (8:00 a.m. and 4:00 p.m. Eastern time) on the day of transmittal. Note: If sent outside of CADTH business hours, the following business day is considered the date of receipt
Collaborative Workspaces	Between business hours (8:00 a.m. to 4:00 p.m. Eastern time) on the day of transmittal. Note: If sent outside of CADTH business hours, the following business day is considered the date of receipt

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Abbreviations

BIA	budget impact analysis
CDEC	CADTH Canadian Drug Expert Committee
CDR	CADTH Common Drug Review
CEDAC	Canadian Expert Drug Advisory Committee
CSR	Clinical Study Report
DPAC	Drug Policy Advisory Committee
NOC	Notice of Compliance
NOC/c	Notice of Compliance with conditions
pCPA	pan-Canadian Pharmaceutical Alliance
RCT	randomized controlled trial

1. Introduction

1.1. About This Document

The objective of this document is to outline the CADTH Common Drug Review (CDR) procedures and provide guidance in the preparation of applications for the review of drug submissions and resubmissions through the CDR process. This document must be read in conjunction with any issues of the *CADTH Pharmaceutical Reviews Update*.

Various templates are hyperlinked throughout this document and are also available on the CADTH website. These templates are to be used by applicants, as directed in the requirement descriptions, when preparing a CDR submission or resubmission.

All references to number of days in this document are in business days unless otherwise specified. Key definitions in this document are defined in Appendix 5.

1.2. Overview of the CADTH Common Drug Review

The objectives of the CDR process are to reduce duplication across jurisdictions, maximize the use of limited resources, and enhance the consistency of drug reviews. CADTH, through its CDR process, undertakes reviews of drug submissions, resubmissions, and requests for advice, it also issues formulary listing recommendations and/or review reports to all federal, provincial, and territorial drug plans that participate in the CDR process (hereafter referred to as “drug plans”).

CADTH’s Drug Policy Advisory Committee (DPAC) provides strategic advice on drug policy issues and drug topics to CADTH. The DPAC Formulary Working Group and the DPAC Optimal Use Working Group have been established to assist DPAC in fulfilling its mandate. For all of the CDR-related operational matters where drug plan input is required, CADTH consults with the DPAC Formulary Working Group, in which members represent the drug plans.

The reimbursement recommendations for drugs reviewed through the CDR process are provided by the CADTH Canadian Drug Expert Committee^a (CDEC) – an appointed, national, expert advisory committee to CADTH that makes drug-related recommendations and provides drug-related advice through the CDR and therapeutic review processes. CDEC is composed of individuals with expertise in drug therapy, drug evaluation, and drug utilization, and public members who bring a lay perspective. The current committee members are listed on the CADTH website.

CDEC follows a deliberative framework and process and takes into consideration the following information when issuing recommendations and advice:

- patient group input
- clinical studies demonstrating the safety, efficacy, and effectiveness of the drug compared with alternatives
- therapeutic advantages and disadvantages relative to current accepted therapy
- cost and cost-effectiveness relative to current accepted therapy.

^a The CADTH Canadian Drug Expert Committee replaced the Canadian Expert Drug Advisory Committee in September 2011.

The CDR process commences with one of the following:

- a manufacturer filing a submission or resubmission
- drug plans filing a submission, resubmission, or request for advice.

A review team prepares CDR clinical and pharmacoeconomic review report(s),^b based on information submitted by manufacturers and studies identified through independent, systematic literature searches.

It is important to note that CDEC recommendations are non-binding to the drug plans. Each drug plan makes its own reimbursement decisions based on the *CDEC Final Recommendation* in addition to other factors, including the plan's mandate, jurisdictional priorities, and financial resources.

1.3. Changes to These Guidelines

CADTH may amend the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and all matters related to CDR. CADTH may request stakeholder feedback for CDR procedural changes and the drug plans are consulted, as required. Amendments to, and clarifications of, the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and all related documents may be effected by means of directives (called *CADTH Pharmaceutical Reviews Update*) issued by CADTH on an as-needed basis between revisions of these documents.

1.4. Interaction Between CADTH and the Manufacturer

Once a CDR application has been filed, CADTH will only address procedure and process-related matters with manufacturers, unless otherwise defined in this document (e.g., a conference call offered during the reconsideration process). Due to the volume of requests and the need to optimize limited resources, CADTH is unable to offer conference calls to manufacturers that have questions regarding the CDR process, and encourages manufacturers that have questions regarding the CDR process to submit a written inquiry to requests@cadth.ca. A written response will be provided in a timely manner. With the exception of pre-submission meetings, in-person meetings will not be offered.

Direct contact between a manufacturer and CDEC members (in their capacity as members of CDEC) or the CADTH review team is not permitted during the review process. Direct approaches in any form to committee members or the CADTH review team may be viewed as introducing conflict of interest and may create an appearance of bias or unfairness. Direct contact by a manufacturer with a CDEC member or member(s) of the CADTH review team may result in a significant delay in the CDR review process because additional steps may be required to obtain an unbiased recommendation on the product.

Consultants working on a CDR submission or resubmission on behalf of a manufacturer are required to copy an official contact for the manufacturer on all email correspondence with CADTH. CADTH will not respond to any email correspondence from a consultant if an official contact for the manufacturer has not been copied.

^b The term "CDR review report(s)" refers to the *CDR Clinical Review Report* and *CDR Pharmacoeconomic Report* typically prepared for a standard CDR review and/or the combined *CDR Clinical and Pharmacoeconomic Review Report* prepared for a tailored CDR review and/or the *CDR Request for Advice* report prepared in response to a request for advice. The term "CDR review report(s)" is used as a shortened title to refer to the report(s) collectively or as applicable to a particular type of review.

1.5. CDR Confidentiality Guidelines

CADTH has developed confidentiality guidelines to protect confidential information obtained through the CDR process (Appendix 1). These confidentiality guidelines ensure that appropriate steps and procedures are in place to protect confidential information, and that this information will be handled in a consistent manner. CADTH will comply with these confidentiality guidelines when handling information as part of the CDR process. A manufacturer will be deemed to have consented to the confidentiality guidelines when it files a submission or resubmission, or when it supplies other information to CADTH. A manufacturer will maintain the confidentiality of documents shared with it by CADTH. The confidentiality guidelines will constitute an agreement between CADTH and the manufacturer.

2. Eligibility for the CDR Process

2.1. Eligible Submissions

This section provides guidance regarding eligibility for the majority of CDR submissions. In some situations, CADTH may consult with drug plans to confirm CDR eligibility of a drug and make a decision on a case-by-case basis. Manufacturers that have questions regarding whether or not a drug is eligible for review through the CDR process are asked to complete an eligibility request form and submit it to requests@cadth.ca. Eligibility should be determined prior to requesting a pre-submission meeting or providing advanced notification.

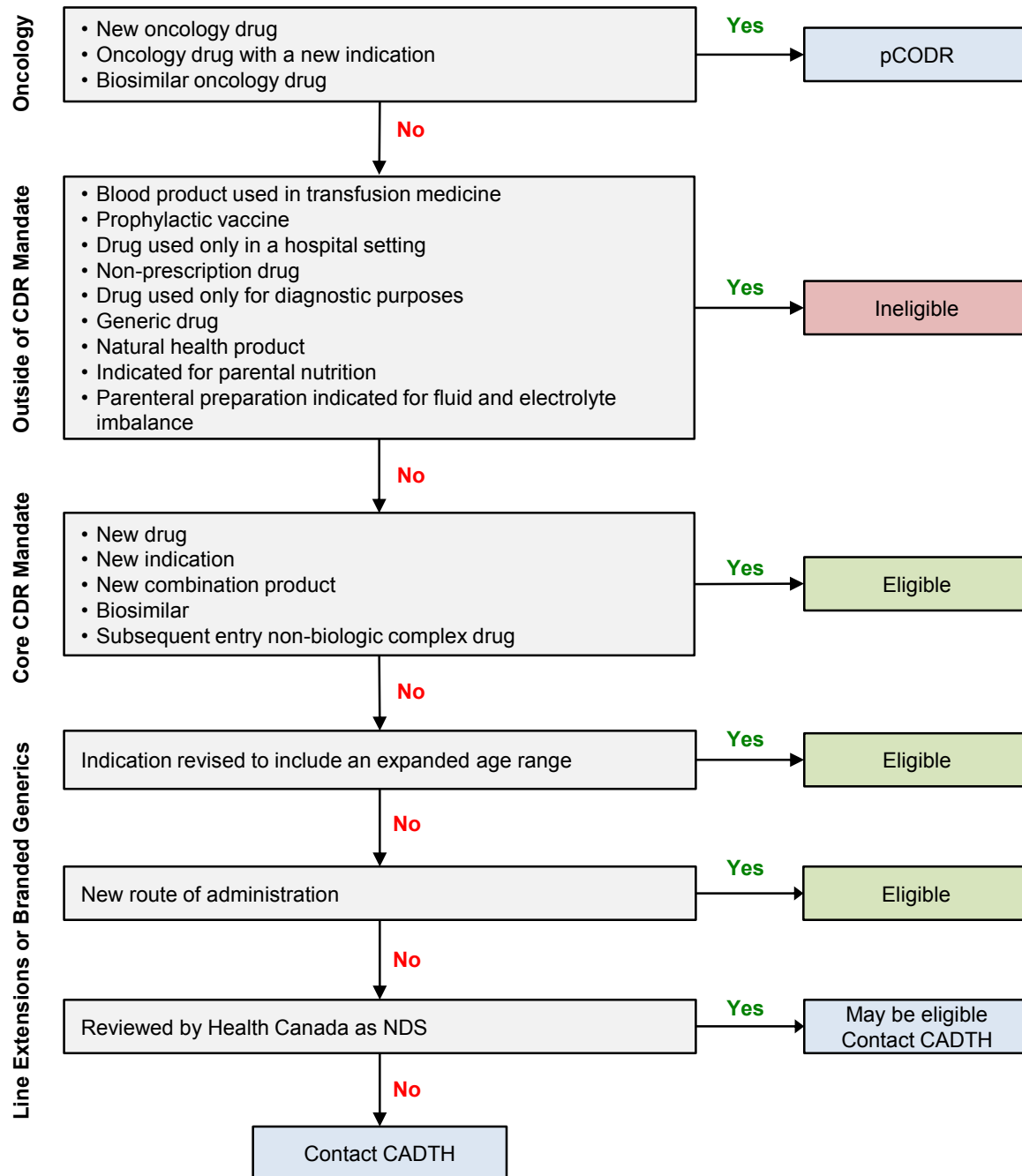
A manufacturer or the drug plans may file a submission for a new drug, a drug with a new indication, a new combination product, or a biosimilar that has received or has a pending Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed. Table 3 provides an overview of each CDR-eligible submission type.

Table 3: Summary of CADTH Common Drug Review Submission Types

Submission Type	Description
New drug	<ul style="list-style-type: none"> • A new active substance that has not been previously marketed in Canada
Drug with a new indication	<ul style="list-style-type: none"> • A drug previously reviewed through the CDR or pCODR processes that has received an NOC or NOC/c for a new indication • A drug marketed before the establishment of CDR that has received an NOC or NOC/c for a new indication • A drug previously reviewed through the CDR process that is approved for use in a new patient population age range
New combination product	<ul style="list-style-type: none"> • Two or more drugs that have not been previously marketed in Canada in that combination
Biosimilar	<ul style="list-style-type: none"> • A biologic drug demonstrating a high degree of similarity to an already authorized biologic drug (i.e., a reference product)

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions; pCODR = CADTH pan-Canadian Oncology Drug Review.

Figure 1: Drugs Eligible for Review Through the Common Drug Review Process



CDR = CADTH Common Drug Review; NDS = new drug submission; pCODR = CADTH pan-Canadian Oncology Drug Review.

2.1.1. New Drug

A new drug, for CDR submission purposes, typically includes one of the following:

- a new active substance that has not been previously marketed in Canada, regardless of when the NOC or NOC/c was issued
- a drug consisting of a single active substance previously reviewed through the CDR process only as an active substance in a combination product
- a new salt of a marketed product
- a drug for which eligibility for review has been confirmed by CADTH in consultation with the drug plans on a case-by-case basis.

A new drug for the purposes of a CDR submission does not include the following variations of existing non-parenteral products containing the same active substance(s) as one or more drugs that have been previously reviewed through the CDR process and/or are currently being funded by the drug plans for the same indication (note: these are considered line extensions for the purposes of CDR):

- a new non-parenteral dosage form with the same route of administration, as long as the new dosage form approval is not accompanied by a change to the indicated population age range (e.g., if a drug in tablet form becomes available in capsule or oral solution dosage form)
- a new strength of the same dosage form (e.g., if a 200 mg tablet becomes available in addition to an already-marketed 100 mg tablet, and the new strength approval is not accompanied by a change to the indicated population age range, a submission for the 200 mg tablet is not required).

New parenteral products or formulations (e.g., intravenous, intramuscular, subcutaneous dosage forms) are not considered line extensions of one another for the purposes of CDR, as they have different routes of administration and, as a result, there may be potential differences in pharmacokinetics and pharmacodynamics, as well as differences in cost. Manufacturers should submit a completed eligibility request form to requests@cadth.ca for guidance on whether a CDR submission is required for a new parenteral formulation.

All submissions for new drugs undergo a standard CDR review.

2.1.2. Drug with a New Indication

A drug with a new indication is:

- a drug previously reviewed through the CDR or pan-Canadian Oncology Drug Review processes that has received an NOC or NOC/c for a new indication
- an active substance marketed before the establishment of CDR (in September 2003) that has received an NOC or NOC/c for a new indication
- a drug previously reviewed through the CDR process that is approved for use in a new patient population age range.

All submissions for drugs with a new indication undergo a standard CDR review.

2.1.3. New Combination Product

A new combination product consists of two or more drugs that have not been previously marketed in Canada in that combination. One or more of the components may be a non-prescription drug, but at least one component must be a prescription drug.

Manufacturers planning to file a submission for a new combination product are required to complete and submit the New Combination Product Considerations Form to CADTH (requests@cadth.ca) prior to filing the submission. CADTH will review the information and, with input from the drug plans (as needed), confirm whether a standard or tailored CDR review should be filed. CADTH will typically provide a response within 10 business days of receiving the form.

2.1.4. Biosimilar

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. Eligible Resubmissions

A resubmission is a review of any drug that has previously been reviewed through the CDR process and for which a CDEC or Canadian Drug Expert Advisory Committee (CEDAC) final recommendation has been issued by CADTH. Resubmission eligibility must be determined prior to requesting a pre-submission meeting or providing advanced notification to CDR (Figure 2).

2.2.1. New Information

A resubmission based on new information consists of one or both of the following:

- new clinical information in support of improved efficacy or safety
- new cost information that significantly affects the cost-effectiveness of the drug.

Any new studies included in the resubmission must address the specific issues identified by the expert review committee in the final recommendation document. Table 4 summarizes the supporting information that must be filed for resubmissions.

Table 4: Summary of New Information Required for Resubmissions

Basis of Resubmission	Supporting Information That Must be Filed
New clinical information supporting improved efficacy or safety	<ul style="list-style-type: none"> • One or more new studies that address specific issues identified by the expert review committee in the final recommendation document • New pharmacoeconomic evaluation • New budget impact analysis (category 2 requirement)
New cost information that significantly affects the cost-effectiveness of the drug	<ul style="list-style-type: none"> • New pharmacoeconomic evaluation • New budget impact analysis (category 2 requirement)

Although not always a requirement, CADTH considers new evidence from one or more randomized controlled trials (RCTs) to be the preferred form of new clinical information for resubmissions based on improved efficacy and/or safety. CADTH considers data from non-randomized studies to be particularly useful in the following situations:

- when the evaluation of important clinical end points and rare adverse events requires longer-term follow-up
- when there is uncertainty regarding the persistence of efficacy of the drug under review because of short-term clinical trials
- when an RCT is impractical because of a limited number of patients
- when it is considered unethical to conduct an RCT
- when randomized studies lack relevant comparators (e.g., an indirect comparison is conducted to evaluate the comparative efficacy and safety of the drug under review relative to appropriate comparators)
- when there is uncertainty regarding the dosage of the drug(s) under review that is used in actual clinical practice
- when the RCTs have limited external validity and additional non-randomized studies could provide meaningful insight into the effectiveness of the treatment in the target population.

2.2.2. Eligibility Assessment for Resubmissions

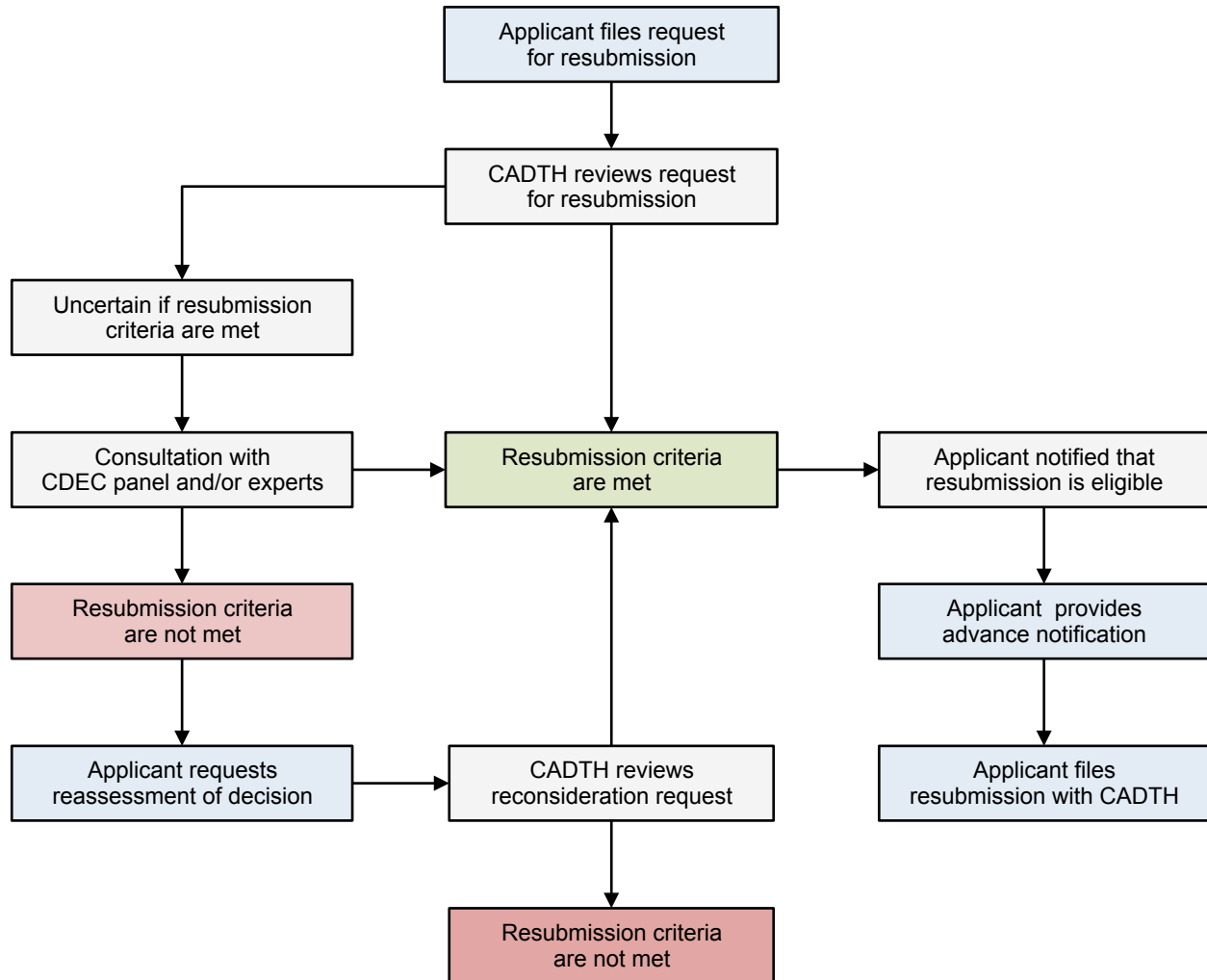
- a) Prior to filing a resubmission, applicants are required to have its eligibility assessed by CADTH. Applicants must provide the following information to requests@cadth.ca for evaluation by CADTH:
 - a completed Resubmission Eligibility Form
 - copies of one or more new studies that address specific issues identified by the expert review committee in the final recommendation document.
- b) CADTH will screen the information provided by the applicant to determine if:
 - the information provided by the applicant represents new information
 - the (one or more) new studies provided by the applicant address specific issues identified by the expert review committee in the final recommendation document.
- c) CADTH may consult with members of the expert review committee and/or clinical experts to determine if the new information filed by the applicant addresses the issues noted in the previous recommendation. However, the final decision regarding whether or not a resubmission will be eligible for review will be determined by CADTH.
- d) CADTH's assessment of eligibility will typically be completed within 10 business days. Applicants will be notified by CADTH if additional time is required to complete the assessment.
- e) If CADTH determines that applicant's resubmission comprises new information and contains at least one study that addresses the specific issues identified by the expert review committee in the final recommendation document, the applicant will be apprised in writing that the resubmission is eligible for review through the CDR process.
- f) If CADTH determines that the applicant's resubmission does not comprise new information or does not address the specific issues identified by the expert review committee in the final recommendation document, the applicant will be apprised in writing that the resubmission is not eligible.

- g) When an applicant has been informed by CADTH that a resubmission is not eligible, the applicant may file one written request for the decision to be reassessed by CADTH. The request for reassessment must clearly outline why the applicant disagrees with CADTH's decision.
- h) Applicants have 10 business days to file a request for reassessment after receiving notification from CADTH regarding the eligibility of a resubmission.
- i) Applicants will only be entitled to have the eligibility decision reassessed once.
- j) CADTH will examine the reassessment request to determine whether the issue(s) raised change the conclusions regarding the eligibility of the resubmission. CADTH may consult with members of the expert review committee and/or clinical experts (as required). The final decision regarding whether or not a resubmission is eligible for review will be determined by CADTH.
- k) CADTH's consideration of each request for reassessment will typically be completed within 10 business days. Applicants will be notified by CADTH if additional time is required to complete the assessment.
- l) CADTH will apprise the applicant in writing of the final decision regarding eligibility of the resubmission.
- m) CADTH will post the results of the resubmission eligibility assessment on the CADTH website.
- n) CADTH will retain and dispose of documents associated with the resubmission in accordance with the CADTH Common Drug Review Confidentiality Guidelines.
- o) All completed resubmission eligibility assessments may be shared by CADTH with the federal, provincial, territorial governments (including their agencies and departments) and the pan-Canadian Pharmaceutical Alliance (pCPA) office.
- p) After receiving confirmation from CADTH that the proposed resubmission is eligible for review through the CDR process, applicants are required to provide CADTH with advance notification for the pending resubmission. Advance notification for resubmissions must be provided in accordance with section 3.2.

2.2.3. Volume of Resubmissions

To ensure fair access to the CDR process for new drug submissions, CADTH may limit the number of resubmissions that can be made and/or initiated within a defined period of time. This decision will be made by CADTH based on the availability of resources, and will be communicated to stakeholders via a *CADTH Pharmaceutical Reviews Update*.

Figure 2: Assessing the Eligibility of Resubmissions



CDEC = CADTH Canadian Drug Expert Committee.

2.3. NOC Status at the Time of Filing the Submission

A CDR submission can be filed on either a pre-NOC or a post-NOC basis (Table 5).^c

Table 5: NOC Status at the Time of Filing

NOC Status	Description
Pre-NOC	Any CDR submission may be filed on a pre-NOC basis up to 180 calendar days in advance of the anticipated receipt of an NOC or NOC/c. If the 180th calendar day falls on a weekend or CADTH holiday, the next business day will be used. This type of submission is accepted with the agreement that some submission requirements (e.g., product monograph) may not be finalized at the time of filing; however, they are to be provided as soon as finalized because the embargoed CDEC recommendation will not be released until all required information, including a copy of the NOC or NOC/c, has been received by CADTH.
Post-NOC	A submission may be filed on a post-NOC or NOC/c basis after the drug has been granted an NOC or NOC/c by Health Canada for the indication(s) to be reviewed through the CDR process.

CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

2.4. Types of CDR Reviews

CADTH conducts either a standard or a tailored CDR review:

- A standard CDR review consists of the review team conducting a systematic review of clinical evidence provided by the manufacturer along with studies identified through its independent, systematic literature search, and an appraisal of the manufacturer-provided pharmacoeconomic evaluation.
- A tailored CDR review consists of the review team conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the manufacturer using a CADTH-provided review template that is specific to the type of drug product to be reviewed.

^c Pre-NOC also includes pre-NOC/c and post-NOC includes post-NOC/c submissions.

Table 6: Types of CDR Reviews Conducted for Submissions and Resubmissions

Type of CDR Review	Type of Submission or Resubmission
Standard review	<ul style="list-style-type: none"> • Submission for a new drug • Submission for a drug with a new indication • Submission for a new combination product (selected) • Resubmission based on new clinical information with or without new cost information
Tailored review	<ul style="list-style-type: none"> • Submission for a new combination product that CADTH has designated as a tailored review • Submission for a subsequent-entry non-biologic complex drug • Resubmission based only on new cost information
Biosimilar review	<ul style="list-style-type: none"> • Submission for a biosimilar

CDR = CADTH Common Drug Review.

Table 6 summarizes the type of CDR review conducted for the different submission and resubmission categories.

2.5. Requests for Advice

Drug plans may file a request for advice through the CDR process regarding a previous CEDAC or CDEC recommendation. The request for advice must be provided to CADTH in a signed letter that clearly describes the issues of interest to the drug plans.

2.6. Drug Plan–Initiated Submissions and Resubmissions

Drug plans may file a submission or resubmission through the CDR process. The submission or resubmission must be filed with CADTH in a signed letter that clearly describes the issues of interest to the drug plans. For these submissions and resubmissions, CADTH supports the drug plans by obtaining and compiling information to conduct the review. CADTH will contact the manufacturer and provide an opportunity to share relevant clinical and pharmacoeconomic data. In general, the review process for a drug plan–filed submission or resubmission will be the same as that used in the review of a submission or resubmission filed by a manufacturer.

3. Pre-submission Procedure

3.1. Pre-submission Meetings

Pre-submission meetings are offered to facilitate the efficient preparation and filing of CDR submissions and resubmissions. The pre-submission meeting provides the opportunity for CADTH staff and the manufacturer to discuss the upcoming submission or resubmission. The goal of the meeting is to assist manufacturers in improving the quality, relevance, and clarity of the information filed in the CDR application. The meeting is not meant to be consultative in nature, outside of clarifying procedural and/or submission or resubmission requirements. This is because at the time of a pre-submission meeting, CADTH has not reviewed the submission or resubmission requirements, and therefore is not in a position to provide final advice on a submission or resubmission.

Pre-submission meetings are scheduled for a maximum of one hour and applicants are limited to one meeting per drug submission or resubmission. The meeting is held at the CADTH office in Ottawa; however, a teleconference option is available for participants unable to attend in person. Manufacturers may bring consultants and/or clinical experts as manufacturer representatives. Representatives from the CDR-participating drug plans and pCPA may attend pre-submission meetings.

Once a submission or resubmission has been filed with CDR, it is no longer eligible for a pre-submission meeting. 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).

3.1.1. Standard Pre-submission Meetings

Manufacturers may request a standard pre-submission meeting with CADTH for a submission or resubmission to be filed within six months of the meeting. To request a standard pre-submission meeting, manufacturers are required to complete the first section of the Pre-submission Meeting Request Form and submit it to CADTH (meetingrequests@cadth.ca).

3.1.2. Early Pre-submission Meetings

CADTH offers opportunities for dialogue between CADTH staff and manufacturers earlier in the pre-submission phase (six to 12 months in advance of filing) for drug submissions with all of the following characteristics:

- the drug is indicated for a relatively small patient population
- clinical data are limited to surrogate end points
- the natural history of the disease is poorly characterized
- a limited number of clinical trials exists and they have small sample sizes
- treatment has a high cost relative to appropriate comparators
- the manufacturer has questions regarding the appropriate type of economic analysis to submit.

Manufacturers are advised to send CADTH supporting information for the aforementioned points and an overall rationale for requesting an early pre-submission meeting as soon as possible after the drug submission has been accepted by Health Canada for review. A decision to accept a manufacturer's request for an early pre-submission meeting will be made by CADTH.

To request an early pre-submission meeting, manufacturers are required to complete both sections of the Pre-submission Meeting Request Form and submit it to CADTH (meetingrequests@cadth.ca).

3.2. Advance Notification Procedure

Manufacturers are required to provide CADTH with a minimum of 30 business days of advance notice for anticipated submissions and resubmissions. All manufacturers are encouraged to provide CADTH with as much notice as possible to facilitate resource planning and budgeting for the CDR program (≥ 120 calendar days is preferred). Manufacturers who provided less than 30 business days' notice will be required to revise the anticipated filing date to meet the minimum requirement. To fulfill the advance notification requirement, manufacturers must complete the CADTH Common Drug Review Advance Notification Form in its entirety and submit it to CADTH (requests@cadth.ca). Information provided to CADTH as part of the advance notification process may be shared with the federal, provincial, and territorial governments, including their agencies and departments, as well as the pCPA office.

For resubmissions, applicants are required to receive confirmation from CADTH that the proposed resubmission is eligible for review through the CDR process, before providing advance notification (see section 2.2). The eligibility assessment and advance notification processes have to occur sequentially to ensure that the patient engagement process is only initiated for eligible resubmissions.

Manufacturers who provide notification of more 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 7). Information regarding a pending CDR submission or resubmission 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).

Table 7: 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

CDR = CADTH Common Drug Review.

^a Required only if more than 30 business days advance notice was provided.

A manufacturer is required to advise CADTH by email (requests@cadth.ca) of changes in the anticipated date of filing a submission or resubmission 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 or resubmission 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 manufacturers from revising the anticipated filing date after the mandatory 30 business day confirmation has been provided. The confirmed anticipated filing date is the basis for determining CADTH resourcing and

timelines. Submissions and resubmissions received at CADTH earlier than the confirmed anticipated filing date will be held and considered received only on the anticipated filing date.

3.3. Health Canada Information Sharing

- As described in *Notice to Industry: Aligned Reviews Between Health Canada and Health Technology Assessment Organizations*, an optional information sharing process has been established to permit Health Canada and CADTH to exchange information regarding the drug under review, for submissions filed with CADTH on a pre-NOC basis. Participation in this process could ensure that CADTH has advance notice of any issues that have the potential to impact CADTH's review of the drug (e.g., changes to the indicated patient population), potentially avoiding delays in the issuance of CADTH's recommendation.
- Manufacturers must indicate on the advance notification form (i.e., received \geq 30 business days in advance of the CDR submission filing date) whether or not they have consented or will be consenting to participate in the information sharing process with Health Canada.
- To promote alignment of regulatory and CADTH reviews, manufacturers should consent to information sharing at the time of, or prior to, submission filing with Health Canada. This may help to minimize the time between issuance of market authorization and CADTH's recommendation.
- If the applicant is unwilling to participate in the information sharing process with Health Canada, CADTH will continue to request information directly from the manufacturer.
- The CADTH Collaborative Workspaces will be used to exchange documents between Health Canada and CADTH.
- In the interest of transparency, CADTH will indicate whether or not a manufacturer has consented to participate in the information sharing process (if applicable).

4. Patient Group Input Procedure

Patient input provides patients' experiences and perspectives of living with a medical condition for which a drug under review is indicated, their experiences with currently available treatments, and their expectations for the drug under review. This information is used by CADTH in the review of submissions, resubmissions based on new clinical information, and requests for advice, and by CDEC in the development of recommendations.

4.1. Call for Patient Input

The call for patient input regarding a submission or resubmission is posted 20 business days in advance of the anticipated filing date (as provided in the advance notification form) or on the same day a request for advice is received by CADTH. Patient groups have a total of 35 business days for preparing and submitting patient input. For post-NOC submissions, a copy of the Health Canada-approved product monograph is posted with the call for patient input.

Open calls for patient input are available via:

- the CADTH website (as a pending drug submission and an open call for patient input)
- E-Alerts to all subscribed patient groups (patient groups can subscribe to E-Alerts by using the "subscribe" option on the CADTH website)
- CADTH Twitter accounts: English, @CADTH_ACMTS and French, @ACMTS_CADTH

4.2. 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 to 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. Upon confirmation that no relevant patient group exists, CADTH will provide interested individuals with the individual patient and caregiver template for completion. The process for providing input, and how CADTH uses and posts that input, remains the same as that for patient groups, with minor modifications, as applicable, for an individual patient or caregiver.
- b) Patient groups are asked to use one of the following patient input templates that are posted on the CADTH website:
 - Standard patient input template: This template has questions and prompts to help guide patients to provide the information that will be most helpful to the review team and CDEC in their work.
 - Biosimilar patient input template: This template has questions and prompts to help guide patients to provide the information that will be most helpful to the pCPA and drug plans.
- c) Patient groups must submit their input as a Microsoft Word document by the posted deadline date for the information to be used by CADTH.

4.3. How Patient Group Input Is Used

- a) All patient group input received for the drug under review is collated and summarized by CADTH. The approximately two-page summary is sent to each of the submitting patient groups 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 patient group to provide comments on the summary document. The patient group input summary is incorporated into CDR review report(s) or a *CADTH Biosimilar Summary Dossier*.
- b) For all submissions, resubmissions, and requests for advice for products (excluding biosimilar submissions), patient group input is used by CADTH in the development of the review protocol. The patient group input summary and the patient group input submissions in their entirety are included in the CDEC brief. CDEC public members present the patient input at the outset of CDEC deliberations (section 8.3), and a summary of the patient input discussion is included in the CDEC recommendation. For a biosimilar review, CADTH collates and summarizes patient group input for consideration by the pCPA and the drug plans that participate in the CDR process.
- c) All patient input submissions are kept on file and may be referred to in future CADTH reviews of the same drug.

4.4. Posting Patient Group Input

- a) CADTH will include the names of the patient groups who provided input within the key milestone table on the CADTH website. The information will be posted for the drug under review after the call for patient input is closed.
- b) The patient group submissions for each drug are consolidated for posting on the CADTH website. Posting will typically occur within two weeks after the call for patient input has been closed.
- c) The conflict of interest information will be included in the posted material.
- d) 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.

5. Requirements for Submissions and Resubmissions

The CDR submission requirements for all eligible submission types are grouped into the following categories:

- category 1 requirements
- category 2 requirements
- additional information.

A brief description of these requirements is provided in Table 8 and detailed descriptions are provided in subsequent sections. For all submission types, the clinical and pharmacoeconomic information provided in the category 1 and category 2 requirements should focus on the indication(s) to be reviewed under the CDR process (unless otherwise specified).

Table 8: Submission Requirement Categories

Requirement Category	Function in the CDR Process	Due
Category 1	Used by the CADTH review team and CDEC for the review and recommendation process	At the time of filing the application
Category 2	Used by the drug plans and not considered as part of the CDR review or recommendation 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 or resubmission was accepted for review
Additional information	Additional information that CADTH may require for completion of the review (e.g., Clinical Study Reports or Health Canada Reviewer’s Report[s])	As soon as possible following a request by CADTH, to avoid delays in the review process

CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

The submission checklists for category 1 and category 2 requirements can be found in Appendix 3. These checklists may assist manufacturers in ensuring that all requirements have been included in the submission. To expedite screening and for efficient use of documents throughout the review, manufacturers must organize all submission information in the order prescribed in the category 1 and category 2 requirements below and follow the electronic file folder format in Appendix 4.

5.1. Category 1 Requirements

Category 1 requirements are used by CADTH and CDEC during the review and recommendation process. One copy of all category 1 requirements must be filed with CADTH as a single submission package and accepted for review by CADTH before it is initiated. The category 1 requirements for standard reviews, tailored reviews, and biosimilar reviews are summarized in Table 9. Category 1 requirements for resubmissions are summarized in Table 10. Detailed descriptions of the information that comprise the category 1 requirements for CDR submissions are subsequently described. Specific requirements for a submission filed on a pre-NOC versus post-NOC basis are delineated in the descriptions that follow the table.

The manufacturer is responsible for ensuring that appropriate copyright permissions have been obtained for electronic copies of articles included in category 1 requirements of a submission, to be shared among CADTH, CDEC, and the drug plans for the review of the submission.

Table 9: Category 1 Requirements for Submissions for Standard Review, Tailored Review, or Biosimilar Review

Section	Specific Items and Criteria	CDR Review Type		
		Standard	Tailored	Biosimilar
General information	• Completed application overview template	Required	Required	Required
	• Signed cover letter	Required	Required	Required
	• Completed executive summary template for a submission	Required	Required	Not required
	• Product monograph	Required	Required	Required
	• Completed declaration letter or biosimilar declaration letter template	Required	Required	Required
Submission template	• Completed tailored review submission template, or • Completed biosimilar submission template	Not applicable	Required	Required
Health Canada documentation	• NOC or NOC/c and Letter of Undertaking, or • A placeholder document specifying the anticipated NOC date	Required	Required	Required
	• Table of Clarimails or Clarifaxes	Required	Required	Not required
Efficacy, effectiveness, and safety information	• Common Technical Document sections 2.5, 2.7.1, 2.7.3, 2.7.4, and 5.2, or • A statement indicating any section(s) are not available	Required	Required	Not required
	• Reference list and copies of key clinical studies and errata	Required	Required	Required
	• Table of studies	Required	Required	Required
	• Reference list and copies of editorial articles	Required	Required	Not required
	• Reference list and copies of new data	Required	Required	Not required
	• Reference list and copies of articles for validity of outcome measure	Required	Required	Not required
	• Indirect comparison with full technical report	May be required	Not required	Not required
Economic information	• Pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) to be reviewed by CADTH	Required	Not required	Not required
	• Unlocked and fully executable economic model	Required	Not required	Not required
	• Economic model supporting documentation	Required	Not required	Not required
Epidemiologic information	• Disease prevalence and incidence data	Required	Required	Not required
	• Number of patients accessing a new drug	May be required	May be required	Not required
Pricing and distribution information	• Submitted price per smallest dispensable unit to four decimal places	Required	Required	Required
	• Method of distribution	Required	Required	Required
Companion Diagnostics	• Reference list and copies of articles that highlight the clinical utility	May be required	May be required	Not required
	• Disclosable price	May be required	May be required	Not required
Pre-NOC letter	• Letter for sending NOC or NOC/c to CADTH	Required	Required	Not required

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

Table 10: Category 1 Requirements for CDR Resubmissions

Section	Specific Items and Criteria	CDR Resubmission Type	
		New Clinical and Cost	New cost Only
General information	• Completed application overview template	Required	Required
	• Signed cover letter	Required	Required
	• Completed executive summary template for a resubmission	Required	Required
	• Product monograph	Required	Required
	• Completed declaration letter	Required	Required
New efficacy and/or safety information	• Reference list and copies of new clinical studies and errata	Required	Not required
	• Reference list and copies of editorial articles	Required	Not required
	• Reference list and copies of articles for validity of outcome measure	Required	Not required
	• Updated table of studies	Required	Required
Economic information	• New pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) to be reviewed by CADTH	Required	Required
	• Unlocked and fully executable economic model	Required	Required
Epidemiologic information	• Disease prevalence and incidence data	Required	Required
Pricing and distribution information	• Submitted price per smallest dispensable unit to four decimal places	Required	Required
	• Method of distribution	Required	Required

CDR = CADTH Common Drug Review.

5.1.1. General Information

Application Overview Template

A completed Application Overview Template.

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 or resubmission being filed (e.g., new drug submission filed on a pre-NOC basis)
- the indication(s) to be reviewed by CADTH
- the requested reimbursement criteria (if applicable)
- the names and contact information (email and phone number) for the primary and backup contact(s) that CADTH can contact regarding the submission. The manufacturer 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.

Executive Summary

A high-level summary of the submission or resubmission using the appropriate template (see following). The document must be referenced and must not exceed five pages (excluding references).

- Executive Summary Template for a Submission
- Executive Summary Template for a Resubmission

Product Monograph

Table 11 summarizes the product monograph requirements for CDR submissions or resubmissions.

Applicants must immediately notify CADTH, up until the time that the *CDEC Final Recommendation* is issued or the *CADTH Biosimilar Summary Dossier* is posted, of any changes to the Health Canada–approved product monograph for the drug under review and provide a revised copy. Failure by the applicant to inform CADTH of any changes to the product monograph could result in temporary suspension of the review. Following notification, 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 CDR review report(s) or *CADTH Biosimilar Summary Dossier*. This could result in the review timelines being delayed, including the submission being considered at a later CDEC meeting or a delay in issuing the *CDEC Final Recommendation*. The applicant will be apprised of any revisions to the anticipated timeline for the review, deferral by CDEC, or the subsequent recommendation not reflecting the most currently available product monograph information relating to the drug under review.

Table 11: Requirements for Filing Product Monograph with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> • At the time of filing the submission or resubmission: 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: <ul style="list-style-type: none"> ◦ 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	<ul style="list-style-type: none"> • A copy of the most current version of the Health Canada–approved product monograph

NOC = Notice of Compliance.

Declaration Letters

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 appropriate CADTH template, printed on company letterhead, and signed by an appropriate senior official.

- Declaration letter template for a standard or tailored review
- Declaration letter template for a biosimilar review

5.1.2. Health Canada Documentation

Health Canada NOC or NOC/c

Table 12 summarizes the NOC requirements for pre-NOC and post-NOC submissions.

Clarimails or Clarifaxes

Table 13 summarizes the requirements regarding Clarimails/Clarifaxes for pre-NOC and post-NOC submissions.

Table 12: Requirements for Filing Notice of Compliance with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> 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 to CADTH 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 CADTH as soon as it is available
Post-NOC	<ul style="list-style-type: none"> A copy of the NOC or NOC/c 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 manufacturer 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

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

Table 13: Requirements for Filing Clarimails/Clarifaxes with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> At time of filing the submission: 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, <i>not</i> chemistry- and manufacturing-related topics) up to the time of filing with CADTH. 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 manufacturer must provide CADTH with revised summary tables to reflect any additional Clarimails/Clarifaxes as aforementioned.
Post-NOC	<ul style="list-style-type: none"> 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, <i>not</i> chemistry- and manufacturing-related topics) up to the point of the NOC or NOC/c being issued. 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.

5.1.3. Efficacy, Effectiveness, and Safety Evidence

Common Technical Document

As shown in Table 14, a copy of selected sections from the Common Technical Document modules. 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.

Table 14: Common Technical Document Module Sections

Section	Title
2.5	Clinical Overview
2.7.1	Summary of Biopharmaceutical Studies and Associated Analytical Methods
2.7.3	Summary of Clinical Efficacy
2.7.4	Summary of Clinical Safety
5.2	Tabular Listing of All Clinical Studies

Clinical Studies

For the clinical studies requirements, CADTH's preference is for any unpublished data to be submitted in manuscript format; however, if unavailable in manuscript format, the information should be provided in accordance with the CONSORT 2010 Statement Checklist, using clearly labelled sections as outlined (i.e., title, abstract, introduction, methods, results, discussion, other information). Should an unpublished study submitted as a category 1 requirement (for the "clinical studies" requirements, or listed in the "table of studies" requirement) become published during the review process of CDR, manufacturers must provide a copy of the published study to CADTH using Collaborative Workspaces. Depending on the nature of the information, CADTH will determine the timelines required to review it and incorporate it into the CDR review report(s). This could result in the submission being considered at a later CDEC meeting. The manufacturer will be apprised of any revisions to the anticipated timelines for the review.

Standard Reviews

A reference list and copies of published and unpublished studies that address key clinical issues for the drug under review must be provided. Applicants must include:

- copies of any supplemental appendices that are associated with published studies
- copies of any errata related to any published studies provided. If there are no errata, a placeholder document with a statement confirming this must be provided

The first file in the folder must be a reference list of the articles and errata included in the folder.

Tailored Reviews

A reference list and copies of source documentation for any data that have been included in the completed tailored CDR review template, but not captured in section, 2.5, 2.7.1, 2.7.3, or 2.7.4 of the Common Technical Document, must be provided. Applicants must include:

- copies of any errata related to any published studies provided. If there are no errata, a placeholder document with a statement confirming this must be provided
- if no further source documentation is applicable, a placeholder document with a statement confirming that there is no further applicable source documentation to be provided.

Biosimilar Reviews

A reference list and copies of published studies that investigated any of the following must be provided:

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

Resubmission Based on New Clinical Information

A reference list and copies of all new clinical information that addresses specific issues identified by the expert review committee in the final recommendation document must be provided. Include copies of any errata related to any published studies provided, or if there are no errata, a placeholder document with a statement confirming this must be provided.

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 the CDR 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 CDR review report(s). This could result in the submission being considered at a later CDEC meeting. The manufacturer will be apprised of any revisions to the anticipated timelines for the review.

Editorials

A reference list and copies of editorials relating to published clinical studies provided in the submission (i.e., published studies included in the “clinical studies” requirement). If no editorials are available, a placeholder document with a statement confirming this must be provided.

New Data

A reference list and copies of new data generated since the last date that data were reported in the studies included in the Health Canada submission. Typically, the clinical studies submitted to CDR are the same as those submitted to Health Canada, and sometimes these studies are ongoing, with data collected after submission to Health Canada. The data that become available after the study has been submitted to Health Canada are required. These data will be accepted in a variety of formats, including late draft, Clinical Study Report, synopsis, abstract, or conference proceedings. If no new data are available, a placeholder document with a statement confirming this must be provided.

Validity of Outcome Measures

A reference list and copies of references supporting the validity of primary outcome measures in clinical studies. If no references are available, a placeholder document is required with a statement confirming that a search was undertaken but no references were located.

Indirect Comparisons

Applicants are required to provide copies of any indirect comparisons that were used in their pharmacoeconomic evaluation. In addition, applicants may elect to provide one or more indirect comparisons to provide evidence of the comparative safety and efficacy of the drug under review relative to appropriate comparators. The indirect comparisons must be provided as a separate report in the submission package.

5.1.4. Economic Information

The pharmacoeconomic submission for a standard review or resubmission consists of a technical report of the pharmacoeconomic evaluation and an economic model, as well as any supporting material relevant to the pharmacoeconomic submission. Details for each component are outlined in this section.

Pharmacoeconomic Evaluation

An appropriate pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) is required. The pharmacoeconomic evaluation should be undertaken in accordance with CADTH's *Guidelines for the Economic Evaluation of Health Technologies: Canada (4th edition)*.

For submissions filed on a pre-NOC basis, where the approved NOC indication differs from the anticipated indication for which the pharmacoeconomic evaluation was conducted, the review may be suspended until a revised pharmacoeconomic submission reflecting the approved indication is provided.

Requirements for the pharmacoeconomic evaluation are:

- The pharmacoeconomic analysis must be in the form of a cost-utility analysis.
- The base case analysis must reflect the Health Canada–approved indication for which the drug is being submitted. If a manufacturer is requesting reimbursement for a specific subgroup of the indicated population or there are any relevant subgroups, these must be provided as scenario analyses.
- All analyses must be conducted probabilistically.
- The specific price(s) submitted to CADTH (to four decimal places) must be used in the manufacturer's base-case analysis.

Requirements for the base-case analysis for the pharmacoeconomic evaluation are:

- The perspective of the publicly funded health payer.
- A discount rate of 1.5% for both costs and quality-adjusted life-years (QALYs).
- All relevant comparators, including treatments that are currently used off-label in Canadian practice. If potentially relevant comparators are excluded from the pharmacoeconomic submission, justification must be provided by the manufacturer and CADTH may request that the manufacturer include these comparators during the review process, which may impact the timelines of the review (i.e. may lead to a later CDEC meeting date). CADTH may suspend the review while a revised model is provided, and the file will not be eligible for a refund if the date of CDEC consideration is delayed.
- Reporting of sequential analysis if more than one comparator is included.

Deviations from these requirements must be discussed with, and accepted by, CADTH in advance of filing the submission. Please contact requests@cadth.ca to provide complete details of the deviations from these requirements. Alternative specifications may be considered in scenario analyses.

For additional information on the reporting of results and details of the pharmacoeconomic evaluation, manufacturers should refer to the *Analysis and Reporting* sections of the *Guidelines for the Economic Evaluation of Health Technologies: Canada (4th edition)*, as well as the worked example.

Economic Model

The model should align with best modelling practices, per the *Modelling* section of the *Guidelines for the Economic Evaluation of Health Technologies: Canada (4th edition)*, and should not be more complex than is required.

An unlocked version of the electronic economic model used in the pharmacoeconomic evaluation is a requirement. The model must be:

- Programmed in Excel, TreeAge, or Arena.
 - Before using other specialized program software, the manufacturer must contact CADTH in advance to ensure that the alternative program software is acceptable. If acceptable, manufacturers will receive direction on how the model and software should be provided as part of the submission information (e.g., licences, laptop with model, and software), which will be returned to the manufacturer at the end of the review process, at the manufacturer's expense.
- Able to function in a standalone environment not requiring access to a web-based platform.
- Provided in its entirety, meaning CADTH must have full access to the programming code (e.g., macros, VBA code) and be able to fully execute the model based on modifications to parameters of interest. CADTH must be able to vary individual parameters, view the calculations, and run the model to generate results.

Basic user information must be provided to ensure clarity on how to modify input parameters and run the model.

Deviations from these requirements must be discussed with and accepted by CADTH in advance of filing the submission. Please contact requests@cadth.ca to provide complete details of the deviations from these requirements.

The submitted economic model should have a reasonable run time. If the model run time is considered by CADTH to be excessive, it may not be possible to complete the review in accordance with the target timelines.

The manufacturer will be notified that the run time is excessive and informed that the review may be delayed as a result. In such circumstances, the following may occur:

- The manufacturer may be able to address the concerns with the model (potentially allowing the review to be completed within the target timeframes). In such cases, the review will be temporarily suspended while the economic model is revised.
- The manufacturer may be unable to address the concerns with the model and the review will be delayed to account for the excessive model run time.

In either of the above scenarios, CADTH may be prevented from achieving the performance metric because of circumstances beyond its control and manufacturers will not be eligible for a partial refund.

Supporting Material

Details regarding information used for input parameters in the pharmacoeconomic evaluation must be provided in detail. This includes:

- If one or more indirect treatment comparison (ITC) is considered within the submitted economic evaluation, the full technical report of the ITC(s) used to inform clinical parameters in the economic model.
- Technical reports of any unpublished studies or analyses used to inform parameters or assumptions (e.g., utility studies, patient registries, unpublished CSRs, expert opinion, etc.). The technical report must provide details of how input parameters were derived, including

a description of the study or data set, the analysis plan, and results of the analyses. Any modification or transformation of the results to use in the economic model must be described.

- If there is a companion diagnostic test associated with the drug under review, the model and pharmacoeconomic evaluation must include relevant costs and consequences (e.g., rates of true- and false-positives, and true- and false-negatives) for these tests in relation to the drug under review. The source(s) and assumption(s) of the relevant inputs should be provided as well.

5.1.5. Epidemiologic Information

Disease Prevalence and Incidence

Provide the prevalence and incidence of the disease(s) or condition(s) for the indication(s) to be reviewed. Include a breakdown of prevalence by participating province, territory, and First Nations populations (where available). References must be provided for this document in the following format:

- in-text citations numbered in their order of appearance
- a numbered reference list in the Citing Medicine format.

Number of Patients Accessing a New Drug

The following information is required only for a new drug submission or a new combination product submission if one of the components is a new drug (as defined in section 2.1):

- For the indication(s) to be reviewed by CADTH, the number of patients in Canada currently accessing the new drug to within 20 business days of filing the submission must be provided.
- This must include the number of patients accessing the drug through each of the different possible mechanisms (such as compassionate use, Health Canada's Special Access Program, and participation in a clinical trial).
- The Number of Patients Accessing New Drug template should be used for providing this information.

5.1.6. Submission Templates for Tailored Reviews and Biosimilar Reviews

Submission Templates for Tailored Reviews

A completed New Combination Product Submission Template or Subsequent Entry Non-Biological Complex Drug Submission Template (as applicable).

Submission Template for a Biosimilar Review

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 or NOC/c has been issued by Health Canada.

5.1.7. Pricing and Distribution Information

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.
- CADTH does not accept confidential submitted prices for applications filed for review through the CDR process. The submitted price is disclosed in all applicable CDR review reports, as well as the CDEC recommendation documents posted on the CADTH website.
- 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 analysis (BIA) (budget impact reports and the models used to produce the results).

Method of Distribution

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

5.1.8. Companion Diagnostics

Clinical Utility of Companion Diagnostic

If applicable, provide a reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s) under review. In this context, clinical utility refers to evidence of improved health outcomes as a result of biomarker testing. If no references are provided, a statement will be required to confirm that a search has been undertaken but no references have been located.

Price of Companion Diagnostic

The disclosable price for the companion diagnostic(s) must also be provided.

5.1.9. Additional Letter for Submissions Filed on Pre-Notice of Compliance Basis

Letter for Sending NOC or NOC/c to CADTH

Once the NOC or NOC/c has been issued, the manufacturer must provide a signed letter, using the Letter for Sending NOC or NOC/c to CADTH template, indicating any wording changes to the Health Canada–approved final product monograph, as compared with the draft product monograph filed in the initial category 1 requirements. The letter should be sent to CADTH using Collaborative Workspaces.

5.2. Category 2 Requirements

CADTH provides secretariat support to the drug plans by ensuring that category 2 requirements have been filed; however, they are not considered as part of the CADTH review or recommendation process. The manufacturer must also provide the category 2 requirements to all drug plans that require copies (see *Contact Information and Requirements for Drug Plans* for details). CADTH does not screen category 2 requirements for completeness. When CADTH notifies a manufacturer that category 2 requirements have been received, it does not imply that the provided information meets the requirements of the individual drug plans. If any of the drug plans have questions regarding the filed category 2 requirements, they will contact the manufacturers directly.

Category 2 requirements may be filed concurrently with category 1 requirements (when available). If not provided at the same time as category 1 requirements, one copy of the category 2 requirements must be provided to CADTH using Collaborative Workspaces within 20 business days of the submission or resubmission being accepted for review by CADTH. Delayed filing of category 2 requirements will not preclude a CDR review from being placed on the agenda of the targeted CDEC meeting; however, the embargoed CDEC recommendation and/or the CADTH Biosimilar Summary Dossier will not be issued until category 2 requirements are received.

5.2.1. Budget Impact Analyses

Budget Impact Reports

Budget impact reports 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 the 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 data from Nova Scotia. The base unit price used in the BIAs must be the same as the price submitted in the category 1 requirements and must be clearly identified in each BIA. Jurisdiction-specific markups or discounts can then be applied, if applicable.

Budget Impact Models

Copies of the models used to produce the BIAs 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 the Non-Insured Health Benefits Program.

5.2.2. Supporting Documentation Used in Budget Impact Analyses

A reference list and copies of all supporting documentation used and/or cited in the BIA. The reference list must be the first file in the folder of the documents. The manufacturer is responsible for ensuring that appropriate copyright permissions have been obtained for electronic copies of all supporting documentation included in category 2 requirements of a submission or resubmission, to be shared among the drug plans.

5.2.3. Companion Diagnostics

If there is a companion diagnostic test associated with the drug, please provide the BIA for drugs and companion diagnostics both in combination and separately, as some jurisdictions fund the two health technologies through separate mechanisms.

5.3. Additional Information

To complete the review CADTH may request additional information from Health Canada or the manufacturer. Note the manufacturer's continuing responsibility to advise CADTH of any harms or safety issues that may arise during the time the submission is under review.

5.3.1. Clinical Study Reports and Periodic Safety Update Reports

CADTH may request complete copies or sections of Clinical Study Reports and Periodic Safety Update Reports from the manufacturer. These documents should be provided in searchable electronic format (i.e., PDF or Microsoft Word).

5.3.2. Health Canada Clinical Reviewer Report(s)

CADTH may request copies of all Health Canada clinical reviewer reports (*Pharmaceutical Safety and Efficacy Assessment* or *Biologics Safety and Efficacy Assessment Report*) pertaining to the evaluation of pivotal safety and efficacy clinical trials – including those associated with any previous negative decision received during any review iteration – for the indication to be reviewed through the CDR process. If the *Pharmaceutical Safety and Efficacy Assessments* or *Biologics Safety and Efficacy Assessment Reports* BSEARs are unavailable from Health Canada at the time the request is received from CADTH, the applicant should provide the reports to CADTH as soon as available (i.e., on the day of, or the business day after, receipt from Health Canada).

6. Application and Screening Procedure

An application filed with CADTH for the review of a drug submission or resubmission through the CDR process represents a submission or resubmission to all of the drug plans. All submission and resubmission requirements must be provided in English.

6.1. Filing a Submission or Resubmission

- a) The appropriate submission or resubmission requirements filed must adhere to the content, format, and organization stipulated in the current version of the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and any applicable *CADTH Pharmaceutical Reviews Update*.
- b) Applicants must be registered with CADTH Collaborative Workspaces before filing a submission or resubmission. For detailed information on how to register please consult CADTH Collaborative Workspaces Registration. Ensure both primary and secondary contacts and any submitting consultants working on a CDR application are registered with Collaborative Workspaces.
- c) Submissions and resubmissions must be filed using Collaborative Workspaces. To file a submission or resubmission, the manufacturers must upload one copy of all category 1 requirements to the corresponding CDR review using Collaborative Workspaces, per the electronic file folder and file format specified in Appendix 4. Submissions and resubmissions must be filed using Collaborative Workspaces during CADTH business hours (between 8:00 a.m. and 4:00 p.m. Eastern time). If filed outside of CADTH business hours, the next business day will be considered the date of transmittal.
- d) CADTH sends an acknowledgement of receipt to the applicant as confirmation the submission has been received.
- e) Applicants who experience difficulties filing a submission or resubmission using Collaborative Workspaces should contact CADTH by email (requests@cadth.ca) for support or to arrange an alternate delivery method for the submission or resubmission requirements (e.g., by email or mailing a USB flash drive or CD).
- 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 or resubmission being accepted for review.
- g) CADTH will provide copies of the category 1 and category 2 requirements to the drug plans to ensure that they have this information prior to the targeted CDEC meetings. Manufacturers are still required to provide copies of their CDR submission or resubmission – 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 manufacturer).

6.2. Screening of Submissions and Resubmissions

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

- a) The date of receipt is considered day zero for the purpose of calculating the 10 business day targeted time frame for initial screening of category 1 requirements.
- b) If the filed category 1 requirements for a submission or resubmission are deficient or require revision in order to meet the requirements, CADTH sends a notice to the

manufacturer 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) Upon receipt of notification of a manufacturer's submission or resubmission, the drug plans may identify questions to be addressed in the review process and submit these to CADTH.
- d) On day 10 of the screening period, CADTH sends a letter to the manufacturer advising whether or not the submission or resubmission requirements have been accepted for review.
- e) Following acceptance for review, the manufacturer must also provide the category 1 requirements to all drug plans that require copies (see *Contact Information and Requirements for Drug Plans* for details).

6.2.1. Finalized Information for Submissions Filed on Pre-NOC Basis

For submissions filed on a pre-NOC basis, some requirements will be outstanding or not finalized at the time that the submission is filed with CADTH (e.g., product monograph). The manufacturer must provide all outstanding and/or finalized category 1 requirements to CADTH as soon as they are 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 CDR review report(s). This could result in the submission being considered at a later CDEC meeting. In the event the finalized information is received after the drug has been discussed by CDEC, CADTH will review the information and determine if the embargoed CDEC recommendation will be issued or if the drug should be placed on a subsequent CDEC agenda. The manufacturer will be apprised of any revisions to the anticipated timelines.
- b) If additional supporting documentation is required, the manufacturer will be apprised of the requirements.
- c) When all outstanding or finalized category 1 submission requirements have been provided to CADTH, the manufacturer must provide a letter to confirm that all information provided in the category 1 requirements for the submission are final.
- d) Once CADTH has notified the manufacturer that the finalized category 1 requirements have been accepted, the manufacturer must ensure that drug plans are provided with a copy of the finalized category 1 requirements.

6.3. Application Fees for the CADTH Common Drug Review

All CDR submissions and resubmissions filed by manufacturers are subject to an application fee. For details please consult *Guidelines on Application Fees for CADTH Pharmaceutical Reviews* (February 2018).

6.4. Targeted Time Frames and Tracking

The key targeted time frames and the status of all CDR reviews are posted on the CADTH website. Table 15 indicates the targeted time frames for key tasks within the CDR process.

Table 15: Targeted Timelines for the CDR Process

Phase of Review	Key Milestone	Business Days
Standard and Tailored CDR Reviews		
Screening and administration	Category 1 requirements received by CADTH	0
	Category 1 requirements screened for acceptance	10
	Review initiated	1 to 10
Review of submission or resubmission	Draft CDR review report(s) prepared and sent to manufacturer for comments	45
	Manufacturer receives draft CDR review report(s) and provides comments	7
	CADTH's responds to comments ^a and final CDR review report(s) prepared	7
CDEC deliberation and recommendation	CDEC brief completed and distributed to CDEC and the drug plans	5
	Review of meeting materials by CDEC and preparation of discussant reports	10
	CDEC meeting	1
	Embargoed CDEC recommendation sent to the drug plans and manufacturer	8 to 10
Embargo period and options	Embargo period	10 to 30 ^b
	Request for clarification or request for reconsideration	Variable ^c
Finalizing and posting	<i>CDEC Final Recommendation</i> issued to drug plans and manufacturer	5
	<i>CDEC Final Recommendation</i> and CDR review report(s) posted	2
Requests for Advice		
Screening and administration	Request for advice received by CADTH	0
	Review approach determined and manufacturer invited to provide information	10
	Review initiated	1 to 10
Review of submission	Draft CDR review report(s) prepared and sent to manufacturer for comments	≤ 45
	Manufacturer receives draft CDR review report(s) and provides comments	7
	CADTH's responds to comments ^a and final CDR review report(s) prepared	7
CDEC deliberation	CDEC brief completed and distributed to CDEC and drug plans	5
	Review of meeting materials by CDEC and preparation of discussant reports	10
	CDEC meeting	1
If no revised CDEC recommendation	<i>CDEC Record of Advice</i> document issued to drug plans and manufacturer	8 to 10
	<i>CDEC Record of Advice</i> document posted	2
If revised CDEC recommendation	Embargoed CDEC recommendation sent to drug plans and manufacturer	8 to 10
	Embargo period	10 to 30 ^b
	Request for clarification or request for reconsideration	Variable ^c
Finalizing and posting	<i>CDEC Final Recommendation</i> issued to drug plans and manufacturer	5
	<i>CDEC Final Recommendation</i> and <i>CDR Request for Advice</i> report posted	2
Biosimilar CDR Reviews		
Screening and administration	Category 1 requirements received by CADTH	0
	Category 1 requirements screened for acceptance	5
	Review initiated	1 to 10
Review	Draft <i>CADTH Biosimilar Summary Dossier</i> prepared	24
	Draft <i>CADTH Biosimilar Summary Dossier</i> sent to applicant	1
	Final <i>CADTH Biosimilar Summary Dossier</i> sent to applicant and drug plans	7
Finalizing and posting	<i>CADTH Biosimilar Summary Dossier</i> is posted on the CADTH website	6

CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

^a Manufacturers will be sent the review team's responses eight business days prior to the CDEC meeting.

^b An extension of up to 20 business days may be requested to prepare a request for reconsideration (i.e., a total of 30 business days).

^c The time frame required to address a request for clarification, or request for reconsideration, depends on the amount of work needed to address the request, as well as the available dates for CDEC meetings.

7. CDR Review Procedure

7.1. Ordering and Initiation of Reviews

- a) Applications for submissions and resubmissions are accepted on an ongoing basis.
- b) Collaborative Workspaces logs the date and time applications for submissions and resubmissions are received.
- c) Applications are screened in the order they are received.
- d) All submissions and resubmissions will be assigned to the CDR work schedule on a first-come, first-served basis, as determined by the date the submission or resubmission is accepted for review by CADTH, with the exception of requests for advice, and drug plan-initiated submissions or resubmissions.
- e) Submissions and resubmissions are typically initiated within 10 business days of acceptance for review. Key dates (including initiation and the targeted CDEC meeting) are provided only once the submission or resubmission has been accepted for review.
- f) The timing of when a request for advice will be considered at a CDEC meeting is based on the nature of the request and the amount of effort required by the review team to address the request. Once completed, requests for advice are generally considered at the earliest available CDEC meeting.
- g) CADTH posts targeted CDEC meeting dates on which submissions and resubmissions may be considered if their reviews are initiated by a given date.
- h) Prior to initiating the review of a submission or resubmission, CADTH:
 - provides the manufacturer with the name of the contact to whom all inquiries about that submission or resubmission are to be directed
 - establishes a review team, based on the nature of the submission or resubmission, and in consideration of the proposed team members' qualifications, expertise, and compliance with the *CADTH Common Drug Review Conflict of Interest Guidelines*. With the exception of the review manager(s), the names of the review team members are not disclosed to the manufacturer
 - determines the appropriate approach for undertaking the review and develops a work plan for the submission or resubmission.

7.2. Reviewing Submissions and Resubmissions

The following sections outline the process for reviewing standard reviews, tailored reviews, resubmissions, requests for advice, and biosimilars.

7.2.1. Standard Reviews

The process for standard reviews is outlined and in Figure 3.

- a) The review team develops a protocol for the review of the submission with input from the drug plans, CDEC members, and other experts (as required).
- b) The review team designs and conducts an independent systematic literature search to address the protocol and to supplement the data provided by the manufacturer. The search strategy and findings from the literature are included in the *CDR Clinical Review Report*.

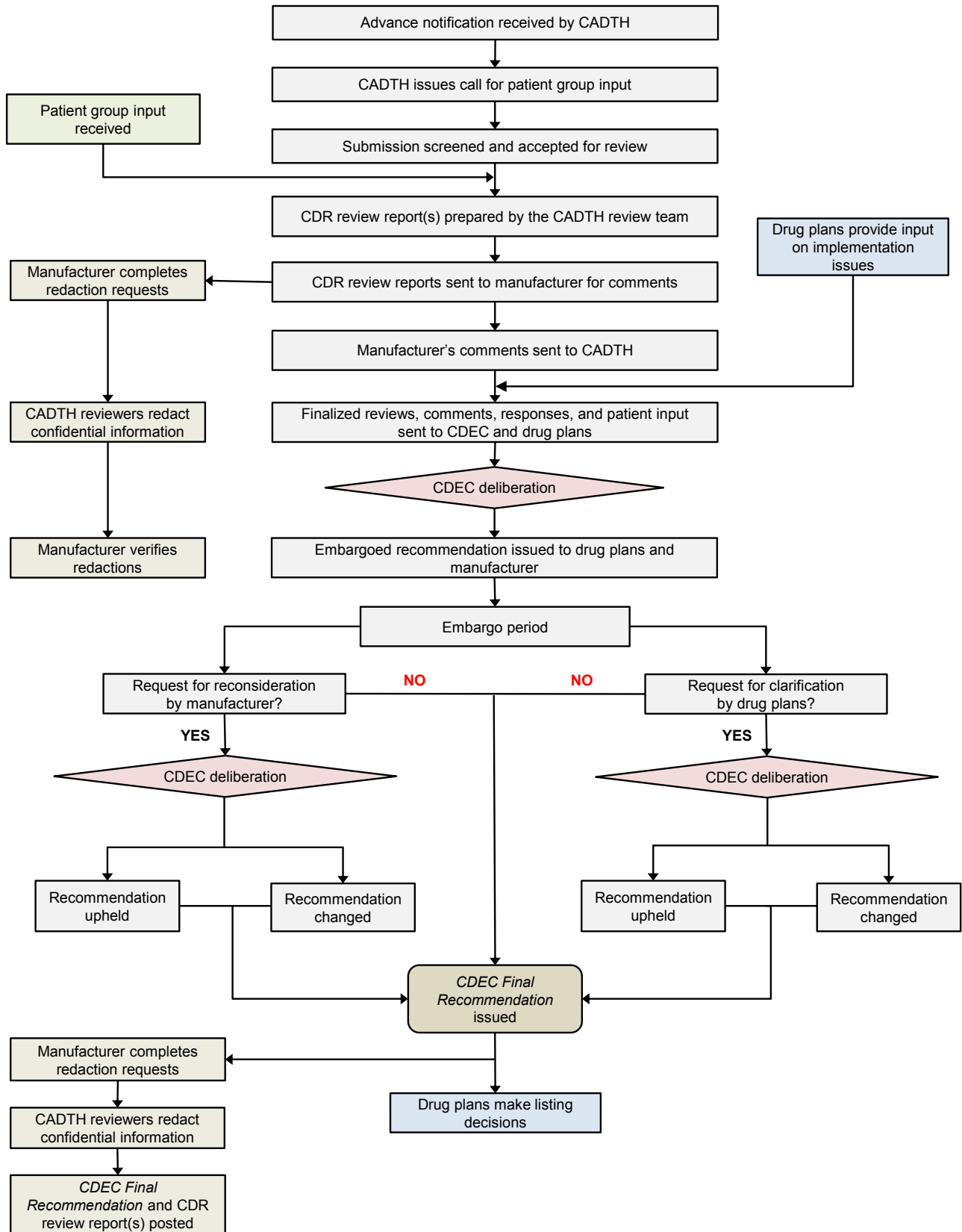
- c) A list of studies included in the systematic review portion of the *CDR Clinical Review Report* is sent to the manufacturer for information. Additional studies that are not included in the CDR systematic review may be used as references in other parts of the *CDR Clinical Review Report*. All studies that are used in the *CDR Clinical Review Report* are referenced.
- d) The review team undertakes a review of the relevant information provided by the manufacturer, by patient groups, and identified through an independent literature search. During this stage, the review team:
 - determines whether additional information from the manufacturer is needed. If so, CADTH will contact the manufacturer. Delays in providing the requested information may result in a temporary suspension of the review due to incomplete information to conduct a thorough review (see section 12.1)
 - prepares a CDR Clinical Review Report in accordance with the review template.
- e) The review team reviews and conducts an appraisal of the pharmacoeconomic information submitted by the manufacturer. The results and conclusions reported in the *CDR Clinical Review Report* are used in the assessment of the pharmacoeconomic information submitted by the manufacturer. During this stage, the review team:
 - determines whether additional information from the manufacturer is needed. If so, CADTH will contact the manufacturer. Delays in providing the requested information may result in a temporary suspension of the review due to incomplete information to conduct an appraisal (see section 12.1)
 - determines whether the submitted pharmacoeconomic evaluation is supported by the available clinical evidence. Results provided by the manufacturer are confirmed, using the supplied economic model. When relevant, the economic model is rerun and revised cost-effectiveness estimates are determined
 - prepares cost comparison tables
 - prepares a CDR Pharmacoeconomic Review Report in accordance with the review template.
- f) Depending on the volume or complexity of material to be reviewed, an extension of the review time frame deadlines may be required. The manufacturer will be notified of any extensions, and the reasons for the extensions.
- g) If a manufacturer submits new information for inclusion in an ongoing review (i.e., after category 1 requirements have been accepted and the review has been initiated), CADTH will determine the timelines required to review the new information and incorporate it into the review reports. This could result in the submission being considered at a later CDEC meeting. The manufacturer would be apprised of any revisions to the anticipated timelines for the review.
- h) The *CDR Clinical Review Report* and *CDR Pharmacoeconomic Review Report* are finalized in accordance with section 7.2.6.
- i) CADTH and Health Canada may communicate as required to clarify information regarding the submission. The manufacturer will be included in or apprised of communications between CADTH and Health Canada.

7.2.2. Tailored Reviews

The process for tailored reviews is outlined below subsequently and in Figure 3.

- a) The review team validates and comments on the information provided by the manufacturer in the tailored CDR review template.
- b) The review team includes its assessment of the submitted information and comments directly into the appropriate sections of the tailored review template, which then becomes the *CDR Clinical and Pharmacoeconomic Review Report*. A single report combining both clinical and pharmacoeconomic information is prepared by CADTH for tailored CDR reviews. During this stage, the review team considers whether it needs additional information from the manufacturer. If so, CADTH will contact the manufacturer. Delays in providing such information may result in a temporary suspension of the review due to incomplete information to conduct an appraisal (see section 12.1).
- c) Depending on the volume or complexity of material to be reviewed, an extension of the review time frame deadlines may be required. The manufacturer will be notified of any extensions, and the reasons for the extensions.
- d) If a manufacturer 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 CDR review report. This could result in the submission being considered at a later CDEC meeting. The manufacturer would be apprised of any revisions to the anticipated timelines for the review.
- e) The *CDR Clinical and Pharmacoeconomic Review Report* for a CADTH–designated tailored CDR review is finalized in accordance with section 7.2.6.
- f) CADTH and Health Canada may communicate as required to clarify information regarding the submission. The manufacturer will be included in or apprised of communications between CADTH and Health Canada.

Figure 3: Common Drug Review Process for Standard and Tailored Reviews



CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

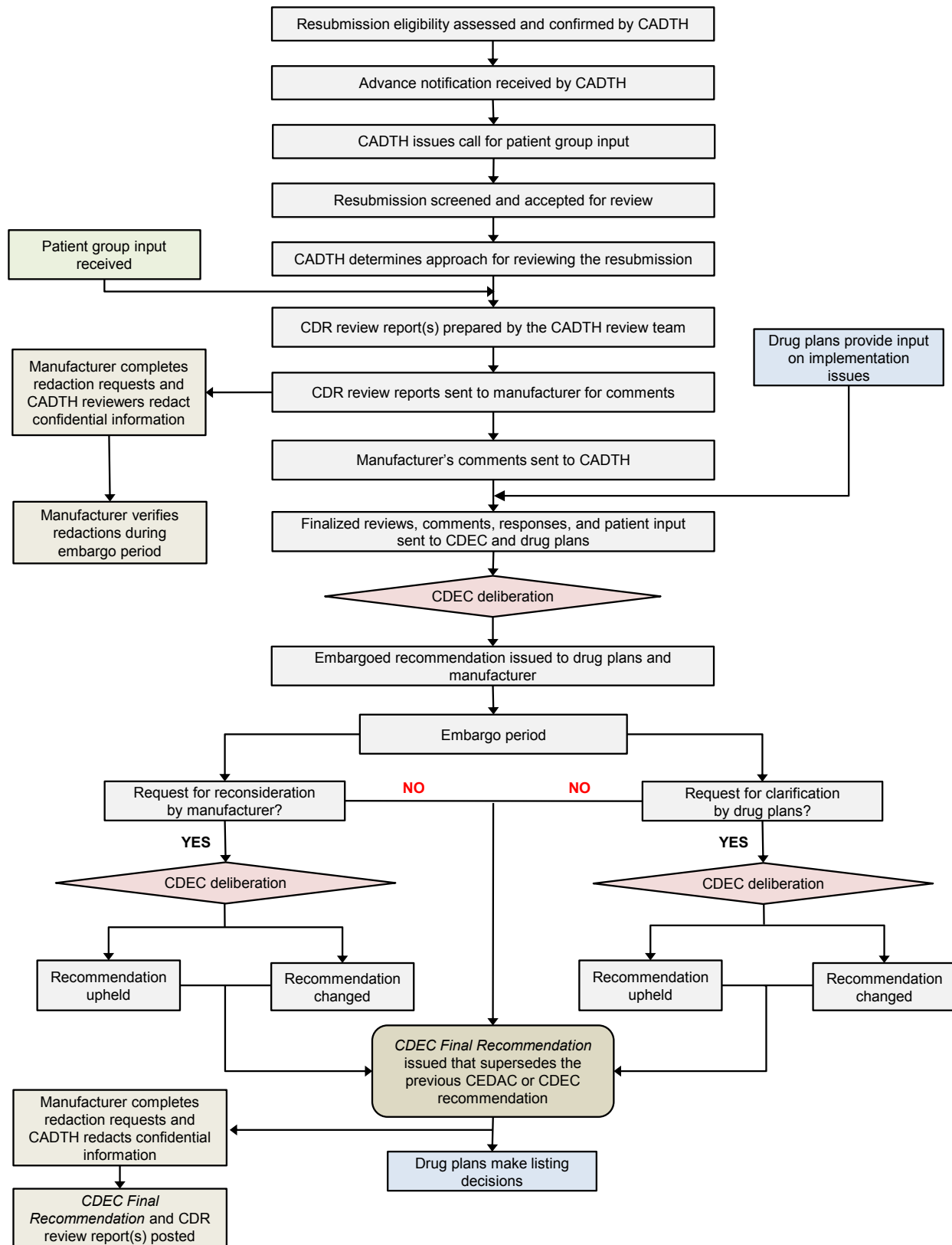
7.2.3. Resubmissions

The process for resubmissions is outlined as follows and in Figure 4.

- a) The resubmission and relevant documents that relate to the initial submission or previous resubmission(s) are reviewed. CADTH determines if a new systematic review is required and decides the appropriate approach to assess the new information.
- b) For resubmissions based on new clinical information, CADTH reviews the relevant clinical information provided in the resubmission and identified in the literature search. CADTH uses this information to prepare a *CDR Clinical Review Report* in accordance with the review template.
- c) For all resubmissions, CADTH conducts an appraisal of the pharmacoeconomic information submitted by the manufacturer and prepares a *CDR Pharmacoeconomic Review Report* in accordance with the review template. CADTH determines whether the submitted pharmacoeconomic evaluation is supported by the available clinical evidence. Results provided by the manufacturer are confirmed, using the supplied economic model. When relevant, the model is rerun and revised cost-effectiveness estimates are determined. CADTH may also prepare cost comparison tables.
- d) When preparing the CDR review report(s), CADTH will determine if additional information is required from the manufacturer. If so, CADTH will contact the manufacturer and request the information. Delays in providing the requested information may result in a temporary suspension of the review due to incomplete information to conduct a thorough review (see section 12.1).
- e) CADTH will determine the length of time required to conduct the review of a resubmission based primarily on the following considerations:
 - Volume and complexity of the new clinical information to be reviewed
 - Complexity of the economic model (e.g., model run-time)
 - Extent of revisions to the economic model relative to the initial submission (e.g., changes in model structure and/or assumptions)
 - Date of filing the resubmission relative to the target CDEC meeting date (e.g., filing earlier in the range provides greater opportunities for CADTH to target an earlier CDEC meeting)
 - The volume of CDR submissions and resubmissions being review concurrently
 - Whether or not the drug underwent an expedited review by Health Canada.

The manufacturer will be notified of the review timelines, including the target CDEC meeting date.
- f) If the manufacturer submits new information for inclusion in an ongoing review (i.e., after category 1 requirements have been accepted and the review had been initiated), CADTH will determine the timelines required to review the new information and incorporate it into the CDR review report(s). This could result in the resubmission being considered at a later CDEC meeting. The manufacturer would be apprised of any revisions to the anticipated timelines for the review.
- g) The *CDR Clinical Review Report* and/or *CDR Pharmacoeconomic Review Report* for a resubmission are finalized in accordance with section 7.2.6.

Figure 4: Common Drug Review Process for Resubmissions



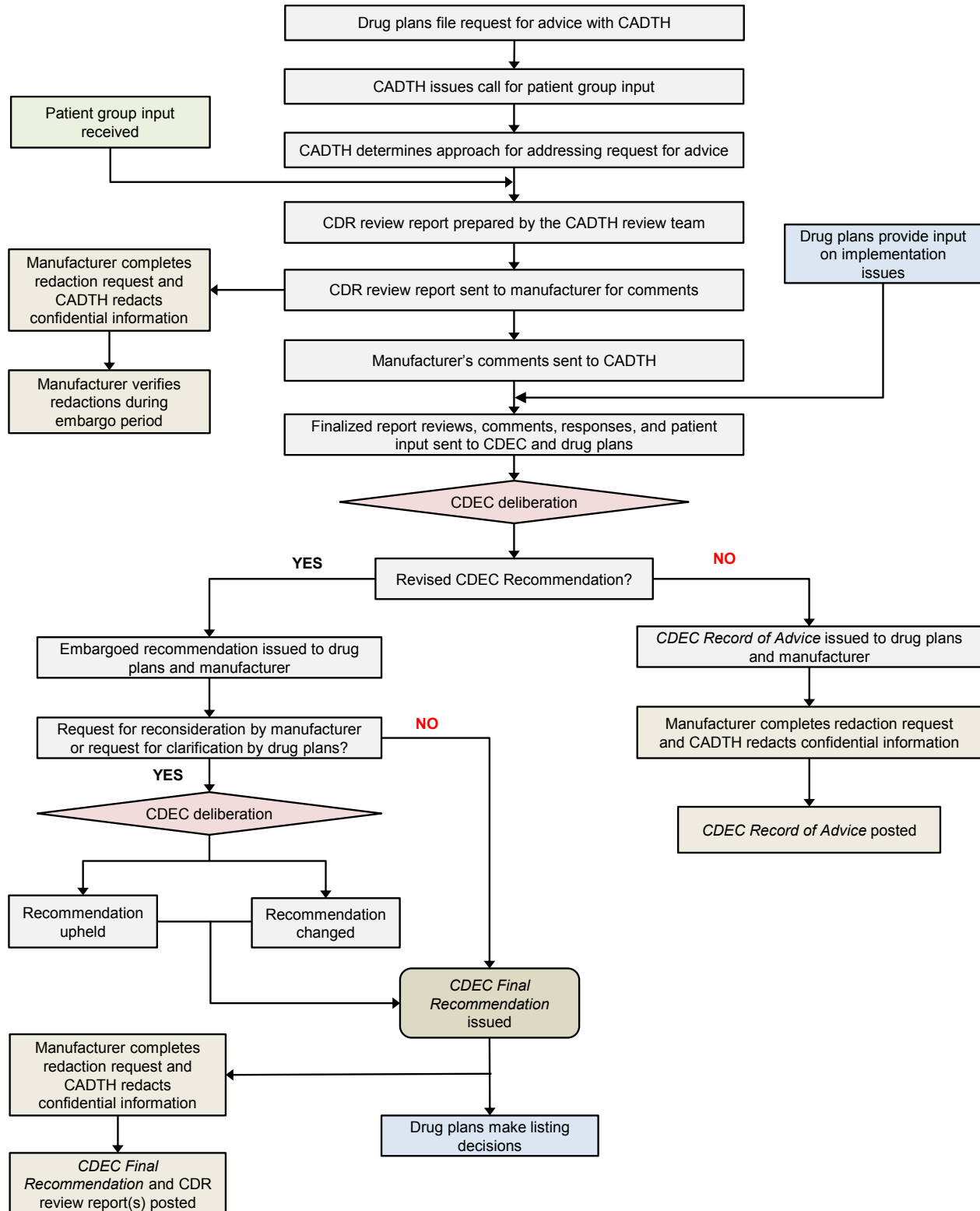
CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

7.2.4. Requests for Advice

In the case of a request for advice filed by the drug plans, the following provisions will apply:

- a) The request for advice will be regarding a previous *CEDAC* or *CDEC Final Recommendation*.
- b) The date on which CADTH receives a request for advice is considered day zero for the purpose of calculating the time frame for determining the approach for the request.
- c) CADTH determines the appropriate approach for responding to the request for advice and develops a work plan for its review within 10 business days of receipt.
- d) CADTH may seek direction from the CDEC chair and members on how to proceed with the request for advice.
- e) CADTH establishes a review team, based on the nature of the request for advice and in consideration of the proposed team members' qualifications, expertise, and compliance with the *CADTH Common Drug Review Conflict of Interest Guidelines*. With the exception of the review manager(s), the names of the review team members will not be disclosed to the manufacturer.
- f) The steps in the review of a request for advice are as follows:
 - the manufacturer(s) of the drug(s) in question is apprised that a review is being undertaken and the reasons for the review, and is/are invited to comment or provide information within 10 business days
 - the review is assigned to a review team
 - a protocol is established
 - the review team conducts a literature search. The studies and materials identified through the literature search and any information or data provided by the manufacturer(s) are supplied to the review team to consider as part of the review.
- g) The *CDR Request for Advice* report is finalized in accordance with section 7.2.6.

Figure 5: Common Drug Review Process for Requests for Advice



CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

7.2.5. Biosimilar Reviews

Review of a Biosimilar Submission Template

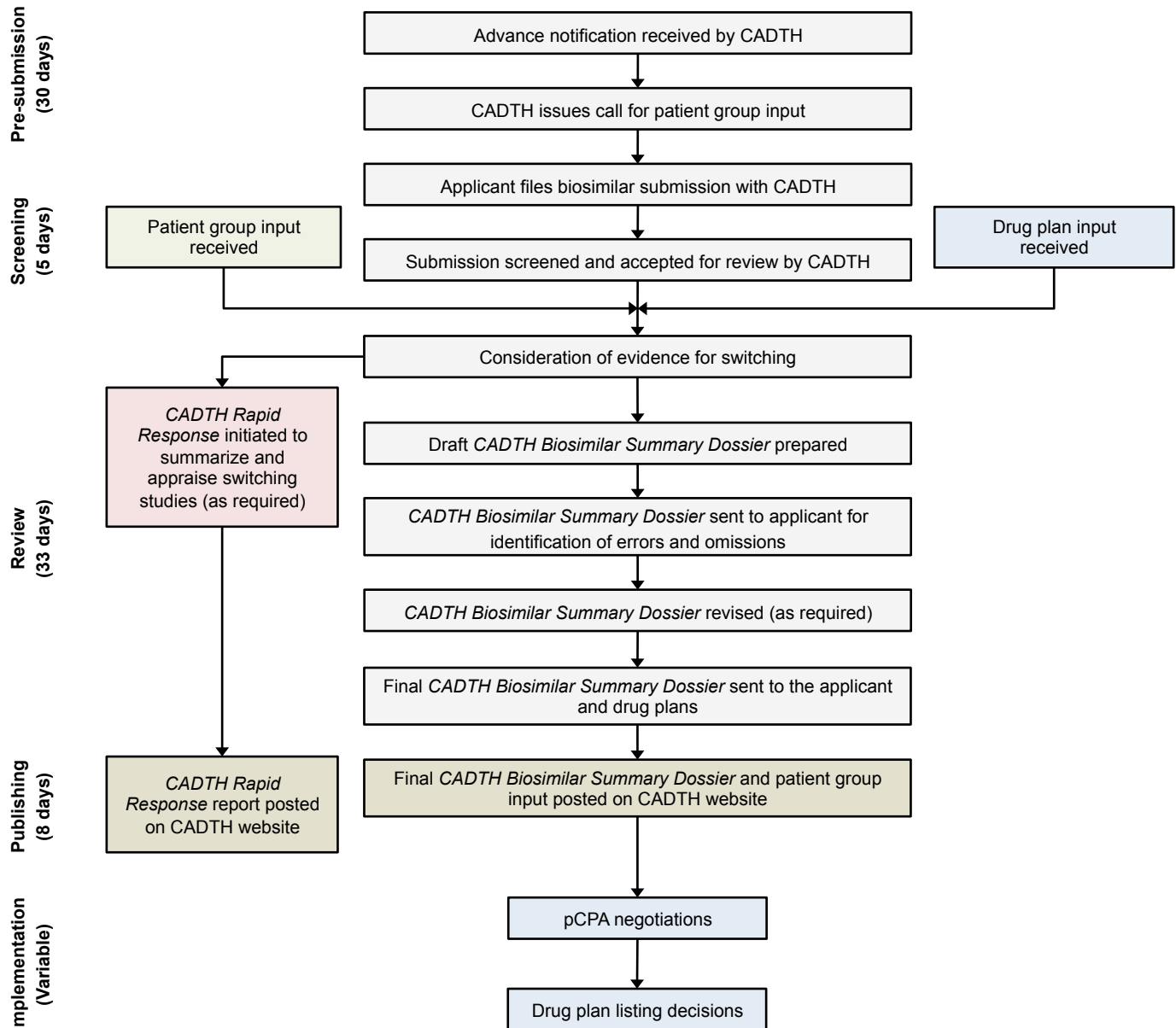
The review process for a biosimilar is outlined below and in Figure 6.

- 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 the 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.
 - 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.
- 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 had been 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.
- g) The draft summary dossier is sent to the applicant for the purposes of identifying errors and omissions.
- h) The applicant has three business days following receipt of the draft summary dossier to review and identify any errors and omissions (using the template provided by CADTH).
- i) 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.
- j) CADTH forwards the final version of the *CADTH Biosimilar Summary Dossier* to the applicant and drug plans.
- k) The *CADTH Biosimilar Summary Dossier* is posted 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.
- l) 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 of the information in the *CADTH Biosimilar Summary Dossier* before these documents are posted.

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 using the CADTH Rapid Response process.
- b) CADTH reviews the 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 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 the 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.

Figure 6: CADTH Common Drug Review Process for Biosimilars



pCPA = pan-Canadian Pharmaceutical Alliance.

7.2.6. Companion Diagnostics

For submissions that include companion diagnostics, CADTH's review process will include the following additional considerations:

Clinical Evidence

As part of the clinical systematic review conducted by CADTH, a subgroup of interest that will be pre-specified in the systematic review protocol will relate to the biomarker status of study participants. This will inform the clinical utility of companion diagnostics by highlighting evidence on the degree to which biomarker testing helps improve outcomes with the corresponding drug treatment.

CADTH reviewers will also review the manufacturer-provided reference list and copies of articles that highlight the clinical utility of the companion diagnostics under review, and may conduct a separate search of the clinical utility of the companion diagnostics. These results will be summarized in an appendix of the clinical review report.

Economic Evidence

As part of the appraisal of the manufacturer-provided pharmacoeconomic evaluation, CADTH reviewers will consider the costs and consequences of any required biomarker testing that manufacturers will incorporate into the submitted analyses.

Patient Input

The patient input template asks patient groups to comment on their expectations and/or experiences with any required biomarker testing for the drug under review. Patient groups are asked to consider answering this question for eligible drugs that have companion diagnostics.

Clinician Input

As part of engaging expert clinicians throughout the review process, CADTH may engage additional experts in pathology and/or laboratory testing who would be able to comment on front line clinical aspects of companion diagnostics (e.g., the timing of biomarker testing in the clinical care pathway, the consistency of the testing protocol with current practice, and the availability of the testing).

Jurisdictional Input

As part of soliciting implementation considerations from its participating jurisdictions, CADTH will also seek insights into the enablers and barriers related to any required biomarker testing.

7.3. CDR Review Report(s)

CADTH forwards the draft CDR review report(s) to the manufacturer for comments and identification of confidential information, and to the drug plans for their information.

7.3.1. Manufacturer's Comments

- a) The manufacturer has seven business days following receipt of the draft CDR review report(s) to review and submit written comments about the report(s) to CADTH. This will be the manufacturer's only opportunity to provide comments.
- b) The manufacturer's combined comments on the draft CDR review report(s) should not exceed 10 pages in length and must be submitted using the template provided by CADTH. The ten-page limit includes any figures, tables, etc., but does not include the list

of references. The formatting of the template document (e.g., page margins, table column widths) is not to be altered.

- c) The manufacturer may waive the opportunity to provide comments by indicating “not applicable” on the comments template or by confirming via email.
- d) The manufacturer’s comments should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the part of the report under discussion.
- e) References should be appropriately cited in the comments documents provided by the manufacturer.
- f) The review team has seven business days to address the comments provided by the manufacturer. If the manufacturer’s comments exceed the ten-page limit, the review team will address only the comments on pages up to the limit.
- g) CADTH forwards the review team’s responses to the manufacturer eight business days prior to the targeted CDEC meeting. The responses are provided to the manufacturer for information only.
- h) The review team’s responses are incorporated into the CDEC brief (see section 8.2) and are shared with drug plans.

7.3.2. Identification of Confidential Information

Manufacturers are responsible for identifying and requesting the redaction of any confidential information supplied by the manufacturer that was used by CADTH in the preparation of the CDR review report(s) before these documents are posted.

- a) The manufacturer has 12 business days following receipt of the draft CDR review report(s) to identify confidential information and submit a request for redaction (see Table 16). This will be the manufacturer’s only opportunity to request redactions from the CDR review report(s).
- b) Manufacturers must identify any confidential information in the report(s) by providing:
 - a completed *Identification of Confidential Information Form*
 - a copy of the CDR review report(s) with confidential information highlighted in yellow.
- c) All requests for redaction must be accompanied by a clearly stated rationale.
- d) The manufacturer may waive the opportunity to request redactions by indicating “not applicable” on the Identification of Confidential Information Form or by confirming via email.
- e) CADTH staff will redact confidential information from CDR review report(s) based on the *Identification of Confidential Information Form* completed by the manufacturer. Redactions will be made in accordance with the *CADTH Common Drug Review Confidentiality Guidelines*.
- f) The redaction form with CADTH’s response will be sent back to the manufacturer with the embargoed recommendation.

7.3.3. Final Versions of CDR Review Report(s)

- a) The draft CDR review report(s) are revised by CADTH, as required, based on the manufacturer’s comments and are included in the CDEC brief.
- b) In the case of a submission filed on a pre-NOC basis, CADTH may revise the CDR review report(s) to reflect the final product monograph or other finalized information provided by the manufacturer as a result of the NOC or NOC/c being granted.

- c) CADTH forwards the final full and redacted CDR review report(s) (if applicable) to the manufacturer and drug plans at the same time the confidential embargoed CDEC recommendation or *CDEC Record of Advice* is sent.
- d) The manufacturer has 10 business days to review and confirm the redactions.
- e) CADTH will post the CDR review report(s) for all submissions, resubmissions, and requests for advice.
- f) In the case of a disagreement expressed by the manufacturer regarding redactions made in the CDR review report(s), CADTH may require additional time to resolve the disagreement in consultation with the manufacturer. This additional time could delay publication of the CDR review report(s); however, any such delays will not affect the timelines for issuing the *CDEC Final Recommendation* or *CDEC Record of Advice*.
- g) CADTH may elect to update a previously posted CDR review report should the redacted information become available in the public domain.

Table 16: Time Allotted for Reviewing and Redacting CDR Review Report(s)

Key Milestone	Description and Timing	Business Days
Manufacturer identifies redactions	Manufacturers are sent the draft CDR review report(s) for comment and identification of confidential information. The manufacturer has 12 business days to submit the <i>Identification of Confidential Information Form</i> to request redactions to the CDR review report(s)	12
Manufacturer verifies redactions	At the same time the confidential embargoed CDEC recommendation or <i>CDEC Record of Advice</i> is sent, manufacturers will be sent the final, full, and redacted CDR review report(s) (if applicable) to review and confirm the redactions	10

CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

8. CDEC Meeting and Recommendation Procedure

8.1. Canadian Drug Expert Committee

- a) CDEC is an advisory body to CADTH that makes drug-related recommendations and provides drug-related advice through the CDR and therapeutic review processes. CDEC's recommendations and advice are provided to CADTH to inform the publicly funded drug plans and a range of stakeholders.
- b) CDEC is established in accordance with the *Canadian Drug Expert Committee Terms of Reference*.
- c) All CDEC members must comply with the following:
 - Conflict of Interest Guidelines for CADTH Expert Committee and Panel Members
 - *Code of Conduct Agreement Form for Members of CADTH Committees and Expert Review Panels*.

8.2. Canadian Drug Expert Committee Brief

CADTH compiles and distributes the CDEC brief to all CDEC members and the drug plans 10 business days before the next scheduled CDEC meeting. The committee members are responsible for reviewing the CDEC briefs for all drugs under consideration at the meeting. Materials contained in a CDEC brief for each drug under review include, but are not limited to:

- patient group input
 - a summary of the submitted patient group input
 - all patient group input submissions in their entirety
- a submission history table of similar drugs reviewed by CDR
- CDR clinical and pharmacoeconomic review report(s)
- manufacturer's comments on the CDR clinical and pharmacoeconomic review report(s) and the CDR review team's responses
- drug plans' listing status for the drug under review and comparators
- additional information
 - reference material (for CDR review report[s])
 - a manufacturer-provided executive summary and table of studies.

Notes: (1) CADTH therapeutic review and optimal use reports are included in the CDEC brief materials when available and relevant. (2) In the case of a request for advice, the CDR clinical and pharmacoeconomic review report(s) related to the submission or resubmission for which the request for advice is made will be included in the CDEC brief. (3) In addition to the materials in the CDEC brief, the committee has access to the complete submission or resubmission materials filed by the applicant.

8.3. Canadian Drug Expert Committee Meeting

Minutes of CDEC deliberations will be taken so that there is a record of attendance at the meeting, of recommendations made, and of the decisions and actions.

8.3.1. Preparation for the Canadian Drug Expert Committee Meeting

- a) The CDEC meeting agenda is set by CADTH and the committee chair.

- b) Three CDEC members, including one public member, are assigned early in the review process as discussants for each drug under consideration at a scheduled committee meeting. The public member prepares a brief written overview report summarizing the patient group input, and the other two discussants each prepare an overview report summarizing the clinical and pharmacoeconomic evidence. No new clinical or economic information (i.e., information that was not submitted by the manufacturer or included by CADTH in the review of the submission or resubmission) is included in the overview reports.
- c) CADTH staff review the discussant reports to ensure the data are accurate and no new information that was not reviewed in the CDR review report(s) is introduced. The final discussant reports are subsequently provided to all CDEC members in advance of the meeting.

8.3.2. Attendees at Canadian Drug Expert Committee Meetings

In addition to CDEC members, the following people may attend a committee meeting in accordance with the *Canadian Drug Expert Committee Terms of Reference*:

- a) Health ministry officials appointed by participating jurisdictions may attend as observers, and may contribute information on practical considerations as described in the decision-making framework, but do not have the right to vote.
- b) Representatives of the pCPA office may attend as observers and may ask clarification questions as needed, but do not have the right to vote.
- c) Relevant CADTH staff and external reviewers contracted by CADTH may actively participate in the presentation of information. The staff role includes provision of administrative and secretariat support. CADTH staff and external reviewers do not have the right to vote.
- d) External experts (including clinical specialists) attend CDEC meetings upon invitation from CADTH. These experts provide input regarding the drug under review, address questions from the committee, and assist in establishing and refining clinical criteria and conditions. They do not vote on the recommendation.

Manufacturers, patients, and others (except as previously described) are not entitled to attend any CDEC meeting, either as observers or to make an oral presentation or submission.

8.3.3. CDEC Deliberative Framework and Process

- a) At the CDEC meeting, committee members consider and discuss each CDEC brief on the meeting's agenda in order to make a recommendation.
- b) Consideration of each submission or resubmission begins with presentations by each of the assigned discussants.
 - a. The public member makes the first presentation, focusing on the perspectives and issues of patients and/or their caregivers related to the condition for which the drug under review is indicated, the impact and unmet needs of current therapy, the treatment outcomes of greatest importance, and the expectations for the drug under review, as identified in the input submitted by patient groups. This information provides context for deliberating the clinical and economic evidence.
 - b. The other two CDEC discussants present their overviews of the clinical and pharmacoeconomic evidence.
- c) Following the discussant presentations, all CDEC members provide input, and the review team and invited external experts provide input (as required).
- d) The key elements supporting CDEC's recommendations include the following information available at the time of the review:

- input from patients and caregivers
 - clinical and economic evidence
 - existing treatment options (e.g., what is or is not reimbursed and who is covered for reimbursement)
 - the submitted price of the drug under review and the publicly available prices of comparators
 - the applicant's requested reimbursement criteria (if any) and the evidence supporting those criteria
 - implementation considerations at the jurisdictional level.
- e) CDEC must make a recommendation or defer if additional clarification is needed. If CDEC needs additional information from CADTH, the applicant, or from external experts, the matter will be deferred to a subsequent CDEC meeting, pending the collection of such information. No new information will be allowed at this time. CADTH will determine whether the additional information provided constitutes new information or not.
- f) Based on the deliberation of the available evidence, CDEC members choose one of three recommendation options: reimburse, reimburse with clinical criteria and/or conditions, or do not reimburse (see also section 8.4.1), and provide reasons for the recommendation.
- g) CDEC members vote on the recommendation;
- only CDEC members vote
 - all CDEC members must vote unless there is a declared conflict of interest that precludes a member from voting
 - CDEC members vote secretly on the recommendation. The reasons for the recommendation are drafted and discussed before committee members vote on a recommendation
 - the CDEC chair validates the voting results and announces if the motion is carried. Results of the vote are determined based upon a simple majority of the voting members. The committee chair votes only in the case of a split vote.

8.4. CDEC Recommendation and Reasons for Recommendation

8.4.1. Canadian Drug Expert Committee Recommendation Options

CDEC may recommend one of the following options for a drug under review: that a drug be reimbursed; that a drug be reimbursed with clinical criteria and/or conditions; or that a drug not be reimbursed. A description of the recommendation options is provided in Table 17.

Table 17: Description of CDEC Recommendations

Reimburse
The drug under review demonstrates comparable or added clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators ^a to recommend reimbursement in accordance with the defined patient population under review, which is typically the patient population defined in the Health Canada–approved indication (as applicable).
Reimburse with Clinical Criteria and/or Conditions^b
Scenarios that could be considered under this category include: <ul style="list-style-type: none"> • The drug under review demonstrates comparable or added clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators in a subgroup of patients within the approved indication. In such cases, the subgroup is specified through “clinical criteria.” • The drug under review demonstrates comparable clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators.^a In such cases, a condition may include that the drug be listed in a similar manner to one or more appropriate comparators.^a • The drug under review demonstrates comparable or added clinical benefit, but the cost/cost-effectiveness relative to one or more appropriate comparators^a is unacceptable. In such cases, a condition may include a reduced price. The drug under review demonstrates clinical benefit, with a greater degree of uncertainty and an acceptable balance between benefits and harms, in a therapeutic area with significant unmet clinical need. In such cases, if the cost/cost-effectiveness relative to one or more appropriate comparators^a is unacceptable, a condition may include a reduced price.
Do Not Reimburse
There is insufficient evidence identified to recommend reimbursement. Scenarios that typically fit this recommendation category include: <ul style="list-style-type: none"> • The drug under review does not demonstrate comparable clinical benefit relative to one or more appropriate comparators.^a • The drug under review demonstrates inferior clinical outcomes or significant clinical harm relative to one or more appropriate comparators.^a

^a An appropriate comparator is typically a drug reimbursed by one or more drug plans for the indication under review. However, the choice of appropriate comparator(s) in the review is made on a case-by-case basis, considering input from jurisdictions and clinical experts. Note: Existing treatment options may include best supportive care and non-pharmaceutical health technologies or procedures.

^b See section 8.4.2 for additional context regarding potential clinical criteria and conditions.

8.4.2. Additional Guidance on the “Reimburse with Clinical Criteria and/or Conditions” Category

a) *Clinical Criteria and Conditions*

The CADTH drug expert committees recommend clinical criteria to provide additional characteristics to identify the patient population for whom reimbursement is being recommended. These are typically provided in addition to any clinical characteristics specified in the Health Canada–approved indication.

The CADTH drug expert committees recommend conditions to provide guidance to the participating jurisdictions on implementation and operational issues related to the drug under review. The examples cited are intended to serve as illustrations only to help guide the reader to better understand some of the factors that CADTH’s drug expert committees will assess as part of their deliberation in formulating a reimbursement recommendation, and are by no means exhaustive or impose any procedural obligations that would constitute grounds for a procedural review. Table 18 lists some of the common considerations regarding clinical criteria and conditions.

Table 18: Examples of Commonly Used Clinical Criteria and Conditions

Clinical criteria	<p>Examples of clinical criteria include, but are not limited to:</p> <ul style="list-style-type: none"> • characteristics that identify a patient subgroup, for example: <ul style="list-style-type: none"> ◦ comorbidity status ◦ inability to use, intolerance, or inadequate response to appropriate comparator(s) ◦ severity of disease or disease progression ◦ disease subtype (e.g., specific mutation) • starting and stopping rules, for example: <ul style="list-style-type: none"> ◦ duration of treatment ◦ response to treatment ◦ patients are receiving appropriate first- and/or second-line therapies and have had a suboptimal response despite an adequate trial.
Conditions	<p>Examples of conditions include, but are not limited to:</p> <ul style="list-style-type: none"> • cost considerations, for example: <ul style="list-style-type: none"> ◦ reduction in price (i.e., cost-effectiveness must be improved) ◦ not to be reimbursed at the submitted price ◦ cost of drug under review not to exceed cost of appropriate comparator. • reimbursement limits, for example: <ul style="list-style-type: none"> ◦ number of doses supported by clinical and cost-effectiveness evidence. • characteristics of the care setting, for example: <ul style="list-style-type: none"> ◦ prescribed by or under the care of an experienced clinical team. • reimbursement of the drug in a manner similar to comparator(s) that are reimbursed by the participating jurisdictions at the time of the review • real-world evidence development for scenarios where there is uncertain clinical benefit, but significant unmet need • considerations related to companion diagnostics, as applicable.

^a The examples cited in Table 18 are not intended to be an exhaustive list of all possible clinical criteria and conditions.

b) Considerations for Significant Unmet Need

In exceptional cases where there is uncertain clinical and pharmacoeconomic evidence, the CADTH drug expert committees may issue a recommendation to reimburse with clinical criteria and/or conditions, due to practical challenges in conducting robust clinical trials and pharmacoeconomic evaluations and in the presence of significant unmet medical need. In these situations, although there is uncertainty with the clinical evidence, the available evidence must reasonably suggest that the drug under review could substantially reduce morbidity and/or mortality associated with the disease. Significant unmet clinical need is identified on a population or subpopulation basis (i.e., not on an individual basis) through the CDR and pan-Canadian Oncology Drug Review processes.

Please note, the scenario examples noted in Table 19 are intended to serve as illustrations only to help guide the reader to better understand some of the factors that CADTH's drug expert committees will assess as part of their deliberation in formulating a reimbursement recommendation, and are by no means exhaustive or impose any procedural obligations that would constitute grounds for a procedural review.

Table 19: Considerations for Significant Unmet Need and Uncertainty of Clinical Benefit

Consideration	Description
Considerations for Significant Unmet Need	
Rarity of condition	<ul style="list-style-type: none"> • The drug under review is approved by Health Canada for the treatment of a rare disease. Specifically, the condition for which the drug is indicated has the following characteristics: <ul style="list-style-type: none"> ◦ is life-threatening, seriously debilitating, or both serious and chronic in nature ◦ affects a relatively small number of patients (incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000) ◦ is often genetically based, onset at birth or early childhood, and leads to a shortened lifespan ◦ places a heavy burden on caregivers and the health care system ◦ is difficult to study because of the small patient population.
Population	<ul style="list-style-type: none"> • Need is identified on a population or subpopulation basis and not on an individual basis.
Absence of alternatives	<ul style="list-style-type: none"> • There is an absence of clinically effective drug or non-drug alternative treatments. • Substantial morbidity and mortality exist despite the available drug or non-drug alternative treatments.
Factors that Contribute to Uncertainty of Clinical Benefit	
Clinical data	<ul style="list-style-type: none"> • Limited number of clinical studies • Small sample sizes (e.g., due to rare disease that affects a relatively small number of patients (incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000) • Absence of comparator groups • Alternative or adaptive trial designs for rare diseases • Short study durations or follow-up • Inability to distinguish disease severity in heterogeneous manifested rare diseases • Limited to surrogate end points • Insufficient evidence on meaningful clinical end points • Greater uncertainty in statistical analyses

Note: The rarity of the condition will not be the sole consideration for defining significant unmet need. In addition, the condition must be identifiable with reasonable diagnostic precision.

8.4.3. Reasons for Recommendation

- a) CDEC recommendations will be accompanied by reasons for the recommendation.
- b) The reasons for recommendation will represent the key considerations and rationale used by CDEC in formulating the recommendation.
- c) CADTH staff may be tasked with preparing the draft reasons for recommendation, for approval by CDEC.

8.5. Requests for Advice

- a) When considering a request for advice, CDEC may address the request by providing one of the following:
 - a revised CDEC recommendation that would supersede a *CEDAC* or *CDEC Final Recommendation*
 - a *CDEC Record of Advice* document containing additional context and/or clarifications regarding a previous *CEDAC* or *CDEC Final Recommendation*.

- b) In the case of a request for advice that results in a revised CDEC recommendation, the embargoed CDEC recommendation will be released as described in section 9.
- c) In the case of a request for advice that does not result in a revised CDEC recommendation, the *CDEC Record of Advice* will be sent to the drug plans and the manufacturer within eight to 10 business days following the applicable CDEC meeting. CADTH will post the *CDEC Record of Advice* for all requests for advice that do not result in a revised CDEC recommendation.
- d) Manufacturers will be responsible for identifying and requesting the redaction of any confidential information supplied by the manufacturer that was used by CADTH in the preparation of the *CDEC Record of Advice* before this document is posted.
- e) If the manufacturer requests that confidential information be redacted from the *CDEC Record of Advice*, CADTH redacts this information in accordance with the *CADTH Common Drug Review Confidentiality Guidelines* (Appendix 2). CADTH will indicate that confidential information was used to make the *CDEC Record of Advice* and that the manufacturer requested that this information be kept confidential, pursuant to the *CADTH Common Drug Review Confidentiality Guidelines*.
- f) All requests for redaction must be accompanied by a clearly stated rationale.
- g) Manufacturers are asked to identify any confidential information in the *CDEC Record of Advice* using the *Identification of Confidential Information Form* template. This form must be submitted to CADTH via Collaborative Workspaces by the date and time specified in the letter provided at the time the *CDEC Record of Advice* was received (typically 1:00 p.m. Eastern time one business day after the *CDEC Record of Advice* was issued).
- h) In the case of a disagreement expressed by the manufacturer regarding redactions made in the *CDEC Record of Advice*, CADTH may require additional time to resolve the disagreement in consultation with the manufacturer. This additional time could delay the timeline for posting the *CDEC Record of Advice*.

9. Embargoed CDEC Recommendations

In accordance with the Procedure and Submission Guidelines for the CADTH Common Drug Review and the CADTH Common Drug Review Confidentiality Guidelines, stakeholders must maintain the confidentiality of the embargoed CDEC recommendation.

9.1. Embargo Period

The embargo period begins with the issuance of the confidential embargoed CDEC recommendation to the manufacturer and the drug plans. The intent of the embargo period is to allow time for the manufacturers and the drug plans to consider the embargoed CDEC recommendation before it is finalized and posted.

During the embargo period, the following may occur with respect to the embargoed CDEC recommendation:

- Drug plans may submit a request for clarification (section 9.3)
- Manufacturers may make a request for reconsideration (section 9.4)

The duration of the embargo period is 10 business days; however, manufacturers may request an extension of up to 20 business days (for a total embargo period of 30 business days) for the purposes of preparing and filing a request for reconsideration.

9.2. Releasing the Embargoed CDEC Recommendation

- a) The confidential embargoed CDEC recommendation will be sent to the manufacturer and drug plans, along with the final and redacted versions of the CDR review report(s), eight to 10 business days following the CDEC meeting at which the recommendation was made.
- b) In the case of a submission that was filed on a pre-NOC basis, the embargoed CDEC recommendation will not be released until CADTH has received a copy of all required information, including a copy of the NOC or NOC/c. CADTH will review the information and determine if the embargoed CDEC recommendation will be issued or if the drug should be placed on a subsequent CDEC agenda. The manufacturer will be apprised of any revisions to the anticipated timelines.
- c) The embargoed CDEC recommendation will not be released until all category 1 and category 2 requirements for a CDR submission or resubmission have been received by CADTH.
- d) During the embargoed period, manufacturers have 10 business days to review the recommendation and notify CADTH in writing whether or not a request for reconsideration will be made.
- e) If a request for reconsideration is accepted by CADTH, the *CDEC Final Recommendation* will not be issued until CDEC has considered the request for reconsideration and made a final recommendation.
- f) The embargoed CDEC recommendation is not publicly available. Drug plans and manufacturers agree not to act on the embargoed recommendation. All stakeholders must maintain its confidentiality.

9.3. Request for Clarification

- a) The drug plans may file a request for clarification of an embargoed CDEC recommendation within 10 business days of notification of the embargoed CDEC recommendation.
- b) A request for clarification is made by filing a written request with CADTH.
- c) The request for clarification will consist of the reason for the request and a brief description of each point requiring clarification. The request for clarification cannot be based on new information.
- d) The manufacturer and CDEC will be notified of the request for clarification.
- e) The request for clarification is tracked on the CADTH website.
- f) CADTH will not issue a *CDEC Final Recommendation* until the drug plans have received a written response to their request for clarification.
- g) CADTH will prepare a written response to the request for clarification for approval by the CDEC chair.
- h) In responding to the request for clarification, CADTH will consult, as required, with the CDEC chair and CDEC, the CADTH review team, and any external expert retained in connection with the submission.
- i) If, in the judgment of the CDEC chair and CADTH, the request for clarification requires input and discussion by the full committee complement, it will be placed on the agenda of a subsequent CDEC meeting.
- j) CADTH will distribute the response to the drug plans, CDEC, and the drug manufacturer within five business days of the committee and CADTH determining the response to the request for clarification.

9.4. Request for Reconsideration of the CDEC Recommendation

9.4.1. Manufacturer's Request for Reconsideration

- a) Every manufacturer of a drug that is the subject of an embargoed CDEC recommendation may file a request for reconsideration of the recommendation during the embargo period.
- b) A request for reconsideration can be made only on one or both of the following grounds:
 - CADTH and/or CDEC failed to act fairly and in accordance with its procedures in conducting the review, and/or
 - the CDEC recommendation is not supported by the evidence that had been submitted or the evidence identified in the CDR review report(s).
- c) A manufacturer is entitled to have the embargoed CDEC recommendation reconsidered once.
- d) A request for reconsideration is filed by submitting a written request to CADTH.
- e) The request for reconsideration will comprise the reason and grounds for the request, the relief sought, and supporting evidence. A request for reconsideration cannot be made solely because the manufacturer disagrees with the recommendation. The request for reconsideration must identify the aspect(s) of the embargoed CDEC recommendation with which the manufacturer disagrees, and state the grounds for the request for reconsideration.
- f) No new information will be considered in the reconsideration.
- g) The manufacturer may only file a request for reconsideration during the embargo period.
- h) In addition to the standard 10-business day embargo period, the manufacturer may request an extension of up to 20 business days (i.e., a total of 30 business days) for the purpose of preparing and filing a request for reconsideration, in accordance with the following:

- The request for the extension must be made in writing within 10 business days of receiving the embargoed CDEC recommendation.
 - The manufacturer must file a request for reconsideration when an extension is granted.
 - The length of the extension will have an impact on the date of the CDEC meeting at which the request for reconsideration will be scheduled.
 - If a manufacturer fails to file a request for reconsideration within the specified time, after requesting and being granted an extension to the embargo period, CADTH may issue a final recommendation in accordance with section 10.
- i) CADTH notifies CDEC and the drug plans of the receipt of the request for reconsideration.
 - j) If the request for reconsideration is accepted, the applicant is offered an optional 45-minute teleconference with CADTH to ensure clarity around the key issues raised in the request for reconsideration so that these can be clearly presented by CADTH to CDEC members. In-person meetings will not be offered.
 - k) CADTH will notify the applicant of the target CDEC meeting date for the reconsideration.

9.4.2. Examination of Request for Reconsideration by CADTH

CADTH will examine, within five business days, each request for reconsideration to determine whether the issue(s) raised can be resolved in discussions with the manufacturer. It may be that the issue(s) can be clarified and the manufacturer will accept the recommendation. It may be that the manufacturer has new information, in which case a resubmission is required. If CADTH is unable to address the issue(s) raised in the manufacturer's request for reconsideration, the request for reconsideration is accepted and will be forwarded to CDEC in accordance with section 9.4.3.

9.4.3. Canadian Drug Expert Committee Reconsideration

- a) CADTH prepares the CDEC brief for the request for reconsideration, which includes, but is not limited to the embargoed CDEC recommendation, the request for reconsideration, a summary of CADTH's reconsideration teleconference with the manufacturer, and a copy of the original CDEC brief for the drug that is the subject of the request for reconsideration.
- b) The CDEC reconsideration brief is delivered to all CDEC members and the drug plans at least 10 business days before the scheduled CDEC meeting.
- c) If CDEC needs clarification from either the CADTH review team or from the manufacturer, or advice from external experts, in order to address the request for reconsideration, the matter will be sent back to CADTH staff to collect such clarification or advice. Consideration of the request for clarification will be moved forward to the next CDEC meeting, pending the collection of the necessary information.
- d) No one attending the CDEC meeting may introduce new information.
- e) CDEC will consider all recommendations categories as described in section 8.4 irrespective of the category of recommendation used for the original embargoed recommendation issued to the drug plans and the manufacturer. CDEC will determine if the original recommendation should be upheld or changed.
- f) Following the reconsideration, the *CDEC Final Recommendation* is issued to the drug plans and the manufacturer, within five business days.
- g) Notification of the *CDEC Final Recommendation* following the reconsideration is made (as described in section 10).

10. CDEC Final Recommendations

- a) After the embargo period has ended, the *CDEC Final Recommendation* will be issued in the following circumstances:
 - a manufacturer does not file a request for reconsideration during the embargo period within the specified time and the drug plans have not filed a request for clarification within the specified time; or the drug plans have filed a request for clarification and written clarification has been provided
 - a manufacturer has filed a request for reconsideration and CDEC has made a recommendation based on the request for reconsideration
 - a manufacturer fails to file either a request for reconsideration of the recommendation after requesting and being granted an extension to the embargo period.
- b) When a *CDEC Final Recommendation* is issued, CADTH will send a notice of the *CDEC Final Recommendation* and a copy of the *CDEC Final Recommendation* to the manufacturer and the drug plans.
- c) All *CDEC Final Recommendations* are posted on the CADTH website. Manufacturers are responsible for identifying and requesting the redaction of any confidential information supplied by the manufacturer that has been included in the *CDEC Final Recommendation* before this document is posted.
- d) If the manufacturer requests that confidential information be redacted from the *CDEC Final Recommendation*, CADTH will redact the confidential information in accordance with the *CADTH Common Drug Review Confidentiality Guidelines*. CADTH will indicate that confidential information was used to make the reimbursement recommendation, and that the manufacturer requested that this information be kept confidential, pursuant to the *CADTH Common Drug Review Confidentiality Guidelines*.
- e) Manufacturers are asked to identify any confidential information they have supplied in the *CDEC Final Recommendation* using the *Identification of Confidential Information Form* provided by CADTH. All requests for redaction must be accompanied by a clearly stated rationale.
- f) Manufacturers are asked to submit the completed form to CADTH via Collaborative Workspaces by the date and time specified in the notice of *CDEC Final Recommendation* (typically 1:00 p.m. Eastern time one business day after the *CDEC Final Recommendation* was issued).
- g) Manufacturers should only request redactions from the *CDEC Final Recommendation* and not from the embargoed CDEC recommendation.
- h) In the case of a disagreement expressed by the manufacturer regarding redactions made in the *CDEC Final Recommendation*, CADTH may require additional time to resolve the disagreement in consultation with the manufacturer. This additional time could delay the timeline for posting the *CDEC Final Recommendation*.

11. Reassessment of Drugs through the CADTH Therapeutic Review Process

As stated in the *CADTH Therapeutic Review Framework and Process*, one of the outputs from a CADTH therapeutic review may be revised CDEC or CEDAC recommendations for drugs that have previously been reviewed through the CDR process.

11.1. Identification of CDEC or CEDAC Recommendations

- a) Existing CDEC recommendations^d that could be revised as a result of the therapeutic review will be identified and communicated to stakeholders during the scoping phase of the therapeutic review process.
- b) This could include drugs where existing CDEC recommendations have not been issued at the time a CADTH therapeutic review is initiated, but will be reviewed through the CDR process before the therapeutic review has been completed.

11.2. Patient Input

- a) Patient engagement opportunities during a therapeutic review are described in detail in the *CADTH Therapeutic Review Framework and Process*.
- b) Patient engagement at the outset of the therapeutic review will include specific questions related to existing CDEC or CEDAC recommendations.
- c) Patient groups will have the opportunity to comment on revisions to existing recommendations that have been proposed by the expert review committee.
- d) Input from patient groups will be collated by CADTH staff and presented by the CDEC public members, in accordance with the *CADTH Therapeutic Review Framework and Process*.

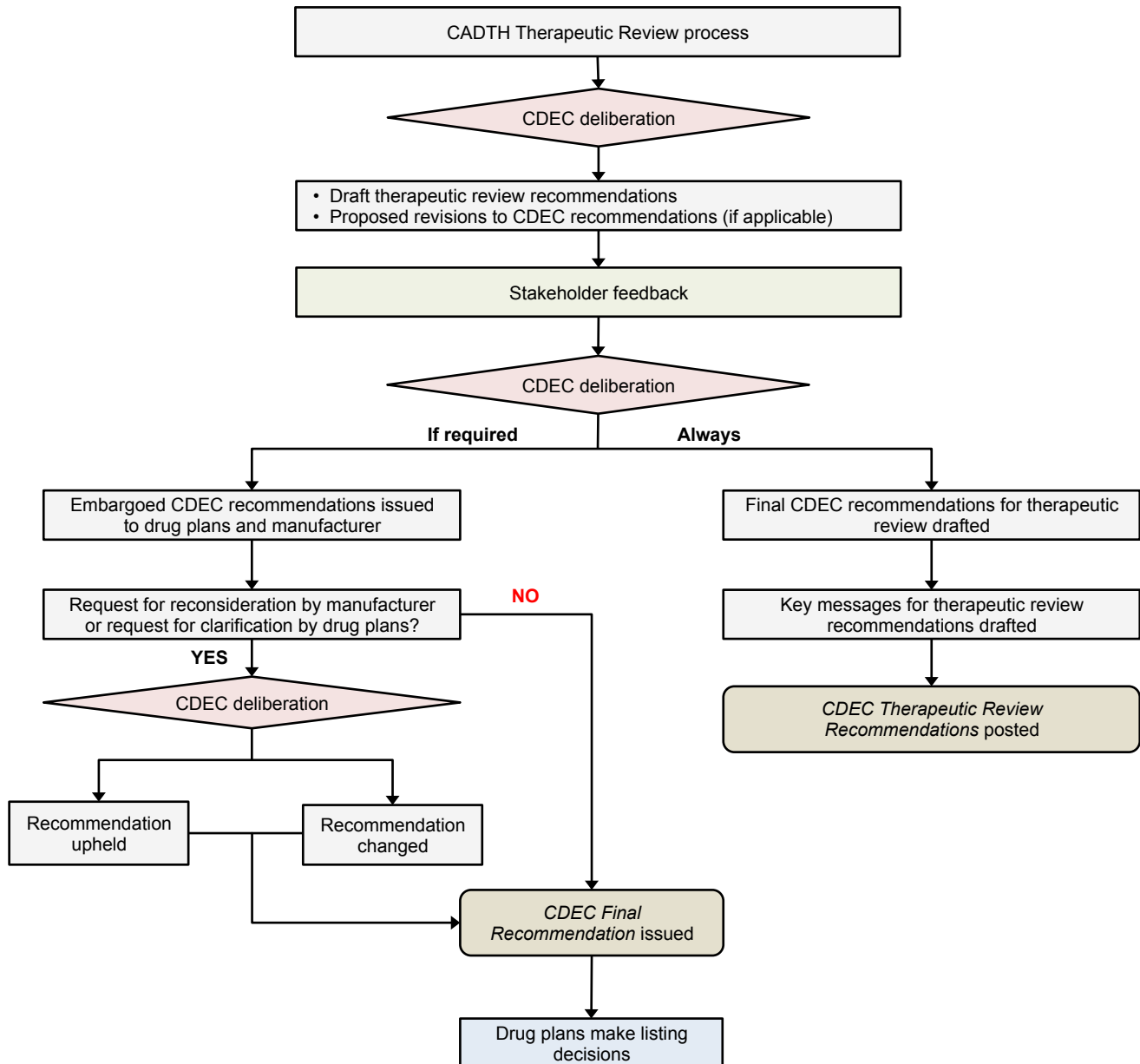
11.3. CDEC Recommendation Process

- a) As part of the deliberative process for therapeutic reviews, CDEC will consider whether or not the results of a therapeutic review suggest that any existing recommendations that were issued through the CDR process should be revised.
- b) When considering revisions to existing CDEC or CEDAC recommendations, the committee will use the recommendation framework described section 8.4.
- c) Proposed revisions to existing CDEC or CEDAC recommendations will be posted for stakeholder feedback at the time the draft therapeutic review recommendations are posted. The following information will be included:
 - the recommendation that may be revised as a result of the therapeutic review
 - the revised reimbursement criteria and/or conditions that are being proposed
 - the rationale for the revision.
- d) Similar to feedback on the draft therapeutic review recommendations, CADTH staff will collate stakeholder feedback on any revisions to existing CDEC or CEDAC recommendations that have been proposed by the committee. The stakeholder feedback is presented and discussed by the committee.

^d This also includes existing recommendations from the Canadian Expert Drug Advisory Committee (CEDAC) which was replaced by CDEC in September 2011.

- e) Once the therapeutic review recommendations have been finalized by CDEC, the committee determines if new recommendations should be issued that will supersede any existing CDEC or CEDAC recommendations that were issued through the CDR process.
- f) The committee considers the stakeholder feedback, the evidence from the therapeutic review, and the final therapeutic review recommendations and determines if any existing CDEC or CEDAC recommendations should be revised. Depending on stakeholder feedback and the final therapeutic review recommendations, this could result in revisions that were not initially identified at the time of stakeholder feedback.
- g) Manufacturers will be notified by CADTH within 10 business days whether or not a revised CDEC recommendation will be issued for one or more of its products.
- h) When CDEC has determined that a previous recommendation should be revised, CADTH will issue a new embargoed CDEC recommendation in accordance with section 9 (i.e., within eight to 10 business days).
- i) Manufacturers with one or more products that have received new CDEC recommendations will have the opportunity to file a request for reconsideration in accordance with section 9.4.
- j) Drug plans will have the opportunity to file a request for clarification in accordance with section 9.3.
- k) CADTH will issue the revised *CDEC Final Recommendation* in accordance with section 10.
- l) The revised recommendation will be an abbreviated document noting the following key information:
 - the drug and indication of interest
 - the recommendation, including any clinical criteria and conditions (if applicable)
 - a statement indicating that the revised recommendation has been issued as a result of a CADTH therapeutic review
 - a disclaimer indicated that the revised recommendation supersedes the previous CDEC or CEDAC recommendation for the drug and indication of interest.
- m) The revised *CDEC Final Recommendation* will contain no confidential information; therefore, manufacturers will not be asked to complete a redaction request form.
- n) Posting of the revised *CDEC Final Recommendation* may occur before posting of the final therapeutic review recommendations.
- o) A disclaimer will be added to the previous *CDEC* or *CEDAC Final Recommendation* stating that it has been superseded by the revised *CDEC Final Recommendation*.

Figure 7: CADTH Therapeutic Review Process for Revising CDEC or CEDAC Recommendations Issued Through the CDR Process



CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review.

12. Temporary Suspension of a Review

12.1. Suspension Due to Incomplete Information

In the event that CADTH is unable to conduct a thorough review and/or an appraisal of a submission or resubmission due to incomplete information, CADTH, in its sole discretion, may temporarily suspend a review in the following manner:

- a) CADTH may temporarily suspend a review pending receipt of all required information.
- b) CADTH will advise the manufacturer in writing that the review has been temporarily suspended. CADTH will indicate the information required in order to re-initiate the review process.
- c) The CDR review report(s) will not be sent to the manufacturer for comment and the submission or resubmission will not be placed on the CDEC agenda until the review team is satisfied that the manufacturer has provided all information.
- d) Once the issue is resolved, depending on the availability of resources, the review will resume at the stage where it was suspended. The manufacturer will be advised, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.
- e) A review may be temporarily suspended at any stage up until the review process has been completed.
- f) A suspended submission or resubmission is tracked on CADTH's website.

12.2. Suspension for Other Reasons

In the event that questions or issues outside of the regular review process arise (for example, but not limited to, legal issues) regarding the submission or resubmission under review, CADTH, in its sole discretion, may temporarily suspend the review in the following manner:

- a) CADTH will advise the manufacturer in writing that the review has been temporarily suspended. CADTH will indicate the anticipated duration of the suspension period. CADTH also has the discretion to extend the temporary suspension as deemed necessary.
- b) CADTH's decision to temporarily suspend the review of a submission that was filed on a pre-NOC basis is made independently of Health Canada's review of that drug.
- c) Once the issue is resolved, depending upon the availability of resources, the review will resume at the stage where it was suspended. The manufacturer will be advised by CADTH, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.
- d) The review may be temporarily suspended for reasons outside of the regular review process during any stage of the review process.
- e) A suspended submission or resubmission is tracked on the CADTH website.

13. Withdrawal from the CDR Process

13.1. Withdrawal Procedure

- a) A submission or resubmission will be withdrawn from the CDR process if:
 - the applicant voluntarily requests withdrawal of the submission or resubmission
 - Health Canada has withdrawn market authorization
 - Health Canada has issued a notice of non-compliance or a notice of deficiency.
- b) An applicant may request voluntary withdrawal from the CDR review process at any time up until 4:00 p.m. Eastern time three business days before the target CDEC meeting for the submission, resubmission, or request for advice is scheduled. For a biosimilar submission, applicants may withdraw from the CDR process at any time before the *CADTH Biosimilar Summary Dossier* is posted on the CADTH website.
- c) In all cases where marketing authorization has been withdrawn or not issued by Health Canada, the manufacturer must advise CADTH, in writing, as soon as possible.
- d) All requests for withdrawal from the CDR process must be provided in writing and contain the following information:
 - name and signature of the applicant
 - reason for the withdrawal from the CDR process
 - the date on which a notice of non-compliance, notice of non-compliance withdrawal letter, notice of deficiency, or notice of deficiency withdrawal letter was issued, along with a copy of the relevant notice and letter
 - if market authorization was withdrawn, the date on which market authorization was withdrawn and a copy of the Health Canada document providing the reason for withdrawal
 - intent to re-file the withdrawn submission or resubmission and anticipated time frame (if applicable).
- e) CADTH will stop the review immediately upon being notified of the withdrawal or non-issuance of market authorization.
- f) CADTH will advise the manufacturer and drug plans that the review has been withdrawn.
- g) The CADTH website will be updated to state that the submission or resubmission has withdrawn.
- h) Manufacturers who withdraw from the CDR process may be entitled to receive a partial refund of the application fees in accordance with the *Guidelines on Application Fees for CADTH Pharmaceutical Reviews*.
- i) CADTH will retain and/or dispose of copies of the withdrawn submission or resubmission (as described in section 14).

13.2. Re-Filing with CADTH After Withdrawal

- a) The applicant is required to re-file a complete submission or resubmission in accordance with section 5.
- b) The re-filed submission or resubmission must include a list of the changes made as compared with the initial submission or resubmission that was withdrawn. All updated documents (not limited to new information – e.g., an updated product monograph) must be provided.

- c) In the case of a withdrawn submission for a drug that was previously filed on a pre-NOC basis and that has subsequently received an NOC or NOC/c, the applicant is required to file the submission on a post-NOC basis.
- d) Submissions and resubmissions being re-filed after withdrawal will be screened according to the procedure described in section 6.
- e) CADTH considers the nature of the submission or resubmission being re-filed and determines the appropriate approach for conducting the review.

14. Document Management

The CDR process is complete when all relevant CADTH documents have been posted on the CADTH website (e.g., recommendation, CDR review report[s], and patient group input). CADTH then undertakes the steps detailed in the *CADTH Common Drug Review Confidentiality Guidelines* regarding the retrieval, disposal, and archiving of files associated with the review. CADTH also follows this document management procedure for a withdrawn submission or resubmission.

Appendix 1: CADTH Common Drug Review Confidentiality Guidelines

Note: These guidelines should be read in conjunction with the applicable sections of the Procedure and Submission Guidelines for the CADTH Common Drug Review, as well as any CADTH Pharmaceutical Reviews Updates issued after the effective date of the procedure and guidelines document.

These guidelines are intended to ensure the confidential information obtained for the purposes of the CADTH Common Drug Review (CDR) is protected and handled in a consistent manner by CADTH. By filing a CDR submission or resubmission with CADTH, or supplying other information to CADTH for the CDR process, a manufacturer or other applicant consents to these guidelines and agrees to be bound by the terms and conditions herein.

Confidential Information

Applicant-supplied information that will be treated by CADTH as confidential includes proprietary scientific, technical, or commercial information about a manufacturer's business or a manufacturer's product received through the exchange of information as part of the CDR process, but does not include information that:

- is or becomes available to the general public other than as a result of a breach of the procedures contained herein (note that information available to the general public includes but is not limited to published articles, drug prices, product monographs, clinical study information available from regulatory agency reports, other health technology assessment agency reports and recommendations, and www.clinicaltrials.gov)
- a third party (who is not under any obligation as to confidentiality or non-disclosure) rightfully discloses to any authorized recipient (as described in section 2 of these guidelines) without restriction as to its use or disclosure.

Confidential information also includes information about a manufacturer's product that is provided to CADTH by Health Canada, with authorization from the manufacturer.

Applicants must clearly identify any confidential information and provide the rationale for requesting the redaction of any confidential information in accordance with *Procedure and Submission Guidelines for the CADTH Common Drug Review*.

Handling Confidential Information

1. Responsibilities of CADTH

- a) CADTH will use reasonable care to prevent the unauthorized use, disclosure, publication, or dissemination of information received by CADTH as part of the CDR process that has been designated confidential.
- b) CADTH will not disclose confidential information in and related to a submission or resubmission to any third party except as permitted by these guidelines, or as required by law or by order of a legally qualified court or tribunal.
- c) CADTH will use the confidential information solely for the purpose of carrying out its responsibilities with respect to the CDR process.

2. Release of Manufacturer's Information

- a) CADTH may release any applicant-supplied information received through the CDR process, including confidential information, to the following authorized recipients:
- CADTH staff and review team members (including contractors and clinical experts)
 - CADTH Canadian Drug Expert Committee (CDEC) members
 - federal government representatives (including their agencies and departments)
 - provincial and territorial government representatives (including their agencies and departments)
 - pan-Canadian Pharmaceutical Alliance office representative(s)
 - members and observers of CADTH's Drug Policy Advisory Committee (DPAC), the DPAC Formulary Working Group, and the DPAC Optimal Use Working Group.
- b) While CADTH is an independent not-for-profit organization and is therefore not subject to access to information legislation, some of the authorized recipients listed previously have their own confidentiality procedures and are subject to freedom of information and access to information legislation over which CADTH has no control.
- c) CADTH staff members are required, as a condition of employment, to comply with CADTH's confidentiality requirements, Code of Conduct, and Conflict of Interest Guidelines.
- d) CADTH does not accept confidential submitted prices for applications filed for review through the CDR process. The submitted price is disclosed in all applicable CDR review reports, as well as the CDEC recommendation documents posted on the CADTH website.
- e) The outputs of economic models (e.g., incremental cost-effectiveness ratios) are not considered confidential and will not be redacted.

3. Documents Shared with Authorized Recipients

- a) The documents that CADTH may share with the authorized recipients include, but are not limited to:
- pre-submission-related materials provided by the applicant
 - the applicant's submission or resubmission
 - information provided by the manufacturer for a drug-plan submission or request for advice
 - redacted and unredacted CDR review report(s)^e
 - manufacturer's comments about CDR review report(s)
 - the CADTH review team's responses to manufacturer's comments about draft CDR review report(s)
 - embargoed CDEC recommendation
 - the redacted and unredacted *CDEC Final Recommendation* or *CDEC Record of Advice*
 - the CDEC brief and CDEC reconsideration brief.

^e The term "CDR review report(s)" in this document refers to the *Common Drug Review Clinical Review Report* and *Common Drug Review Pharmacoeconomic Report* typically prepared for a standard CDR review and/or the combined *Common Drug Review Clinical and Pharmacoeconomic Review Report* prepared for a tailored CDR review and/or the *Common Drug Review Request for Advice Report* prepared in response to a request for advice. The term "CDR review report(s)" is used as a shortened title to refer to the report(s) collectively or as applicable to a particular type of review.

- b) CADTH provides the following documents to the applicant (of which the applicant must maintain confidentiality):
 - draft CDR review report(s)
 - the CADTH review team's responses to manufacturer's comments about draft CDR review report(s)
 - an embargoed CDEC recommendation
 - the *CDEC Final Recommendation* (until posted on CADTH website)
 - a response to request for clarification (if applicable).
- c) The documents that CADTH may post on its website include:
 - a tracking document indicating the status of a CDR review, including a submission filed on a pre-NOC basis
 - CDR review report(s) with confidential information redacted
 - a *CDEC Final Recommendation* with confidential information redacted
 - a *CDEC Record of Advice* with confidential information redacted
 - a product monograph for the drug under review (typically for the duration of the patient input process).

4. Making Reference to Confidential Information in Public CADTH CDR Documents

CADTH may use confidential information supplied by the manufacturer in the preparation of CDR review report(s), CDEC recommendations, and *CDEC Record of Advice* documents. Before these documents are posted in the public domain, the manufacturer will be asked to identify any confidential information for redaction in accordance with the *Procedure and Submission Guidelines for the CADTH Common Drug Review*.

- The following principles and provisions will apply to any confidential information that the manufacturer has provided and requests to be redacted from CDR review report(s), *CDEC Final Recommendation*, or the *CDEC Record of Advice*:
- CADTH will redact the confidential information using redaction software and will indicate that the manufacturer requested that the confidential information be redacted, pursuant to the *CADTH Common Drug Review Confidentiality Guidelines*.
- CADTH may provide a general description of the type of information that was redacted.
- Submitted prices and the outputs of economic models (e.g., incremental cost-effectiveness ratios) are not considered confidential and will not be redacted.
- In the case of a disagreement expressed by the manufacturer regarding redactions made in the CDR review report(s) and/or *CDEC Final Recommendation*, CADTH may require additional time to resolve the disagreement, in consultation with the manufacturer. This additional time could delay posting of these documents; however, any such delays will not affect the timelines for issuing the *CDEC Final Recommendation* to authorized recipients.

5. Archiving of Documents Containing Confidential Information

- a) CADTH may retain copies of all documents associated with the review of a drug, for as long as there may be a need to consult them.
- b) CADTH will determine at its sole discretion if there is a need to consult this information.
- c) CADTH staff undertakes regular reviews of archived material. Any material that CADTH determines to be no longer required will be disposed of.

Appendix 2: List of Templates

Various hyperlinked templates (e.g., for letters, tailored CADTH Common Drug Review reviews, and tables) are provided throughout this document and are to be used when filing a Common Drug Review application for a submission or resubmission. These templates are also available on the CADTH website.

Pre-Submission Phase Forms

- [Pre-submission meeting request form](#)
- [CADTH Common Drug Review advance notification form](#)
- [New combination product considerations form](#)
- [Resubmission eligibility form](#)
- [Submission eligibility form](#)

Templates for Category 1 Requirements

- [Application overview template](#)
- [Executive summary template for a submission](#)
- [Executive summary template for resubmission](#)
- [Table of studies template](#)
- [Letter for sending NOC or NOC/c to CADTH](#)
- [Declaration letter template for a standard or tailored review](#)
- [Declaration letter template for a biosimilar review](#)
- [Number of Patients Accessing New Drugs](#)

Templates for Comments and Redactions

- [Manufacturer comments for a standard or tailored review](#)
- [Identification of errors or omissions for a biosimilar review](#)
- [Identification of confidential information template](#)

CADTH Submission Templates

- [Biosimilar submission template](#)
- [New combination product submission template](#)
- [Subsequent entry non-biological complex drug submission template](#)

Appendix 3: Checklists for Preparing CDR Applications

Manufacturers may use the checklists used by CADTH, as provided in this appendix, to help ensure that all submission or resubmission requirements for a CADTH Common Drug Review application have been included.

Category 1 Requirements	
A.	New drug, drug with a new indication, or new combination product submission filed on a pre-NOC basis
B.	New drug, drug with a new indication, or new combination product submission filed on a post-NOC basis
C.	New combination product (funded components or CADTH–designated tailored CDR review) filed on a pre-NOC basis
D.	New combination product (funded components or CADTH–designated tailored CDR review) submission filed on a post-NOC basis
E.	Biosimilar submission filed on a pre-NOC basis
F.	Biosimilar submission filed on a post-NOC basis
G.	All resubmissions
Category 2 Requirements	
H.	All submissions
I.	All resubmissions

CDR = CADTH Common Drug Review; NOC = Notice of Compliance.

A. Category 1 Requirements for a Standard Review Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	<ul style="list-style-type: none"> Completed application overview template 	<input type="checkbox"/>
Signed cover letter	<ul style="list-style-type: none"> Clear description of submission filed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> The indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Anticipated date of NOC or NOC/c for indication(s) to be reviewed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Requested reimbursement criteria, if applicable 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Names and contact information for primary and backup contacts 	<input type="checkbox"/>
Executive summary	<ul style="list-style-type: none"> Completed executive summary template for a submission 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Maximum five pages (excluding references) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Product monograph	At the time of filing: <ul style="list-style-type: none"> A copy of the most recent draft product monograph 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Draft product monograph with tracked clinical and label review changes up to time of Health Canada approval 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Clean and dated version of Health Canada–approved product monograph 	<input type="checkbox"/>
Declaration letter	<ul style="list-style-type: none"> Completed declaration letter template 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Health Canada Documentation		
NOC	At the time of filing: <ul style="list-style-type: none"> A placeholder document indicating the anticipated NOC date for the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Copy of NOC or NOC/c granted for the indication(s) under review Letter of Undertaking (only if NOC/c granted) 	<input type="checkbox"/> <input type="checkbox"/>
Clarimails/clarifaxes	At time of filing: <ul style="list-style-type: none"> Summary table of clinical Clarimails/Clarifaxes up to time of filing 	<input type="checkbox"/>
	Ongoing basis until NOC or NOC/c is issued: <ul style="list-style-type: none"> Revised clinical Clarimail/Clarifax summary table(s) 	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common Technical Document	• Section 2.5	<input type="checkbox"/>
	• Section 2.7.1	<input type="checkbox"/>
	• Section 2.7.3	<input type="checkbox"/>
	• Section 2.7.4	<input type="checkbox"/>
	• Section 5.2	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies and errata	• Reference list of key clinical issues studies (published and unpublished) and any errata	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
	• Copies of any errata (or a document stating that none found)	<input type="checkbox"/>
Table of studies	• Completed table of studies template	<input type="checkbox"/>
Editorials	• Reference list of editorial articles (or document stating none found)	<input type="checkbox"/>
	• Copies of editorial articles	<input type="checkbox"/>
New data	• Reference list of new data (or statement that none available)	<input type="checkbox"/>
	• Copies of new data available	<input type="checkbox"/>
Validity of outcome measures	• Reference list (or statement that none available)	<input type="checkbox"/>
	• Copies of validity of outcome measure references available	<input type="checkbox"/>
Indirect Comparison	• Copies of any indirect comparisons used in pharmacoeconomic evaluation	<input type="checkbox"/>
	• Technical report	<input type="checkbox"/>
Economic Information		
Pharmacoeconomic evaluation	• Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH	<input type="checkbox"/>
Economic model	• A copy of the unlocked and fully executable economic model	<input type="checkbox"/>
Supporting documentation	• Required economic model supporting documentation	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown (if available)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Number of patients accessing a new drug	<ul style="list-style-type: none"> Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.) Use the Number of Patients Accessing New Drug template 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Pricing and Distribution Information		
Price and distribution method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	• Reference list	<input type="checkbox"/>
	• Copies of articles that highlight the clinical utility of the companion diagnostic(s)	
	• Disclosable price for the companion diagnostic(s)	<input type="checkbox"/>
Additional Letter for Submissions Filed on Pre-NOC Basis		
Letter for sending NOC or NOC/c to CADTH	<p>After NOC or NOC/c is issued:</p> <ul style="list-style-type: none"> • A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (used the provided letter template) 	<input type="checkbox"/>

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

B. Category 1 Requirements for a Standard Review Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	• Completed application overview template	<input type="checkbox"/>
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement criteria, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Executive summary	• Completed executive summary template for a submission	<input type="checkbox"/>
	• Maximum five pages (excluding references)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Health Canada Documentation		
NOC	• A copy of the NOC or NOC/c granted for the indication(s) to be reviewed	<input type="checkbox"/>
	• Letter of Undertaking (only if NOC/c granted)	<input type="checkbox"/>
Clarimails/Clarifaxes	• Summary table of any clinical Clarimails/Clarifaxes up to the time of NOC or NOC/c being issued	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common Technical Document	• Section 2.5	<input type="checkbox"/>
	• Section 2.7.1	<input type="checkbox"/>
	• Section 2.7.3	<input type="checkbox"/>
	• Section 2.7.4	<input type="checkbox"/>
	• Section 5.2	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies and errata	• Reference list of key clinical issues studies (published and unpublished) and any errata	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
	• Copies of any errata (or a document stating that none found)	<input type="checkbox"/>
Table of studies	• Completed table of studies template	<input type="checkbox"/>
Editorials	• Reference list of editorial articles (or a document stating none found)	<input type="checkbox"/>
	• Copies of editorial articles	<input type="checkbox"/>
New data	• Reference list of new data (or statement that none available)	<input type="checkbox"/>
	• Copies of new data available	<input type="checkbox"/>
Validity of outcome, measures	• Reference list (or statement that none available)	<input type="checkbox"/>
	• Copies of validity of outcome measure references available	<input type="checkbox"/>
Indirect Comparison	• Copies of any indirect comparisons used in pharmacoeconomic evaluation	<input type="checkbox"/>
	• Technical Report	<input type="checkbox"/>
Economic Information		
Pharmacoeconomic evaluation	• Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH	<input type="checkbox"/>
Economic model	• A copy of the unlocked and fully executable economic model	<input type="checkbox"/>
Supporting documentation	• Required economic model supporting documentation	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Epidemiologic Information		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown (if available)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Number of patients accessing a new drug	<ul style="list-style-type: none"> • Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.) • Use the Number of Patients Accessing New Drug template 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	• Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s)	<input type="checkbox"/>
	• Copies of articles that highlight the clinical utility of the companion diagnostic(s)	
	• Disclosable price for the companion diagnostic(s)	<input type="checkbox"/>

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

C. Category 1 Requirements for a Tailored Review Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	<ul style="list-style-type: none"> Completed application overview template 	<input type="checkbox"/>
Signed cover letter	<ul style="list-style-type: none"> Clear description of submission filed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> The indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Requested reimbursement criteria, if applicable 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Names and contact information for primary and backup contacts 	<input type="checkbox"/>
Executive summary	<ul style="list-style-type: none"> Completed executive summary template for a submission 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Maximum five pages (excluding references) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Product monograph	At the time of filing: <ul style="list-style-type: none"> A copy of the most recent draft product monograph 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Draft product monograph with tracked clinical and label review changes up to time of Health Canada approval 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Clean and dated version of Health Canada–approved product monograph 	<input type="checkbox"/>
Declaration letter	<ul style="list-style-type: none"> Completed declaration letter template 	<input type="checkbox"/>
Submission template		
Tailored CDR review template	<ul style="list-style-type: none"> Completed tailored review template 	<input type="checkbox"/>
Health Canada Documentation		
NOC	At the time of filing: <ul style="list-style-type: none"> A placeholder document indicating the anticipated NOC date for the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Copy of NOC or NOC/c for the indication(s) under review 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Letter of Undertaking (only if NOC/c granted) 	<input type="checkbox"/>
Clarimails and Clarifaxes	At time of filing: <ul style="list-style-type: none"> Summary table of clinical Clarimails/Clarifaxes up to time of filing 	<input type="checkbox"/>
	Ongoing basis until NOC or NOC/c is issued: <ul style="list-style-type: none"> Revised clinical Clarimail/Clarifax summary table(s) 	<input type="checkbox"/>
Bioequivalence, Efficacy, and Safety Evidence		
Common Technical Document	<ul style="list-style-type: none"> Section 2.5 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Section 2.7.1 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Section 2.7.3 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Section 2.7.4 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Section 5.2 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Or a statement indicating which section(s) were not required by Health Canada 	<input type="checkbox"/>
Clinical studies and errata	<ul style="list-style-type: none"> Additional source documentation for data reported in the tailored CDR review template 	<input type="checkbox"/>
Disease Prevalence and Incidence		
Disease prevalence and incidence	<ul style="list-style-type: none"> Disease prevalence and incidence with specified breakdown (if available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Pricing and Distribution Information		
Price and distribution Method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
Additional Letter for Submissions Filed on Pre-NOC Basis		
Letter for sending NOC or NOC/c to CADTH	After NOC or NOC/c is issued: <ul style="list-style-type: none"> • A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (used the provided letter template) 	<input type="checkbox"/>

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

D. Category 1 Requirements for a Tailored Review Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	• Completed application overview template	<input type="checkbox"/>
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement criteria, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Executive summary	• Completed executive summary template for a submission	<input type="checkbox"/>
	• Maximum five pages (excluding references)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Health Canada Documentation		
NOC	• Copy of NOC or NOC/c for the indication(s) to be reviewed	<input type="checkbox"/>
	• Letter of Undertaking (only if NOC/c granted)	<input type="checkbox"/>
Clarimails/Clarifaxes	• Summary table of any clinical Clarimails/Clarifaxes up to the time of NOC or NOC/c being issued	<input type="checkbox"/>
Submission template		
Tailored CDR review template	• Completed tailored review template	<input type="checkbox"/>
Bioequivalence, Efficacy, and Safety Evidence		
Common Technical Document	• Section 2.5	<input type="checkbox"/>
	• Section 2.7.1	<input type="checkbox"/>
	• Section 2.7.3	<input type="checkbox"/>
	• Section 2.7.4	<input type="checkbox"/>
	• Section 5.2	<input type="checkbox"/>
	• Or a statement indicating any section(s) not required for the Health Canada submission	<input type="checkbox"/>
Disease Prevalence and Incidence		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown if available	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>

CDR = CADTH Common Drug Review; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

E. Category 1 Requirements for a Biosimilar Review Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	<ul style="list-style-type: none"> Completed application overview template 	<input type="checkbox"/>
Signed cover letter	<ul style="list-style-type: none"> Clear description of submission filed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> The indication(s) to be reviewed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Requested reimbursement criteria 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Names and contact information for primary and backup contacts 	<input type="checkbox"/>
Product monograph	At the time of filing: <ul style="list-style-type: none"> A copy of the most recent draft product monograph 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Draft product monograph with tracked changes 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Clean and dated version of Health Canada–approved product monograph 	<input type="checkbox"/>
Declaration letter	<ul style="list-style-type: none"> Completed declaration letter template for a biosimilar 	<input type="checkbox"/>
Health Canada Documentation		
NOC	At the time of filing: <ul style="list-style-type: none"> A placeholder document specifying the anticipated NOC date for the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Copy of NOC or NOC/c granted for the indication(s) under review 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Letter of Undertaking (only if NOC/c granted) 	<input type="checkbox"/>
Submission Template		
Submission template	At the time of filing: <ul style="list-style-type: none"> Completed biosimilar submission template 	<input type="checkbox"/>
	After NOC or NOC/c is issued: <ul style="list-style-type: none"> Updated biosimilar submission template 	<input type="checkbox"/>
Evidence for Switching		
Table of studies	<ul style="list-style-type: none"> Completed table of studies 	<input type="checkbox"/>
Copies of published studies	<ul style="list-style-type: none"> Copies of published studies that investigated any of the following: <ul style="list-style-type: none"> switching from reference product to the biosimilar under review switching from a biosimilar to the biosimilar under review 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	<ul style="list-style-type: none"> Submitted unit pricing to four decimal places 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Method of distribution 	<input type="checkbox"/>

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

F. Category 1 Requirements for a Biosimilar Review Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Application overview	• Completed application overview template	<input type="checkbox"/>
Signed cover letter	• Clear description of submission being filed	<input type="checkbox"/>
	• The indication(s) to be reviewed	<input type="checkbox"/>
	• Requested reimbursement criteria	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Product monograph	• A copy of the most recent product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template for a biosimilar	<input type="checkbox"/>
Health Canada Documentation		
NOC	• Copy of NOC or NOC/c for the indication(s) under review	<input type="checkbox"/>
	• Letter of Undertaking (only if NOC/c granted)	<input type="checkbox"/>
Submission Template		
Submission template	• Completed biosimilar submission template	<input type="checkbox"/>
Evidence for Switching		
Table of studies	• Completed table of studies	<input type="checkbox"/>
Copies of published studies	• Copies of published studies that investigated any of the following:	<input type="checkbox"/>
	◦ 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	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>

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

G. Category 1 Requirements for All Resubmission Types

Section	Specific Items and Criteria	Included
General Information		
Application overview	<ul style="list-style-type: none"> Completed application overview template 	<input type="checkbox"/>
Signed cover letter	<ul style="list-style-type: none"> Clear description of resubmission being filed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> The indication(s) to be reviewed 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Requested reimbursement criteria, if applicable 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Names and contact information for primary and backup contacts 	<input type="checkbox"/>
Executive summary	<ul style="list-style-type: none"> Completed executive summary template for a resubmission 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Maximum five pages (excluding references) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document referenced with all supporting references 	<input type="checkbox"/>
Product monograph	<ul style="list-style-type: none"> A copy of the most current version of the Health Canada–approved product monograph 	<input type="checkbox"/>
Declaration letter	<ul style="list-style-type: none"> Completed declaration letter template 	<input type="checkbox"/>
New and Updated Efficacy and/or Safety Information		
New clinical studies	<ul style="list-style-type: none"> Reference lists of all new clinical studies and errata, (or r document stating none is available) included in the resubmission that were not provided in the initial submission, or a previous resubmission 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of all new clinical information and errata 	<input type="checkbox"/>
Editorials	<ul style="list-style-type: none"> Reference list of editorial articles (or document stating none found) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of editorial articles 	<input type="checkbox"/>
Validity of Outcome Measures	<ul style="list-style-type: none"> Reference list for validity of outcome measures (or document stating none found) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of validity of outcome measure references available 	<input type="checkbox"/>
Table of studies	<ul style="list-style-type: none"> An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template 	<input type="checkbox"/>
New and Updated Economic Information		
Pharmacoeconomic evaluation	<ul style="list-style-type: none"> Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
Economic model	<ul style="list-style-type: none"> A copy of the unlocked and fully executable economic model 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Required economic model supporting documentation 	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	<ul style="list-style-type: none"> Disease prevalence and incidence data, with specified breakdown (if available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	<ul style="list-style-type: none"> Submitted unit pricing to four decimal places 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Method of distribution 	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	<ul style="list-style-type: none"> Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Disclosable price for the companion diagnostic(s) 	<input type="checkbox"/>

H. Category 2 Requirements for all Submissions and Resubmissions

Requirement	Specific Items and Criteria	Included
BIA reports	• BIA report British Columbia	<input type="checkbox"/>
	• BIA report Alberta	<input type="checkbox"/>
	• BIA report Saskatchewan	<input type="checkbox"/>
	• BIA report Manitoba	<input type="checkbox"/>
	• BIA report Ontario	<input type="checkbox"/>
	• BIA report New Brunswick	<input type="checkbox"/>
	• BIA report Nova Scotia	<input type="checkbox"/>
	• BIA report Prince Edward Island	<input type="checkbox"/>
	• BIA report Newfoundland and Labrador	<input type="checkbox"/>
	• BIA report Non-Insured Health Benefits	<input type="checkbox"/>
BIA models	• BIA model British Columbia	<input type="checkbox"/>
	• BIA model Alberta	<input type="checkbox"/>
	• BIA model Saskatchewan	<input type="checkbox"/>
	• BIA model Manitoba	<input type="checkbox"/>
	• BIA model Ontario	<input type="checkbox"/>
	• BIA model New Brunswick	<input type="checkbox"/>
	• BIA model Nova Scotia	<input type="checkbox"/>
	• BIA model Prince Edward Island	<input type="checkbox"/>
	• BIA model Newfoundland and Labrador	<input type="checkbox"/>
• BIA model Non-Insured Health Benefits	<input type="checkbox"/>	
Supporting BIA documentation	• Reference list of all supporting documentation used and/or cited in BIAs	<input type="checkbox"/>
	• Copies of all supporting documentation used and/or cited in BIAs	<input type="checkbox"/>

BIA = budget impact analysis.

Appendix 4: Electronic File Structure and Naming Format

Instructions for Manufacturers

Please carefully review the following electronic file structure and naming convention before assembling the CADTH Common Drug Report (CDR) submission or resubmission requirements. If you have any questions, 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 Collaborative Workspaces. To file a submission, manufacturers 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 1GB. 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; therefore, manufacturers 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, manufacturers must 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; therefore, manufacturers are asked to use abbreviations as necessary.

A. Category 1 Requirements for a Standard CDR Review

 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 - Executive Summary

 4 - Product Monograph

 5 - Declaration letter

2_Brand Name_Health Canada Documentation

 1 - Health Canada NOC

 2 - Letter of Undertaking (Note: only if applicable)

 3 - Table of Clarimails

3_Brand Name_Clinical Information

3.1_Common Technical Document

 1 - Section 2.5

 2 - Section 2.7.1

 3 - Section 2.7.3

 4 - Section 2.7.4

 5 - Section 5.2

3.2_Clinical Studies and Errata

 _List of Studies and Errata

 1 - Trial Name_Author_Year

 2 - Trial Name_Author_Year Erratum

3.3_Table of Studies

 Table of Studies






- 3.4_Editorials
 - _List of Editorials
 - 1 - Author_Year
- 3.5_New Data
 - _List of New Data
 - 1 - Trial Name_Author_Year
- 3.6_Validity of Outcomes
 - _List of References
 - 1 - Author_Year
- 3.7_Indirect Comparison
 - Indirect Comparison
 - Technical Report
- 4_Brand Name_Economic
 - Pharmacoeconomic evaluation
 - Economic model
 - Economic model supporting documentation
- 5_Brand Name_Epidemiologic Information
 - Disease Prevalence and Incidence
 - Number Patients Accessing New Drug (Note: only if applicable)
- 6_Brand Name_Pricing and Distribution
 - Pricing and Distribution
- 7_Companion Diagnostic
 - 7.1_Clinical Utility
 - _List of References
 - 1 - Author_Year
 - 7.2_Price
 - Companion Diagnostic Price

B. Category 1 Requirements for a Tailored CDR Review Submission




 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 - Executive Summary
-  4 - Product Monograph
-  5 - Declaration Letter

2_Brand Name_Health Canada Documentation






-  1 - Health Canada NOC
-  2 - Letter of Undertaking (Note: only if applicable; adjust following file numbers if necessary)
-  3 - Table of Clarimails

3_Brand Name_Submission Template




-  1 – CDR Tailored Review Submission Template

4_Brand Name_Clinical Information

4.1_Common Technical Document

-  1 - Section 2.5
-  2 - Section 2.7.1
-  3 - Section 2.7.3
-  4 - Section 2.7.4
-  5 - Section 5.2


4.2_Source Documentation

-  _List of Documentation
-  1 - Name_Year
-  2 - Name_Year


5_Brand Name_Epidemiologic Information

-  Disease Prevalence and Incidence

 6_Brand Name_Pricing and Distribution

 Pricing and Distribution

 Commitment for Submitted Price

 7_Companion Diagnostic

 7.1_Clinical Utility

 _List of References

 1 – Author_Year

 7.2_Price





 Companion Diagnostic Price

C. Category 1 Requirements for a Biosimilar Submission



 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

D. Category 1 Requirements for All Resubmissions

 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 - Executive Summary
-  4 - Product Monograph
-  5 - Declaration letter

2_Brand Name_New Clinical Information



2.1_New Clinical Studies

-  _List of New Clinical Studies
-  1 - Trial Name_Author_Year
-  2 - Trial Name_Author_Year

2.2_ New Editorials and Errata

-  _List of Editorials and Errata
-  _No Editorials or No Errata (*Note: placeholder document, only if applicable*)
-  1 - Author_Year_Editorial
-  2 - Trial Name_Author_Year_Erratum




2.3_Validity of Outcomes

-  _List of References
-  1 – Author_Year

2.4_Updated Table of Studies

-  Table of Studies

3_Brand Name_Economic

-  Pharmacoeconomic evaluation
-  Economic model
-  Economic model supporting documentation

 4_Epidemiologic Information

 Disease Prevalence and Incidence

 5_Brand Name_Pricing and Distribution

 Pricing and Distribution

E. Category 2 Requirements for all Submissions and Resubmissions

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





 **Brand Name – Category 2**

 2_Brand Name BIAs



 2.1_BIA Reports

-  1 - BIA Report BC
-  2 - BIA Report AB
-  3 - BIA Report SK
-  4 - BIA Report MB
-  5 - BIA Report ON
-  6 - BIA Report NB
-  7 - BIA Report NS
-  8 - BIA Report PEI
-  9 - BIA Report NL
-  10 - BIA Report NIHB

 2.2_BIA Models

-  1 - BIA Model BC
-  2 - BIA Model AB
-  3 - BIA Model SK
-  4 - BIA Model MB
-  5 - BIA Model ON
-  6 - BIA Model NB
-  7 - BIA Model NS
-  8 - BIA Model PEI
-  9 - BIA Model NL
-  10 - BIA Model NIHB

 2.3_BIA Supporting Documentation

-  _List of References
-  1 - Name of document

Appendix 5: Key Definitions

The following are high-level definitions for key terms used in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* document. Readers should consult the appropriate sections of the document for more detailed context as it relates to some terms.

Active Substance: A therapeutic substance that has pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease (see new active substance).

Additional Information: Any information that is requested from the manufacturer by CADTH in addition to the category 1 requirements that is required to complete the review of the submission or resubmission, or to clarify information related to the submission or resubmission.

Applicant: A person, corporation, or entity eligible to file an application for a CDR submission or resubmission. The applicant could be a manufacturer, a supplier, a corporation, or entity recruited by the manufacturer or the supplier.

Application: Written documentation filed by an applicant to have a drug reviewed through the CDR process.

Appropriate Comparator: Typically a drug listed by one or more drug plans for the indication under review. However, the choice of appropriate comparator(s) in reviews by CADTH is made on a case-by-case basis.

Biosimilar: A biosimilar is a biologic drug (i.e., a drug derived from living sources versus a chemically synthesized drug), demonstrating a high degree of similarity to an already authorized biologic drug (i.e., a “reference product” that has been authorized in Canada, or in some circumstances can be an authorized non-Canadian biologic from a jurisdiction that has an established relationship with Health Canada).

Budget Impact Analysis (BIA): A forecast of the impact of listing a drug on the drug plans’ expenditures.

Business Day: Any day (other than a Saturday, Sunday, statutory holiday, or company holiday) on which the CADTH office in Ottawa (Ontario, Canada) is open for business during regular business hours. Please refer to the CADTH website “Contact Us” section for a listing of the CADTH Holiday Schedule.

Business Hours: Any weekday (excluding statutory and company holidays) from 8:00 a.m. to 4:00 p.m. Eastern time.

CADTH Review Team: A team assembled by CADTH to undertake the review of a submission or resubmission, or to prepare a report in response to a request for advice. The review team may include CADTH staff, contracted reviewers, and external experts with appropriate qualifications and expertise.

Calendar Days: All days including Saturday, Sunday, statutory holidays, and company holidays.

Canadian Drug Expert Committee (CDEC): An appointed, national, independent advisory committee to CADTH that makes drug-related recommendations and provides drug-related advice through the CDR and therapeutic review processes. CDEC is composed of individuals with expertise in drug therapy, drug evaluation and drug utilization, and public members to bring a lay perspective. CDEC replaced the Canadian Expert Drug Advisory Committee (CEDAC) in September 2011.

Canadian Drug Expert Committee (CDEC) Brief: A compilation of the materials regarding a drug under review by CDR, prepared by CADTH staff for the members of CDEC. The CDEC brief includes patient group input, CDR review report(s), manufacturer's comments on the CDR review report(s) and the CDR review team's responses, and the manufacturer's executive summary.

Canadian Drug Expert Committee (CDEC) Final Recommendation: A document that provides guidance to the drug plans participating in CDR to make a funding decision regarding the drug under review. *CDEC Final Recommendations* are non-binding to the drug plans. Each drug plan makes its own drug-listing decisions based on the *CDEC Final Recommendation* in addition to other factors, including the plan's mandate, jurisdictional priorities, and financial resources.

Canadian Drug Expert Committee (CDEC) Record of Advice: The advice document issued by CDEC in response, in cases where a request for advice has not resulted in a revised CDEC recommendation

Canadian Expert Drug Advisory Committee (CEDAC): CEDAC was replaced by the CADTH Canadian Drug Expert Committee (CDEC) in September 2011. CEDAC was a CADTH advisory body composed of individuals with expertise in drug therapy and drug evaluation and public members. For drugs reviewed through the CDR process, CEDAC made formulary listing recommendations for use by the participating federal, provincial, and territorial publicly funded drug plans.

Common Drug Review (CDR) Process: A single technology drug review process by which CADTH conducts an objective, rigorous, evidence-based, health technology assessment of the relative therapeutic merits and cost-effectiveness of drugs, incorporating patient group-submitted input.

Common Drug Review (CDR) Queuing: Queuing is a delay in the initiation of the review of a CDR submission or resubmission.

Companion Diagnostic Test: A companion diagnostic test is a medical device that provides information that is essential for the safe and effective use of corresponding drugs or biological products. They can identify patients who are likely to benefit or experience harms from particular therapeutic products, or monitor clinical response to optimally guide treatment adjustments. Companion diagnostics detect specific biomarkers that predict more favourable responses to particular therapeutic products.

Conflict of Interest Guidelines: The conflict of interest guidelines adopted by CADTH.

Date of Acceptance for Review: The date on which CADTH has confirmed with the applicant that the key requirements for initiating the review process for a submission or resubmission (i.e., category 1 requirements as delineated in the *Procedure and Submission Guidelines for the CADTH Common Drug Review*) have been met.

Date of Filing: The date on which a submission or resubmission is received by CADTH.

Date of Initiation of a Review: The date on which the assigned CDR review team begins work on a review.

Drug: An active substance considered to be a drug under the Canadian Food and Drugs Act and Food and Drug Regulations that has been granted (or will be granted in the case of a submission filed on a pre-Notice of Compliance [NOC] basis), a Health Canada NOC or Notice of Compliance with conditions (NOC/c), and is approved for human use.

Drug Plans: The federal, provincial, and territorial drug plans participating in the CDR process.

Embargo Period: Refers to the period of time following the issuance of an embargoed CDEC recommendation, during which the embargoed CDEC recommendation is neither acted on by drug plans nor is publicly available. During this period, the manufacturer may submit a request for reconsideration or the drug plans may submit a request for clarification.

Embargoed Canadian Drug Expert Committee (CDEC) Recommendation: An evidence-based recommendation issued by CADTH. The embargoed CDEC recommendation is released to the manufacturer and drug plans only, and is not publicly available. The manufacturer must maintain the confidentiality of this document.

External Expert: An individual with appropriate qualifications and expertise required for some aspect of the review of the submission or resubmission, and whose services are obtained on a contract basis, as required.

Formulary: A list of drugs covered as benefits, as determined by each federal, provincial, and territorial drug plan.

Formulary Working Group (FWG): A working group of the CADTH Drug Policy Advisory Committee (DPAC). The FWG is composed of representatives from the federal, provincial, and territorial drug plans. FWG provides advice to CADTH on pharmaceutical issues and helps with the effective jurisdictional sharing of pharmaceutical information. FWG members are observers at CDEC meetings.

Generic Drugs: Copies of Canadian reference products (i.e., Health Canada–approved brand name drugs) that demonstrate bioequivalence on the basis of pharmaceutical equivalence (i.e., they contain identical amounts of the identical active medicinal ingredients, in comparable dosage forms, but do not necessarily contain the same non-medicinal ingredients as the Canadian reference product, and the conditions of use fall with those of the Canadian reference product) and bioavailability characteristics, where applicable, with the Canadian reference product. Generic drugs are not reviewed through the CDR process.

Initiation Range: Refers to time frame which CDR submissions or resubmissions are initiated and the corresponding CDEC meeting date.

New Active Substance: A therapeutic substance that has never before been approved for marketing in Canada in any form. It may be:

- a chemical or biological substance not previously approved for sale in Canada as a drug
- an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

New Combination Product: Consists of two or more drugs that have not been previously marketed in Canada in that combination. It may consist of either two or more new drugs, two or more previously marketed drugs, or a combination of new drug(s) and previously marketed drug(s). Combination products (funded components), a category of new combination products, contain components that are already funded by drug plans and are eligible for a tailored review by CDR and for modified submission requirements.

New Drug: A therapeutic substance that has never before been approved for marketing in any form, regardless of when the Notice of Compliance or Notice of Compliance with conditions was issued. It may be:

- a chemical or biological substance not previously approved for sale in Canada as a drug
- an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

New Indication: A disease condition for which the use of a particular drug has not previously been approved by Health Canada.

New Information: New clinical information and/or new cost information that was not part of an originally filed submission or resubmission.

Notice of Compliance (NOC): Authorization issued by Health Canada to market a drug in Canada when regulatory requirements for the safety, efficacy, and quality are met.

Notice of Compliance with conditions (NOC/c): Authorization issued by Health Canada to market a drug under the Notice of Compliance with conditions policy. This indicates that the sponsor has agreed to undertake additional studies to confirm the clinical benefit of the product.

Patient Group: An organized group of patients or caregivers in Canada.

Patient Group–Submitted Input: Information, submitted by a patient group, that describes the experiences and perspectives of patients living with the condition for which a drug in a CDR submission or resubmission is indicated and the impact of drug therapy on the lives of those with that illness or condition.

Post-Notice of Compliance (NOC): The timing of filing a CDR submission after Health Canada has granted a Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed under the CDR process.

Pre-Notice of Compliance (NOC): The timing of filing a CDR submission before Health Canada has granted a Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed under the CDR process, and for which the anticipated date of NOC or NOC/c is within 180 calendar days of the submission being filed.

Reasons for Recommendation: These represent the key considerations and rationale used by CDEC in formulating the recommendation.

Request for Advice: A written request made by drug plans for CDEC advice regarding a previous *CEDAC* or *CDEC Final Recommendation*. A request for advice can result in a revised CDEC recommendation or a *CDEC Record of Advice*.

Request for Clarification: A written request from drug plans for clarification of an embargoed CDEC recommendation.

Request for Reconsideration: A written request from a manufacturer for an embargoed CDEC recommendation to be reconsidered.

Request for Voluntary Withdrawal: A written request by an applicant to withdraw a submission or resubmission from the review process. These may be filed any time before the *CDEC Final Recommendation* has been issued.

Resubmission: An application filed to review a previous submission or resubmission for the same indication(s) on the basis of new information after a *CDEC Final Recommendation* has been issued.

Standard Common Drug Review (CDR) Review: Consists of the CDR review team conducting a systematic review of clinical evidence provided by the manufacturer along with studies identified through its independent, systematic literature search, and an appraisal of the manufacturer-provided pharmacoeconomic evaluation.

Stopped Review: The cessation of the review of a submission or resubmission under the CDR process before all steps of the review process are completed. Work on a stopped submission or resubmission does not resume.

Submission: An application filed for an initial review of a drug under the CDR process for a specific indication(s), for any of the following CDR-eligible drug submission types: new drug, drug with a new indication, new combination product, or a biosimilar.

Submitted Price: 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.

Suspended Review: Refers to the temporary cessation of the review of a submission or resubmission under the CDR process. This occurs if questions or issues arise outside of the regular review process or if the CDR review team is unable to perform a thorough assessment of the submission or resubmission due to incomplete or non-transparent information. Once the issue is resolved, the review proceeds from the point at which it was suspended. The applicant is not required to file a submission or resubmission to re-initiate the review.

Tailored Common Drug Review (CDR) Review: Consists of the CDR review team conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the manufacturer using a CADTH-provided review template that is specific to the type of drug product to be reviewed.

Therapeutic Review: An evidence-based review of publicly available sources regarding a therapeutic category of drugs (e.g., antihypertensive drugs) or a class of drugs (e.g., angiotensin-converting enzyme inhibitors [ACEIs]) in order to support drug reimbursement and policy decisions and encourage the optimization of drug therapy. The scope and depth of the review are determined by jurisdictional needs. An important characteristic of a therapeutic review is that it may inform CDR submission reviews and associated CDEC listing recommendations, which in turn advise drug plan decisions. However, CADTH therapeutic reviews may not always coincide with a CDR submission.