

CADTH COMMON DRUG REVIEW

Procedure for the CADTH Common Drug Review

AUGUST 2014

CADTH

RECORD OF UPDATES TO THE PROCEDURE FOR THE CADTH COMMON DRUG REVIEW

| Update | Version of the <i>Procedure for the CADTH Common Drug Review</i> |
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| 14 | September 2011 |
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| 17 | August 2014 |

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ABBREVIATIONS

| | |
|-------|---|
| CDR | CADTH Common Drug Review |
| F/P/T | federal, provincial, territorial |
| CDEC | Canadian Drug Expert Committee |
| CEDAC | Canadian Expert Drug Advisory Committee |
| DPAC | Drug Policy Advisory Group |
| SEB | subsequent entry biologic |
| NOC | Notice of Compliance |
| NOC/c | Notice of Compliance with conditions |
| pCODR | pan-Canadian Oncology Drug Review |
| PMPRB | Patented Medicine Prices Review Board |

1. INTRODUCTION

1.1 About This Document

The objective of this document is to describe the CADTH Common Drug Review (CDR) procedures to be followed by all participants involved in the CDR process.

This document should be read in conjunction with the [Submission Guidelines for the CADTH Common Drug Review](#) and any issues of the [CDR Update](#) posted after *CDR Update — Issue 108*. Revisions from all applicable *CDR Update* issues 86 to 108 are included in this version of the *Procedure for the CADTH Common Drug Review*.

All references to number of days in this document are in business days unless otherwise specified. Please refer to the [CADTH website](#) “Contact Us” section for a current listing of the CADTH holiday schedule and business hours.

Key terms in this document are defined in APPENDIX 3: KEY DEFINITIONS.

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. An overview of the CDR process is presented in Figure 1 and the targeted time frames are presented in Table 1, Table 2, and Table 3. CADTH, through its CDR process, undertakes reviews of drug submissions, resubmissions, and requests for advice and issues formulary listing recommendations to all federal, provincial, and territorial (F/P/T) 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 listing recommendations for drugs reviewed through the CDR process are provided by the [Canadian Drug Expert Committee](#)¹, 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. The Canadian Drug Expert Committee is composed of individuals with expertise in drug therapy, drug evaluation, and drug utilization, and public members who bring a lay perspective. The identities of committee members are available on the CADTH website.

The Canadian Drug Expert Committee follows a deliberative framework and process and takes into consideration the following information when issuing recommendations and advice:

- patient group input

¹ The Canadian Drug Expert Committee replaced the Canadian Expert Drug Advisory Committee in September 2011.

- 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.

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),² based on information submitted by manufacturers and studies identified through independent, systematic literature searches.

It is important to note that Canadian Drug Expert Committee 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.

All submissions and resubmissions filed by manufacturers for drugs that receive a Health Canada Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) on or after September 1, 2014 are subject to an application fee. For details regarding the CDR application fees, see APPENDIX 1.

1.3 Changes to the CADTH Common Drug Review Procedure

From time to time, CADTH may amend the *Procedure for the CADTH Common Drug Review* and all matters related to CDR. The drug plans are consulted as required. Amendments to, and clarifications of, the procedure and all related documents may be effected by means of directives (called [CDR Updates](#)) issued by CADTH on an “as-needed” basis, between revisions of these documents. Generally, changes that are corrections or clarifications become effective immediately.

1.4 Interaction Between CADTH and the Manufacturer

Once a CDR application has been filed, CADTH will hold teleconferences with the manufacturers only to discuss procedure and process-related matters, unless otherwise defined in the *Procedure for the CADTH Common Drug Review* (e.g., conference call offered during the reconsideration process).

Direct contact between a manufacturer and Canadian Drug Expert Committee members, in their capacity as members of the Canadian Drug Expert Committee, or the review team of the CDR (hereafter referred to as “CDR review team”) is not permitted during the review process. Direct

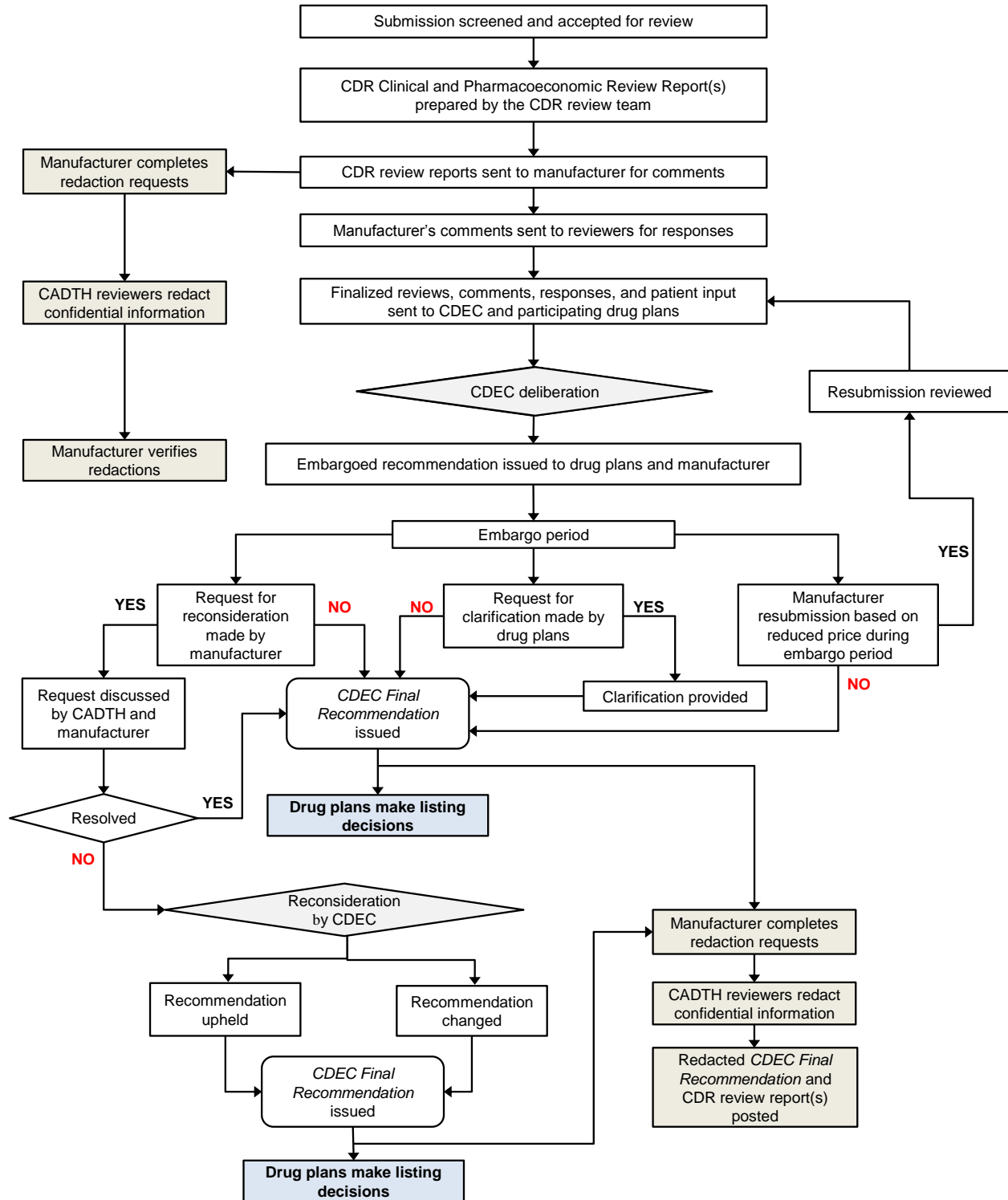
² The term “CDR review report(s)” refers to the *Common Drug Review Clinical Review Report* and *Common Drug Review Pharmacoeconomic Report* typically prepared for a standard CDR review and/or the combined *Common Drug Review Clinical and Pharmacoeconomic Review Report* prepared for a tailored CDR review 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.

approaches in any form to committee members or the CDR 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 Canadian Drug Expert Committee member or member(s) of the CDR review team may result in a significant delay in the review process of CDR because additional steps may be required to obtain an unbiased recommendation on the product.

1.5 CADTH Common Drug Review Confidentiality Guidelines

CADTH has developed confidentiality guidelines to protect confidential information obtained for the Common Drug Review (APPENDIX 2). 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 supplies other information to CADTH. A manufacturer will maintain the confidentiality of documents, shared with the manufacturer by CADTH, that are labelled as “confidential.” The confidentiality guidelines will constitute an agreement between CADTH and the manufacturer.

Figure 1: CADTH Common Drug Review Process



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

Table 1: Targeted Time Frames for Key Milestones in the CDR Process for Submissions and Resubmissions

| Phase of Review | Key Milestone | Business Days |
|--|---|-----------------------|
| Screening and Administration | • Category 1 requirements received by CADTH | 0 |
| | • Category 1 requirements screened for acceptance | 10 |
| | ▪ <i>Priority review request screened and assessed</i> | 15 |
| | • Additional copies of category 1 requirements received by CADTH | 5 |
| | • Submission or resubmission received by CDR review team | 3 |
| Order of Review | • Order and timing for initiating the review determined | Variable ^a |
| Review of Submission | • Review initiated • Protocol developed • Draft CDR Clinical and Pharmacoeconomic Review Report(s) prepared • Draft CDR review report(s) sent to manufacturer for comments | 45 |
| | • Manufacturer receives draft CDR review report(s) for comments • Manufacturer's comments sent to CADTH | 7 |
| | • CDR review team's responses to manufacturer's comments prepared • Final CDR review report(s) prepared | 7 |
| | | |
| CDEC Deliberation and Recommendation | • CDEC brief completed and distributed to CDEC and drug plans | 5 |
| | • CDEC meeting | 10 to 40 |
| | • Embargoed CDEC recommendation document drafted • Embargoed CDEC recommendation sent to drug plans and manufacturer | 5 to 7 |
| Embargo Period and Options | Embargo period ^b During the embargo period, the following scenarios may occur: | 10 to 30 ^c |
| | • Request for clarification at drug plans' request; OR | Variable ^d |
| | • Request for reconsideration at manufacturer's request; OR | Variable ^d |
| | • Resubmission based on reduced price at manufacturer's request; OR | Variable ^d |
| | • No request for clarification AND no request for reconsideration or resubmission based on reduced price | — |
| Finalizing and Posting Recommendation and Reports | • <i>CDEC Final Recommendation</i> drafted | 5 |
| | • <i>CDEC Final Recommendation</i> issued to drug plans and manufacturer | |
| | • <i>CDEC Final Recommendation</i> posted on CADTH website | Variable |
| | • Final CDR Clinical and Pharmacoeconomic Review Report(s) posted | Variable |

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

^a Submissions and resubmissions are generally reviewed on a first-come, first-served basis unless priority review status is requested and granted.

^b The embargoed CDEC recommendation is to be held in confidence by all stakeholders and not acted upon until after CADTH has issued the notice of *CDEC Final Recommendation* accompanied by the actual *CDEC Final Recommendation*.

^c A manufacturer may request an extension of up to 20 business days solely for the purpose of preparing and filing a request for reconsideration or a resubmission based on a reduced price during the embargo period (i.e., a total of 30 business days).

^d The time frame required to address a request for clarification, a request for reconsideration, or a resubmission based on reduced price during the embargo period depends on the amount of work required to address the request and the available dates for CDEC meetings.

Table 2 Targeted Time Frames for Key Milestones in the CDR Process for Requests for Advice

| Phase of Review | Key Milestone | Business Days |
|--|---|-----------------------|
| Screening and Administration | • Request for advice received by CADTH | 0 |
| | • Request for advice approach determined | 10 |
| | • Manufacturer is apprised that a review is being undertaken and invited to comment or provide information | 10 |
| Order of Review | • Order and timing for initiating the review determined | Variable ^a |
| Review of Submission | • Review initiated • Protocol developed • Draft <i>Common Drug Review Request for Advice</i> report prepared • Draft <i>Common Drug Review Request for Advice</i> report sent to manufacturer for comments | 45 |
| | • Manufacturer receives draft <i>Common Drug Review Request for Advice</i> report for comments • Manufacturer's comments are sent to CADTH | 3 |
| | • CDR review team's response to manufacturer's comments are prepared • Final <i>Common Drug Review Request for Advice</i> report is prepared | 3 |
| | | |
| CDEC Deliberation and Recommendation | • CDEC brief completed and distributed to CDEC and drug plans | 5 |
| | • CDEC meeting | 10 to 40 |
| | If the request for advice does not result in a revised CDEC recommendation: | |
| | • <i>CDEC Record of Advice</i> document issued to drug plans and manufacturer | 5 to 7 |
| | • <i>CDEC Record of Advice</i> document posted | Variable |
| | If the request for advice results in a revised CDEC recommendation: | |
| | • Embargoed CDEC recommendation drafted and sent to drug plans and manufacturer | 5 to 7 |
| Embargo Period and Options | Embargo period (when the request for advice results in a revised CDEC recommendation) ^b During the embargo period, the following scenarios may occur: | 10 to 30 ^c |
| | • Request for clarification at drug plans request; OR | Variable ^d |
| | • Request for reconsideration at manufacturer's request; OR | Variable ^d |
| | • No request for clarification AND no request for reconsideration | — |
| Finalizing and Posting Recommendation and Reports | • Final Recommendation drafted and issued to drug plans and manufacturer | 5 |
| | • Final Recommendation posted | Variable |
| | • Final <i>CDR Request for Advice</i> report posted | Variable |

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

^a Requests for advice are not queued. The timing of when a request for advice will be considered at a CDEC meeting is based on the nature of the request, the variable amount of effort required by reviewers to address each request, and the needs of the drug plans. Once completed, requests for advice are generally considered at the earliest available CDEC meeting.

^b The embargoed CDEC recommendation is to be held in confidence by all stakeholders and not acted upon until after CADTH has issued the notice of *CDEC Final Recommendation* accompanied by the *CDEC Final Recommendation*.

^c A manufacturer may request an extension of up to 20 extra business days solely for the purpose of preparing and filing a request for reconsideration (i.e., a total of 30 business days).

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

| Document | Key Milestone | Business Days |
|--|--|---------------|
| CDR Review Reports | Manufacturer identifies redactions: At the same time as manufacturers are asked to provide comments on the draft CDR review report(s), they are asked to identify any confidential information and submit a form identifying confidential information to be redacted. | 12 |
| | CADTH staff redact confidential information | Variable |
| | Manufacturers verify redactions: Manufacturers will be sent the CDR review report(s) with redactions at the same time as they are sent the confidential embargoed CDEC recommendation to review and confirm the redactions. | 10 |
| | CDR review report(s) are posted on the CADTH website: The CDR review report(s) will generally be posted at the same time as the <i>CDEC Final Recommendation</i> is posted on the CADTH website. | Variable |
| | CDR review report(s) updated: CADTH may elect to update a previously posted CDR review report should the redacted information become available in the public domain. | Optional |
| CDEC Final Recommendation or Record of Advice | Manufacturer identifies redactions: When the <i>CDEC Final Recommendation</i> or <i>CDEC Record of Advice</i> is issued, the manufacturer will be asked to identify any confidential information and submit a form identifying confidential information to be redacted, | 1 |
| | CADTH staff redact confidential information | 1 |
| | CDEC Final Recommendation or CDEC Record of Advice is posted on the CADTH website. | Variable |

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

2. CADTH COMMON DRUG REVIEW – ELIGIBLE APPLICATIONS

2.1 CADTH Common Drug Review Submissions

This section provides guidance regarding eligibility for the majority of CDR submissions. However, there may be situations where CADTH may consult with the drug plans to confirm the CDR eligibility of a drug and make a decision on a case-by-case basis, if necessary.

A manufacturer or the drug plans may file a submission for a new drug, a drug with a new indication, a new combination product, a new combination product (funded components), or a subsequent entry biologic (SEB) that

- has received a NOC or a Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed; or
- has a pending NOC or NOC/c for the indication(s) to be reviewed.

Table 4 provides an overview of each CDR-eligible submission type.

Table 4: 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. See the full description (section 2.1.1) regarding new salts and line extensions. |
| Drug with a new indication | <ul style="list-style-type: none"> A drug previously reviewed by CDR that has received an NOC or NOC/c for a new indication; or A drug marketed before the establishment of CDR that has received an NOC or NOC/c for a new indication. |
| New combination product | <ul style="list-style-type: none"> Two or more drugs that have not been previously marketed in Canada in that combination. It may consist of: <ul style="list-style-type: none"> two or more new drugs two or more previously marketed drugs a combination of new drug(s) and previously marketed drug(s). See the full description (section 2.1.3) regarding a new combination product (funded components). |
| Subsequent entry biologic | <ul style="list-style-type: none"> 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.

2.1.1 New Drug

A new drug is a new active substance that has not been previously marketed in Canada, regardless of when the NOC or NOC/c was issued. A new drug submission includes a new salt of a marketed product, but does not include the following variations of existing products being funded by drug plans (line extensions) containing the same active substance(s):

- New dosage form with the same route of administration (e.g., if a drug in tablet form becomes available in capsule form, a submission for the capsule is not required).
Note: New parenteral products or formulations (e.g., intravenous, intramuscular, subcutaneous dosage forms) are not considered line extensions of one another, for 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 are asked to contact CADTH at requests@cadth.ca for guidance on whether a submission is required for parenteral line extensions.
- 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, a submission for the 200 mg tablet is not required).

2.1.2 Drug with a New Indication

A drug with a new indication is either:

- a drug previously reviewed by CDR that has received an NOC or NOC/c for a new indication; or
- a drug marketed before the establishment of CDR (in September 2003) that has received an NOC or NOC/c for a new indication.

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. New combination products may consist of:

- two or more new drugs
- two or more previously marketed drugs
- a combination of new drug(s) and previously marketed drug(s).

A new combination product (funded components) is a new combination product containing two or more drugs that are already funded by the drug plans. All submissions for new combination products (funded components) will undergo a tailored review by CDR (hereafter referred to as a “tailored CDR review”). All submissions for other new combination products will typically undergo a standard review by CDR (hereafter referred to as “standard CDR review”); however, a decision to conduct a tailored CDR review may be made by CADTH on a case-by-case basis. Manufacturers planning to file a submission for any new combination product are required to complete and submit the following template to CADTH (requests@cadth.ca) before filing the submission:

- [New Combination Product Considerations Form](#)

CADTH will review the provided information and, with input from the drug plans, determine if the new combination product should undergo a tailored or standard CDR review.

2.1.4 Subsequent Entry Biologic

An SEB 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). Similarity between an SEB and the reference product is established in accordance with Health Canada’s [Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics \(SEBs\)](#), for the authorized indications.

2.2 Notice of Compliance Status at the Time of Filing the Submission

A CDR submission can be filed on either a pre-NOC or a post-NOC basis.³

2.2.1 Submissions Filed Pre-NOC or NOC/c

When Health Canada is highly likely to issue an NOC or NOC/c for the indications to be reviewed by CDR within 90 calendar days, a submission may be filed on a pre-NOC basis for a new drug, drug with a new indication, new combination product, new combination product (funded components), or an SEB. 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

³ Pre-NOC also includes pre-NOC/c and post-NOC includes post-NOC/c submissions.

filing; however, they are to be provided as soon as finalized because the embargoed Canadian Drug Expert Committee recommendation will not be released until all required information is received. Although Health Canada cannot provide assurance that an NOC or NOC/c will be issued on a particular date or at all, manufacturers may consider filing a submission with CDR up to 90 calendar days in advance of the anticipated NOC or NOC/c if no significant issues have been raised by Health Canada to date during the review process.

2.2.2 Submissions Filed Post-NOC or NOC/c

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 by CDR.

2.3 Drugs Not Eligible for Review Under the CADTH Common Drug Review Process

Applications for oncology drugs used for the active treatment of cancer should be filed through the [pan-Canadian Oncology Drug Review](#) (pCODR) process.

Submissions should be made directly to drug plans for the following items until further notice:

- Line extensions of marketed products, including new dosage forms with the same route of administration and new strengths of the same dosage form. For other line extensions (including new parenteral products or formulations that are not administered through the same route of administration), contact CADTH for direction.
- Generic products.

Whenever there is doubt as to whether a drug submission should be made to CDR, manufacturers are invited to contact CADTH by email at requests@cadth.ca for direction. CADTH may consult with the participating drug plans in those cases where drugs do not clearly fall into a category described above.

2.4 CADTH Common Drug Review Resubmissions

A resubmission from a manufacturer or the drug plans may be filed for a new drug, drug with a new indication, new combination product, new combination product (funded components or CADTH-designated tailored CDR review), or an SEB that has previously been reviewed through the CDR process and for which a *CDEC Final Recommendation* has been issued by CADTH. To be eligible for a resubmission, the applicant must submit new information that was not previously provided in the initial submission or previous resubmission(s). The new information must consist of one or both of the following:

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

If the new information is in support of improved efficacy, it must be from a randomized controlled trial. If the new information is in support of improved safety, case-control or cohort studies will be accepted if randomized controlled trials are unavailable.

Manufacturers or drug plans are not limited in the number of resubmissions that they may file; however, resubmissions must meet the requirement of new information to be eligible for CDR process.

2.5 CADTH Common Drug Review Submissions, Resubmissions, and Requests for Advice Filed by Drug Plans

2.5.1 Requests for Advice

Drug plans may file a request for advice through the CDR process regarding a previous Canadian Expert Drug Advisory Committee (CEDAC) or Canadian Drug Expert Committee 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.

2.5.2 CADTH Common Drug Review 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 submission or resubmission filed by a manufacturer.

2.6 Priority Review Status

2.6.1 Impact of Priority Review Status

- a) A submission or resubmission that is granted priority review will not be queued.
- b) A submission or resubmission designated for priority review will be given preferred status on the Canadian Drug Expert Committee agenda.
- c) A submission or resubmissions granted priority review status must undergo all steps in the review process of CDR and will generally follow the estimated CDR time frames for review.
- d) The granting of priority review status has no impact on the type of recommendation issued by the Canadian Drug Expert Committee.

2.6.2 Requesting Priority Review Status

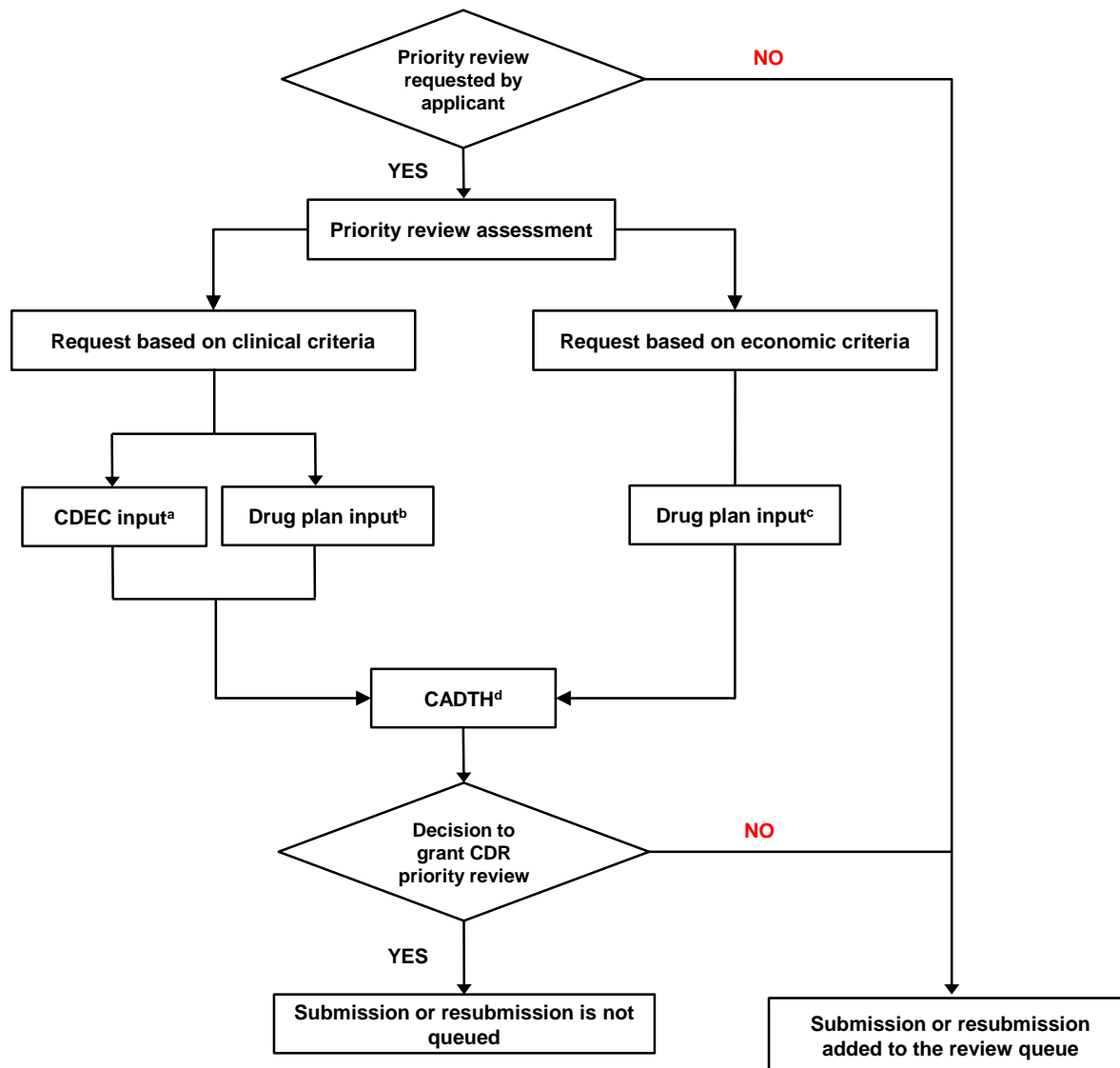
- a) Manufacturers may request priority review status at the time of filing a submission or resubmission by including a completed [Priority Review Application Template](#).
- b) A submission or resubmission may be granted priority review status based on clinical criteria if **all** of the following criteria are demonstrated:
 - The drug is indicated or anticipated to be indicated for an immediately life-threatening or other serious disease
 - The drug addresses an unmet medical need
 - The drug offers substantial improvement in clinically important outcome measures of efficacy and effectiveness, when compared with other appropriate comparators.
- c) A submission or resubmission may be granted priority review status based on economic criteria if the following criterion is demonstrated:

- For the drug under review, the projected combined cost savings for the drug plans is an average of at least \$7.5 million per year for the first three years the product is marketed in Canada, when compared with appropriate comparators.
- d) A drug that qualifies for a priority review under Health Canada provisions must meet the CDR priority review criteria to be eligible for a CDR priority review.

2.6.3 Assessing a Priority Review Request

- a) The process used by CADTH in the assessment of a CDR priority review request depends on whether the applicant is requesting priority review based on clinical criteria or based on economic criteria (see summary diagram in Figure 2).
- Priority review status based on clinical criteria will be determined by CADTH in consultation with the Canadian Drug Expert Committee chair, one of the two Canadian Drug Expert Committee public members, external clinical expert(s) (as required), as well as representatives from the drug plans.
 - Priority review status based on economic criteria will be determined by CADTH in consultation with representatives from the drug plans.
- b) The final decision regarding priority review status will be determined by CADTH. There is no provision for requesting reconsideration of the decision.
- c) The time period for assessing a priority review request based on clinical or economic priority review criteria will be 15 business days. The date the submission or resubmission is received is considered day zero for the purposes of calculating this targeted time frame for the assessment of a priority review request. If any priority review requirement filed is incomplete, CADTH will notify the applicant and the 15-day time frame for the priority review assessment will begin when the required information is received and accepted for review by CADTH.
- d) CADTH will inform manufacturers in writing if a priority review has been granted.
- e) CADTH is unable to offer a conference call to discuss the decision regarding a priority review request.

Figure 2: Schematic Diagram of CADTH Common Drug Review Process for Priority Review Assessment



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

^a Input from CDEC will be provided by the CDEC chair with input from one of the two CDEC public members and, if needed, input from an external clinical expert(s).

^b Input from the drug plans will be led by the chair of the DPAC Formulary Working Group, who may consult with clinical experts as needed.

^c Priority review requests based on economic criteria are assessed based on their potential budget savings for the drug plans; therefore, this assessment is performed by the drug plans and is independent of CDEC.

^d The final decision regarding priority review status will be determined by CADTH.

3. PRE-SUBMISSION PROCEDURE

3.1 Pre-submission Meetings

3.1.1 Standard Pre-submission Meetings

To facilitate the efficient preparation and filing of submissions for review under the CDR process, manufacturers may request pre-submission meetings with CADTH for pending submissions to be filed within six months. These meetings provide an opportunity for the manufacturer to introduce a drug to CADTH and discuss submission requirements. Pre-submission meetings are intended to offer the opportunity for dialogue between CADTH staff and manufacturers and are not meant to be consultative in nature, outside of clarifying submission requirements. Manufacturers are also invited to provide information on drugs in their pipeline so that CADTH can plan for future submissions. Pre-submission meetings are scheduled for a maximum of one hour and applicants are limited to one meeting per pending drug submission.

To request a pre-submission meeting, manufacturers are required to complete the first section of the following form and submit it to CADTH (meetingrequests@cadth.ca): [Pre-submission Meeting Request Form](#).

3.1.2 Early Pre-submission Meetings

CADTH offers opportunities for dialogue between CDR staff and manufacturers earlier in the pre-submission phase, 6 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
- natural history of the disease is poorly characterized
- there is a limited number of clinical trials 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 points listed above 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 on a case-by-case basis. Pre-submission meetings are intended to offer the opportunity for dialogue between CADTH staff and manufacturers and are not meant to be consultative in nature.

To request an early pre-submission meeting, manufacturers are required to complete the following form and submit it to CADTH (meetingrequests@cadth.ca): [Pre-submission Meeting Request Form](#).

3.2 CADTH Common Drug Review Advanced Notification Procedure

CADTH uses the following two-step process for obtaining information regarding pending CDR submissions and resubmissions, as applicable:

3.2.1 Voluntary Pipeline Notification of Pending CADTH Common Drug Review Submissions

Manufacturers are encouraged to voluntarily provide advanced notification of a pending CDR submission at the time of regulatory filing (i.e., providing advanced notification of approximately 12 months). Manufacturers willing to participate in this voluntary process are asked to complete and submit the advanced notification template to requests@cadth.ca:

- [CADTH Common Drug Review Voluntary Pipeline Notification Template](#)
- [CADTH Common Drug Review Advanced Notification Instructions](#).

3.2.2 Mandatory Notification of Pending Submission or Resubmission

Manufacturers are required to provide CADTH with advanced notification of a pending submission or resubmission at least 20 business days before filing with CDR. All manufacturers must complete and submit the appropriate advanced notification template for a submission or resubmission by email to requests@cadth.ca. Failure to provide notification at least 20 business days in advance of filing may result in a delay in the processing and review of the submission or resubmission by CADTH. The date that the advanced notification template is received by CADTH is considered day zero (for purposes of counting back 20 business days in advance of the date on which CADTH will receive the submission).

- [CADTH Common Drug Review Mandatory Notification Submission Template](#)
- [CADTH Common Drug Review Mandatory Notification Resubmission Template](#)
- [CADTH Common Drug Review Advanced Notification Instructions](#).

4. CADTH COMMON DRUG REVIEW APPLICATION PROCEDURE

4.1 Filing Applications for Submissions or Resubmissions

- a) The appropriate submission or resubmission requirements filed must adhere to the content, format, and organization stipulated in the current [Submission Guidelines for the CADTH Common Drug Review](#).
- b) Submissions and resubmissions must be delivered to CADTH by courier, registered mail, or in person (APPENDIX 4). The only exceptions are resubmissions based on a reduced price during the embargo period, which may be submitted by email.
- c) When filing a submission or resubmission, the manufacturer should initially deliver only one copy of the submission or resubmission to CADTH.
- d) CADTH screens the application in accordance with the requirements described in the *Submission Guidelines for the CADTH Common Drug Review*. Once the submission or resubmission is accepted for review under the CDR process, the manufacturer will be

advised and asked to provide the required number of copies as described in the *Submission Guidelines for the CADTH Common Drug Review*.

- e) In the case of a submission or resubmission from the drug plans, the submission or resubmission must be filed with CADTH in a signed letter that clearly describes the issues of interest to the drug plans.

4.1.1 Finalized Information for Submissions Filed on Pre-NOC Basis

For submissions filed on a pre-NOC basis, some information may be outstanding (e.g., Health Canada reviewers' report) or not finalized at the time that an application is filed with CADTH. It is the responsibility of the manufacturer to provide such information as soon as it is available.

- a) CADTH will assess finalized information upon receiving it. Depending on the nature and extent of changes to the information compared with what was originally filed, CADTH will determine the timelines required to review it and incorporate it into the CDR review report(s). This could result in the submission being considered at a later Canadian Drug Expert Committee meeting. The manufacturer will be apprised of any revisions to the anticipated timelines for the review.
- b) If additional supporting documentation is required, the manufacturer will be apprised of the requirements.
- c) When all 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.

4.2 Application Fees for the CADTH Common Drug Review

All submissions and resubmissions filed by manufacturers for drugs that receive a Health Canada NOC or NOC/c on or after September 1, 2014 are subject to an application fee. For details regarding the application fees for CDR, see APPENDIX 1.

4.3 Screening of Submissions From Manufacturers

- a) CADTH screens applications for submissions in accordance with the requirements described in the [Submission Guidelines for the CADTH Common Drug Review](#).
- b) The date of receipt of a submission is considered day zero for the purpose of calculating the targeted time frames for application screening. These targeted time frames are posted in the submission status reports in the CDR database section of the CADTH website.
- c) When not provided at the same time as category 1 requirements, category 2 requirements should be submitted at least 20 business days before the targeted Canadian Drug Expert Committee meeting at which the submission will be considered. Incomplete category 2 requirements will not preclude CDR reviews from being placed on the agenda of the targeted Canadian Drug Expert Committee meeting; however, the *CDEC Final Recommendation* will not be issued until all category 2 requirements are complete.

- d) An initial screening of a submission is completed by CADTH as follows:
- within 10 days for category 1 (with or without category 2) requirements
 - within five days for category 2 requirements, when not filed at the same time as category 1 requirements.
- e) If the filed category 1 or category 2 requirements for a submission are deficient or require revision in order to meet the requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*, 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 or category 2 requirements is completed by CADTH as soon as possible after receipt, but may take up to five days.
- f) When category 1 requirements for a submission have been accepted for review by CADTH:
- CADTH sends an acknowledgement to the manufacturer and requests that the manufacturer provide five additional copies (for a total of six) of the category 1 requirements in electronic format on separate CDs, DVDs, or USB flash drives.
 - CADTH may request additional copies if required.
 - The manufacturer must ensure that the drug plans are provided with a copy of the category 1 requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*.
- g) As described in section 4.1.1, when a CDR submission has been filed on a pre-NOC basis, the manufacturer must provide all outstanding and/or finalized category 1 requirements as soon as they are available. Once CADTH has notified a 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.
- h) When category 2 requirements for a submission are complete:
- CADTH sends an acknowledgement to the manufacturer.
 - No further copies of category 2 requirements are required by CADTH.
 - The manufacturer must ensure that the drug plans are provided with a copy of the category 2 requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*.
- i) Upon receipt of notification of a manufacturer's submission, the drug plans may identify questions to be addressed in the review process and submit these to CADTH.

4.4 Screening Resubmissions From Manufacturers

The following provisions apply to all resubmissions filed by manufacturers or drug plans, with the exception of resubmissions based on reduced price during embargo period (section 8.5).

- a) CADTH screens applications for resubmissions in accordance with the requirements described in the [Submission Guidelines for the CADTH Common Drug Review](#).
- b) The date of receipt of a resubmission is considered day zero for the purpose of calculating the targeted time frames for application screening. These targeted time frames are posted in the submission status reports in the CDR database section of the CADTH website.
- c) When not provided at the same time as category 1 requirements, category 2 requirements (as applicable) should be submitted at least 20 business days before the targeted

Canadian Drug Expert Committee meeting at which the resubmission will be considered. Incomplete category 2 requirements will not preclude reviews by CDR from being placed on the agenda of the targeted Canadian Drug Expert Committee meeting; however, the *CDEC Final Recommendation* will not be issued until all category 2 requirements are complete.

- d) An initial screening of a resubmission is completed by CADTH as follows:
 - within 10 days for category 1 (with or without category 2) requirements
 - within 5 days for category 2 requirements, as applicable, when not filed at the same time as category 1 requirements.
- e) If the filed category 1 or category 2 requirements (outside of the new information requirements) for a resubmission are deficient or require revision in order to meet the requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*, 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 or category 2 requirements is completed by CADTH as soon as possible after receipt, but may take up to five days.
- f) If CADTH determines that the information in the resubmission does not comprise new information, CADTH will advise the manufacturer and drug plans of this finding and that the resubmission has been rejected. CADTH will retain and dispose of copies of the rejected submission in accordance with the *CADTH Common Drug Review Confidentiality Guidelines*.
- g) When category 1 requirements for a resubmission based on new clinical information with or without new cost information have been accepted by CADTH for review:
 - CADTH sends an acknowledgement to the manufacturer and requests that the manufacturer provide five additional copies (for a total of six) of the category 1 requirements on separate CDs, DVDs, or USB flash drives.
 - CADTH may request additional copies if required.
 - The manufacturer must ensure that the drug plans are provided with a copy of the category 1 requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*.
- h) When category 1 requirements for a resubmission based on new cost information only have been accepted for review by CADTH:
 - CADTH sends an acknowledgement to the manufacturer and requests that the manufacturer provide three additional copies (for a total of four) of the category 1 requirements on separate CDs, DVDs, or USB flash drives.
 - CADTH may request additional copies if required.
 - The manufacturer must ensure that the drug plans are provided with a copy of the category 1 requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*.
- i) When category 2 requirements for a resubmission are complete:
 - CADTH sends an acknowledgement to the manufacturer.
 - No further copies of category 2 requirements are required by CADTH.
 - The manufacturer must ensure that the drug plans are provided with a copy of the category 2 requirements as outlined in the *Submission Guidelines for the CADTH Common Drug Review*.

- j) Upon receipt of notification of a manufacturer's resubmission, the drug plans may identify questions to be addressed in the review process and submit these to CADTH.

4.5 Tracking

CADTH posts submission status reports with key targeted time frames and the status of the review for all submissions, resubmissions, and requests for advice on the [CADTH website](#). Table 1 and Table 2 indicate the targeted time frames for key tasks within the CDR process. CADTH typically updates these reports weekly, as applicable.

5. PATIENT GROUP INPUT PROCEDURE

Patient group 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 the CDR review team in the review of submissions, resubmissions based on new clinical information, and requests for advice and by Canadian Drug Expert Committee in the development of recommendations.

5.1 Notifying Patient Groups about Calls for Patient Input

CADTH posts the name of a drug to be reviewed along with the deadline date for receiving patient group input on the CADTH website. CADTH also notifies all subscribed patient groups by email. Patient groups can subscribe to receive E-Alerts by using the "subscribe" option on the CADTH website. CADTH also tweets about calls for patient input to those who follow CADTH's Twitter accounts (English: @CADTH_ACMTS and French: @ACMTS_CADTH). When CADTH posts a call for patient input, it also posts a copy of the Health Canada–approved product monograph, which provides information about the drug. Product monographs are not available for submissions filed on a pre-NOC basis.

5.2 Deadline for Patient Group Input

The call for patient input regarding a submission or resubmission is posted 20 business days in advance of the manufacturer's anticipated date of filing the application, as indicated in the mandatory advanced notification template (section 3.2.2). Patient groups have a total of 35 business days for preparing and submitting patient input for all drug submissions, resubmissions based on new clinical information, and requests for advice.

5.3 Submitting Patient Group Input

- a) Patient input is submitted to CADTH by patient groups. Individual patients or caregivers who wish to provide input are encouraged to work with a patient group that represents their condition and have that patient group include their information in its patient input submission to CDR.
- b) Patient groups are asked to use one of the two templates posted on the CADTH website — the [Patient Input Template](#) for all drugs **except** SEBs and the [SEB Patient Input Template](#) for SEBs only. Each of the templates has questions and prompts to help guide patients to

provide the information that will be most helpful to the CDR review team and the Canadian Drug Expert Committee in their work.

- c) Patient groups must submit their input by the posted deadline date in order that the information can be used by the CDR review team to develop the protocol — a critical step that takes place early in the review of a submission.
- d) Patient groups are asked not to include any private information in their patient input submission to CDR, because when permission is granted, the patient group input is posted on the CADTH website in its entirety. It is the responsibility of the patient group to exclude any private information.

5.4 How Patient Group Input Is Used

- a) All patient group input received by CADTH for the drug under review is collated and summarized by CADTH staff. This summary and the patient group input submissions in their entirety are provided to the CDR review team to use in the development of the protocol.
- b) The approximately two-page summary is also sent to each of the patient groups that provided input for their review and comments. Patient groups are asked to comment on whether the summary reflects the main issues and outcomes of importance to them and to ensure that no private information is included in the summary.
- c) The patient group input summary is incorporated into its own section in the *CADTH Common Drug Review Clinical Review Report*. Additionally, patient input is incorporated into other sections of the *CADTH Common Drug Review Clinical Review Report* when relevant. The patient group input summary and the patient group input submissions in their entirety are included in the Canadian Drug Expert Committee brief.
- d) The Canadian Drug Expert Committee public members present the patient input at the outset of the Canadian Drug Expert Committee deliberations about the drug (section 7.3).
- e) The patient input is included, as relevant, in the Canadian Drug Expert Committee recommendation document. A summary of the patient input discussed during the deliberation is included in its own section of the document.
- f) The patient group input submissions in their entirety are also shared with the drug plans and posted on the CADTH website.
- g) All patient input submissions are kept on file and may be referred to in future CDR reviews of the same drug.

5.5 Posting Patient Group Input

- a) All patient group input submissions received on and after February 1, 2014 are posted on the CADTH website in their entirety.
- b) The primary contact for each patient group is asked to provide permission for posting the patient group input on the CADTH website.
- c) If the primary contact does not grant permission to post the patient group input, CADTH will indicate on the website that patient group input had been received; however, it was not posted at the request of the patient group.

- d) The name of the patient group and conflict of interest information will be included in the posted material. The name and contact information of the author will not be posted.
- e) CADTH takes reasonable precautions to remove any private information 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.
- f) The target time frame for posting patient group input on the CADTH website is at the same time the CDR review report(s) are posted.

6. CDR REVIEW PROCEDURE

6.1 Order of Review

- a) Applications for submissions and resubmissions are accepted on an ongoing basis.
- b) Applications for submissions and resubmissions are logged when received so that there is a record of the date of receipt. CADTH sends an acknowledgement of receipt to the applicant.
- c) Applications are screened in the order that they are received.
- d) The date of receipt is considered day zero for the purpose of calculating the targeted time frames for application screening. These targeted time frames are posted in the submission status reports on the CADTH website.
- e) 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 submissions and resubmissions granted priority review status, requests for advice, and drug plan-initiated submissions or resubmissions.
- f) Requests for advice are not assigned to the review queue. The timing of when a request for advice will be considered at a Canadian Drug Expert Committee meeting is based on the nature of the request and the amount of effort required by the CDR review team to address the request. Once completed, requests for advice are generally considered at the earliest available Canadian Drug Expert Committee meeting.
- g) CADTH posts, on the [CADTH website](#), targeted Canadian Drug Expert Committee meeting dates on which submissions and resubmissions may be considered if their reviews are initiated by a given date.

6.2 Initiation of Review

When the review of a submission or resubmission is initiated, CADTH:

- a) Provides the manufacturer with the name of the contact to whom all inquiries about that submission or resubmission are to be directed.
- b) 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*. The names of the review team members are not disclosed to the manufacturer.

- c) Determines the appropriate approach for undertaking the review and develops a workplan for review of the submission or resubmission.

6.3 Review of a Submission

6.3.1 Types of CDR Reviews Conducted for Submissions and Resubmissions

The CDR review team conducts either a standard CDR review or a tailored CDR review, depending on the type of submission or resubmission filed by a manufacturer.

- A standard 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.
- A tailored 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.

Table 5 summarizes the type of CDR review conducted for the different submission and resubmission categories.

| Type of CDR Review | Type of Submission or Resubmission |
|---------------------|---|
| Standard CDR Review | <ul style="list-style-type: none"> • New drug submission • Drug with a new indication submission • New combination product submission • Resubmission based on new clinical information with or without new cost information |
| Tailored CDR Review | <ul style="list-style-type: none"> • New combination product (funded components or CADTH-designated tailored CDR review) submission • Subsequent entry biologic submission • Resubmission based only on new cost information |

CDR = CADTH Common Drug Review.

6.3.2 Standard CDR Reviews for New Drugs, Drugs with a New Indication, and New Combination Products

- a) The CDR review team develops a protocol for the review of the submission with input from the drug plans, Canadian Drug Expert Committee members, and other experts, as required.
- b) The CDR 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 *Common Drug Review Clinical Review Report*.
- c) A list of studies included in the systematic review portion of the *Common Drug Review 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 *Common Drug Review Clinical Review Report*. All studies that are used in the *Common Drug Review Clinical Review Report* are referenced.
- d) The CDR review team undertakes a review of the relevant information provided by the manufacturer, by patient groups, and identified through an independent literature search.

The clinical review is completed in accordance with the review template. During this stage, the review team:

- Determines whether it needs additional information from the manufacturer. 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 (section 11.1)
 - Prepares a *Common Drug Review Clinical Review Report* in accordance with the [review template](#).
- e) The CDR review team reviews and conducts an appraisal of the pharmacoeconomic information submitted by the manufacturer. The results and conclusions reported in the *Common Drug Review Clinical Review Report* are used in the assessment of the pharmacoeconomic information submitted by the manufacturer. During this stage, the review team:
- Determines whether it needs additional information from the manufacturer. 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 (section 11.1)
 - 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 *Common Drug Review Pharmacoeconomic Review Report* in accordance with the [review template](#).
- f) Depending on the volume or complexity of material to be reviewed, extension of the review time frame deadlines may be required. The manufacturer will be notified of any extensions, and reasons for the extensions, granted by CADTH.
- g) The *Common Drug Review Clinical Review Report* and *Common Drug Review Pharmacoeconomic Review Report* are finalized in accordance with section 6.6.
- h) 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 CDR and Health Canada.

6.3.3 Tailored CDR Reviews for New Combination Products (Funded Components or CADTH-Designated Tailored CDR Reviews) and SEBs

- a) The CDR review team validates and comments on the information provided by the manufacturer in the new combination product (funded components or CADTH-designated tailored CDR review) template or the SEB template.
- b) The CDR 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 *Common Drug Review Clinical and Pharmacoeconomic Review Report*.⁴ During this stage, the CDR review team considers whether it needs additional information from the

⁴ Only a single report combining both clinical and pharmacoeconomic information is prepared by the CDR review team for tailored CDR reviews.

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 (section 11.1).

- c) Depending on the volume or complexity of material to be reviewed, extension of the review time frame deadlines may be required. The manufacturer will be notified of any extensions, and reasons for the extensions, granted by CADTH.
- d) The *Common Drug Review Clinical and Pharmacoeconomic Review Report* for a new combination product (funded components or CADTH-designated tailored CDR review) or an SEB is finalized in accordance with section 6.6.
- e) 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 CDR and Health Canada.

6.4 Review of a Resubmission

6.4.1 Review of Resubmission Based on New Cost Information

In the event a resubmission is filed based on new cost information (i.e., new cost information not included in the initial submission or previous resubmission[s]) that significantly affects the cost-effectiveness of the drug, the following provisions shall apply:

- a) The resubmission and relevant documents that relate to the initial submission or previous resubmission(s) are reviewed by the CDR review team.
- b) The CDR review team conducts an independent literature search to supplement the data provided by the manufacturer.
- c) The review team conducts an appraisal of the pharmacoeconomic information submitted by the manufacturer. The results and conclusions reported in the previous *Common Drug Review Clinical Review Report(s)* on the drug are used in the assessment of the pharmacoeconomic information submitted by the manufacturer. During this stage, the review team:
 - Determines 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 (section 11.1)
 - 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 *Common Drug Review Pharmacoeconomic Review Report* in accordance with the [review template](#).
- d) 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 reasons for the extensions, granted by CADTH.
- e) The *Common Drug Review Pharmacoeconomic Review Report* for a resubmission based on new cost information is finalized in accordance with section 6.6.

6.4.2 Review of Resubmission Based on New Clinical Information

When a resubmission is filed based on new clinical information, the following provisions shall apply:

- a) Based on a review of the resubmission and relevant documents from the initial submission, the CDR review team determines if a new systematic review is required and determines the appropriate approach to assess the new information.
- b) The CDR review team conducts an independent literature search to identify any new relevant information and to supplement the data provided by the manufacturer.
- c) The CDR review team reviews the relevant clinical information provided in the resubmission and the information identified in the literature search. During this stage, the review team:
 - Determines whether it needs additional information from the manufacturer. 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 (section 11.1)
 - Prepares a *Common Drug Review Clinical Review Report* in accordance with the [review template](#).
- d) The review team conducts an appraisal of the pharmacoeconomic information submitted by the manufacturer. The results and conclusions reported in the *Common Drug Review Clinical Review Report* are used in the assessment of the pharmacoeconomic information submitted by the manufacturer. During this stage, the review team:
 - Determines 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 (section 11.1)
 - 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 model is rerun and revised cost-effectiveness estimates are determined
 - Prepares cost-comparison tables
 - Prepares a *Common Drug Review Pharmacoeconomic Review Report* in accordance with the [review template](#).
- e) 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 reasons for the extensions, granted by CADTH.
- f) The *Common Drug Review Clinical Review Report* and *Common Drug Review Pharmacoeconomic Review Report* for a resubmission based on new clinical information are finalized in accordance with section 6.6.

6.5 Review of a Request 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 Canadian Expert Drug Advisory Committee 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 workplan for its review within 10 business days of receipt.
- d) CADTH may seek direction from the Canadian Drug Expert Committee 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*. 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 CDR review team
 - a protocol is established
 - the review team conducts a literature search. The studies and material 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 6.6.

6.6 CDR Review Report(s)

6.6.1 Manufacturer's Comments

- a) CADTH forwards the draft CDR review report(s) to the manufacturer for comment and to drug plans for information.
- b) 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.
- c) The manufacturer's combined comments on the draft CDR review report(s) should not exceed six pages in length.
- d) The manufacturer may waive the opportunity to provide comments.
- e) 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.
- f) References should be appropriately cited in the comments documents provided by the manufacturer.

6.6.2 CDR Review Team's Responses to Manufacturer's Comments

- a) CADTH forwards the manufacturer's written comments, if any, to the CDR review team.
- b) The CDR review team has seven business days to address the comments provided by the manufacturer. If the manufacturer's comments exceed the six-page limit, the review team will address only the comments on pages up to the limit.

- c) When preparing responses to a manufacturer’s comments, the CDR review team should clearly identify the comments to which they are responding and address them succinctly, whenever possible. References should be provided, if appropriate.
- d) The CDR review team’s responses are shared with the Canadian Drug Expert Committee; however, they are not distributed to the manufacturer.

6.6.3 Final Versions of CDR Review Report(s)

- a) The CDR review report(s) are revised by the CDR review team, as required, on the basis of the manufacturer’s comments, and are included in the Canadian Drug Expert Committee 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 versions of the CDR review report(s) to the manufacturer and drug plans when it releases the embargoed Canadian Drug Expert Committee recommendation.

6.6.4 Redaction and Posting of CDR Review Report(s)

- a) CADTH will post the CDR review report(s) on the CADTH website for all submissions, resubmissions, and requests for advice.
- b) Manufacturers will be responsible for identifying any confidential information in the CDR review report(s) and for requesting any redactions before these reports are posted on the CADTH website.
- c) All requests for redaction must be accompanied by a clearly stated rationale.
- d) At the same time as manufacturers are asked to provide comments on the CDR review report(s), they are asked to identify any confidential information and submit a request for redactions.
- e) Although manufacturers must provide comments on the CDR review report(s) within the time frames described in 6.6.1, they have an additional five business days to identify the confidential information and submit a request for redactions (see Table 6).

| Table 6: Time Allotted for Reviewing and Redacting CDR Review Report(s) | | |
|--|--|---|
| Time for Manufacturer’s Comments on CDR Review Report(s) | Additional Time to Identify Confidential Material | Total Time Available for Identifying Confidential Material |
| 7 days | 5 days | 12 days |

CDR = CADTH Common Drug Review.

- f) 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* (APPENDIX 2).
- g) The manufacturers are sent the CDR review report(s) with redactions at the same time as they are sent the confidential embargoed Canadian Drug Expert Committee recommendation. At this point, the manufacturers will have 12 business days to review and confirm the redactions.

- h) The CDR review report(s) will generally be posted at the same time as the *CDEC Final Recommendation* is posted on the CADTH website.
- i) CADTH may elect to update a previously posted CDR review report should the redacted information become available in the public domain.
- j) 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*.

7. CANADIAN DRUG EXPERT COMMITTEE MEETING AND RECOMMENDATION PROCEDURE

7.1 The Canadian Drug Expert Committee

- a) The Canadian Drug Expert Committee is an advisory body to CADTH that makes drug-related recommendations and provides drug-related advice through the CDR and therapeutic review processes. The Canadian Drug Expert Committee's recommendations and advice are provided to CADTH to inform the publicly funded drug plans and a range of stakeholders.
- b) The Canadian Drug Expert Committee is established in accordance with the [Canadian Drug Expert Committee Terms of Reference](#).
- c) All Canadian Drug Expert Committee 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*

7.2 Canadian Drug Expert Committee Brief

CADTH compiles and distributes the Canadian Drug Expert Committee brief to all Canadian Drug Expert Committee members and the drug plans 10 business days before the next scheduled Canadian Drug Expert Committee meeting. The committee members are responsible for reviewing the Canadian Drug Expert Committee briefs for all drugs under consideration at the meeting. Materials contained in a Canadian Drug Expert Committee 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
- Submission history table of similar drugs reviewed by CDR
- *CADTH Common Drug Review Clinical and Pharmacoeconomic Review Report(s)*
- Manufacturer's comments on the *CADTH Common Drug Review 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])
- Manufacturer-provided executive summary and table of studies.

Notes: (1) CADTH Therapeutic Review and Optimal Use reports are included in the Canadian Drug Expert Committee brief materials when available and relevant. (2) In the case of a request for advice, the *CADTH Common Drug Review 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 Canadian Drug Expert Committee brief. (3) Although the manufacturer's full submission or resubmission will be available at the Canadian Drug Expert Committee meeting, it will not routinely be sent to committee members in advance, but will be available on request.

7.3 Canadian Drug Expert Committee Meeting

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

7.3.1 Preparation for the Canadian Drug Expert Committee Meeting

- a) The Canadian Drug Expert Committee meeting agenda is set by CADTH and the committee chair.
- b) The Canadian Drug Expert Committee brief for each drug to be considered at a particular Canadian Drug Expert Committee meeting will be delivered to all committee members and the drug plans at least 10 business days in advance of the scheduled Canadian Drug Expert Committee meeting date.
- c) Three Canadian Drug Expert Committee 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 the CDR review team in the review of the submission or resubmission) is included in the overview reports.
- d) 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 Canadian Drug Expert Committee members in advance of the meeting.

7.3.2 Attendees at Canadian Drug Expert Committee Meetings

In addition to Canadian Drug Expert Committee 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) 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.
- c) Specialist experts attend the Canadian Drug Expert Committee meeting upon invitation but do not vote on the recommendation.
- d) Manufacturers, patients, and others (except as described above) are not entitled to attend any Canadian Drug Expert Committee meeting, either as observers or to make an oral presentation or submission.

7.3.3 Canadian Drug Expert Committee Deliberative Framework and Process

- a) At the Canadian Drug Expert Committee meeting, committee members consider and discuss each Canadian Drug Expert Committee 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.
- c) 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.
- d) The other two Canadian Drug Expert Committee discussants present their overviews of the clinical and pharmacoeconomic evidence.
- e) Following the discussant presentations, all Canadian Drug Expert Committee members provide input, and the CDR review team and invited external experts provide input as required.
- f) Canadian Drug Expert Committee members' deliberations include:
 - 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.
- g) The Canadian Drug Expert Committee must make a recommendation or defer if additional clarification is needed. If the Canadian Drug Expert Committee needs additional information from the CDR review team, the applicant, or from external experts, the matter will be sent back to CADTH to collect the additional information and the matter will be deferred to a subsequent Canadian Drug Expert Committee 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.
- h) Based on the deliberation of the available evidence, Canadian Drug Expert Committee members choose one of four recommendation options: list, list with clinical criteria and/or conditions, do not list at the submitted price, or do not list (section 7.4.1) and provide reasons for the recommendation.

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- i) Canadian Drug Expert Committee members vote on the recommendation.
- Only Canadian Drug Expert Committee members vote
 - All Canadian Drug Expert Committee members must vote unless there is a declared conflict of interest that precludes a member from voting
 - Canadian Drug Expert Committee members vote secretly on the recommendation. The reasons for recommendation are drafted and discussed before committee members vote on a recommendation
 - The Canadian Drug Expert Committee 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.

7.4 Canadian Drug Expert Committee Recommendation and Reasons for Recommendation

7.4.1 Canadian Drug Expert Committee Recommendation Options

The Canadian Drug Expert Committee may recommend one of the following options for a drug under review: that a drug be listed; that a drug be listed with clinical criteria and/or conditions; that a drug not be listed at the submitted price; or that a drug not be listed. A description of the recommendation options is provided in Table 7.

Table 7: Description of Canadian Drug Expert Committee Recommendations

| |
|--|
| List |
| A drug ^a demonstrates comparable or added clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators. ^b |
| List with clinical criteria and/or conditions |
| <p>Scenarios that typically fit this listing category include:</p> <ul style="list-style-type: none"> • A drug^a 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.” • A drug^a demonstrates added clinical benefit, but the cost/cost-effectiveness relative to one or more appropriate comparators^b is unacceptable. In such cases, a condition may include a reduced price. • A drug^a demonstrates comparable clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators.^b In such cases, a condition may include that the drug^a be listed in a similar manner to one or more appropriate comparators. <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) • characteristics of the care setting (e.g., prescribed by or under the care of an experienced clinical team) • starting and stopping rules (e.g., response to treatment). <p>Examples of conditions include, but are not limited to^c:</p> <ul style="list-style-type: none"> • pricing considerations • reimbursement limits (e.g., number of doses supported by clinical and cost-effectiveness evidence) • current formulary listing status of one or more appropriate comparators (e.g., if a drug under review is similar to a listed appropriate comparator[s], the condition may be to list the drug in a similar manner to the listed comparator[s]). <p>Note: The use of “and/or” in the “List with clinical criteria and/or conditions” allows for three subcategories of this listing category: clinical criteria and conditions, clinical criteria only, conditions only.</p> |
| Do not list at the submitted price |
| <p>Scenarios that typically fit this listing category include:</p> <ul style="list-style-type: none"> • A drug^a demonstrates no added clinical benefit and the cost/cost-effectiveness relative to one or more appropriate comparators^b is unacceptable. • A drug^a demonstrates added clinical benefit, but the cost/incremental cost-effectiveness ratio far exceeds that of existing treatment options^d and precludes a recommendation to list with clinical criteria and/or conditions. <p>Note: The “Of Note” section in the recommendation may provide additional context regarding price, comparator(s), patient subgroups to whom the drug might be restricted, and other relevant considerations.</p> |
| Do not list |
| <p>A scenario that typically fits this listing category includes:</p> <ul style="list-style-type: none"> • A drug^a does not demonstrate comparable clinical benefit relative to one or more appropriate comparators.^b |

^a Refers to a drug under review.

^b An appropriate comparator is typically a drug listed by one or more drug plans for the indication under review. However, the choice of appropriate comparator(s) in the CDR reviews is made on a case-by-case basis.

^c Although not listed as conditions, evidence gaps and the need for evidence development may be highlighted in the Canadian Drug Expert Committee recommendation document as appropriate.

^d Existing treatment options may include best supportive care.

7.4.2 Reasons for Recommendation

- a) The Canadian Drug Expert Committee's recommendations will, in every case, be accompanied by reasons for the recommendation. A CADTH staff member may be tasked with the responsibility of preparing a draft statement of reasons for recommendation, for approval by the Canadian Drug Expert Committee.
- b) The reasons for recommendation will represent the key considerations and rationale used by the Canadian Drug Expert Committee in formulating the recommendation.

7.5 Requests for Advice

When considering a request for advice, the Canadian Drug Expert Committee may address the request by providing one of the following:

- a revised Canadian Drug Expert Committee recommendation that would supersede a previous Canadian Expert Drug Advisory Committee or *CDEC Final Recommendation*
 - a *CDEC Record of Advice* document containing additional context and/or clarifications regarding a previous Canadian Expert Drug Advisory Committee or *CDEC Final Recommendation*.
- a) In the case of a request for advice that results in a revised Canadian Drug Expert Committee recommendation, the embargoed Canadian Drug Expert Committee recommendation will be released as described in section 8.
 - b) In the case of a request for advice that does not result in a revised Canadian Drug Expert Committee recommendation, the *CDEC Record of Advice* will be sent to the drug plans and the manufacturer within five to seven business days following the applicable Canadian Drug Expert Committee meeting. The *CDEC Record of Advice* will be posted on the CADTH website.

8. THE EMBARGOED CDEC RECOMMENDATION

8.1 Embargo Period

During the embargo period, stakeholders limit the distribution of the confidential, embargoed recommendation in accordance with the *Procedure for the CADTH Common Drug Review* and the *CADTH Common Drug Review Confidentiality Guidelines*. The intent of the embargo period is to allow time for the manufacturers and the jurisdictions to consider the embargoed Canadian Drug Expert Committee recommendation before it is made public.

During the embargo period, the following may occur with respect to the embargoed Canadian Drug Expert Committee recommendation:

- Drug plans may submit a request for clarification (section 8.3)
- Manufacturers may make a request for reconsideration (section 8.4)
- Manufacturers may file a resubmission based on a reduced price (section 8.5).

The duration of the embargo period is 10 business days; however, manufacturers may request an extension of up to 20 business days for the purposes of preparing and filing a request for reconsideration or a resubmission at a reduced price during the embargo period.

8.2 Releasing the Embargoed CDEC Recommendation

- a) In the case of a submission that was filed on a pre-NOC basis, the embargoed Canadian Drug Expert Committee recommendation will not be released until CADTH has received a copy of the NOC or NOC/c.
- b) The embargoed Canadian Drug Expert Committee recommendation will be sent to the manufacturer and the drug plans within five to seven business days following the Canadian Drug Expert Committee meeting at which the recommendation was made.
- c) If a request for reconsideration is accepted or a resubmission based on a reduced price is accepted, the notice of *CDEC Final Recommendation* will not be issued until the Canadian Drug Expert Committee has considered the request for reconsideration or has considered the resubmission based on a reduced price and made a recommendation in either case.
- d) Until the notice of *CDEC Final Recommendation* has been issued (section 9), the embargoed Canadian Drug Expert Committee recommendation is not publicly available. Drug plans and manufacturers agree not to act on the embargoed recommendation. All stakeholders shall maintain its confidentiality.

8.3 Request for Clarification

8.3.1 Drug Plans' Request for Clarification

- a) The drug plans may file a request for clarification of an embargoed Canadian Drug Expert Committee recommendation within 10 business days of notification of the embargoed Canadian Drug Expert Committee 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 Canadian Drug Expert Committee will be notified of the request for clarification.
- e) The request for clarification is tracked in the submission status report on the CADTH website.

8.3.2 Response to Request for Clarification

- a) CADTH will not issue a notice of *CDEC Final Recommendation* until the drug plans have received a written response to their request for clarification.
- b) CADTH will prepare a written response to the request for clarification for approval by the Canadian Drug Expert Committee chair.
- c) In responding to the request for clarification, CADTH will consult, as required, with the Canadian Drug Expert Committee chair and the Canadian Drug Expert Committee, the CDR review team, and any external expert retained in connection with the submission.
- d) If, in the judgment of the Canadian Drug Expert Committee 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 Canadian Drug Expert Committee meeting.

- e) CADTH will distribute the response to the drug plans, the Canadian Drug Expert Committee, and the drug manufacturer within five business days of the committee and CADTH determining the response to the request for clarification.

8.4 Request for Reconsideration of the CDEC Recommendation

8.4.1 Manufacturer's Request for Reconsideration

- a) Every manufacturer of a drug that is the subject of an embargoed Canadian Drug Expert Committee recommendation may file a request for reconsideration of the recommendation.
- b) A request for reconsideration can be made only on one or both of the following grounds:
 - CDR and/or the Canadian Drug Expert Committee failed to act fairly and in accordance with its procedures in conducting the review, and/or
 - The Canadian Drug Expert Committee recommendation is not supported by the evidence that had been submitted or the evidence identified in the CDR review report(s).
- c) A manufacturer shall only be entitled to have the embargoed Canadian Drug Expert Committee recommendation reconsidered once.
- d) Concurrent filing of a resubmission based on a reduced price during the embargo period and a request for reconsideration is not allowed.
- e) A request for reconsideration is filed by submitting a written request to CADTH.
- f) 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 Canadian Drug Expert Committee recommendation with which the manufacturer disagrees, and state the grounds for the request for reconsideration.
- g) No new information will be considered in the reconsideration.
- h) The manufacturer has 10 business days after receiving notification of the embargoed Canadian Drug Expert Committee recommendation to file a request for reconsideration.
- i) In addition to the standard 10 business days of the 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 Canadian Drug Expert Committee recommendation
 - The manufacturer must provide adequate reasons for the requested extension and must indicate when the request for reconsideration will be submitted
 - 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 Canadian Drug Expert Committee 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 9.

- j) CADTH notifies the Canadian Drug Expert Committee and the drug plans of the receipt of the request for reconsideration.

8.4.2 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, then the request for reconsideration will be forwarded to the Canadian Drug Expert Committee in accordance with section 8.4.3.

8.4.3 Canadian Drug Expert Committee Reconsideration

- a) CADTH prepares the Canadian Drug Expert Committee brief for the request for reconsideration, which includes, but is not limited to the embargoed Canadian Drug Expert Committee recommendation, request for reconsideration, a summary of CADTH's discussions with the manufacturer, and a copy of the original Canadian Drug Expert Committee brief for the drug that is the subject of the request for reconsideration. Five business days are allocated for this task.
- b) The Canadian Drug Expert Committee reconsideration brief is delivered to all Canadian Drug Expert Committee members and the drug plans at least 10 business days before the scheduled Canadian Drug Expert Committee meeting.
- c) If the Canadian Drug Expert Committee needs clarification from either the CDR 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 Canadian Drug Expert Committee meeting, pending the collection of the necessary information.
- d) No one attending the Canadian Drug Expert Committee meeting may introduce new information.
- e) The Canadian Drug Expert Committee will consider all recommendations categories as described in section 7.4 irrespective of the category of recommendation used for the original embargoed recommendation issued to the drug plans and the manufacturer. The Canadian Drug Expert Committee will determine if the original recommendation should be upheld or changed.
- f) The *CDEC Final Recommendation* following the reconsideration is issued to the drug plans and the manufacturer, within five business days following the committee meeting.
- g) Notification of the *CDEC Final Recommendation* following the reconsideration is made as described in section 9.

8.5 Request to Submit Reduced Price During Embargo Period

8.5.1 Resubmission Based on a Reduced Price During the Embargo Period

- a) Every manufacturer that has filed the submission or resubmission for a drug that is the subject of an embargoed Canadian Drug Expert Committee recommendation may file a resubmission based on a reduced price during the embargo period in accordance with section 8.5.1(b) below. A manufacturer may not file a resubmission based on a reduced price during the embargo period if the drug plans have filed the submission, resubmission, or request for advice; however, the manufacturer may file a resubmission in accordance with the [Submission Guidelines for the CADTH Common Drug Review](#) and its review will follow the usual procedure and review timelines.
- b) The resubmission based on a reduced price during the embargo period can be made on the following grounds:
 - The embargoed Canadian Drug Expert Committee recommendation is “Do not list at the submitted price”; **or**
 - The embargoed Canadian Drug Expert Committee recommendation is “List with clinical criteria and/or conditions” where
 - there is a condition of a reduced price in comparison to the submitted price; or
 - cost/cost-effectiveness has been identified as a reason for the recommendation; or
 - cost/cost-effectiveness has been identified as a factor in the “Of Note” section of the recommendation.
- c) A manufacturer shall be entitled to make a resubmission based on a reduced price only once during the embargo period.
- d) Concurrent filing of a request for reconsideration and a resubmission based on a reduced price during the embargo period is not allowed.
- e) A resubmission based on a reduced price during the embargo period is filed by submitting a written request to CADTH.
- f) For any resubmission based on a reduced price during the embargo period, the only new information that will be accepted and reviewed is the reduced price and pharmacoeconomic analyses based on the new price. Other proposals to improve the cost-effectiveness of the drug, including but not limited to product listing agreements, rebates, budget caps, and changes to the indicated population, will not be considered. No new clinical information will be considered.
- g) The submitted reduced price may be a confidential price that will become effective following release of the *CDEC Final Recommendation*. The manufacturer must guarantee that the reduced price will be available to all drug plans.
- h) The manufacturer has 10 business days after receiving notification of the embargoed Canadian Drug Expert Committee recommendation to file a resubmission based on a reduced price during embargo period.
- i) In addition to the standard 10 business days of the 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 the resubmission based on a reduced price during the embargo period, in accordance with the following:

- The request for the extension must be made in writing within 10 business days of receiving the embargoed Canadian Drug Expert Committee recommendation
 - The manufacturer must provide adequate reasons for the requested extension and must indicate when the resubmission based on a reduced price will be submitted
 - The manufacturer must file a resubmission based on a reduced price during the embargo period when an extension is granted
 - The length of the extension will have an impact on the date of the Canadian Drug Expert Committee meeting at which the resubmission based on a reduced price during the embargo period will be scheduled
 - If a manufacturer fails to file a resubmission based on a reduced price during the embargo period 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 9.
- j) CADTH notifies the Canadian Drug Expert Committee and the drug plans of the receipt of the resubmission based on a reduced price during the embargo period.
- k) A resubmission based on a reduced price during the embargo period that is accepted proceeds as quickly as possible for consideration by Canadian Drug Expert Committee. The date of the targeted Canadian Drug Expert Committee meeting for such a resubmission will be determined based on the amount of pharmacoeconomic information related to the price reduction, and the effort required for its review.
- l) If the notice of *CDEC Final Recommendation* has been issued and the manufacturer wishes to resubmit based on a reduced price, the manufacturer will be required to file a resubmission based on new cost information as described in section 2.4.

8.5.2 Review of Resubmission Based on a Reduced Price During the Embargo Period

- a) CADTH will update the *CADTH Common Drug Review Pharmacoeconomic Review Report* (including the pharmacoeconomic evaluation and relevant cost tables) using the reduced price.
- b) The updated *CADTH Common Drug Review Pharmacoeconomic Review Report* will be forwarded to the Canadian Drug Expert Committee in accordance with section 8.5.3, but will not be sent to the manufacturer for comments.
- c) No changes or updates will be made to the *CADTH Common Drug Review Clinical Review Report*.

8.5.3 The Canadian Drug Expert Committee's Consideration of the Resubmission Based on a Reduced Price During the Embargo Period

- a) CADTH prepares the Canadian Drug Expert Committee brief for the resubmission based on a reduced price during the embargo period, which includes, but is not limited to:
- the embargoed Canadian Drug Expert Committee recommendation
 - the request to file a resubmission based on a reduced price during the embargo period
 - the reduced price
 - an updated *CADTH Common Drug Review Pharmacoeconomic Review Report*.

- b) The Canadian Drug Expert Committee brief for the resubmission based on a reduced price during the embargo period is delivered to all Canadian Drug Expert Committee members and the drug plans at least 10 business days before the scheduled Canadian Drug Expert Committee meeting at which it will be considered.
- c) No one attending the Canadian Drug Expert Committee meeting may introduce any other new information.
- d) The Canadian Drug Expert Committee shall review and consider the Canadian Drug Expert Committee brief for the resubmission based on a reduced price during the embargo period. The committee will determine if the original recommendation should be upheld or changed.
- e) The Canadian Drug Expert Committee will make a recommendation and provide reasons for its recommendation regarding the resubmission based on reduced price during the embargo period.
- f) The new embargoed Canadian Drug Expert Committee recommendation regarding the resubmission based on reduced price during the embargo period is issued to the manufacturer and drug plans within five to seven business days following the Canadian Drug Expert Committee meeting.

8.5.4 Potential Outcomes of the Embargoed Canadian Drug Expert Committee Recommendation Following Canadian Drug Expert Committee Consideration of a Resubmission Based on a Reduced Price During the Embargo Period

- a) There shall be no right to file a second resubmission based on a reduced price during the embargo period. If manufacturers wish to file a resubmission based on a price that has been reduced further, they will be required to file a resubmission based on new cost information (section 2.4).
- b) Manufacturers may file a request for reconsideration of the embargoed Canadian Drug Expert Committee recommendation (section 8.4), within 10 business days of receiving the document. If a request for reconsideration is accepted, a *CDEC Final Recommendation* will not be issued until the Canadian Drug Expert Committee has considered the request for reconsideration.
- c) Drug plans may file a request for clarification of the embargoed Canadian Drug Expert Committee recommendation regarding the resubmission based on reduced price during the x-refembargo period within 10 business days of receiving it (section 8.3).
- d) Until the *CDEC Final Recommendation* has been issued (section 9), the embargoed Canadian Drug Expert Committee recommendation regarding the resubmission based on reduced price during the embargo period is not publicly available and drug plans agree not to act on it. All stakeholders shall maintain its confidentiality.

9. NOTICE OF *CDEC FINAL RECOMMENDATION*

9.1 *CDEC Final Recommendation*

- a) The *CDEC Final Recommendation* will be issued in the following circumstances:
- when an embargoed Canadian Drug Expert Committee recommendation has been issued and:
 - a manufacturer does not file, or waives the right to file, a request for reconsideration of the recommendation or a resubmission based on a reduced price during the embargo period within the specified time; and
 - the drug plans have not filed a request for clarification of the recommendation within the specified time; or
 - the drug plans have filed a request for clarification of the recommendation and a clarification has been provided.
 - when an embargoed Canadian Drug Expert Committee recommendation has been issued and:
 - a manufacturer has filed a request for reconsideration, and the Canadian Drug Expert Committee has made a recommendation based on the request for reconsideration; or
 - a manufacturer has filed a resubmission based on a reduced price during the embargo period and the Canadian Drug Expert Committee has made a recommendation regarding the resubmission based on a reduced price during the embargo period for which a request for reconsideration has not been filed.
 - when an embargoed Canadian Drug Expert Committee recommendation has been issued and:
 - a manufacturer fails to file either a request for reconsideration of the recommendation or a resubmission based on a reduced price, after requesting and being granted an extension to the embargo period.
- b) When a *CDEC Final Recommendation* is issued, CADTH will send the following documents to the drug plans and the manufacturer:
- a notice of the *CDEC Final Recommendation*
 - a copy of the *CDEC Final Recommendation*.
- c) 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* (APPENDIX 2) and the redaction procedure described in section 6.6.4. CADTH will indicate that confidential information was used to make the listing decision, and will indicate that the manufacturer requested that this information be kept confidential, pursuant to the *CADTH Common Drug Review Confidentiality Guidelines* (APPENDIX 2).

9.2 Plain Language Version of the *CDEC Final Recommendation*

- a) The *CDEC Final Recommendation* document is rewritten in plain (non-technical) language for use by the general public.⁵
- b) The plain language version of the *CDEC Final Recommendation* is sent to the manufacturer in Microsoft Word format 10 business days following the notice of final Canadian Drug Expert Committee recommendation.
- c) The manufacturer has 10 business days to:
 - Review the plain language *CDEC Final Recommendation* for any confidential information that should be removed.
 - Identify the confidential information to be removed by using the Identification of Confidential Information Form.
 - Identify any errors or inaccuracies in an accompanying letter. The errors or inaccuracies identified by the manufacturer should be presented clearly, their location in the document must be provided, and any proposed corrections should be presented clearly and succinctly.
- d) Based on the manufacturer's response, CADTH corrects any inaccuracies and removes the content that is identified as confidential in accordance with the *CADTH Common Drug Review Confidentiality Guidelines* (APPENDIX 2).
- e) If the manufacturer has not responded to CDR within 10 business days of receipt of the plain language *CDEC Final Recommendation*, CDR will remove any confidential information removed in the corresponding technical version of the *CDEC Final Recommendation* document pursuant to the *CADTH Common Drug Review Confidentiality Guidelines* (APPENDIX 2).
- f) CADTH posts the final version of the plain language *CDEC Final Recommendation* on the CADTH website.

9.3 Drug Plan Decision

- a) Canadian Drug Expert Committee 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.
- b) Drug plans are requested to share their listing decisions with CADTH.

⁵ CADTH has placed a hold on the preparation and posting of plain-language versions of *CDEC Final Recommendations*.

10. WITHDRAWAL FROM THE CADTH COMMON DRUG REVIEW PROCESS

10.1 Withdrawal or Non-Issuance of Market Authorization by Health Canada

- a) If at any time during the CDR process Health Canada withdraws or does not issue marketing authorization for a drug that is the subject of a submission or resubmission to be reviewed or that is actively under review by CDR, the provisions of this section will apply.
- b) In all cases where marketing authorization has been withdrawn or not issued by Health Canada, the manufacturer must advise CADTH, in writing, within five business days and must provide the following information:
 - In the case of submission or resubmission filed on a post-NOC basis, the date on which the marketing authorization was withdrawn and a copy of the Health Canada document providing the reason for withdrawal of marketing authorization.
 - In the case of an application filed on a pre-NOC basis, 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, and a copy of the relevant notice and letter.
- c) CADTH will stop the review of an application immediately upon being notified of, or learning about, the withdrawal of marketing authorization for the drug (or new indication[s]) under review or Health Canada's decision not to issue an NOC or NOC/c for the drug (or new indication[s]).
- d) CADTH will advise the manufacturer and drug plans, in writing, that the review has been stopped. The CDR review process for this drug will not continue, and CADTH will retain a record of the review up to the point that it was stopped.
- e) CADTH will retain and/or dispose of copies of the withdrawn submission or resubmission as described in section 12.
- f) If and when Health Canada issues an NOC or NOC/c or reinstates the marketing authorization, and the applicant wants the drug to be reviewed under the CDR process, the applicant will be required to file a complete submission or resubmission (depending on whether the review that was under way at the time of withdrawal was a submission or resubmission) in accordance with the [Submission Guidelines for the CADTH Common Drug Review](#). The re-filed submission or resubmission must contain information that addresses the reason(s) for the withdrawal and provide either a copy of the Health Canada documentation indicating reinstatement of the marketing authorization, or issuing a marketing authorization (i.e., NOC or NOC/c).
- g) When Health Canada withdraws marketing authorization for a drug for which CADTH has issued a notice of *CDEC Final Recommendation*, the submission status report on the CADTH website will be updated accordingly.

10.2 Voluntary Withdrawal by the Applicant

An applicant may request that a submission or resubmission be withdrawn from the review process at any time up to the targeted date on which CADTH is scheduled to issue the notice of *CDEC Final Recommendation* (as indicated in the CDR submission status report for that submission, resubmission, or request for advice on the CADTH website). The applicant must submit to CADTH a dated written request for withdrawal that has the following information:

- the name and signature of the applicant
- the reason that the request for withdrawal is being made
- whether or not the applicant expects to re-file the withdrawn submission, resubmission, or request for advice again, and if so, the anticipated time frame.

a) A Request for Withdrawal by the Manufacturer

Upon receipt of a request for withdrawal from a manufacturer, CADTH will withdraw the submission or resubmission as follows:

- CADTH will remove the submission or resubmission from the review queue if the review has not been initiated, or will stop its review of the submission or resubmission, and will inform the manufacturer in writing of having done this.
- CADTH will notify the drug plans when it receives a request for withdrawal of a submission or resubmission from a manufacturer.
- CADTH will post “voluntary withdrawal” by the manufacturer as the reason for the withdrawal on the CADTH website.
- CADTH will retain and/or dispose of the withdrawn submission or resubmission as described in section 12.

b) A Request for Withdrawal by the Drug Plans

Upon receipt of a request for withdrawal from the drug plans regarding a submission, resubmission, or request for advice that was filed by the drug plans, CADTH will withdraw the submission, resubmission, or request for advice as follows:

- If the review has not been initiated, CADTH will remove the submission or resubmission from the review queue.
- If the review has been initiated, CADTH will stop its review of the submission, resubmission, or request for advice.
- CADTH will inform the drug plans in writing of having withdrawn the submission, resubmission, or request for advice.
- CADTH will notify the drug manufacturer when it receives a request for withdrawal of a submission, resubmission, or request for advice from the drug plans.
- CADTH will post “voluntary withdrawal” by the drug plans as the reason for the withdrawal on the CADTH website.
- CADTH will retain and/or dispose of the withdrawn submission, resubmission, or request for advice as described in section 12.

10.3 Re-Filing Submissions and Resubmissions After Withdrawal

- a) The applicant is required to re-file a complete submission or resubmission in accordance with the [Submission Guidelines for the CADTH Common Drug Review](#).
- 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., 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 a NOC/c, the applicant is required to file a complete submission following the requirements for a submission filed on post-NOC basis in accordance with the *Submission Guidelines for the CADTH Common Drug Review* in order for the review to proceed.
- d) Submissions being re-filed after withdrawal will be screened according to the procedure described in section 4.3 and resubmissions being re-filed after withdrawal will be screened according to the procedure described in section 4.4.
- e) CADTH considers the nature of the submission or resubmission being re-filed and determines the appropriate approach for reviewing it. The applicant is apprised.

11. TEMPORARY SUSPENSION OF A REVIEW

11.1 Temporary Suspension of a CDR Review Due to Incomplete Information

In the event that the CDR review team 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, in its sole discretion, may temporarily suspend a review pending receipt of all required information.
- b) CADTH will advise the manufacturer in writing that the review of the submission or resubmission is temporarily suspended. CADTH will indicate the information that is required by the CDR review team in order to re-initiate the review process.
- c) The *CADTH Common Drug Review Clinical and Pharmacoeconomic Review Report(s)* will not be sent to the manufacturer for comment and the submission or resubmission will not be placed on the Canadian Drug Expert Committee agenda until the review team is satisfied that the manufacturer has provided all information required to conduct a thorough review of the submission or resubmission.
- d) 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, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.
- e) The review of the submission or resubmission may be temporarily suspended during any stage of the review process before the CDR review report(s) are sent to the manufacturer for comments and redaction requests.

- f) A suspended submission or resubmission is tracked in the submission status report on CADTH's website.

11.2 Temporary Suspension of a CDR Review 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 of the submission or resubmission in the following manner:

- a) CADTH will advise the manufacturer in writing that the review of the submission or resubmission is 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 CDR 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 of the submission or resubmission 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 in the submission status report on the CADTH website.

12. DISPOSITION OF SUBMISSION AND RESUBMISSION DOCUMENTS

The issuance of the notice of *CDEC Final Recommendation* and the posting of the CDR review report(s) signal the completion of the CDR review of a submission, resubmission, or request for advice. CADTH then undertakes the steps detailed in the *CADTH Common Drug Review Confidentiality Guidelines* (APPENDIX 2) regarding the retrieval, disposal, and archiving of media storage devices and files associated with the review. CADTH also follows this document disposition procedure for a withdrawn submission or resubmission.

APPENDIX 1: GUIDELINES FOR MANUFACTURERS ON APPLICATION FEES FOR THE CADTH COMMON DRUG REVIEW

1. INTRODUCTION

This document provides guidelines to manufacturers on the application fee for the review of a drug submission or resubmission filed with the CADTH Common Drug Review. CADTH may amend, from time to time, the *Guidelines for Manufacturers on Application Fees for the CADTH Common Drug Review* (hereafter referred to as the Guidelines on Application Fees) and all matters related to the Common Drug Review. Amendments to, and clarifications of, the Guidelines on Application Fees may be effected by means of directives (called [CDR Updates](#)) issued by CADTH on an “as needed” basis between formal revisions of the document. Any changes to the Guidelines on Application Fees will be applied prospectively.

The Guidelines on Application Fees were established to ensure that the appropriate amounts of CADTH Common Drug Review fees are being recovered from the applicants in accordance with the mandate of the Conference of Deputy Ministers of Health. The fees will supplement existing federal, provincial, and territorial funding and will be used to help finance an increase in the number of drugs CADTH reviews annually.

1.1 Scope

This document applies to all drug review applications filed by manufacturers with the CADTH Common Drug Review for drug submissions, resubmissions, requests for a resubmission based on a reduced price during the embargo period, and requests for reconsideration. The Guidelines on Application Fees must be read in conjunction with the following documents found on CADTH’s website.

- [Submission Guidelines for the CADTH Common Drug Review](#)
- [Procedure for the CADTH Common Drug Review](#)
- [Targeted Time Frames for Key Milestones in the CADTH Common Drug Review Process](#).

1.2 Background

Application fees are required for all drug submissions and resubmissions filed by manufacturers for review through the CADTH Common Drug Review process, which is a pan-Canadian process for conducting objective, rigorous reviews of the clinical effectiveness and cost-effectiveness, as well as reviews of patient input for drugs and providing formulary listing recommendations to Canada’s publicly funded drug plans, excluding that of Quebec. Application fees will not apply to any submission, resubmission, or request for advice filed by the CADTH Common Drug Review participating drug plans.

2. IMPLEMENTATION GUIDELINES

This section provides information on the fee amounts, the types of fees charged, and guidelines on refunds.

2.1 General Contact Information

For questions regarding invoicing and the timing of the application fees payment or questions about your account, please contact Accounts Receivable by phone at 613 226 2553 ext. 1314, fax 613 226 5392, or email at accountsreceivable@cadth.ca. Please have your customer and invoice numbers readily available.

For questions regarding the type of fee charged for your application, please contact CADTH Central Intake by phone 613 226 2553, fax 613 226 5392, or email at requests@cadth.ca.

2.2 Fee Payment Procedures

All payments must be made in Canadian funds. Payments must be made payable to either “CADTH” or the “Canadian Agency for Drugs and Technologies in Health.”

2.2.1 Application Fee Schedule

Application fees will be charged based on the schedule in Table 1 plus applicable taxes. Applicable taxes include GST/HST, or QST.

| Schedule | Application Type ^a | Fee |
|----------|---|----------|
| A | Submission for a new drug for review of a single indication | \$72,000 |
| | Submission for an existing drug for the review of a new indication | |
| | Submission for a new combination product for review of a single indication | |
| B | Each subsequent new indication ^b filed at the same time or sequentially for the three application types listed in schedule A | \$57,600 |
| | Resubmission based on new clinical information with or without new cost information | |
| C | Submission for a new combination product (funded components or CADTH designated tailored reviews) | \$36,000 |
| | Submission for a subsequent entry biologic | |
| D | Resubmission based on new cost information only | \$7,000 |
| | Request for a resubmission based on a reduced price during the embargo period | |
| | Request for reconsideration of an embargoed CDEC recommendation | |

CDEC = Canadian Drug Expert Committee.

^a Application types under schedules A and B would typically undergo a standard CDR review. Application types under schedule C would typically undergo a tailored CDR review. The various application fee schedules reflect the relative difference in estimated effort for the review of the various application types.

^b When an application is filed for the review of multiple indications at the same time and CADTH decides to conduct a standard CDR review for each indication, an application fee of \$72,000 will apply to only one of these indications and an application fee of \$57,600 (20% discount) will apply to each of the other indication(s) to be reviewed. In addition, for each subsequent indication for a drug filed sequentially at a later date, an application fee of \$57,600 will apply.

Fees will be charged at two Common Drug Review process milestones for Schedule A, Schedule B, and Schedule C submissions. Schedule D fees will be charged at one milestone. Table 2 sets out the milestones.

| Schedule | Milestone 1 | | | Milestone 2 | | | Total Fee |
|----------|----------------------|--------------|------------|-------------------------------------|--------------|------------|-----------|
| | Description | Per Cent Due | Amount Due | Description | Per Cent Due | Amount Due | |
| A | Initiation of review | 70% | \$50,400 | Sending reports to the manufacturer | 30% | \$21,600 | \$72,000 |
| B | | 70% | \$40,320 | | 30% | \$17,280 | |
| C | | 70% | \$25,200 | | 30% | \$10,800 | |
| D | Request accepted | 100% | \$7,000 | NA | 0% | \$0 | \$7,000 |

NA = not applicable.

2.2.2 Submission of Payment

An initial invoice for the application fee owing will be sent once a submission or resubmission accepted for review by CADTH has been initiated. For a request for reconsideration or a resubmission based on a reduced price during the embargo period, an invoice for the application fee will be sent once the request has been accepted by CADTH for consideration at the next available Canadian Drug Expert Committee (CDEC) meeting.

Payments are to be sent to:

CADTH

Attn: Accounts Receivable
 600–865 Carling Avenue
 Ottawa, ON
 K1S 5S8
 Canada

All CADTH Common Drug Review application fees are due within 30 calendar days of receipt of an invoice. If fee payment for a submission, resubmission, resubmission based on a reduced priced during the embargo period, or request for reconsideration is not received within 30 days, the following will occur:

- A reminder will be provided indicating that payment is past due. It is the sole responsibility of the applicant to pay any fees by the due date and although it is CADTH’s intention to send subsequent reminders of unpaid fees, it shall not be obligated to do so.
- If payment remains outstanding after 45 calendar days, all work on the drug review will be temporarily suspended. Once a review is suspended, there is no assurance that the review will be completed in time for the originally targeted CDEC meeting. If the review of an application has been temporarily suspended due to non-payment of fees, CADTH makes no commitments or guarantees as to the date on which such work will be resumed, or the CDEC meeting at which the application will be considered.
- Once payment in full is received, CADTH will resume its work on the suspended application as soon as it can be reasonably accommodated based on available resources and application volumes.

- In the case of a request for reconsideration, the *CDEC Final Recommendation* will not be issued until full payment is received by CADTH.

Acceptable forms of payment include cheques, money orders, international bank drafts, credit cards (Visa, MasterCard), and wire transfers. Only Canadian funds are accepted.

Cheques, money orders, and international bank drafts should be made payable to “CADTH” or the “Canadian Agency for Drugs and Technologies in Health.” Cheques drawn from non-Canadian banks must be issued in coordination with a referenced Canadian bank (that is, referenced on the cheque); otherwise they will not be accepted. If insufficient fees are received, the drug submission, resubmission, or request for clarification or resubmission based on a reduced price during the embargo period will be returned to the applicant. Fees paid by a cheque that is not cleared through the CADTH bank account due to insufficient funds (NSF) will be considered outstanding. Any fees associated with the NSF cheque incurred by CADTH will be charged to the manufacturer. Any other fees associated with stop payment requests, closed account fees, or any other such charges will also be charged back to the manufacturer. Post-dated payments will not be accepted. Any overpayments will be refunded to the applicant.

Credit card payments (Visa, MasterCard) are accepted if the following information is provided:

- Cardholder’s full credit card number
- Cardholder’s name (as it appears on the credit card), address, and telephone number
- Expiry date of the credit card.

To pay by credit card, please complete the appropriate section on the invoice and return it to CADTH at the address provided on the previous page or call CADTH Accounts Receivable at 613 226 2553 ext. 1314.

Wire payments of invoiced fees will be accepted only when wired in Canadian funds as specified on the invoice.

Please include your company name, product name, and invoice number with any wire payments.

Please ensure all service charges, including fees charged by your bank or any intermediary banks, are covered by your payment. CADTH is not responsible for any fees charged during the transfer process. Failure to pay the full amount outstanding will result in a balance owing on your account. Any payments sent in non-Canadian funds will be rejected. If problems occur with the transaction, please contact TD Canada Trust at 613 783 6619.

2.2.3 Performance Metrics for the CADTH Common Drug Review Process

| Table 3: Performance Metrics | | | |
|---|---------------------------|--------------------------|----------------------------------|
| Submissions | Performance Metric | Compliance Target | Refund for Non-Compliance |
| Screening of submission or resubmission and “Acceptance for Review” | 10 business days | 100% | NA |

Table 3: Performance Metrics

| Submissions | Performance Metric | Compliance Target | Refund for Non-Compliance |
|--|--------------------|-------------------|---|
| Date of "Acceptance for Review" to date of issuance of embargoed CDEC recommendation | 180 calendar days | 95% | 25% of the application fee payable back to the manufacturer |

CDEC = Canadian Drug Expert Committee; NA = not applicable.

Subject to the exceptions set forth below, if a refund is payable to an applicant based on non-compliance with the metric (i.e., not meeting the timelines for date of "Acceptance for Review" to date of issuance of embargoed CDEC recommendation), a refund as per Table 3 will be provided.

There may be instances in which CADTH is prevented from achieving the performance metric due to circumstances beyond the reasonable control of CADTH, including without limitation those circumstances set forth in Table 4 below. CADTH shall not be in breach of the performance metrics and shall not incur any liability to the applicant or be responsible for any refund of application fees if and to the extent it is delayed and prevented from achieving the performance metrics due to circumstances beyond its control. During the period that such circumstances continue, the timelines shall be suspended. CADTH shall resume its work as soon as reasonably possible and the performance metric timelines shall resume from the date on which CADTH is reasonably able to resume its work.

Table 4: Factors^a That May Influence Common Drug Review Timelines

| Scenario |
|---|
| • Voluntary withdrawal by the applicant |
| • Time required for the applicant to provide additional information |
| • Temporary suspension of a review by CADTH due to incomplete information |
| • Substantial deviation between the proposed indication provided at the time of filing a submission on a pre-NOC basis and the final indication approved by Health Canada |
| • Temporary suspension of a review by CADTH due to non-payment of the application fee |
| • Deferral of the recommendation by CDEC pending clarification on specific issues |
| • Withdrawal of marketing authorization for a drug by Health Canada |
| • Non-issuance of marketing authorization by Health Canada |
| • Delay in issuing marketing authorization by Health Canada |

CDEC = Canadian Drug Expert Committee; NOC = Notice of Compliance.

^a Further context for these factors is provided in the *Procedure for the CADTH Common Drug Review*.

Please refer to the [Procedure for the CADTH Common Drug Review](#) and any applicable [CDR Updates](#) (subsequent to *CDR Update – Issue 108*) for details regarding each of the scenarios noted in Table 4.

There may be other factors not included in the preceding table that are beyond CADTH's control and may impact the timing of a review. The determination as to whether a circumstance leading to a delay is beyond the reasonable control of CADTH shall be made by CADTH, acting reasonably, and shall be final and binding on the applicant and all other parties. CADTH shall

advise the applicant in writing, as soon as practicable after such circumstances arise, of the delay and the circumstances beyond the control of CADTH that have resulted in the delay.

2.2.4 Refunds of Application Fees

Except as expressly provided for in this guidance document, application fees are non-refundable regardless of the *CDEC Final Recommendation*.

Manufacturers who voluntarily withdraw from the CDR process shall be entitled to receive a partial refund of the application fees in the following circumstances:

- Those who voluntarily withdraw from the CDR process after initiation of a review and before the *CDR Clinical and Pharmacoeconomic Review Report(s)* are sent to the manufacturer shall receive a refund of 50% of the total amount invoiced.
- Those who voluntarily withdraw after the *CDR Clinical and Pharmacoeconomic Review Report(s)* have been sent to the manufacturer, but before the date of the CDEC meeting at which the drug is scheduled to be reviewed, shall receive a refund of 25% of the total amount invoiced.

No refunds will be issued for voluntary withdrawal after the submission or resubmission has been reviewed by CDEC.

Fees for requests for a resubmission at a reduced price during the embargo period are always non-refundable.

| Refund Amount | Time of Voluntary Withdrawal From the CADTH Common Drug Review Process |
|----------------------|--|
| 50% refund | Before the CDR review reports are sent to the manufacturer |
| 25% refund | After the manufacturer has received the CDR review reports, but before the targeted CDEC meeting |
| No refund | On or after the date of the targeted CDEC meeting |

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

2.3 Deferred Fees and Fee Exemptions

Application fees for submissions, resubmissions, requests for resubmission based on a reduced price during the embargo period, and requests for reconsideration are not eligible for any application fee deferral or exemptions.

APPENDIX 2: CADTH COMMON DRUG REVIEW CONFIDENTIALITY GUIDELINES

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

Confidential Information

Manufacturer's must clearly and obviously label or mark any confidential information as such. Only information labelled in this manner will be considered as confidential, and CADTH will only be bound by the terms of these guidelines for labelled information. Confidential information includes any non-public 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 which does not include information that:

- was already in the possession of CADTH, external reviewer(s) assigned to review the submission or resubmission, Canadian Drug Expert Committee members, external experts (when contracted to provide specific information in relation to the submission or resubmission), federal, provincial, territorial (F/P/T) governments (including their agencies and departments) or the Patented Medicine Prices Review Board (PMPRB); without restriction as to its use or disclosure
- is or becomes available to the general public other than as a result of a breach of the procedures contained herein (information available to the general public includes but is not limited to published articles, drug prices, and product monographs)
- a third party (who is not under any obligation as to confidentiality or non-disclosure) rightfully discloses to CADTH, external reviewer(s) assigned to review the submission or resubmission, Canadian Drug Expert Committee members, external experts (when contracted to provide specific information in relation to the submission or resubmission), F/P/T governments (including their agencies and departments), or PMPRB; 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.

Handling Confidential Information

1. Responsibilities of CADTH

- CADTH will use reasonable care to prevent the unauthorized use, disclosure, publication, or dissemination of confidential information that is labelled confidential and included in and related to submissions and resubmissions
- 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
- CADTH will use the submission or resubmission and confidential information solely for the purpose of carrying out its responsibilities with respect to the Common Drug Review

- CADTH shall utilize secure filing and storage, websites, and tracking processes for handling submissions or resubmissions and confidential information.

2. Release of Manufacturer's Information

- a) CADTH may release a manufacturer's submission or resubmission, including confidential information, to the following "authorized recipients":
 - CADTH staff
 - CDR review team members (including contractors and clinical experts)
 - Canadian Drug Expert Committee members
 - F/P/T government representatives (including their agencies and departments)
 - PMPRB representatives.
- 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 above have their own confidentiality procedures and are subject to freedom of information and access to information legislation over which CADTH has no control. By filing a submission or resubmission, manufacturers consent to their information, including confidential information, being exchanged with F/P/T governments (including their agencies and departments) and the PMPRB by signing a template letter provided in the *Submission Guidelines for the CADTH Common Drug Review*.
- 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) All CDR review team members, Canadian Drug Expert Committee members, and external experts must abide by the confidentiality clauses contained in their Code of Conduct and/or Conflict of Interest Guidelines and/or contracts.
- e) CADTH's Drug Policy Advisory Committee (DPAC) Formulary Working Group (FWG) members are required to sign a non-disclosure agreement requiring them to comply with these confidentiality guidelines.

3. Documents Shared with Authorized Recipients

- a) The documents which CADTH may share with the authorized recipients include:
 - Manufacturer's submission or resubmission
 - Redacted and unredacted CDR review report(s)⁶
 - Manufacturer's comments about CDR review report(s)
 - CDR review team's responses to manufacturer's comments
 - Embargoed Canadian Drug Expert Committee recommendation
 - *CDEC Final Recommendation*
 - *CDEC Record of Advice*
 - CDEC brief

⁶ The term "CDR review report(s)" in this document refers to the CADTH *Common Drug Review Clinical Review Report* and *Common Drug Review Pharmacoeconomic Report* typically prepared for a standard CDR review and/or the combined CADTH *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.

- CDEC reconsideration brief.
- b) CADTH provides the following documents to the submitting manufacturer. The manufacturer shall maintain the confidentiality of these documents.
- CDR review report(s)
 - Embargoed Canadian Drug Expert Committee recommendation
 - Canadian Drug Expert Committee recommendation on reconsideration
 - Technical version of the *CDEC Final Recommendation* (until posted on CADTH website)
 - Plain language version of the *CDEC Final Recommendation* (until posted on CADTH website)
 - Response to request for clarification (if applicable).
- c) The documents which CADTH may post on its website include:
- Tracking document indicating the status of a CDR review, including a submission filed on a pre-NOC basis.
 - *CDEC Final Recommendation* with confidential information redacted (both the technical version and the plain language version).
 - CDR review report(s) with confidential information redacted, as per the current *Procedure for the CADTH Common Drug Review*.
 - *CDEC Record of Advice*.

4. Making Reference to Confidential Information in Public CADTH Common Drug Review Documents

CADTH may use confidential information supplied by the manufacturer in the preparation of the CDR review report(s), Canadian Drug Expert Committee recommendations, *CDR Request for Advice* reports, 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. The following principles and provisions shall apply:

The following provisions will apply to any confidential information which the manufacturer requests to be redacted from the 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 (e.g., confidential price, unpublished study results) that was redacted.
- Confidential submitted prices will be redacted; however, 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), 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*.

5. Archiving of Documents Containing Confidential Information

- a) CADTH may retain two master copies of electronic documents, including documents containing confidential information associated with the review of a drug, for as long as there may be a need to consult them, as follows:
 - one copy is kept securely on a CADTH server
 - one copy is kept on the manufacturer-provided media (CDs, DVDs or USB flash drives) in secure storage.
- b) One complete set of all hard copy documents,⁷ including documents containing confidential information associated with the review of a drug, is kept on file by CADTH in secure storage for as long as there may be a need to consult them.
- c) CADTH will determine at its sole discretion if there is a need to consult this information.
- d) CADTH staff undertakes regular reviews of archived material. Any material that CADTH determines to be no longer required is disposed of, as described in section 6.

6. Disposal of Documents Containing Confidential Information

- a) CADTH disposes of extra hard copies⁷ of the submission or resubmission.
- b) CADTH disposes of electronic documents on any manufacturer-provided media (CDs, DVDs, USB flash drives), other than the copies which are retained as per paragraph 5 a) of these guidelines.
- c) At the completion of a review, reviewers are directed to delete all electronic documentation that was provided during the review, which includes confidential information that may have been stored on the hard drive of a computer or in emails.

⁷ If applicable. CADTH discontinued the requirement for hard copies of category 1 requirements for all CDR submissions received on or after October 9, 2013.

APPENDIX 3: KEY DEFINITIONS

The following are high-level definitions for key terms used in the *Procedure for the CADTH Common Drug Review* and [Submission Guidelines for the CADTH Common Drug Review](#) documents. Readers should consult the appropriate sections of the documents 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 CDR is made on a case-by-case basis.

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 current listing of CADTH business days.

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.

Common Drug Review (CDR) 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 CDR review team may include CADTH staff, contracted reviewers, and external experts with appropriate qualifications and expertise.

Canadian Drug Expert Committee (CDEC) — an appointed, national, independent advisory committee to CADTH that makes drug-related recommendations and provides drug-related advice through CDR and Therapeutic Review processes. The Canadian Drug Expert Committee

is composed of individuals with expertise in drug therapy, drug evaluation and drug utilization, and public members to bring a lay perspective. The Canadian Drug Expert Committee 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 the Canadian Drug Expert Committee. The Canadian Drug Expert Committee 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 — 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 the Canadian Drug Expert Committee in response, in cases where a request for advice has not resulted in a revised Canadian Drug Expert Committee recommendation.

Canadian Expert Drug Advisory Committee (CEDAC) — CEDAC was replaced by the Canadian Drug Expert Committee 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.

Confidentiality Guidelines — refer to the *CADTH Common Drug Review Confidentiality Guidelines* document (Appendix 2).

Confidential Price — a price per unit that is submitted in confidence, as part of the CDR submission requirements and to which the provisions of the *CADTH Common Drug Review Confidentiality Guidelines* apply.

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 [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's reception desk.

Date of Initiation of a Review — the date on which the CDR review team kicks off 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 CDR.

Embargo Period — refers to the period of time following the issuance of an embargoed Canadian Drug Expert Committee recommendation, during which the embargoed Canadian Drug Expert Committee recommendation is neither acted on by drug plans nor is publicly available. During this period, the manufacturer may submit a request for reconsideration or a resubmission based on a reduced price, 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 Canadian Drug Expert Committee 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 Canadian Drug Expert Committee 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.

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 NOC or NOC/c 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 90 calendar days of the submission being filed.

Priority Review — a preferred status in the review queue for drugs meeting the CDR priority review criteria. All steps in the CDR process are completed and timelines are not truncated.

Queuing — see **CDR Queuing**

Reasons for Recommendation — these represent the key considerations and rationale used by the Canadian Drug Expert Committee in formulating the recommendation.

Request for Advice — a written request made by drug plans for Canadian Drug Expert Committee advice regarding a previous Canadian Expert Drug Advisory Committee or *CDEC Final Recommendation*. A request for advice can result in a revised Canadian Drug Expert Committee recommendation or a *CDEC Record of Advice*.

Request for Clarification — a written request from drug plans for clarification of an embargoed Canadian Drug Expert Committee recommendation.

Request for Reconsideration — a written request from a manufacturer for an embargoed Canadian Drug Expert Committee recommendation to be reconsidered.

Request for 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.

Review Team — see **CDR Review Team**

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, new combination product (funded components), or a subsequent entry biologic.

Submission Guidelines — the guidelines adopted by CADTH that outline how submissions and resubmissions from manufacturers must be prepared and submitted.

Submission or Resubmission Requirements — information that is required by CADTH to review a submission or resubmission through the CDR process.

Submission Status Report — a document posted on the CADTH website for every CDR submission, resubmission, or request for advice filed with CADTH that provides key targeted time frames and the status of the review. The report is generally updated on a weekly basis.

Submitted Price — the price per unit that is submitted to CDR and that must not be exceeded for any of the drug plans following release of a *CDEC Final Recommendation*,⁸ irrespective of the type of recommendation made and whether or not the Canadian Drug Expert Committee criteria for listing are the same as the criteria requested by the manufacturer.

Subsequent Entry Biologic (SEB) — 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). Similarity between an SEB and the reference product is established in accordance with Health Canada’s [Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics \(SEBs\)](#), for the authorized indications.

⁸ A *CDEC Final Recommendation* is non-binding on the drug plans. Each of the drug plans subsequently makes its own drug-listing decisions based on the Canadian Drug Expert Committee recommendation in addition to other factors, including the plan’s mandate, jurisdictional priorities, and financial resources.

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 — a review of publicly available evidence regarding a single drug, a therapeutic category of drugs, or a pharmacologic class of drugs. The scope and depth of the review are determined by jurisdictional needs. An important characteristic of a therapeutic review is that it is conducted to coincide with a CDR submission review, and thus informs the CDR submission review and listing recommendation and informs drug plan decisions.

APPENDIX 4: CADTH CONTACT AND CADTH COMMON DRUG REVIEW APPLICATION FILING INFORMATION

| Table 8: How and Where to Direct CDR-Related Inquiries or CDR Applications | |
|---|---|
| Type of Inquiry or CDR Application | How and Where to Direct |
| <ul style="list-style-type: none"> • General CDR inquiries • CDR process or procedure-related inquiries | In writing to: Email: requests@cadth.ca Fax: 613-226-5392 Mail⁹: Central Intake CADTH 600-865 Carling Avenue Ottawa, ON K1S 5S8 |
| Filing CDR applications for a submission or resubmission | By registered mail, ⁹ courier, or in person to: Central Intake CADTH 600-865 Carling Avenue Ottawa, ON K1S 5S8 |
| Inquiries regarding a CDR application for which the review has been initiated | By email to: The designated submission coordinator contact provided by CADTH in the category 1 requirement acceptance letter |
| Inquiries regarding CDR application fees | In writing to: Email: requests@cadth.ca |

CDR = CADTH Common Drug Review.

| Table 9: Delivery Times | |
|---|--|
| Means of Delivery | When Considered to Have Been Delivered |
| By courier, registered mail, regular mail, in person | <ul style="list-style-type: none"> • On the day of receipt by CADTH's reception desk |
| Email or fax | <ul style="list-style-type: none"> • On the day of transmittal if sent during CADTH business hours • On the business day that normal business hours next occur, if sent outside of CADTH business hours <p>For CADTH business hours and holiday schedule, please check the CADTH website www.cadth.ca, under "Contact Us."</p> |

⁹ If the party sending a CADTH Common Drug Review–related inquiry or other correspondence, or filing a CADTH Common Drug Review application knows, or should reasonably know, of any disruption or difficulty with the postal system that might affect the delivery of mail, any such inquiry, correspondence, or CADTH Common Drug Review application should not be mailed, and should instead be delivered to CADTH by electronic means, if applicable (e.g., resubmissions based on a reduced price during the embargo period may be submitted by email; CADTH Common Drug Review applications cannot be filed electronically), by courier, or in-person delivery.