Proposal to Revise Category 1 Requirements for CADTH Single Technology Reviews

1 Proposal Objectives

CADTH would like to invite stakeholder comments on a proposal to revise category 1 requirements to further support single technology reviews through both the CADTH Common Drug Review (CDR) and the CADTH pan-Canadian Oncology Drug Review (pCODR) programs. Proposed additions to category 1 requirements include:

- a systematic review of the clinical literature
- complete clinical study reports
- current reimbursement status table
- a budget impact analysis.

The requirements for submission will be dependent upon the CADTH review type, as described in Table 1.

Table 1: Proposed New Category 1 Requirements

Proposed Requirements	CADTH Review Type	
	Standard	Tailored
Systematic Review	Required	Not required
Clinical Study Reports	Required	Required
Reimbursement Status Table	Required	Required
Budget Impact Analysis	Required	Required

2 Proposed Changes to Category 1 Requirements

2.1 Systematic Review of the Literature

In the existing CDR and pCODR processes, CADTH conducts both standard and tailored reviews, depending upon the type of submission being filed.

- **Standard review:** consists of CADTH conducting a systematic review of the submitted clinical evidence in addition to clinical studies identified through its independent systematic literature search, and an appraisal of the submitted pharmacoeconomic evaluation.
- **Tailored review:** consists of CADTH conducting an appraisal of both the submitted clinical evidence and pharmacoeconomic evaluation using a CADTH-provided review template that is specific to the type of drug product to be reviewed.

Standard reviews are typically conducted for new drugs and drugs with new indications, and tailored reviews are typically conducted only for a subset of new combination products (e.g., those where the individual components are already reimbursed by the public drug plans). A key difference between the standard and tailored review processes is that the standard review process involves CADTH conducting a systematic literature review and summarizing the relevant clinical evidence (see section 7.2.1. of the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and section B4.1 of the *pCODR Procedures* for additional details on the current standard review process).

CADTH is proposing that a systematic literature review be a category 1 requirement for all submissions and resubmissions being reviewed through the standard review process.

Major components of the systematic review should include:

- an explicit protocol that describes the scope of the systematic review with respect to the PICOS (patient population — including relevant subgroups, intervention, comparators, outcomes, study designs)
- a description of the search strategy, process for screening, study selection, and data extraction
- a flow chart for the selection of included studies, a list of included and excluded studies
- a description of study characteristics for each individual-included study (design, participants, interventions, outcomes, statistical analysis plan)
- a description of the individual study results in terms of baseline and demographic characteristics, patient disposition, and efficacy and safety results for the full patient population and relevant subgroups.

Submitters will be encouraged to make use of the opportunity for pre-submission meetings with CADTH to discuss the specifics of their proposed protocol.

As part of the review process, CADTH will prepare a clinical review report that includes:

- a validation and critical appraisal of the submitted systematic review
- a summary and critical appraisal of all relevant indirect treatment comparisons (either submitted and/or identified by CADTH)
- the identification, synthesis, and critical appraisal of additional relevant evidence from studies that do not meet the systematic review protocol but that address important gaps in the evidence
- an integration of stakeholder perspectives, including patient groups, clinical experts, and public drug programs
- an overall interpretation of the available clinical evidence for the drug under review relative to appropriate comparators.

CADTH's clinical report may cite for public disclosure data or other types of evidence obtained from any of the category 1 requirements (e.g., systematic review, sections of the common technical document, publications, clinical study reports, full technical reports of any indirect treatment comparisons) or pursuant to a request from CADTH to the manufacturer for additional information.

Stakeholders should also note the following: Both the submitted systematic review and CADTH's clinical report will be posted on the CADTH website without redactions following the posting of the final recommendations. This is accordance with the ongoing consultation *Proposal to Enhance Transparency of CADTH's Review Reports and Recommendations.*

2.2 Complete Clinical Study Reports

Clinical study reports are not currently a category 1 requirement. However, routine requests by CADTH to manufacturers to provide clinical study reports are almost universally complied with. Clinical study reports provide the most complete details regarding the design, conducting of, and results of clinical trials, and will be required by CADTH to validate information provided in the systematic review. To ensure fairness for all, CADTH is proposing to make complete clinical study reports a category 1 requirement. Final or interim clinical study reports should be provided in full and include both the complete study protocol and analysis plan.

2.3 Reimbursement Status for Comparators

For all CADTH reviews conducted through the CADTH CDR and pCODR processes, information regarding the reimbursement status of relevant drugs is summarized for consideration by the review teams and expert committees. The approach to obtaining this information currently differs between the standard and tailored review processes:

- Applicants are required to complete a table summarizing the reimbursement status of drugs in the tailored review process.
- CADTH summarizes the reimbursement status of relevant comparator drugs in the standard review process, with input from the drug plans.

CADTH has reviewed its processes and determined that there would be value in having the applicant provide a summary of the reimbursement status for all relevant comparator drugs at the time a submission or resubmission is filed. This would help facilitate screening of the pharmacoeconomic submission requirements and reduce the risk of potential delays during the review process.

CADTH is proposing that the following standardized template be used to summarize the reimbursement status of relevant comparator drugs.

2.3.1 Proposed Template for Reimbursement Status for Comparators

Please provide the publicly available listing status and criteria for all relevant comparators. CADTH may update the information provided by the applicant with new information provided by the participating drug programs, as required.

Step 1: Please use a separate table for each indication being reviewed by CADTH.

Step 2: Add the non-proprietary and brand names for each relevant comparator and use a separate row for each comparator.

Step 3: Use the following abbreviations to complete the table:

Abbreviation	Description
EX	Exception item for which coverage is determined on a case-by-case basis
FB	Full benefit
NB	Not a benefit
RES	Restricted benefit with specified criteria (e.g., special authorization, exception drug status, limited use benefit)
CADTH	Under review by CADTH
pCPA	Under negotiation by the pan-Canadian Pharmaceutical Alliance
FPT	Under consideration by the federal, provincial, and territorial drug plans
–	Information not available

Table 2: Reimbursement Status for Relevant Comparators for the Treatment of (State the Indication)

Comparators	Participating Drug Plans													
	BC	AB	SK	MB	ON	NB	NS	PE	NL	YT	NT	NIHB	DND	VAC
Brand (Generic)														
Brand (Generic)														

Brand (Generic)														
Brand (Generic)														

AB = Alberta, BC = British Columbia, DND = Department of National Defence; MN = Manitoba; NIHB = Non-Insured Health Benefits Program; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan; VAC = Veterans Affairs Canada; YT = Yukon.

Step 4: For all restricted benefit entries (RES), please state the criteria used by each drug plan. Use a separate table for each indication and add or delete rows, as necessary.

Table 3: Reimbursement Criteria for (Comparator) for (State the Indication)

Drug Plan	Criteria for Restricted Benefit
Add name	State the exact criteria
Add name	State the exact criteria
Add name	State the exact criteria

2.4 Budget Impact Analysis

CADTH currently conducts a review and appraisal of a pan-Canadian budget impact analysis (BIA) as part of the CADTH pCODR process for oncology drugs. For non-oncology drugs, this work is provided as implementation support for the pan-Canadian Pharmaceutical Alliance (pCPA) and the participating drug programs on a case-by-case basis. To promote alignment across CADTH's drug review processes and to provide additional support for the jurisdictions, CADTH will be including a review and appraisal of a manufacturer-submitted BIA as part of the CADTH CDR process.

2.4.1 Proposed Category 1 Submission Requirements for Budget Impact Analyses

The BIA information description that follows will be a category 1 requirement for all submissions and resubmissions. Any deviations from these requirements would require discussion and acceptance by CADTH prior to filing.

Aggregate pan-Canadian Budget Impact Report:

- a budget impact report that provides an overall aggregate BIA for all the participating drug plans (i.e., a pan-Canadian analysis)
- the base-unit price used in the BIA must be the same as the price submitted in the category 1 requirements and must be clearly identified in each BIA; jurisdiction-specific markups or discounts can then be applied, if applicable.

Aggregate Budget Impact Model:

- a copy of the model used to produce the aggregate pan-Canadian BIA for all of the CDR-participating drug plans
- the BIA model should be flexible enough to be applied to the context of any participating ministry of health or provincial cancer agency, which may differ with respect to the funding of comparators or the design of the program responsible for drug funding.

Supporting Documentation Used in Budget Impact Analysis:

- a reference list and copies of all supporting documentation used and/or cited in the BIA
- the manufacturer is responsible for ensuring that appropriate copyright permissions have been obtained for the electronic copies of all supporting documentation included in the submission or resubmission, to be shared among the drug plans.

Companion Diagnostic:

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

2.4.2 Proposed Category 2 Submission Requirements for Budget Impact Analyses

- The BIA reports and models for each of the individual participating drug plans will remain as category 2 requirements for all submissions and resubmissions.
- The target date for filing these BIAs will remain 20 business days after the submission or resubmission has been accepted for review by CADTH.

2.4.3 Proposed Review Procedure for Budget Impact Analysis

CADTH Pharmacoeconomic Review Report:

- The CADTH review team will critically appraise the aggregate pan-Canadian BIA filed by the manufacturer and conduct a reanalysis in order to model alternative scenarios, as required.
- The summary, appraisal, and reanalysis of the aggregate BIA will be included in the *CADTH Pharmacoeconomic Review Report* and posted on the CADTH website.
- Manufacturers will have the opportunity to review and comment on CADTH's summary, appraisal, and reanalysis when they are provided with the draft review reports for comment.

CADTH Canadian Drug Expert Committee Deliberations and Recommendations:

- The CADTH Canadian Drug Expert Committee (CDEC) may include commentary in its recommendations regarding how the budget impact of a drug may affect the ability of the participating drug plans to implement a recommendation.

3 How to Submit Feedback

To provide feedback on the proposals, please use the feedback template. The completed template must be saved in one of the following formats:

- Microsoft Word document (.doc or.docx)
- unlocked PDF document that permits copying and pasting of text.

The completed templates must be uploaded sent to feedback@cadth.ca.

Feedback should be presented clearly and succinctly in 11-point font and must be received by CADTH by **5:00 p.m. EDT on Friday, September 13, 2019**. For feedback to be considered, you must identify yourself to CADTH. Only one response per organization will be considered. If more than one response is received, only the first will be considered.

If you have any questions about the feedback process, please email us at feedback@cadth.ca. We thank you in advance for your interest.

Appendix 1: Frequently Asked Questions

Q: What do the proposed changes mean for those making submissions to CADTH Common Drug Review and CADTH pan-Canadian Oncology Drug Review?

For submissions of new drugs or drugs with new indications that will undergo a standard review, CADTH's proposal will require the submission of a systematic review of the literature, based on a detailed protocol consistent with best practices and in accordance with CADTH requirements. For both standard and tailored reviews, clinical study reports, a reimbursement status table, and a budget impact analysis will become category 1 requirements. Select submission requirements may be waived at the discretion of CADTH if the submitter is not the manufacturer of the drug being submitted and does not have access to all the information required

Q: What do the proposed changes mean for patient groups?

CADTH's proposal is focused on the requirements for those groups submitting a request for review and does not involve any revisions to the existing patient engagement processes.

Q: What do the proposed changes mean for clinicians?

CADTH's proposal is focused on the submission requirements for those groups submitting a request for review and does not involve any revisions to the existing clinician engagement processes.

Q: Would the proposed changes result in reduced review timelines for CADTH?

CADTH is not proposing any revisions to the current review timelines for the CADTH CDR and pCODR processes (i.e., the existing performance metric will remain at 180 calendar days or less). CADTH will continue to accept submissions up to 180 calendar days prior to the anticipated date of approval by Health Canada, allowing stakeholders to benefit from the shortest possible intervals between market authorization and CADTH recommendations.

Q: Would the proposed changes result in changes to the application fee structure?

CADTH is not proposing any revisions to the current application fee structure for the pharmaceutical review processes as a result of this consultation.

Q: When could the proposed changes be implemented by CADTH?

CADTH is currently targeting to implement the revised submission and review processes for any submissions or resubmissions that are filed on or after April 1, 2020.