pan-Canadian Oncology Drug Review
Pre-Submission, Submission and Resubmission Guidelines

August 2019
## RECORD OF UPDATES

<table>
<thead>
<tr>
<th>Update</th>
<th>Version</th>
<th>Reported on CADTH Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>June 2019</td>
<td>June 12, 2019</td>
</tr>
<tr>
<td>1</td>
<td>August 2019</td>
<td>August 22, 2019</td>
</tr>
</tbody>
</table>
INQUIRIES

Inquiries and correspondence about CADTH’s pan-Canadian Oncology Drug Review (pCODR) program should be directed to:

CADTH pan-Canadian Oncology Drug Review
154 University Avenue, suite 300
Toronto, ON
M5H 3Y9

Telephone: 1-866-988-1444
Fax: 1-866-662-1778
Email: pcodrinfo@cadth.ca
Website: www.cadth.ca/pcodr
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECORD OF UPDATES</td>
<td>ii</td>
</tr>
<tr>
<td>INQUIRIES</td>
<td>iii</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>iv</td>
</tr>
<tr>
<td>1 Purpose</td>
<td>1</td>
</tr>
<tr>
<td>2 Introduction</td>
<td>1</td>
</tr>
<tr>
<td>3 Definitions</td>
<td>1</td>
</tr>
<tr>
<td>4 The Pre-Submission Process</td>
<td>2</td>
</tr>
<tr>
<td>4.1 Requirements for Advance Notification of a Submission or Resubmission to the pCODR Program</td>
<td>2</td>
</tr>
<tr>
<td>4.2 Pre-submission information for New Submissions to pCODR</td>
<td>2</td>
</tr>
<tr>
<td>4.3 Pre-submission information for Resubmissions to pCODR</td>
<td>3</td>
</tr>
<tr>
<td>4.4 Pre-submission Meetings</td>
<td>4</td>
</tr>
<tr>
<td>4.5 Frequency and Duration of Pre-submission Meetings</td>
<td>4</td>
</tr>
<tr>
<td>4.6 Pre-submission Meeting Requirements</td>
<td>4</td>
</tr>
<tr>
<td>5 The Submission Process</td>
<td>4</td>
</tr>
<tr>
<td>5.1 Pending Submission Requirements</td>
<td>4</td>
</tr>
<tr>
<td>5.2 Submissions</td>
<td>4</td>
</tr>
<tr>
<td>5.2.1 Eligible Submissions</td>
<td>4</td>
</tr>
<tr>
<td>5.2.1.1 Post-NOC or Post-NOC/c Submissions</td>
<td>4</td>
</tr>
<tr>
<td>5.2.1.2 Pre-NOC or Pre-NOC/c Submissions</td>
<td>5</td>
</tr>
<tr>
<td>5.2.2 Commencement of Process</td>
<td>6</td>
</tr>
<tr>
<td>5.2.3 Filing of Submissions</td>
<td>7</td>
</tr>
<tr>
<td>5.2.4 Screening of Submission for Completeness</td>
<td>7</td>
</tr>
<tr>
<td>5.2.5 Tracking</td>
<td>8</td>
</tr>
<tr>
<td>5.2.6 Priority and Order of Review</td>
<td>8</td>
</tr>
<tr>
<td>5.2.7 Inquiries</td>
<td>9</td>
</tr>
<tr>
<td>5.2.8 Disclosure of Information</td>
<td>10</td>
</tr>
<tr>
<td>5.3 Post-NOC or Post-NOC/c Submission Requirements</td>
<td>11</td>
</tr>
<tr>
<td>5.3.1 Category 1 Post-NOC or Post-NOC/c Submission Requirements</td>
<td>11</td>
</tr>
<tr>
<td>5.3.2 Additional Information</td>
<td>19</td>
</tr>
<tr>
<td>5.4 Pre-NOC or Pre-NOC/c Submission Requirements</td>
<td>20</td>
</tr>
<tr>
<td>5.4.1 Category 1 Pre-NOC or Pre-NOC/c Submission Requirements</td>
<td>21</td>
</tr>
<tr>
<td>5.4.2 Category 2 Pre-NOC or Pre-NOC/c Submission Requirements</td>
<td>22</td>
</tr>
<tr>
<td>5.4.2.1 Category 2 Requirements at time of NOC or NOC/c</td>
<td>23</td>
</tr>
<tr>
<td>5.4.3 Additional Information (see section 5.3.2)</td>
<td>23</td>
</tr>
<tr>
<td>6 The Resubmission Process</td>
<td>24</td>
</tr>
<tr>
<td>6.1 Resubmissions</td>
<td>24</td>
</tr>
<tr>
<td>6.1.1 Eligible Resubmissions</td>
<td>24</td>
</tr>
<tr>
<td>6.1.2 Filing of Resubmissions</td>
<td>25</td>
</tr>
<tr>
<td>6.1.3 Screening of Resubmission for Completeness</td>
<td>25</td>
</tr>
<tr>
<td>6.1.4 Priority and Order of Review</td>
<td>25</td>
</tr>
<tr>
<td>6.1.5 Inquiries</td>
<td>25</td>
</tr>
<tr>
<td>6.1.6 Confidentiality</td>
<td>25</td>
</tr>
<tr>
<td>6.2 Resubmission Requirements</td>
<td>25</td>
</tr>
<tr>
<td>6.2.1 For Resubmissions Filed (as described in first three bullets in Table 2)</td>
<td>26</td>
</tr>
<tr>
<td>6.2.2 For All Resubmissions</td>
<td>26</td>
</tr>
<tr>
<td>APPENDIX A: pCODR Definitions</td>
<td>30</td>
</tr>
<tr>
<td>APPENDIX</td>
<td>Title</td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>B</td>
<td>Participating P/T Ministries of Health and Provincial Cancer Agencies</td>
</tr>
<tr>
<td>C</td>
<td>pCODR Pre-submission Information Requirements Form - Submissions</td>
</tr>
<tr>
<td>D</td>
<td>pCODR Pre-submission Information Requirements Form - Resubmissions</td>
</tr>
<tr>
<td>E</td>
<td>CADTH pan-Canadian Oncology Drug Review Resubmission Eligibility Form</td>
</tr>
<tr>
<td>F</td>
<td>Guidance to PAG and Tumour Groups when Making pCODR Submissions</td>
</tr>
<tr>
<td>G</td>
<td>Delivery of Mail</td>
</tr>
<tr>
<td>H</td>
<td>Electronic File Format Requirements</td>
</tr>
<tr>
<td>I</td>
<td>Submission and Resubmission Checklists</td>
</tr>
<tr>
<td>I1</td>
<td>Post NOC or NOC/c Submission Requirements Checklist</td>
</tr>
<tr>
<td>I2</td>
<td>Pre-NOC or Pre-NOC/c Submission Requirements Checklist</td>
</tr>
<tr>
<td>I3</td>
<td>Resubmission Requirements Checklist</td>
</tr>
<tr>
<td>I4</td>
<td>General Requirements Checklist</td>
</tr>
<tr>
<td>J</td>
<td>CONSORT Reporting Standard for Documenting Patient Flow</td>
</tr>
<tr>
<td>K</td>
<td>Template for Listing Canadian and International Published and Unpublished Studies</td>
</tr>
<tr>
<td>L</td>
<td>Template for Confirming Disclosure of All Known Unpublished Studies</td>
</tr>
<tr>
<td>M</td>
<td>Letter Template for Authorizing Unrestricted Sharing of Information</td>
</tr>
<tr>
<td>N</td>
<td>Guidance on Pharmacoeconomic Information for pCODR Program</td>
</tr>
</tbody>
</table>
1 Purpose

The purpose of the pan-Canadian Oncology Drug Review (pCODR) Pre-Submission, Submission and Resubmission Guidelines (hereinafter referred to as “Guidelines”) is to:

- provide guidance to Sponsors on the type of information and timing required by the pCODR program prior to a Submission or Resubmission being filed with the pCODR program and to provide guidance around Pre-submission Meetings between the pCODR program and the Sponsor
- provide guidance to Sponsors in the preparation of Submissions and Resubmissions
- ensure Submissions and Resubmissions meet the needs of the pCODR program and the participating jurisdictions

By filing a Pre-Submission Information Form, Submission or Resubmission or by supplying other information to the pCODR program once a Submission or Resubmission has been filed, each Sponsor/Contributor hereby consents to the requirements specified in these Guidelines and the pCODR Procedures and constitutes an agreement between CADTH and the Sponsor on its application.

2 Introduction

CADTH, through the pCODR program, evaluates clinical evidence and cost-effectiveness information on new cancer drugs and uses this evaluation to provide cancer drug funding recommendations to Federal drug plans, provincial/territorial Ministries of Health (excluding Quebec) and provincial cancer agencies. These recommendations are used by jurisdictions to guide their drug funding decisions.

The review process is initiated when a Drug Submission is made to the pCODR program for a New Oncology Drug or an Oncology Drug with a New Indication used for active treatment of cancer. Submissions of Drugs not used for active treatment of cancer, including supportive treatments that may be used in the care of patients with cancer, are to be sent to the Common Drug Review. More information on the Common Drug Review can be found at www.cadth.ca/cdr.

The pCODR process, with its detailed assessment of evidence conducted by an expert review committee, and opportunity for input at various stages of the review process by patients, clinicians, pharmaceutical manufacturers, the Provincial Advisory Group (PAG) and the Sponsor, which may be a provincially recognized clinician-based tumour group, reduces duplication of this effort by each individual federal, provincial and territorial drug plan and cancer agency and ensures reviews are done in a timely manner.

The creation of the pCODR program brings consistency and clarity to the cancer drug review process, allowing for greater understanding by all stakeholders, while ensuring individual federal, provincial and territorial governments can make funding decisions informed by evidence that has been carefully evaluated by experts.

The pCODR pre-submission and submission review processes are presented in Figure 1 and Figure 2, respectively. Complete details of the pCODR procedures are outlined in the pCODR Procedures document available on the pCODR section of the CADTH website (www.cadth.ca/pcodr).

3 Definitions

The capitalized terms in this document are defined in Appendix A.

All references to number of days in this document are in pCODR Business Days, as defined in Appendix A, unless otherwise specified.
4 The Pre-Submission Process

Before a drug submission is made to CADTH, the pCODR program works with the Sponsor to prepare them for the submission process. This preparation includes receiving advance notification from a Sponsor of an upcoming Submission or Resubmission, holding a pre-submission meeting with the Sponsor, setting up supports to assist both the Sponsor and stakeholder groups through the review process, obtaining input from PAG, and notifying appropriate stakeholder groups of the pending review. It also involves determining the appropriate membership for clinical and economic guidance panels, identifying additional resources and expertise that will be part of the review, including either the creation of an ad hoc clinical panel and/or online survey of clinical leads affiliated with provincial cancer agencies, to support the development of a provisional algorithm based on their clinical expertise.

Note: Subject to the pCODR Procedures and the requirements set out in these Guidelines regarding the disclosure of information, all Pre-submission Information provided by the Sponsor to the pCODR program will remain confidential.

4.1 Requirements for Advance Notification of a Submission or Resubmission to the pCODR Program

Sponsors of drugs for pCODR review are requested to provide the Pre-submission Information before the anticipated date of filing the complete Submission or Resubmission. To facilitate the pCODR review process, Sponsors of drugs for pCODR review must provide the Pre-submission Information at least 120 calendar days before the anticipated date of filing the complete Submission or Resubmission. If the anticipated submission received date falls on a weekend or statutory holiday, the following business day will be applied. If a Sponsor fails to meet the 120 calendar days advance notification requirement, a Sponsor will be required to refile the Pre-submission Information with the corrected information and the time will be reset back to day zero for the Sponsor until the requirement is fulfilled (i.e., the new starting date will be from the time of the receipt of the refilled date of the Pre-Submission Requirement Information Form). The reset of the time will not apply to the updated information in the Pre-Submission Requirement Information Form filed at the time of the Submission or Resubmission. The pCODR program will monitor this requirement for all Pre-submission Information submitted through its process. Sponsors include pharmaceutical manufacturers, provincially recognized clinician-based Tumour Groups and the pCODR Provincial Advisory Group (PAG).

The information required by the pCODR program during the pre-submission phase is detailed in the Pre-submission Information Requirements Form. Requirements for Pre-submission Information are different for Submissions and Resubmissions; see Appendices C and D for illustrative examples. In order to ensure that the information remains secured, a sponsor must be registered with the pCODR program in order to access the form through the secure Collaborative Workspaces. Details about the registration process can be found here: https://www.cadth.ca/pcodr/registration. Pre-submission Information should be provided to the pCODR program using the online form available at:

- pCODR Pre-submission Information Requirements Form - Submissions
- pCODR Pre-submission Information Requirements Form - Resubmissions

4.2 Pre-submission information for New Submissions to pCODR

Pre-submission information is required by the pCODR program in order to optimize the submission planning and review process. A Sponsor will be required to complete the Pre-submission Information Requirements Form using the online form. To meet the 120 calendar days advance
notification requirements, all Pre-submission Information requirements must be completed using
the online Pre-submission Information Requirements Form and submitted to the pCODR program.
The Pre-submission Information Requirements Form will not be accepted if the mandatory fields
are not completed. A Sponsor will be required to refile the Pre-submission Information with the
completed information and the time will be reset back to day zero for the Sponsor until the
requirement is fulfilled (i.e., the new starting date will be from the time of the receipt of the
refiled date of the Pre-Submission Information Form). While some allowances may be made where
information is not available to complete the economic section of the form, the pCODR program
reserves the right to request further information be provided before scheduling a pre-submission
meeting.

Tumour Groups will need to work with one of their jurisdictional PAG members to bring forward
their intention to make a Submission or Resubmission to the pCODR program through the
completion of the Pre-submission Information Requirements Form. The PAG will assist in
determining if the Submission or Resubmission would be of local or national scope before the
Tumour Group would file a Submission or Resubmission.

Sponsors are requested to advise the pCODR program of changes in the anticipated date of filing a
Submission or Resubmission as soon as possible. Sponsors should confirm the anticipated date of
filing the complete Submission or Resubmission and the requested reimbursement criteria at least
five (5) business days prior to the posting date of a pending submission. Pending submissions are
issued one month in advance of the anticipated filing date.

If the Pre-submission Information is not provided as outlined in these Guidelines or the anticipated
Submission or Resubmission filing date is not confirmed in accordance with the above
requirements, there may be a delay in the processing and review of the Submission or
Resubmission by pCODR. The Pre-submission Information Requirements Form must be completed
and updated at the time of filing a submission or resubmission to the pCODR program.

Sponsors should contact the pCODR program if they encounter difficulties obtaining the
information necessary to complete the Pre-submission Information Requirements Form.

4.3 Pre-submission information for Resubmissions to pCODR

In addition to the above requirements outlined in sections 4.1 and 4.2 of these Guidelines,
Sponsors will be required to complete the CADTH pan-Canadian Oncology Drug Review
Resubmission Eligibility Form (see Appendix E).

Both the Pre-submission Information for a Resubmission and the CADTH pan-Canadian Oncology
Drug Review Resubmission Eligibility Form must be filed together on the same day. The Pre-
submission Information for a Resubmission can be filed using the online form available through the
secure Collaborative Workspaces. The CADTH pan-Canadian Oncology Drug Review Resubmission
Eligibility Form should be submitted in Word document format to pCODR through the secure
Collaborative Workspaces, which is accessed through the pCODR section of the CADTH website.

If a Resubmission is because new information becomes available during the review process but
before the pERC Final Recommendation is issued, Pre-submission Information does not need to be
provided to the pCODR program.
4.4 Pre-submission Meetings

The purpose of a pre-submission meeting is to provide an opportunity for the Sponsor to introduce a drug to the pCODR program. Information may be sought from the pCODR program on the submission requirements for the drug, including the approach to the clinical and economic evaluation and a dialogue to support the development of a provisional algorithm. Sponsors may also wish to discuss and clarify general submission requirements and procedures for a specific drug or indication. In addition, Sponsors are encouraged to provide information about drugs/indications in the pipeline (i.e., drugs or indications for which Submissions will be filed more than 12 months from the meeting date) during pre-submission meetings. Sponsors will also be asked to confirm if the anticipated submission date remains on schedule.

Manufacturers may bring consultants and/or clinical experts as manufacturer representatives. The pCODR program may invite relevant experts (as appropriate) and representatives from PAG, as needed.

The information and advice provided by the pCODR program at the pre-submission meeting will be based on the Guidelines in effect at the time of the meeting and the information provided will be non-binding. The meeting will be recorded by the pCODR program for internal purposes. At the time of filing the complete Submission, Sponsors should ensure that the Submission conforms to the requirements in effect at that time. Sponsors should note that the pCODR program may request Additional Information or material after receipt of the Submission in order to complete the review.

If the Sponsor is a Tumour Group, the Pre-submission meeting may also be used to determine which Submission Requirements, as outlined in the Guidelines, may be waived. The PAG member representing the Tumour Group’s Provincial Cancer Agency or Ministry of Health may also be invited to attend the pre-submission meeting.

4.5 Frequency and Duration of Pre-submission Meetings

A pre-submission meeting will be scheduled by teleconference for each Submission and Resubmission, pending the completion of the Pre-submission Information Requirements Form. Sponsors may request an in-person pre-submission meeting with the pCODR program, but this will be limited to one meeting in a six month period in order to ensure fair access to CADTH staff and relevant experts (if appropriate) involved in the pCODR review process.

All pre-submission meetings will be scheduled for a maximum of up to one hour and Sponsors are limited to one meeting per drug submission or resubmission.

Manufacturers are encouraged to provide information on drugs in their pipeline.

4.6 Pre-submission Meeting Requirements

Sponsors will be required to provide a completed Pre-submission Information Requirements Form (see Appendix C and D) in order to receive a pre-submission meeting date. Within 5 business days of receiving confirmation of the meeting date and time, the Sponsor must provide the pCODR program with a draft meeting agenda and list of proposed attendees. The pCODR program will collaborate with the Sponsor on the draft agenda and may include additional key topic areas to be discussed at the meeting. In these cases, the pCODR program will send the additional topics within 5 business days of receiving the draft agenda from the Sponsor.

Five business days prior to the scheduled meeting, Sponsors are required to provide a final agenda, the list of confirmed attendees and presentation slides to allow CADTH staff sufficient
time to prepare for the discussion otherwise the meeting may be rescheduled without prejudice to the Submission or Resubmission.
Figure 1. pCODR Pre-Submission Process

120 Calendar Days

Mandatory 120 Calendar Days
(4 months)

**4a Prepare & Submit Pre-Submission Form for New Submission**

**4b Prepare & Submit Pre-Submission Form for Re-Submission + Eligibility Form**

4c Prepare Agenda & Materials in Collaboration with pCODR for Pre-Submission Meeting

4d Receive Input from PAG on Provisional Algorithm & Clarify Preliminary Set of Implementation Issues

4e Hold Pre-Submission Meeting

4f Set up Clinical & Economic Guidance Panels

4g Establish Ad Hoc Panel and/or Conduct Online Survey

4h Pending Submission: Seek Input from Registered Clinicians & Patients

4i Submission Process See Figure 2

4j Develop New or Revise Existing Provisional Algorithm


**Pre-Submission Advance Notification should be made at least 4 months in advance of anticipated filing date of the Submission.

Refer to "Process in Brief" for a Full Description of pCOUR Process Steps on CADTH Website.

@CADTH-pCODR June 2019
Figure 2. pCODR Standard Review Process

**Includes Review/Comment of Provisional Algorithm**

1. Conduct Pre-Submission Planning activities including getting input from PAG and notifying Patient Groups

2. Prepare & Submit Request for Drug Review

3.1 Screen Submission and Initiate Review Process

3.2a Collect Patient Group (or Individual Patients - No Patient Groups) input

3.2b Collect Registered Clinician input

4.1** Conduct Clinical Review

4.1/4.2.2 Clarify info with Submitter during review

4.2 Conduct Economic Review

5.1** CASCA Board of Directors to Review/Confirm Implementation considerations

5.2 Summarize & Review with pERC

6.** Prepare & Publicly Post Initial Recs, Post Reviews

7.1** Get Feedback from Submitter

7.1a** Get Feedback from Patient Group (or Individual Patients when there are no Patient Groups)

7.1b** Get Feedback from Registered Clinician

7.2** Get Feedback from pERC

7.4 Eligible for Early Conversion?

8. Summarize & Review with pERC

6. Prepare & Publish Post Final Recs & Post Input

End

Estimated 99 – 149 business days

Note: Next steps could include Recommendation Implementation, Procedural Review or Resubmission.

Refer to "Process in Brief" for a Full Description of pCODR Process Steps on CADTH Website.
5 The Submission Process

A Submission to the pCODR program represents a Submission to all Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies (excluding Quebec). A Submission must adhere to the content, format, and organization guidelines stipulated in these Guidelines.

While the Guidelines describe the information that the pCODR program requires to conduct the review of the Drug, the Federal drug plans, individual participating P/T Ministries of Health and Provincial Cancer Agencies may require more information to be submitted, for regulatory or decision-making purposes. Federal drug plans and individual P/T Ministries of Health conduct an assessment of their own submission and will advise the Manufacturer on the completeness of their submission for their individual purposes. Sponsors will need to work with each Provincial Cancer Agency to determine if additional requirements must be met for completeness of the submission. Please see Appendix B for a list of contacts from Federal drug plans, each P/T Ministry of Health and Provincial Cancer Agency.

5.1 Pending Submission Requirements

Sponsors should confirm the targeted date of filing the complete Submission and the requested reimbursement criteria at least five (5) business days prior to the posting date of a pending submission. Pending submissions are issued one month in advance of the anticipated filing date. Advance notice of this filing date will allow stakeholders to be notified and is intended to afford them sufficient time to prepare input on a Pending Submission.

Failure to provide the required Pre-submission Information or to confirm the anticipated filing date one month in advance may result in a delay in the processing and review of a Drug Submission by the pCODR program.

5.2 Submissions

5.2.1 Eligible Submissions

Eligible Submissions include New Oncology Drugs and Oncology Drugs with New Indications that have or have not received a Notice of Compliance (NOC) or a Notice of Compliance with Conditions (NOC/c) from Health Canada. New Oncology Drugs and Oncology Drugs with New Indications that have received a NOC or NOC/c are referred to in the pCODR review process as “Post-NOC or Post-NOC/c Submissions”. New Oncology Drugs with a pending NOC or NOC/c and Oncology Drugs with New Indications that have a pending NOC or NOC/c or for which an application has not been submitted to Health Canada for review are referred to in the pCODR review process as “Pre-NOC or Pre-NOC/c Submissions”. Following are descriptions for each of these types of eligible submissions:

Note: Submissions for Biosimilars should be filed directly with the pan-Canadian Pharmaceutical Alliance office and jurisdictions. pCODR reserves the right to request that a Biosimilar Submission undergo a standard review in limited cases. The pCODR program reserves the right to waive Submission Requirements as needed in exceptional circumstances. Please contact the pCODR program for further guidance.

5.2.1.1 Post-NOC or Post-NOC/c Submissions

A Post-NOC or Post-NOC/c Submission for a New Oncology Drug or those for New Active Substances that have a NOC or NOC/c and that have not been marketed in Canada, regardless of when the NOC or NOC/c was
issued. New Oncology Drugs include new salts of marketed products but do not include the following variations of existing products (line extensions) containing the same Active Substance(s):

- New dosage forms 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)
- 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).

A Post-NOC or Post-NOC/c Submission for an Oncology Drug with New Indication(s) are those for a New Indication(s) of a Drug that has either previously been reviewed by the pCODR or marketed prior to the establishment of the pCODR and:

- That has received a NOC or NOC/c for the indication
- The Drug has defined funding criteria by one or more of the Federal drug plans, P/T Ministry of Health / Provincial Cancer Agency and the P/T Ministries of Health, the Provincial Advisory Group (PAG) or Provincial Cancer Agencies have agreed that it should be submitted for review by pCODR; or
- The Drug is not funded by any of the Federal drug plans, P/T Ministries of Health / Provincial Cancer Agencies and the P/T Ministries of Health, PAG, or Provincial Cancer Agencies have agreed that it should be submitted for review by pCODR; or
- The Federal drug plans, P/T Ministries of Health, PAG or Provincial Cancer Agencies have requested the review of the Drug with New Indication(s).

### 5.2.1.2 Pre-NOC or Pre-NOC/c Submissions

A Pre-NOC or Pre-NOC/c Submission is one for a New Drug for which Health Canada is highly likely to issue a NOC or NOC/c within 6 months of the Sponsor filing a Submission with the pCODR. In the case of Pre-NOC or Pre-NOC/c Submissions for New Oncology Drugs, the only Sponsor that will be allowed to make a submission is the Manufacturer. This is because the Manufacturer is the only Sponsor who will likely have the needed information on product price or anticipated product price to conduct an appropriate economic assessment.

A Pre-NOC or Pre-NOC/c Submission for an Oncology Drug with a New Indication(s) is one for which Health Canada is highly likely to issue a NOC or NOC/c within 6 months of the Sponsor filing a Submission with the pCODR or for which the indication is not likely to be submitted to Health Canada for review. Pre-NOC or Pre-NOC/c Submissions for Oncology Drugs with a New Indication may be filed by any Sponsor type (see Appendix A for definition of Sponsor). For Oncology Drugs with New Indications with no pending NOC (i.e., the indication is not likely to be submitted to Health Canada for review), the indication being submitted would reflect the current established standard of practice.

Although Health Canada cannot provide assurance that an NOC or NOC/c will be issued on a particular date or at all, Sponsors may consider filing a
Submission with pCODR if there have not been any significant issues raised by Health Canada.

Note: If the submission is for an Oncology Drug with a New Indication that has not received a NOC or a NOC/c and is not likely to be submitted to Health Canada, please contact the pCODR program for further guidance.

All New Oncology Drugs and Oncology Drugs with New Indication(s) that are for active cancer treatment and that may be potentially funded by one or more of the participating Federal drug plans, P/T Ministries of Health/Provincial Cancer Agencies should be submitted to the pCODR for review to be eligible for funding consideration. Submissions may be made either Pre-NOC or Post-NOC.

Submissions for non-Oncology Drugs, including supportive treatments that may be used in the care of patients with cancer, are to be sent to the Common Drug Review. More information on the Common Drug Review can be found at www.cadth.ca/cdr.

Whenever there is uncertainty about whether a Submission should be made to the pCODR, Sponsors are encouraged to contact the pCODR program for clarity. The pCODR program may consult with the participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies and the Common Drug Review in those cases where Drugs do not clearly fall into a category described above.

Note: Submissions should continue to be made directly to Federal drug plans, P/T Ministries of Health/Provincial Cancer Agencies for the following Oncology Drugs until further notice:

- New single source products that do not contain New Drugs (i.e., combination products),
- Line extensions of existing products, including new dosage forms with the same route of administration and new strengths of the same dosage form. For other line extensions, contact the pCODR program for direction,
- Generic products to be used in currently funded regimens.

5.2.2 Commencement of Process

The pCODR process is initiated either:

- by the Manufacturer, a provincially recognized clinician-based Tumour Group, or the PAG filing a Submission with the pCODR program; or
- by the PAG or the pCODR Advisory Committee, filing a Request for Advice with the pCODR program; or
- by the Manufacturer, a provincially recognized clinician-based Tumour Group, or the PAG, filing a Resubmission with the pCODR program.

Note: If the Submission is being made by a provincially recognized clinician-based Tumour Group or the PAG, please see Appendix F for further guidance and/or contact the pCODR Program for additional clarity. If the Submission pertains to an Oncology Drug with a New Indication that has not received a NOC or a NOC/c and is not likely to be submitted to Health Canada for review, contact the pCODR program for additional clarity.
5.2.3 Filing of Submissions

Sponsors are requested to file a Submission using the secure Collaborative Workspaces; however, a Sponsor must first register on the pCODR section of the CADTH website if a Sponsor has not already registered. Details on registration can be found at: https://www.cadth.ca/pcodr/registration.

In exceptional cases, Submissions may also be delivered to the pCODR program by mail or courier (see Appendix G). Submissions are to be provided on CD/DVD or on a memory stick and not in hard copy. See Appendix H for the format and naming of the files.

At the same time as filing a Submission with pCODR, Sponsors should contact individual Federal drug plans, P/T Ministries of Health/Provincial Cancer Agencies, to determine if additional information is required. These individual Federal drug plans, P/T Ministries of Health/Provincial Cancer Agencies will conduct their own assessment of the submission based on their specific requirements and applicable regulations.

- Sponsors should not wait until both Category 1 and Category 2 Submission or Resubmission Requirements are satisfied before sending copies to the participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies (see section 5.3 and 5.4 for Category 1 and Category 2 Requirements).

- Instead, Sponsors should upload to the secure Collaborative Workspaces or send CD/DVD copies or memory stick, as applicable, of Category 1 Submission and Resubmission Requirements to the participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR program that the Category 1 Requirements have been met.

- Additionally, Sponsors should send CD/DVD copies or memory stick, as applicable, of Category 2 Submission and Resubmission Requirements to the participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR program that the Category 2 Requirements have been met.

5.2.4 Screening of Submission for Completeness

A screening of the Submission is conducted by the pCODR program within ten (10) business days of receipt to ensure that it meets the pCODR requirements outlined in this Guideline.

A Sponsor should ensure that all relevant documents are submitted at the time of filing (see Appendices I1 or I2 for the appropriate Checklists). If the Submission is incomplete, the pCODR program sends a notice to the Sponsor advising what information is needed to complete the Submission. The timeline for the review will not be initiated until the Submission is deemed complete and the Submission will not enter in the review queue until the requirements are satisfied.

When the Submission is complete, the pCODR program sends an acknowledgement to the Sponsor and publicly posts the date it was deemed complete.
5.2.5 Tracking

The pCODR program posts the status of the review of all Submissions, Resubmissions, and Requests for Advice on the pCODR section of the CADTH website including target dates in the review process such as the target pERC meeting date.

In general, approximately one month prior to the anticipated submission date, after receiving confirmation from the Sponsor to do so, the pCODR program will post details of a Pending Submission including the Sponsor and the target submission date. Stakeholders will also be notified of the funding conditions and/or criteria being requested by the Sponsor. This posting is essential to adequately notify stakeholders who may provide input into the pCODR review process.

5.2.6 Priority and Order of Review

All Submissions, Resubmissions, and Requests for Advice made to pCODR are assigned to a tiered queue for review and placement on the pCODR Expert Review Committee (pERC) meeting agenda. The assignment to the review queue and placement on the pERC meeting is made jointly by the pCODR program and the pERC Chair. Consultation with the Provincial Advisory Group (PAG) is sought as required.

Submissions are accepted on an ongoing basis. The pCODR program publishes, on the pCODR section of the CADTH website, the targeted pERC meeting upon date on which a Submission may be deliberated. If adequate pre-submission notification is provided to pCODR for resource planning purposes, the targeted pERC meeting date is based on the posted pCODR review times (see Figure 2). In certain circumstances, including but not limited to, unavailability of review resources, the pCODR program may need to schedule the placement of a Submission or Resubmission on a pERC meeting agenda other than the posted targeted pERC meeting date. This will be communicated to the Sponsor and the new targeted pERC meeting date will be publicly posted.

Submissions are logged when they are received, so that there is a record of the date and time of receipt. The date of receipt of a complete Submission is considered day zero (0) for the purpose of calculating targeted time frames for reviewing the Submission, and the date a Submission is received is posted on the pCODR section of the CADTH website.

Only complete Submissions and Resubmissions, satisfying all of the Submission and Resubmission Requirements, respectively, are entered in the review queue.

Submissions are reviewed in the order received (i.e., first come, first served).

Please Note: The pCODR priority review process has been put on hold effective August 9, 2018. Pending submissions (issued one month in advance of the anticipated filing date) posted on the CADTH website on or before August 9, 2018, that have requested priority review will have their requests assessed upon submission and, if granted, maintained until they have received a Notification to Implement a pERC Final Recommendation or they have been withdrawn. In the future, CADTH will review the pCODR priority review process, as required, in consultation with the jurisdictions and stakeholders. This change aligns with the CADTH Common Drug Review program.
At the time of filing, Sponsors may request that a Submission or Resubmission be assessed to determine whether or not it meets priority review criteria. The Sponsor must provide justification for the request. This request will be considered by a three-person panel consisting of the pERC Chair, the pERC Vice Chair and one additional pERC member, according to the following priority review criteria:

- a New Oncology Drug, or Oncology Drug with a New Indication and employed for the active treatment of cancer, where use offers potential substantial improvements on significant outcomes, such as (but not limited to):
  - improved overall survival in the adjuvant setting; or
  - elimination or substantial reduction of treatment side effects associated with standard of care; or
  - measurable and substantial improvements in quality of life over other available therapies in Canada

OR

- a New Oncology Drug, or Oncology Drug with a New Indication and employed for the active treatment of cancer, where no other comparable drug/treatment is currently marketed in Canada

For Submissions meeting priority review criteria, the review timeline is not condensed and prioritization only has an impact if a review queue exists.

The review queue and placement on the pERC meeting agenda is as follows:

- Any Submission meeting priority review criteria
- Any Resubmission meeting priority review criteria
- Submissions for New Oncology Drugs or Oncology Drugs with a New Indication (Pre-NOC, Pre-NOC/c, Post-NOC or Post NOC/c)
- A Request for Advice
- Reconsiderations of an Initial Recommendation
- Resubmissions

5.2.7 Inquiries

All inquiries, including clarification of Submission Requirements and the Drug review process, should be directed to the pCODR program (refer to Inquiries, page ii, for contact information).

The pCODR program will provide the Sponsor with the name of the CADTH staff member who will be the contact regarding the Submission.

The pCODR program reserves the right to waive Submission or Resubmission Requirements as needed in exceptional circumstances.
5.2.8 Disclosure of Information

pCODR is committed to providing an open and transparent drug review process and
to the need to be accountable for its recommendations to patients and the public.
As such, pCODR considers it essential to be able to outline the evidence upon which
the pERC recommendations are made. In view of these principles, the pCODR
program has outlined a general approach to managing the disclosure of information
which is detailed in the *pCODR Disclosure of Information Guidelines*, available on
the pCODR section of the CADTH website ([www.cadth.ca/pcodr](http://www.cadth.ca/pcodr)). During the
submission screening, a high-level assessment will be conducted to determine if the
information has been made disclosable (e.g. price of the Drug and its relevant
comparator(s), price of companion diagnostics, if applicable, submitted estimates
of the incremental cost-utility or cost-effectiveness ratios, that is, the ICURs or
ICERs) in order for the review to be deemed complete and proceed through the
process. A more detailed assessment of Disclosable and Non-Disclosable
Information is completed at the pCODR Checkpoint Meeting.

As a principle, it is expected that Non-Disclosable Information within a Submission
will be kept to a minimum. The definitions of Disclosable Information and Non-
Disclosable Information are outlined in the *pCODR Disclosure of Information
Guidelines*. At the time of filing a Submission it is the responsibility of the Sponsor to:

- Clearly highlight specific information in the Submission documents that is Non-
  Disclosable.
- Complete a summary table, as outlined in the template included in Appendix C
  of the *pCODR Disclosure of Information Guidelines*, that identifies: the Non-
  Disclosable Information, the location in the submission, the exact wording of
  the Non-Disclosable Information and the general justification for deeming it
  Non-Disclosable. The justification should identify which type of Non-
  Disclosable Information is included, as defined in the *pCODR Disclosure of
  Information Guidelines*. This table is to be provided as a component of the
  Submission. If pCODR does not receive a completed table with a Submission or
  Resubmission or Additional Information submitted, all of the information in the
  submission will be considered disclosable by the pCODR program.
- Provide a structured summary of information related to the submitted
  economic model and budget impact analysis that may be released into the
  public domain, as outlined in the template included in Appendix A of the
  *pCODR Disclosure of Information Guidelines*. Information provided in this
  summary may be included in reports or recommendations posted on the pCODR
  section of the CADTH website.

Please refer to the *pCODR Disclosure of Information Guidelines* for definitions of
Disclosable Information and Non-Disclosable Information for the pCODR review
purposes, requirements for the structured summary of economic information, any
structured summaries of clinical information that are submitted and detailed
information on how Non-Disclosable Information is managed by the pCODR
program.

A Sponsor is deemed to have consented to the *pCODR Disclosure of Information
Guidelines* when it files a Submission or supplies other information related to the
Submission to the pCODR program. The *pCODR Disclosure of Information Guidelines*
constitute an agreement between CADTH and the Sponsor.
5.3 **Post-NOC or Post-NOC/c Submission Requirements**

These requirements outline information that the pCODR program needs to undertake the Clinical and Economic Reviews of New Oncology Drugs or Oncology Drugs with a New Indication(s) that have received a NOC or NOC/c. Submission requirements are outlined separately for New Oncology Drugs or Oncology Drugs with New Indication(s) that do not have a NOC or NOC/c (Pre-NOC or Pre-NOC/c Submissions) in section 5.4.

| Submissions for Oncology Drugs with New Indication(s) are to contain clinical and economic information relating to the New Indication(s) only. |

To expedite the screening of Submissions for completeness and to facilitate the efficient use of documents, Sponsors must provide the information in the order prescribed (sections 5.3.1 and 5.3.2) and in accordance with the electronic file requirements (see Appendix H). See Appendix I for Submission Checklists. Submission requirements must be submitted to the pCODR program only electronically (e.g., secured Collaborative Workspaces) and not as hard copies.

Submission Requirements are subdivided into Category 1, Category 2, and Additional Information.

- Category 1 information must all be included when the Submission is filed in order for the review to proceed.
- There are presently no Category 2 requirements for post-NOC or post-NOC/c submissions.
- Additional Information includes information the pCODR program requires for completion of the review. The pCODR program may request Additional Information from Health Canada or the Sponsor. The Sponsor also has the responsibility of advising the pCODR program regarding any harm or safety issues, including both domestic and global alerts that may arise during the time that the Submission is under review. This may include any communiqués (e.g. “Dear Doctor” letters regarding harm and safety) and any confirmed labeling changes agreed to with international regulatory agencies (e.g. FDA, EMEA) relevant to the Submission while the Submission is under review by the pCODR program.

5.3.1 **Category 1 Post-NOC or Post-NOC/c Submission Requirements**

a) **Signed Cover Letter**

A signed cover letter (an electronic signature is acceptable) from the Sponsor, confirming that all the required information has been provided. It should also indicate:

- A clear description of the Submission being filed (i.e., Category 1 requirements for Post-NOC or Post-NOC/c Submission);
- The updated or new information that was not provided in the Pre-submission Information;
- The New Indication when filing a Submission for an Oncology Drug with a New Indication;
- A statement clarifying whether the submitted price is the current marketed price or the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation [section 4.3.1(h)];
• The names of the primary and backup contact(s) that the pCODR program can contact regarding the Submission. [Note: The Sponsor may designate the consultant(s) preparing the Submission as primary and/or backup contact(s)].

b) Updated Pre-submission Information Requirements Form

Pre-submission Information Requirements are outlined in section 4 of these Guidelines. Updates to Pre-submission Information should include but not be limited to:

• Revising any information that has changed since the Pre-submission Information was provided to pCODR, including all relevant comparators, which may include those that received an initial or final pCODR Expert Review Committee recommendation, or are undergoing negotiations through the pan-Canadian Pharmaceutical Alliance, or is publicly funded including case-by-case funding.
• If a specific population has been defined in a submitted request for funding criteria, the rationale and supporting references for the specified population should be clearly identified.

c) Summary Table Listing Submitted Non-Disclosable Information

Requirements for the Summary Table Listing Submitted Non-Disclosable Information are outlined in the pCODR Disclosure of Information Guidelines, which are available on the pCODR section of the CADTH website (www.cadth.ca/pcodr). Please ensure that this information is submitted in a Word format.

d) Health Canada NOC or NOC/c

A copy of the NOC or NOC/c, dated and signed by Health Canada. If the Drug in the Submission has received an NOC/c, the Manufacturer must provide a copy of the Letter of Undertaking that outlines the confirmatory studies intended to verify the Drug’s clinical benefit, including an indication of time frames.

e) Product Monograph

The Product Monograph should show the date it was approved by Health Canada and the company and product names.

f) Efficacy, Effectiveness, and Safety Evidence

The following are required:

• a copy of the Clinical Overview (Module 2.5) and Clinical Summary (Modules 2.7.1, 2.7.3, 2.7.4, and 2.7.6) from Module 2 of the Common Technical Document; OR
• a copy of the Clinical Studies section of the Comprehensive Summaries or equivalent documentation accepted by Health Canada (as described in Health Canada’s New Drug Submission Guideline) if the Submission is not filed with Health Canada in the Common Technical Document format; and
• copies of published and unpublished studies that address key clinical issues. Head-to-head comparison clinical trials between the submitted drug product and principal comparators are of particular interest. If there are no head-to-head clinical trials, where possible, provide indirect data analyses comparing the drug under review to relevant comparators. While
almost any study design may be considered, the pCODR Expert Review Committee (pERC) will, as part of the pERC Deliberative Framework, assess the level of uncertainty in trial results introduced by different study designs. *Note: Phase 1 studies and letters from clinicians should be not be provided.*

- a copy of the study protocol for the pivotal study(ies)
- a copy of the statistical analysis plan

Where applicable, a copy of published and unpublished studies that address sequencing of therapies in relation to the submitted Drug for review, including the search strategy for those studies. Search strategies for sequencing of therapies should include all search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required.

It is preferred that unpublished data are submitted in manuscript format; however, if unavailable in manuscript format, the following information should be included in clearly labelled sections:

- Objective and rationale of study
- Interventions
- Study population (including eligibility criteria, baseline characteristics, and sample size)
- Methods (including randomization method, blinding method, handling of withdrawals and drop-outs, allocation concealment, and outcome measurement)
- Information about pre-planned extension of trial (if relevant)
- Results (all beneficial and harmful patient effects, including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs with reasons; and measures of dispersion, such as standard deviation or standard error, must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)
- Data analysis
- Conclusions

*Note: Unpublished information provided to pCODR will be managed according to the pCODR Disclosure of Information Guidelines, which are available on the pCODR section of the CADTH website (www.cadth.ca/pcodr). If unpublished data include Non-Disclosable Information, as defined in the pCODR Disclosure of Information Guidelines, a structured summary of clinical information for disclosure may be included.*

- Diagrams following the CONSORT reporting standards or similar diagrams that document the flow of patients through the trials, identified as pivotal trials in Health Canada documentation. (Appendix J contains an example of the format and type of required information.) All information in the sections of the sample diagram is to be provided, including reasons for discontinuation and loss to follow-up at each stage of the study. If applicable, the following are to be incorporated into the CONSORT or similar diagram:
o Additional phases of the study (e.g., screening, washout, baseline, treatment, follow-up) and reasons for discontinuing between phases;

o Assessments at different time points and reasons for discontinuing between time points; and

o Analysis populations for each outcome if they differ (primary outcome, key secondary outcomes, harms) and reasons why patients were excluded from each outcome analysis.

o Copies of editorial articles and errata relating to published studies included in the Submission (Note: If none are available, a statement confirming this should be provided.)

o New data, generated since the last date that data were reported in the studies included in the Submission. (Typically, the studies submitted to the pCODR are the same as those submitted to Health Canada, and sometimes these studies are ongoing, with data collected after submission to Health Canada. The data resulting after the study has been submitted to Health Canada is required.) These data will be accepted in a variety of formats, including late draft, Clinical Study Report excerpts, synopsis, abstract, or conference proceedings. (Note: If none are available, a statement confirming this should be provided.)

- Copies of references supporting the validity of outcome measures (e.g., appropriate references could include disease dependent information that are informed by literature or key opinion leaders research, as well as numerous cancer-related research consortia that can be referred to for guidance) in studies (if available). If no references are provided, a statement is required to confirm that a search has been undertaken but no references have been located.

- A tabulated list of Canadian and international published and unpublished clinical trials. (See Appendix K table template. The template can be downloaded from the secure Collaborative Workspaces. All parts of the template must be completed as per instructions in footnotes below the table).

- A list of all completed published studies, including editorial articles and errata relating to them, and unpublished studies included in the Submission and where they are located in the Submission, including the section in the Submission and the Submission page number, and, when available, a PDF copy of the abstract or publication should be inserted in the table. (Note: All Phase 3 studies, described in the Common Technical Document, are to be listed.)

- Search strategies used to locate published studies in medical literature databases. All search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required. Search results are not required.

- A list of all completed published and unpublished studies not included in the Submission (Note: For Drugs available for 10 years or more in Canada or internationally, the pCODR program should be contacted for guidance as to what to include in the table.)

- A list of all ongoing studies for all indications.
• A signed declaration that all known, unpublished clinical trials have been disclosed (see Appendix L letter template). The template may be downloaded from the secure Collaborative Workspaces.

Note: As per the pCODR Disclosure of Information Guidelines, information that the Sponsor determines may be Non-Disclosable Information and that is provided in any of these documents must be specifically identified by highlighting and should be listed in the Summary Table Listing Submitted Non-Disclosable Information.

g) Economic and Epidemiologic Information

i) Pharmacoeconomic Evaluation

Requirements for the pharmacoeconomic evaluation include:
• The pharmacoeconomic analysis base case must be in the form of a cost-utility analysis or cost-effectiveness analysis.
• If there are relevant subgroups within the specific reimbursement criteria requested by the sponsor, these should be provided as scenario analyses.
• All analyses must be conducted probabilistically within a reasonable model run time. If the model runtime exceeds one business day (8 hours) it will be considered by CADTH to be excessive and it may not be possible to complete the review in accordance with the target timelines. The model should include the ability to conduct or present deterministic analyses for assessment of face validity of differences in data inputs based on specific characteristics.
• The price submitted to CADTH (to four decimal places) must be used in the sponsor’s base case analysis.

Requirements for the base case analysis for the pharmacoeconomic evaluation include:
• The perspective of the publicly funded health payer (i.e., all participating F/P/T Ministries of Health/Provincial Cancer agencies).
• All relevant comparators, which may include those that are currently publicly funded products including case-by-case funding, those that are currently under review (i.e., received an initial pERC recommendation) or under negotiations that could potentially be funded.
• If relevant comparators are excluded from the pharmacoeconomic submission, justification must be provided by the sponsor and the pCODR program may request that the sponsor include these comparators during the review process, which may impact the timelines of the review.
• Reporting of sequential analyses if more than one comparator is included. If such analyses are not provided by the sponsor, the pCODR program may request that the sponsor include these analyses during the review process, which may lead to a delay in the review.

Deviations from these requirements must be discussed with, and accepted by the pCODR program in advance of the submission. Alternative specifications may be considered in scenario analyses.

For additional details on the Reporting of results and details of the pharmacoeconomic evaluation, manufacturers should refer to the Analysis and
Reporting sections of the *Guidelines for the Economic Evaluation of Health Technologies: Canada (4th edition)*, including the *worked example*. Please also refer to Appendix L for additional guidance and suggested content for pharmacoeconomic submissions to the pCODR program.

ii) Economic Model

The model should align with best modelling practices, as per the Modelling section of the *Guidelines for the Economic Evaluation of Health Technologies: Canada (4th edition)*, and should not be more complex than is required. The model run time should not preclude the pCODR program from appropriately testing the robustness of the model. The pCODR program may inform the sponsor of an unacceptable model run time during the review process, which may lead to a delay in the review.

A fully unlocked and executable version of the electronic economic model used in the pharmacoeconomic evaluation is a requirement. The model must be:

- Programmed in an acceptable software platform: Excel
- Provided in its entirety, meaning that the pCODR program must have full access to the programming code (e.g., macros, VBA code) and be able to fully execute the model based on modifications to parameters of interest. pCODR must be able to specify inputs, vary individual parameters, view the calculations, and run various analyses to generate results.
- Able to function in a standalone environment not requiring access to a web-based platform.

Documentation detailing the methods used in the modeling exercise and basic user information must be provided to ensure clarity on how to modify input parameters and run the model.

Deviations from these requirements must be discussed with and accepted by the pCODR program in advance of the submission. Please contact the pCODR program for further guidance.

Sponsors must ensure that economic models submitted to CADTH are free from harmful components and, in particular, that they do not contain any harmful code, such as program routine, device, malware, or other undisclosed feature. This includes, without limitation, a time bomb, virus, software lock, drop dead device, malicious logic, worm, Trojan horse, or trap door that is designed to delete, disable, deactivate, interfere with or otherwise harm CADTH’s hardware, data, or other programs, or adversely affect the functionality of CADTH systems.

iii) Supporting Material

In addition to a structured summary of economic information as outlined in the *pCODR Disclosure of Information Guidelines*, details regarding information used for input parameters in the pharmacoeconomic evaluation must be provided in detail. This includes:

- Technical reports of any unpublished studies or analyses used to inform parameters or assumptions (e.g., utility studies, patient registries, unpublished clinical study reports, expert opinion, etc.). The technical report must provide details of how input parameters were derived, including: a description of the study or data set, the analysis plan, results
of the analyses. Any modification or transformation of the results to use in the economic model must be described.

- Where the inputs for efficacy and/or safety are derived from indirect comparisons, the full technical report of the indirect treatment comparison(s) used to inform clinical parameters must be provided. This must include a full report detailing the objectives, methods, results, limitations, and conclusions related to the indirect comparison.
- Cost/price information table including data sources and assumptions
- If there is a companion diagnostic test associated with the drug, the model and pharmacoeconomic evaluation should include relevant costs and consequences of any required biomarker testing. The source(s) and assumption(s) of the relevant inputs should be provided as well.

The pCODR program must be able to vary individual parameters, view the calculations, and run the model to generate results. The following table identifies the type of information that the pCODR program requires for its examination of the model and the preferred format for receiving it:

<table>
<thead>
<tr>
<th>Information Elements</th>
<th>Preferred Format</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basis for the pharmacoeconomic study (model, spreadsheet)</td>
<td>A model (or a spreadsheet) that is unlocked (or executable). The user should be able to specify inputs, view calculations, and run various analyses.</td>
</tr>
<tr>
<td>Media</td>
<td>Uploaded to the secure <a href="#">Collaborative Workspaces</a>, CD-ROM/DVD or memory stick</td>
</tr>
<tr>
<td>Software requirements</td>
<td>The software and system requirements to run the model must be in Excel format.</td>
</tr>
<tr>
<td>Basic user guide to the model</td>
<td>Electronic format</td>
</tr>
<tr>
<td>Model documentation (manuscripts or a summary of the model report may be submitted)</td>
<td>Electronic format</td>
</tr>
<tr>
<td>Description of the statistical analyses included in the model (data sources, methods, and results)</td>
<td>Electronic format</td>
</tr>
<tr>
<td>Cost/price information table including data sources and assumptions</td>
<td>Electronic format</td>
</tr>
</tbody>
</table>

*Note: The model will not be released to any third parties.*

iv) Budget Impact Analysis

The following budget impact analysis (BIA) information is required in the Submission filed with the pCODR program:

- One non-specific BIA model and report that evaluates the perspective of Canada as a whole, and includes the perspective of each participating jurisdiction in the pCODR program. 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 funding of comparators or the design of the program responsible for drug funding.

- The following supporting documentation for the non-specific BIA:
  - all market research information used in the BIA
  - documents cited in the BIA
  - Disease prevalence — the prevalence or incidence of the disease(s) or condition(s) for which the Drug is under review should be provided for the Canadian population.
  - For Drugs which require reconstitution or dose preparation, the method of dose preparation, dose stability and specifics around potential drug wastage should be addressed.
  - If there is a companion diagnostic test associated with the drug, please provide the budget impact analyses for drugs and companion diagnostics in combination and separately, as some jurisdictions fund the two health technologies through separate mechanisms.

Deviations from these requirements must be discussed with, and accepted by the pCODR program in advance of the submission. Please contact the pCODR program for further guidance.

Note: Province/program specific BIAs must be provided directly to each of the participating F/P/T Ministries of Health/Provincial Cancer agencies in accordance with their requirements in addition to a copy of the non-specific BIA included in the pCODR Submission.

Sponsors must ensure that the BIA models submitted to CADTH are free from harmful components and, in particular, that they do not contain any harmful code, such as program routine, device, malware, or other undisclosed feature. This includes, without limitation, a time bomb, virus, software lock, drop dead device, malicious logic, worm, Trojan horse, or trap door that is designed to delete, disable, deactivate, interfere with or otherwise harm CADTH's hardware, data, or other programs, or adversely affect the functionality of CADTH systems.

h) Pricing and Availability Information

Submitted prices, reported as price per smallest unit to four decimal places and per smallest dispensable unit for all dosage forms, strengths, and package sizes.

Note: The price that is submitted to CADTH must be made available to all the participating public drug programs and cancer agencies following the completion of a pCODR review. It can be:

- the current market price in Canada or
- the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation.

Note 1: If applicable, the disclosable price for a companion diagnostic(s) must be provided in the structured summary of economic information.

Note 2: If applicable, the disclosable price of the relevant comparator(s) must also be provided in the structured summary of economic information.
i) **Letter Authorizing Unrestricted Sharing of Information**

This letter from the holder of the NOC or NOC/c, on company letterhead and signed by an appropriate senior official (an electronic signature is acceptable), should permit unrestricted sharing of information regarding the Drug product between and within CADTH and:

- Participating Provincial Cancer Agencies
- Participating Federal Drug Plans and P/T Ministries of Health
- F/P/T governments, including their agencies and departments
- P/T health authorities, including regional health authorities
- Canadian Association of Provincial Cancer Agencies
- Pan-Canadian Pharmaceutical Alliance Office
- Health Canada
- Patented Medicine Prices Review Board

This letter template is provided in Appendix M. The template may also be downloaded from the secure Collaborative Workspaces of the pCODR section of the CADTH website.

*Note: When a third party (e.g., NOC holder, Manufacturer, or distributor) is involved in filing a Submission, a letter is required from all of the parties that may have information regarding the product on file with Health Canada.*

j) **Companion Diagnostics**

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

### 5.3.2 Additional Information

The following additional information may be requested by the pCODR program, and is assessed on a case-by-case basis. Additional Information is information the pCODR program requires for completion of the review and generally pertains to design, methodology and clinical data results. The pCODR program may request Additional Information from Health Canada or the Sponsor. The Sponsor also has the responsibility of advising the pCODR program regarding any harm or safety issues, including both domestic and global alerts that may arise during the time that the Submission is under review. This may include any communiqués (e.g. “Dear Doctor” letters regarding harm and safety) and any confirmed labeling changes agreed to with international regulatory agencies (e.g. FDA, EMEA) relevant to the Submission while the Submission is under review by pCODR.

Examples of Additional Information that may be requested include:

a) **Health Canada Reviewers’ Report**

The pCODR program may request the Health Canada Reviewers’ Report for each Submission. To avoid delays in providing the report to the pCODR program, Manufacturers are encouraged to request the report from Health Canada.
Canada as soon as they are assured that a NOC or NOC/c will be issued and to forward it immediately to the pCODR program upon receipt.

b) **Periodic Safety Update Reports (PSURs)**

   The pCODR program may contact the Manufacturer for this information.

c) **Clinical Study Report**

   The pCODR program may request the Clinical Study Report or parts of it in searchable electronic format (Microsoft Word or searchable PDF).

d) **Copies of Clarifaxes**

   The pCODR program may request copies of Clarifaxes concerning responses relating to the NOC or NOC/c being issued by Health Canada, or that would be relevant to pCODR (Note: Clarifaxes on animal toxicology and chemistry, and/or manufacturing and control may not be relevant; it is up to the Sponsor to determine whether or not these clarifaxes have an impact on labelling for use in humans).

e) **Revised economic model and report**

   The pCODR program may request the Sponsor to provide an updated economic model and report based on clarification requests during the review. In these cases, the Sponsor must provide both a clean and track changed version of the updated report, as well as a revised structured summary of economic information.

f) **Revised budget impact analysis model and report**

   The pCODR program may request the Sponsor to provide an updated budget impact analysis model and report based on clarification requests during the review. In these cases, the Sponsor must provide both a clean and track changed version of the updated report, as well as revised structured summary of economic information.

All Additional Information provided will be managed in accordance with the pCODR Disclosure of Information Guidelines, which are available on the pCODR section of the CADTH website (www.cadth.ca/pCODR).

Providing this information does not affect the review queue; however, if there is a delay in providing it or if the quantity and complexity of the requested information is significant, there may be a consequent delay in completion of the review.

Note: For Additional Information received during the review, please contact individual pCODR participating members to see if they require this information as part of their provincial Submission.

5.4 **Pre-NOC or Pre-NOC/c Submission Requirements**

   Note: Pre-NOC or Pre-NOC/c Submissions for New Oncology Drugs will only be accepted if made by the Manufacturer. This is because the Manufacturer is the only Sponsor who will likely have the needed information on product price or anticipated product price to conduct appropriate an economic assessment. Other Sponsor types may not have this information available. Pre-NOC or Pre-NOC/c submissions for drugs with New Indications may be filed by any Sponsor type (see definition of Sponsor). For New Oncology Drugs
filed Pre-NOC or Pre-NOC/c, the Drug must have received the NOC or NOC/c before it will be placed on the pERC agenda.

Although most of the Pre-NOC or Pre-NOC/c Submission Requirements are the same as those for other Submissions (section 5.2), the additional/different requirements for Pre-NOC or Pre-NOC/c Submissions are listed below.

- Category 1 information must be included when the Submission is filed in order for the review to proceed.
- Category 2 information must be provided to the pCODR program as soon as the NOC or NOC/c has been issued, and must be provided at least six Business Days prior to the targeted pERC meeting date. Please note any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda.

Note: If the Submission pertains to an Oncology Drug with a New Indication that has not received a NOC or a NOC/c and is not likely to be submitted to Health Canada for review, contact the pCODR program for additional clarity.

5.4.1 Category 1 Pre-NOC or Pre-NOC/c Submission Requirements

a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the Sponsor, confirming that all the required information has been provided. It should also indicate:

- The updated or new information that was not provided in the Pre-submission Information;
- The New Indication when filing a Submission for an Oncology Drug with a New Indication and if it has been submitted to Health Canada for review;
- A clear description of the Submission being filed (i.e., Category 1 requirements for Pre-NOC or Pre-NOC/c Submission);
- Intention to provide Category 2 requirements at the time of NOC or NOC/c as soon as the NOC or NOC/c has been issued, and must be provided at least six Business Days prior to the targeted pERC meeting date. Please note that any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda;
- A statement to confirm if the Sponsor agrees that Health Canada can share information and documents with CADTH as described in the Notice to Industry: Aligned Reviews Between Health Canada and Health Technology Assessment Organizations;
• A statement clarifying whether the submitted price is the current marketed price or the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation [section 5.3.1(h)];
• The names of the primary and backup contact(s) that the pCODR program can contact regarding the Submission. [Note: The Sponsor may designate the consultant(s) preparing the Submission as primary and/or backup contact(s)].

b) Health Canada Screening Acceptance Letter
A copy of the Screening Acceptance Letter indicating that an application has been accepted by Health Canada to review the Drug for sale in Canada.

c) Updated Pre-submission Information Requirements Form (see section 5.3.1)

d) Draft Health Canada Product Monograph
A draft Product Monograph only is required at the time of filing a Submission. The draft Product Monograph should show the company and product names that correspond to the NOC.

e) Summary Table Listing Submitted Non-Disclosable Information (see section 5.3.1)

f) Efficacy, Effectiveness, and Safety Evidence (see section 5.3.1)

g) Economic and Epidemiologic Information (see section 5.3.1)
Note: For pre-NOC submissions, where the approved NOC differs from the anticipated indication for which the pharmacoeconomic evaluation was conducted, the review may be suspended until a revised pharmacoeconomic submission reflecting the approved indication is provided.

h) Pricing and Availability Information (see section 5.3.1)

i) Letter Authorizing Unrestricted Sharing of Information (see section 5.3.1)

j) Table Listing Clarifaxes
A table listing the Clarifaxes and the responses during the Health Canada review of the Drug that have been received at the time the Submission is filed with pCODR. The topic for clarification, date, response, and date of responses are to be provided.

k) Copies of Clarifaxes
Copies of all Clarifaxes and responses to the point of the NOC or NOC/c being issued by Health Canada.

As with all other documents provided to pCODR as part of the Submission, specific information in the clarifaxes that may be potentially Non-Disclosable Information, as per the pCODR Disclosure of Information Guidelines, should be clearly highlighted.

l) Companion Diagnostics (see section 5.3.1)

5.4.2 Category 2 Pre-NOC or Pre-NOC/c Submission Requirements

Category 2 information must be provided to the pCODR program as soon as the NOC or NOC/c has been issued to allow the review to be completed without delay, and
must be provided at least six Business Days prior to the targeted pERC meeting date. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda.

5.4.2.1 Category 2 Requirements at time of NOC or NOC/c

a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the Sponsor, confirming that all the required information has been provided. It should also indicate:

- A clear description of the Submission being filed (i.e., Category 2 requirements for a Pre-NOC or Pre-NOC/c Submission at time of NOC or NOC/c);
- the date the NOC or NOC/c was received;
- Intention to provide the remaining Category 2 requirements, for Pre-NOC/c submissions, as soon as the NOC or NOC/c has been issued to allow the review to be completed without delay, and must be provided at least six Business Days prior to the targeted pERC meeting date. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda.

b) Health Canada NOC or NOC/c

A copy of the NOC or NOC/c, dated and signed by Health Canada, as soon as it has been issued.

c) Product Monograph

The Health Canada-approved Final Product Monograph (showing the date it was approved by Health Canada) and the company and product names that correspond to the NOC or NOC/c should be provided at the time of NOC or NOC/c, to allow the review to proceed as quickly as possible. The Final Product Monograph should be accompanied by a version showing the revisions (with track changes visible) that occurred following the Product Monograph meeting. This is required so that review team members are able to focus on any changes that may have occurred from the initially provided version and the final labelling.
6 The Resubmission Process

6.1 Resubmissions

Manufacturers, provincially recognized clinician-based Tumour Groups and the PAG may file Resubmissions when New Information becomes available that was not provided in the original Submission.

New Information is either (1) new clinical information (not previously submitted) in support of improved efficacy or safety or (2) new cost information that significantly impacts the cost-effectiveness of the Drug. In cases where pERC has issued an initial or final recommendation, New Information must address the specific issues identified in the pERC recommendation.

If the New Information is in support of improved efficacy and/or in support of improved safety, it should be from a randomized controlled trial. Notwithstanding, New Information may be from a non-randomized study when a randomized controlled trial is not available.

Note: Information requested by the pCODR program to clarify a Submission, such as Additional Information outlined in section 5.3.2, is not considered New Information and does not affect the place of a Submission in the review queue.

6.1.1 Eligible Resubmissions

Resubmissions from Manufacturers, provincially recognized clinician-based Tumour Groups, and the PAG are limited to New Oncology Drugs or Oncology Drugs with New Indications that have a NOC or NOC/c and Pre-NOC or Pre-NOC/c Submissions that are undergoing review through the pCODR process or for which Final Recommendation has been issued by the pCODR program.

A Resubmission will be assessed by the pCODR program to determine its eligibility prior to its initiation. A Sponsor must provide a completed pCODR Resubmission Eligibility Form via email to pcodrsubmissions@cadth.ca or through the secure Collaborative Workspaces before a Resubmission can be initiated. Please refer to the pCODR Procedures for additional information.

The pCODR program may accept Resubmissions under the following circumstance(s):

- New Information becomes available after a pERC Final Recommendation has been issued; or
- New Information becomes available during the review process before the pERC Final Recommendation has been issued; or
- New Information becomes available that affects funding conditions and/or criteria recommended by pERC and accepted by participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies in their decisions to fund.

The Sponsor of the New Information does not need to be the same as the Sponsor of the original Submission or Resubmission.
6.1.2 Filing of Resubmissions

Resubmissions may be filed through the secure Collaborative Workspaces; however, a Sponsor must first register on the pCODR section of the CADTH website. In exceptional cases, Resubmissions may also be delivered to the pCODR program by mail or courier (Appendix G). Sponsors should wait until the Resubmission has been deemed complete by pCODR before sending information to individual Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies.

6.1.3 Screening of Resubmission for Completeness

An initial screening of the Resubmission is conducted by the pCODR program within ten (10) days of receipt to ensure that it is complete. The pCODR program verifies whether the Resubmission is complete in accordance with these Guidelines. A Sponsor should ensure that all relevant documents are submitted at the time of filing (see Appendix 13). If the Resubmission is incomplete, the pCODR program sends a notice to the Sponsor advising what information is needed to complete the Resubmission. The timeline for the review will not be initiated until the Resubmission is deemed complete and the Submission will not enter in the review queue until the requirements are satisfied.

When the Resubmission is complete, the pCODR program sends an acknowledgement to the Sponsor and publicly posts the date the Resubmission was deemed complete.

6.1.4 Priority and Order of Review

Contained in section 5.2.6 of these Guidelines. The information for Submissions applies to Resubmissions as well.

6.1.5 Inquiries

Contained in section 5.2.7 of these Guidelines. The information for Submissions applies to Resubmissions as well.

6.1.6 Confidentiality

Contained in section 5.2.8 of these Guidelines. The information for Submissions applies to Resubmissions as well.

6.2 Resubmission Requirements

The following table identifies the type of information that the Sponsor must provide in filing a Resubmission, depending on when the Resubmission is being filed relative to the status of the Drug in the pCODR process and the reason the Sponsor is resubmitting. In all cases, where pERC has issued an initial or a final recommendation, New Information must address the specific issues identified in the pERC recommendation.
### Table 2. Guidance for Filing a Resubmission

<table>
<thead>
<tr>
<th>When During the Review Process is the Resubmission Being Filed</th>
<th>Reason For Filing a Resubmission</th>
<th>What the Sponsor Must Submit to pCODR</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Resubmission is filed before Final Recommendation is issued</td>
<td>New clinical information supporting improved efficacy or improved safety</td>
<td>• New randomized controlled clinical trial(s) or, when a randomized controlled clinical trial is impractical and/or considered unethical, new non-randomized study(s) that address the specific issue(s) identified in the pERC recommendation</td>
</tr>
<tr>
<td>• Resubmission is filed after Final Recommendation is issued</td>
<td></td>
<td>• New pharmacoeconomic evaluation</td>
</tr>
<tr>
<td>• Resubmission is based on New Information that affects coverage criteria and is filed after Final Recommendation is issued</td>
<td>New cost information</td>
<td>• New pharmacoeconomic evaluation and BIA</td>
</tr>
<tr>
<td>• Resubmission is filed after withdrawn market authorization has been re-instated</td>
<td></td>
<td>• If Submission is withdrawn — all Submission requirements; If Resubmission is withdrawn — all Resubmission requirements. For both, Health Canada information addressing reason for withdrawal and reinstatement of market authorization.</td>
</tr>
<tr>
<td>• Resubmission is filed after voluntary withdrawal</td>
<td></td>
<td>• Depending if Submission, Resubmission, or Request for Advice is withdrawn — all Submission, Resubmission, or Request for Advice requirements; updated documents (e.g., revised Product Monograph), any New Information (if applicable) and a list of changes since withdrawal.</td>
</tr>
</tbody>
</table>

6.2.1 **For Resubmissions Filed (as described in first three bullets in Table 2)**

New Information, data, and reference material that were not included in the original Submission are required in addition to the information described in the following section “For All Resubmissions.”

6.2.2 **For All Resubmissions**

The following information must be supplied when making any Resubmission and organized in the manner as set out in Appendix E with clearly labelled identifying sections.
a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the Sponsor, confirming that the information is new and stating the anticipated change or outcome.

The letter should also provide:

- justification for the Resubmission — the rationale for the Resubmission
- statement clarifying whether the submitted price is the current marketed price or the disclosable price that may become effective and disclosed following release of the pERC Initial Recommendation [Section 6.2.2 (g)]
- the names of the primary and backup contact(s) the pCODR program can contact regarding the Resubmission. [Note: The Manufacturer may designate the consultant(s) preparing the Submission as primary and/or backup contacts.]

b) Updated Pre-submission Information Requirements Form

Pre-submission Information Requirements are outlined in section 4 of these Guidelines. Updates to Pre-submission Information for Resubmissions should include but not be limited to:

- Correcting any information that has changed since the Pre-submission Information was submitted to pCODR, including all relevant comparators, which may include those that are currently funded, those that are currently under review (i.e., received a pERC initial recommendation) or under negotiations that could potentially be funded.
- If a specific population has been defined in a submitted request for funding criteria, the rationale and supporting references for the specified population should be clearly identified.

c) Product Monograph

A copy of the most recent product monograph, showing the date it was approved by Health Canada and the company and product names that correspond to the NOC or NOC/c.

d) New Information

- A list of all New Information not included in the original Submission, or previous Resubmissions, which is being included in the current Resubmission
- Copies of all New Information and supporting documentation.

Diagrams following the CONSORT reporting standards or similar diagrams that document the flow of patients through the trials, identified as pivotal trials in Health Canada documentation (Appendix J contains an example of the format and type of required information.) All information in the sections of the sample diagram is to be provided, including reasons for discontinuation and loss to follow-up at each stage of the study. If applicable, the following are to be incorporated into the CONSORT or similar diagram:

- Additional phases of the study (e.g., screening, washout, baseline, treatment, follow-up) and reasons for discontinuing between phases; and
- Assessments at different time points and reasons for discontinuing between time points; and
• Analysis populations for each outcome if they differ (primary outcome, key secondary outcomes, harms) and reasons why patients were excluded from each outcome analysis.

An updated tabulated list of Canadian and international published and unpublished clinical trials that were not identified in the original Submission to pCODR (see Appendix K table template). The template can also be downloaded from the secure Collaborative Workspaces of the pCODR section of the CADTH website. The list should include a list of all completed published studies, including editorial articles and errata relating to them, unpublished studies, and a list of all ongoing studies for all indications.

Search strategies used to locate published studies in medical literature databases. All search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required. Search results are not required.

A signed declaration that all known, unpublished clinical trials have been disclosed (Appendix L letter template). The template may be downloaded from the secure Collaborative Workspaces of the pCODR section of the CADTH website.

Note: As per the pCODR Disclosure of Information Guidelines, information that the Sponsor determines may be Non-Disclosable Information and that is provided in any of these documents must be specifically identified by highlighting and should be listed in the Summary Table Listing Submitted Non-Disclosable Information.

e) Information if Drug has a Notice of Compliance with Conditions (NOC/c)

• Status of the confirmatory studies listed in the Letter of Undertaking if the Resubmission is for a Drug with an NOC/c
• Most recent interim analysis results for confirmatory studies listed in the Letter of Undertaking.

f) Economic and Epidemiologic Information

Note: refer to clause 5.3.1(g) for requirements that must be provided.

Note: The price that is submitted to CADTH must be made available to all the participating public drug programs and cancer agencies following the completion of a pCODR review. It can be:

• the current market price in Canada or
• the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation.

Note 1: If applicable, the disclosable price for a companion diagnostic(s) must be provided in the structured summary of economic information.

Note 2: If applicable, the disclosable price of the relevant comparator(s) must also be provided in the structured summary of economic information.
h) **Companion Diagnostics**

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

i) **Letter Authorizing Unrestricted Sharing of Information**

This letter from the holder of the NOC or NOC/c, on company letterhead and signed by an appropriate senior official, should permit unrestricted sharing of information regarding the Drug product between and within the CADTH and:

- Participating Provincial Cancer Agencies
- Participating Federal Drug Plans and P/T Ministries of Health
- P/T governments, including their agencies and departments
- P/T health authorities, including regional health authorities
- Canadian Association of Provincial Cancer Agencies
- Pan-Canadian Pharmaceutical Alliance Office
- Health Canada
- Patented Medicine Prices Review Board.

This letter template is provided in Appendix M. The template may also be downloaded from the secure Collaborative Workspaces of the pCODR section of the CADTH website.

*Note: When a third party (e.g., NOC holder, Manufacturer, or distributor) is involved in filing a Submission, a letter is required from all of the parties that may have information regarding the product on file with Health Canada.*

j) **List of Funding Decisions by pCODR Participants**

A summary of the funding status of the Drug by all participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies at the time of the Resubmission, including all funding conditions and/or criteria if applicable.
**APPENDIX A: pCODR Definitions**

The following definitions shall apply to this document, unless otherwise stated.

**Additional Information:** Any information that is requested by pCODR, Guidance Panel, pERC, and required to complete the review of the Submission or Resubmission, or to explain or clarify information related to the Submission or Resubmission. Providing this information does not affect the review queue; however, if there is a delay in providing it or if the quantity and complexity of the requested information is significant, there may be a consequent delay in completion of the review. In exceptional cases, PAG may request additional information on a Submission which extends beyond the submitted scope of the review. Revision of review scope may be considered by pCODR in very limited instances, based on jurisdictional input, feasibility to conduct the revised review and clinical importance. All three criteria must be met for scope modification.

**Biosimilar:** 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 a biosimilar and the reference product is established in accordance with Health Canada’s *Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs*, for the authorized indications.

**Business Day:** Any day (other than a Saturday, Sunday, statutory holiday, or company holiday) on which CADTH is open for business.

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

**CDR:** Common Drug Review

**Clarifax:** A Health Canada request for clarification that is faxed to the manufacturer. The purpose of a Clarifax is to expand on, add precision to or re-analyze existing information or data in the submission. Clarifaxes do not contain requests for new data, such as new Clinical and/or Pre-Clinical information, including bioavailability data that were not previously submitted.

**Contributor:** Anyone who has an opportunity to provide input into the pCODR review process for a specific drug review and includes the Sponsor, the manufacturer of the drug product if they are not the Sponsor, the Provincial Advisory Group, registered clinician(s) and patient group(s).

**Disclosable Information:** Has the meaning given to it in the *pCODR Disclosure of Information Guidelines*.

**Disclosure of Information Guidelines:** The guidelines adopted by the pCODR program to ensure the appropriate protection and disclosure of information obtained through the pCODR review process. The Disclosure of Information Guidelines outline the steps and procedures that the pCODR program put into place to ensure disclosure of information is handled in a consistent manner.

**Drug:** An active substance considered to be a Drug under the Canadian Food and Drugs Act and Food and Drug Regulations, which is sold for human use (e.g., includes biosimilars, radiopharmaceuticals, among others).

**Manufacturer:** A Drug Manufacturer, also known as a Pharmaceutical Manufacturer.
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
- a biological substance previously approved for sale in Canada as a Drug, but differing in molecular structure, nature of the source material, or manufacturing process.

New Oncology Drug: A therapeutic substance for the active treatment of cancer 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
- a biological substance previously approved for sale in Canada as a Drug, but differing in molecular structure, nature of the source material, or manufacturing process.

Non-Disclosable Information: Has the meaning given to it in the pCODR Disclosure of Information Guidelines.

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.

Oncology Drug with a New Indication: A Drug for the active treatment of cancer that was either previously reviewed by the pCODR or marketed prior to the establishment of the pCODR and that has or has not received a NOC or NOC/c for a New Indication(s) and:

- the Drug has defined funding criteria by one or more Drug Plans / Provincial Cancer Agencies and the Federal drug plans, P/T Ministries of Health, PAG or Provincial Cancer Agencies have agreed that it should be submitted; or
- the Drug is not funded by any of the Federal drug plans, P/T Ministries of Health / Provincial Cancer Agencies and the P/T Ministries of Health, PAG, or Provincial Cancer Agencies have agreed that it should be submitted; or
- the Federal drug plans, P/T Ministries of Health, PAG or Provincial Cancer Agencies have requested the review of the Drug with New Indication(s).

P/T: Provincial and Territorial.

PAG: Provincial Advisory Group provides operational, as well as some strategic advice, to ensure pERC recommendations are useful to drug funding decision makers. The PAG consists of appointed representatives from the Federal drug plans, each of the provincial Ministries of Health and provincial cancer care agencies participating in the pCODR. The PAG is accountable to the pCODR Advisory Committee.

Provincial Cancer Agencies: Those provincially funded organizations or programs mandated with implementing a broad range of cancer-related health services, such as cancer control strategies, provision of care delivery, and cancer research and systems innovation.

pCODR Director: CADTH staff person hired to provide leadership, development, and delivery of the pCODR program.
**pCODR program:** The Director and staff make up the pCODR program. The Director is responsible for the leadership, development, and delivery of the pCODR program. The pCODR program staff is responsible for the administrative duties associated with the pCODR process.

**pCODR Advisory Committee:** Provides strategic advice for pCODR's ongoing development and management, and provides advice on cancer-specific issues to ensure the pCODR program meets the needs of the federal, provincial/territorial (P/T) governments and cancer agencies.

**pERC:** The pCODR Expert Review Committee assesses the clinical evidence and cost effectiveness of new cancer drugs, and uses this information to make recommendations to the federal, provincial and territorial governments to guide their drug funding decisions. The pERC is an advisory body composed of up to 16 individuals with expertise in drug therapy / drug evaluation and patient members.

**PMPRB:** Patented Medicine Prices Review Board. The PMPRB is an independent quasi-judicial body established by Parliament in 1987 under the *Patent Act*. The PMPRB has a dual role: (1) Regulatory - To ensure that prices charged by patentees for patented medicines sold in Canada are not excessive; and (2) Reporting - To report on the pharmaceutical trends of all medicines and on the research and development spending by pharmaceutical patentees.

**Pre-NOC or Pre-NOC/c Submission:** Those submissions made to pCODR prior to and in the absence of authorization issued by Health Canada. The submission may be for a New Drug or New Indication for which Health Canada is highly likely to issue a NOC or NOC/c within 6 months of the Sponsor filing a Submission with the pCODR. In the case of Pre-NOC or Pre-NOC/c Submissions for New Drugs, the only Sponsor that will be allowed to make a submission is the Manufacturer. In the case of Pre-NOC or Pre-NOC/c Submissions for Oncology Drugs with New Indications, any Sponsor type may file the Submission.

**Pre-submission Information:** The information required by pCODR during the pre-submission phase, as detailed in a Pre-Submission Information Requirements Form, in order to optimize the submission planning and review process. Sponsors are requested to file this information at least 120 calendar days before the anticipated date of filing the complete submission. If the 120th day falls on a weekend or statutory holiday, the following business day will be applied.

**Request for Advice:** A written request made by the PAG or the pCODR Advisory Committee, through PAG, to the pERC for advice on specific therapeutic, clinical or pharmacoeconomic issues, or regarding a pERC Recommendation, which may result in a new Recommendation.

**Sponsor:** The person, corporation, or entity filing a Submission or Resubmission.

**Submission:** A submission to the pCODR program consisting of:

- an electronic request (e.g., on CD/DVD or memory stick)or on-line submission through the password-protected area of the pCODR section of the CADTH website) provided by the Sponsor with supporting documentation, to have a Drug funded by a Federal drug plan, P/T Ministry of Health or Provincial Cancer Agency participating in the pCODR process; or
- a request, together with supporting documentation, if any, made by the PAG, to consider the funding status of Drugs already funded or previously reviewed for funding by one or more of the participating Federal drug plans, P/T Ministries of Health or Provincial Cancer Agencies, as required.

**Submission Guidelines:** The guidelines adopted by the pCODR program that outline how Submissions and Resubmissions must be prepared and submitted.

**Submission Requirements:** Information that is required by the pCODR program to undertake the Clinical and Economic Reviews of Drugs and other information that is required by the Federal drug plans, P/T Ministries of Health or Provincial Cancer Agencies in making funding decisions. The Requirements apply to Submissions and Resubmissions.
**Tumour Groups:** A clinical and/or research group, officially affiliated with a Provincial Cancer Agency or a P/T Ministry of Health, where medical/surgical cancer specialists, health care professionals and researchers with common interest/expertise in managing tumours related to a specific area of the body (e.g. breast or lung) work together to share information, make new discoveries and develop consistent protocols/best practices for treating patients.
**APPENDIX B: Participating P/T Ministries of Health and Provincial Cancer Agencies**

**Note:** The Sponsor may not need to wait until both Category 1 and 2 Submission Requirements, if applicable, are satisfied before sending copies to the participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies, unless otherwise stated. Please refer to the table below for contact information on what to send and the timing of their applications.

Sponsors are strongly encouraged to contact the relevant Federal drug plans, Ministry of Health or Provincial Cancer Agencies to determine if additional requirements are needed for their local reviews.

For Resubmissions, Sponsors should wait until the Resubmission has been deemed complete by pCODR before sending information to individual Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies.

In addition to Category 1 and Category 2 Submission Requirements or Resubmission Requirements, as applicable, Sponsors must also prepare and provide a program/plan specific BIA for each of the Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies.

<table>
<thead>
<tr>
<th>Province</th>
<th>Contact/Send Submission to:</th>
<th>What to Send</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>Provincial Pharmacy Director BC Cancer&lt;br&gt;600-750 West Broadway Vancouver, BC V5Z 1H1</td>
<td>• Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.&lt;br&gt;• Sponsors should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td>Alberta</td>
<td>Executive Director Pharmaceutical Funding and Guidance Branch Alberta Health and Wellness&lt;br&gt;10025 Jasper Avenue, 11th Floor&lt;br&gt;P.O. Box 1360, STN Main&lt;br&gt;Edmonton, AB T5J 2N3</td>
<td>• Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
</tr>
<tr>
<td>Province</td>
<td>Contact Information</td>
<td>Requirements</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Alberta</td>
<td><strong>Sponsor</strong> should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Director, Cancer Services</strong></td>
<td><strong>Sponsor</strong> should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td>Holy Cross Site</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2210-2nd Street SW</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calgary, Alberta T25 3C3</td>
<td></td>
</tr>
<tr>
<td>Saskatchewan</td>
<td><strong>Sponsor</strong> should send USB stick/flash drive copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
<td><strong>Sponsor</strong> should send USB stick/flash drive copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td>Saskatchewan Cancer Agency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c/o Saskatoon Cancer Centre</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 Campus Drive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saskatoon, SK S7N 4H4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>And</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Director of Oncology Pharmacy Services</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saskatchewan Cancer Agency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c/o Saskatoon Cancer Centre</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharmacy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 Campus Drive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saskatoon, SK S7N 4H4</td>
<td></td>
</tr>
<tr>
<td>Manitoba</td>
<td><strong>Sponsor</strong> should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
<td><strong>Sponsor</strong> should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical Consultant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Provincial Drug Programs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Manitoba Health</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1014 - 300 Carlton Street</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Winnipeg, MB R3B 3M9</td>
<td></td>
</tr>
<tr>
<td>Province</td>
<td>Contact Details</td>
<td>Steps</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Manitoba      | Director of Provincial Oncology Drug Program <br>CancerCare Manitoba <br>675 McDermot Avenue <br>Winnipeg, Manitoba R3E 0V9 | • Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.  
• Sponsors should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met. |
| Ontario       | Director, Ontario Public Drug Programs Ontario Ministry of Health and Long-Term Care <br>5700 Yonge Street 3rd Floor <br>Toronto, ON M2M 4K5 | • Sponsors should send copies of submissions after receiving confirmation from the pCODR Secretariat that the requirements for Category 1 and Category 2 have been met.  
• Sponsors must provide one full hard copy and two electronic copies for each submission. For electronic copies, the Ministry will accept CDs, DVDs, and USB keys. |
<table>
<thead>
<tr>
<th>Province</th>
<th>Role</th>
<th>Address</th>
<th>Submission Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ontario</td>
<td>Director</td>
<td>Provincial Drug Reimbursement Programs</td>
<td>• Submission content information should be consistent with what is being sent to OPDP.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cancer Care Ontario</td>
<td>• Submission via USB stick or CD only, with shorter file names (difficulty in transferring files with lengthy names).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>620 University Avenue</td>
<td>• Category 1 and 2 submission files</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toronto ON M5G 2L7</td>
<td>• Resubmission files</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Ontario-specific BIAs</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>Executive Director</td>
<td>Pharmaceutical Services</td>
<td>• Sponsors should provide on CD/DVD/USB stick a copy of Category 1 Submission Requirements after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>New Brunswick Department of Health</td>
<td>• Sponsors should provide on CD/DVD/USB stick a copy of Category 2 Submission Requirements after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PO Box 5100</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>520 King Street, HSBC Place</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fredericton, NB E3B 5G8</td>
<td></td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>Director, Pharmaceutical Services</td>
<td>Nova Scotia Department of Health</td>
<td>• Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and Wellness</td>
<td>• Sponsors should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PO BOX 488 - 1690 Hollis Street</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Halifax, NS B3J 2R8</td>
<td></td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>Medical Lead</td>
<td>Provincial Medical Oncology Program</td>
<td>• Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cancer Care Nova Scotia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4th Floor, Bethune Bldg.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1275 South Park Street</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Halifax, NS B3H 2Y9</td>
<td></td>
</tr>
<tr>
<td>Province</td>
<td>Contact Information</td>
<td>Submission Requirements</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>
| Prince Edward Island  | Pharmacy Consultant  
Pharmacy Consultant  
Health System Planning & Development  
Department of Health and Wellness  
20 Fitzroy Street, Charlottetown  
Prince Edward Island, C1A 7N8 | Sponsors should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met. |
| Prince Edward Island  | Medical Director  
Medical Director  
Queen Elizabeth Hospital  
PEI Cancer Treatment Centre  
60 Riverside Dr  
Charlottetown, PE  C1A 8T5 | Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met. |
| Newfoundland and Labrador | Clinical Pharmacist  
Department of Health and Community Services, Pharmaceutical Services Division, Newfoundland and Labrador | Manufacturers should submit requests for drug coverage through NLPDP according to national minimum submission requirements for brand name and single source drugs as follows: |
| Newfoundland and Labrador | Clinical Chief Cancer Care Program, Eastern Health Dr. H. Bliss Murphy Cancer Centre 300 Prince Philip Drive St. John's, NL A1B 3V6 | • Sponsors should send CD/DVD copies of Category 1 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 1 Requirements have been met.  
• Sponsors should send CD/DVD copies of Category 2 Submissions Requirements to participating P/T Ministries of Health and Provincial Cancer Agencies after receiving confirmation from the pCODR Secretariat that the Category 2 Requirements have been met. |

*Refer to the website for Federal drug plans and P/T Ministry of Health requirements.*
APPENDIX C: pCODR Pre-submission Information Requirements Form - Submissions

Please access the online form at: pCODR Pre-submission Information Form - Submissions

Select PRINT button above to print or save a pdf copy of the completed form.

pCODR Pre-submission Information Requirements Form – Submissions
Please see the pCODR Pre-submission, Submission and Resubmission Guidelines for details on completing this template.

NOTE: Data entered in this form will be lost after 45 minutes of inactivity or if the application is closed before submitting.

› SPONSOR / MANUFACTURER INFORMATION

› DRUG INFORMATION

› COMPANION DIAGNOSTIC

› HEALTH CANADA REVIEW TYPE

› HEALTH CANADA CONSENT LETTER

› KEY DATE INFORMATION

› PRESUBMISSION MEETING

› CANADIAN TRIALS & PATIENT ACCESS PROGRAMS

› CLINICAL OVERVIEW

› ECONOMIC OVERVIEW

› INDIRECT TREATMENT COMPARISONS

› INTERNATIONAL COMPARISONS

Submit  Cancel
APPENDIX D: pCODR Pre-submission Information Requirements Form - Resubmissions

Please access the online form at: pCODR Pre-submission Information Form - Reubmissions

Select PRINT button above to print or save a pdf copy of the completed form.

pCODR Pre-submission Information Requirements Form – Resubmissions

Please see the pCODR Pre-submission, Submission and Resubmission Guidelines for details on completing this template.

NOTE: Data entered in this form will be lost after 45 minutes of inactivity or if the application is closed before submitting.

- SPONSOR / MANUFACTURER INFORMATION
- DRUG INFORMATION
- KEY INFORMATION DATES
- COMPANION DIAGNOSTIC
- HEALTH CANADA REVIEW TYPE
- HEALTH CANADA CONSENT LETTER
- PRESUBMISSION MEETING
- CANADIAN TRIALS & PATIENT ACCESS PROGRAMS
- RESUBMISSION INFORMATION
- CADTH PAN-CANADIAN ONCOLOGY DRUG REVIEW RESUBMISSION ELIGIBILITY FORM
- CLINICAL OVERVIEW
- NEW ECONOMIC INFORMATION
- INDIRECT TREATMENT COMPARISONS
- INTERNATIONAL COMPARISONS
**APPENDIX E: CADTH pan-Canadian Oncology Drug Review Resubmission Eligibility Form**

1. **APPLICANT INFORMATION (TO BE COMPLETED BY SPONSOR)**
   
   Name of sponsor/manufacturer:

   Primary contact for resubmission:
   *Provide name, title, email, phone number*

   Back-up/secondary contact for resubmission:
   *Provide name, title, email, phone number*

2. **DRUG INFORMATION (TO BE COMPLETED BY SPONSOR)**
   
   Name of drug (non-proprietary and brand):

   Indication:

   Requested reimbursement criteria:

   Date of Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) (issued or anticipated): DD-MM-YYYY

   Anticipated resubmission filing date: DD-MM-YYYY

3. **RATIONALE FOR THE RESUBMISSION INFORMATION (TO BE COMPLETED BY SPONSOR)**
   
   Indicate if the reason for the proposed resubmission is for new clinical and/or new economic evidence.

   Check all that apply:

   New clinical information
   - *Improved efficacy*
   - *Improved safety*
   - *Randomized Controlled Trial(s)*

   New economic information

4. **ISSUES ADDRESSED BY THE NEW INFORMATION (TO BE COMPLETED BY SPONSOR)**
   
   - Using the table below, identify the issues raised in the CADTH pCODR Expert Review Committee (pERC) recommendation that the new information addresses. Add or remove rows as required.

   | Issue raised in the pERC recommendation document (applies to the initial recommendation if a final recommendation has not been issued) | Identify new evidence that addresses the issue |
   | Clear state the issue identified in the pERC recommendation | Add brief summary of new evidence |
   | Clear state the issue identified in the pERC recommendation | Add brief summary of new evidence |
### 5. SUMMARY OF NEW CLINICAL INFORMATION (TO BE COMPLETED BY SPONSOR)

This section should not exceed three (3) pages in length, using a minimum 11 point font on 8 ½” by 11” paper, and should include:

- a description of any new clinical information that was not available at the time of the last pCODR review
- a brief overview of new clinical studies including a description of the study design, population, intervention, comparators and outcomes
- a brief summary of the key results from the new studies
- citations and hyperlinked URLs to main articles or pivotal trial, if clinical data are published, or to an abstract or poster, if clinical data are published
- NCI clinical trial number and URL

### 6. SUMMARY OF NEW ECONOMIC INFORMATION (TO BE COMPLETED BY SPONSOR)

This section should not exceed three (3) pages in length, using a minimum 11 point font on 8 ½” by 11” paper, and should include:

- a description of any new economic information that was not available at the time of the last pCODR review.

### 7. ELIGIBILITY ASSESSMENT (FOR CADTH USE ONLY)

<table>
<thead>
<tr>
<th>Issue raised in pERC recommendation document</th>
<th>CADTH assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>To be completed by CADTH</td>
<td>To be completed by CADTH</td>
</tr>
</tbody>
</table>
### 8. CONCLUSION (FOR CADTH USE ONLY)

Based on the information provided by the Sponsor, it is concluded that the resubmission:
- **Meets the eligibility criteria for the pCODR process**
- **Does not meet the eligibility criteria for the pCODR process**

Date of Decision:

### 9. REASON(S) FOR CONCLUSION (FOR CADTH USE ONLY)

*To be completed by CADTH*

### 10. REQUEST FOR RE-EVALUATION (IF APPLICABLE, TO BE COMPLETED BY SPONSOR)

*This section should not exceed one page in length, using a minimum 11 point font on 8 ½” by 11” paper, and should include:*
  - **a description of any discrepancies or errors**

### 11. CADTH RESPONSE & DECISION (FOR CADTH USE ONLY)

*To be completed by CADTH*

Date of Decision:
APPENDIX F: Guidance to PAG and Tumour Groups when Making pCODR Submissions

It is expected that when making a Submission to pCODR, Tumour Groups and PAG may not have the same access to information as a Manufacturer. Therefore, guidance is provided below outlining how information may be obtained or when Submission requirements may be waived.

Other details relevant to Tumour Groups and PAG Sponsors can be found in the pCODR Procedures document on the pCODR section of the CADTH website (www.cadth.ca/pcodr).

a) **Signed Cover Letter**
   Provide as per section 5.3.1(a). In addition, outline any Submission Requirements that may have been waived in consultation with the pCODR Program.

b) **Updated Pre-submission Information**
   All Sponsors should complete the Pre-submission Information Requirement Form as outlined in section 4 of this *Guideline*.

   In addition, PAG and Tumour Group Sponsors may wish to include the following information:
   - Rationale for the Submission
   - Role of the Manufacturer in the Submission process
   - Status of reviews by other Provincial Cancer Agencies
   - Role and collaboration with other Provincial Cancer Agencies in a pCODR Submission
   - Plan for obtaining pharmacoeconomic evidence
   - Plan for obtaining clinical evidence
   - Completed COI forms

c) **Summary Table Listing Submitted Non-Disclosable Information**
   If Non-Disclosable Information is provided in a Submission that a Tumour Group or PAG does not want put into the public domain (e.g. reviews conducted within provincial cancer agencies, specific jurisdictional data, academic manuscripts under embargo), a Summary Table Identifying Submitted Non-Disclosable Information should be provided as described in the *pCODR Disclosure of Information Guidelines*.

d) **Health Canada NOC or NOC/c**
   Requirement waived if manufacturer not involved in the Submission or if Submission is for an Oncology Drug with a New Indication that has not been submitted to Health Canada.

e) **Product Monograph**
   Provide as per section 5.3.1(e).

f) **Efficacy, Effectiveness and Safety Evidence**
   Clinical information usually available only to the Manufacturer, may be waived if it cannot be obtained such as:
   - Excerpts from the Common Technical Document
   - Clinical Study Reports
   - Periodic Safety Update Report
• Health Canada Reviewer Reports

The Sponsor should ensure that they have attempted to systematically identify all available clinical information within the scope of the Submission they are submitting to pCODR. Systematic reviews conducted within Provincial Cancer Agencies may be provided as a component of the clinical information supporting efficacy, effectiveness and safety evidence. As part of a systematic search, lead authors or principal investigators should be contacted when clinical information includes unpublished studies or non-industry sponsored trials.

A tabulated list of all published and unpublished studies must be provided. If these studies are not identified with the support of the Manufacturer, unpublished studies should be identified through clinical trial registries.

The requirement for a signed declaration that all known studies and information known to the Sponsor have been disclosed may be waived if the Manufacturer is not involved in the Submission.

All other clinical information should be provided as per section 5.3.1(f).

g) Economic and Epidemiologic Information

Provide as per section 5.3.1(g). Provincial Cancer Agencies may wish to work with the Manufacturer and/or agencies and organizations that can provide pharmacoeconomic expertise when preparing their Submission. If needed, the Sponsor should contact pCODR who may be able to provide direction on where and how support for economic Submission requirements can be found.

h) Pricing and Availability Information

Provide as per section 5.3.1(h).

i) Letter Authorizing Unrestricted Sharing of Information

Provide as per section 5.3.1(i).

j) Companion Diagnostics

Provide as per section 5.3.1(j).
APPENDIX G: Delivery of Mail

To the pCODR Program:

pan-Canadian Oncology Drug Review Program, Director
154 University Avenue, suite 300
Toronto, ON
M5H 3Y9

a) Delivery Times

Any Communications will be considered to have been delivered:

- on the day of actual delivery, if by personal delivery
- on the fifth (5th) day following deposit in the mail, if by registered or regular mail
- on the day of transmittal if sent during the normal business hours of the recipient or on the Business Day during which such normal business hours next occur, if by electronic means.

If the party sending Communications knows, or ought reasonably to know, of any disruption or difficulty with the postal system that might affect the delivery of mail, any such Communications shall not be mailed but shall be given by personal delivery or by electronic communication.

b) Determining Time Frames

The date on which the Submission or Resubmission is received is considered day zero (0) for the purpose of calculating time frames.
APPENDIX H: Electronic File Format Requirements

Specifications:

Sponsors are requested to file a Submission using the secure Collaborative Workspaces; however, a Sponsor must first register on the pCODR section of the CADTH website if a Sponsor is not already registered. Details on registration can be found at: https://www.cadth.ca/pcodr/registration.

Only in exceptional cases, Submissions may also be delivered to the pCODR program by mail or courier (see Appendix G). Submissions are to be provided on CD or DVD or on a memory stick and not in hard copy.

When filing a Submission or Resubmission, please ensure the following:

- Documents must be provided in MS WORD or PDF format that is unlocked, searchable and printable; the preference would be in MS WORD format. Users must have the ability to extract information or combine documents.
- Documents must be easily identified, and thus, labelled as follows:
  - Brand name_Indication_document type (e.g., product monograph, Module 2.5, etc).pdf or doc

Sponsors must ensure that the electronic files submitted to CADTH are free from harmful components and, in particular, that they do not contain any harmful code, such as program routine, device, malware, or other undisclosed feature. This includes, without limitation, a time bomb, virus, software lock, drop dead device, malicious logic, worm, Trojan horse, or trap door that is designed to delete, disable, deactivate, interfere with or otherwise harm CADTH’s hardware, data, or other programs, or adversely affect the functionality of CADTH systems.

Format for Electronic Files for Submissions:

The proposed folders and files reflect the requirements and the order of the requirements for Post-NOC or Post-NOC/c submissions. Other submissions types (e.g., Pre-NOC or Pre-NOC/c submissions) and Resubmissions would be required to meet the same format and naming conventions for the electronic files but would follow the order for including the information as specifically outlined for these submission types.

Note: As outlined in the pCODR Disclosure of Information Guidelines, all confidential information should be summarized in a table and saved in the first folder (e.g., 01.03_Brand Name_Non-Disclosable Information Table). In addition, a structured summary of economic information that may be disclosed should be provided in the fourth folder (e.g., 04.02_Brand Name Economic Information for Disclosure). If structured summaries of clinical information for disclosure are included, they should be provided in second folder. Please see the pCODR Disclosure of Information Guidelines on the pCODR section of the CADTH website (www.cadth.ca/pcodr) for more details.

Legend

- Represents one folder and
- Represents a PDF or Word file (document), unlocked and searchable and printable.
01_Brand Name_Condition_General Information
- 01.01_Brand Name_Signed Cover Letter
- 01.02_Brand Name_Updated Presub Info
- 01.03_Brand Name_ Non-Disclosable Info Table (in Word format)
- 01.04_Brand Name_HC NOC or NOC/c
- 01.05_Brand Name_PM

02_Brand Name_Condition_Clinical Information
  - 02.01 Brand Name_HC Module 2
    - 02.01.01_Brand Name_Module 2.5
    - 02.01.02_Brand Name_Module 2.7.1
    - 02.01.03_Brand Name_Module 2.7.3
    - 02.01.04_Brand Name_Module 2.7.4
    - 02.01.05_Brand Name_Module 2.7.6

Note 1: Critical studies and all trials discussed in the clinical evidence portion of the submission should be included in this folder (Brand Name_Condition_Clinical Information). Each trial should be a separate document. When feasible the trial should be numbered with the same number as listed in the reference list and the name should be short and concise. For example:

  01. Smith et al.CMAJ.2007.pdf
  03. manufacturer.unpublished.2010.pdf

Note 2: If structured summaries of clinical information for disclosure are part of the submission, they should be included in this folder (Brand Name_Condition_Clinical Information)

- 02.02_Brand Name_Condition_CONSORT
  (Note: may be CONSORT-like diagram)
  - 02.02.01_Brand Name_CONSORT diagram (Study x)
  - 02.02.02_Brand Name_CONSORT diagram (Study y)
02.03_Brand Name_Condition_New data generated after NDS
(See Note 1 above for recommendation on labelling references.)

02.04_Brand Name_Condition(Editorial articles and errata)
(See Note 1 above for recommendation on labelling references.)

02.05_Brand Name_Condition_References supporting outcome measures
(See Note 1 above for recommendation on labelling references.)

02.06_Brand Name_Condition_Table-Published Unpublished studies
- Brand Name_Table of studies

02.07_Brand Name_Condition_Disclosure-unpublished studies
- Brand Name_Signed Disclosure of Unpublished Studies

02.08_Brand Name_Condition_Statistical Analysis Plan
- Brand Name_Statistical Analysis Plan

02.09_Brand Name_Condition_Study Protocol
- Brand Name_Study Protocol

02.10_Brand Name_Condition_Search strategies
- Brand Name_Search strategy

03_Brand Name_Condition_Epidemiologic Information
- 03.01_Brand Name_Disease Prevalence and Incidence

04_Brand Name_Condition_Pharmacoeconomic Evaluation
- 04.01_Brand Name_PE
- 04.02_Brand Name_Economic Information for Disclosure (in Word format)
- 04.03_Brand Name_Economic Model
- 04.04_Brand Name_Economic Documentation
04.05_Brand Name_Indirect Treatment Comparison

05_Brand Name_Condition_BIA

05.01_Brand Name_Condition_BIA_Non-Specific

05.02_Brand Name_Supporting Documentation for BIAs

05.03_Brand Name_Condition_Pricing, Ability to Supply, Sharing of Information

05.03.01_Brand Name_Pricing and Availability Information

05.03.02_Brand Name_Letter-Unrestricted Sharing of Information

06_Brand Name_Condition_Cat 2 and Other Information

Note: Other information may include copies of published and unpublished studies that address sequencing of therapies in relation to the submitted Drug for review, including the search strategy for those studies.

Guidance for Submitting Additional Information Request:

AddInfo_YYYY-MM-DD

Note: Examples of additional information requested include but are not limited to

- HCRviewersReport_YYYY-MM-DD
- PSURs
- ClinicalStudyReport
- HCClarifax_ YYYY-MM-DD
- Brand Name_Economic Model_[VERSION]_YYYY-MM-DD
- Brand Name_BIA_[VERSION]_YYYY-MM-DD
- Brand Name_UpdatedNon-DisclosableInfoTable_[VERSION]_YYYY-MM-DD
# APPENDIX I: Submission and Resubmission Checklists

Drug Name: _________________________________________________________________

Sponsor (Name and Type): ______________________________________________________

**Category and Designation:**
- • Post-NOC or Post-NOC/c Review □
  - • New Oncology Drug □
  - • Oncology Drug with New Indication □
- • Pre-NOC or Pre-NOC/c Review □
  - • New Oncology Drug □
  - • Oncology Drug with New Indication □

**Submission Type:**
- • First review □
- • Resubmission □

**Administrative Issues:**
Complete set of Category 1 Submission Requirements provided
(See list of Submission Requirements) ____________

Category Two Requirements (for Pre-NOC or Pre-NOC/c) provided
at Time of Submission ____________

Number of Zipped File Folders Making a complete Submission ____________

If not online, number of CD/DVDs or USB Making a Complete Submission ____________
### APPENDIX I1: Post NOC or NOC/c Submission Requirements Checklist

#### Category 1

<table>
<thead>
<tr>
<th>Signed Cover Letter</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Description of Submission being filed</td>
<td>□</td>
</tr>
<tr>
<td>• The New Indication when submitting a Drug with New Indications</td>
<td>□</td>
</tr>
<tr>
<td>• Clarification if submitted price is current market price or disclosable price that may become effective and disclosed following release of the pERC Initial Recommendation</td>
<td>□</td>
</tr>
<tr>
<td>• Names of primary and backup contacts to be contacted regarding Submission</td>
<td>□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Updated Pre-submission Information</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Supporting references for specified listing when requested by Sponsor</td>
<td>□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Summary Table Identifying Submitted Non-Disclosable Information (in Word format)</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Health Canada NOC or NOC/c (dated and signed)</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Letter of Undertaking (if NOC/c)</td>
<td>□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product Monograph</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Product Monograph</td>
<td>□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Efficacy, Effectiveness, and Safety Evidence</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinical Overview and Clinical Summary, including Synopses of Individual Studies (Common Technical Document, Modules 2.5, 2.7.1, 2.7.3, 2.7.4, and 2.7.6) OR Clinical Studies section of Comprehensive Summary in hard copy and Word or searchable PDF format on CD/DVD</td>
<td>□</td>
</tr>
<tr>
<td>• Critical studies that address key clinical issues (published and unpublished)</td>
<td>□</td>
</tr>
<tr>
<td>• Protocol of pivotal studies that address key clinical issues (published and unpublished)</td>
<td>□</td>
</tr>
<tr>
<td>• Statistical Analysis Plan</td>
<td>□</td>
</tr>
<tr>
<td>• Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies</td>
<td>□</td>
</tr>
<tr>
<td>• New data generated since the last date that data were reported in studies included in Submission</td>
<td>□</td>
</tr>
<tr>
<td>• Copies of editorial articles and errata relating to published studies</td>
<td>□</td>
</tr>
<tr>
<td>• Copies of references supporting validity of outcome measures OR statement confirming that a search did not identify any</td>
<td>□</td>
</tr>
<tr>
<td>• Copies of published and unpublished studies that addresses sequencing of therapies in relation to the submitted Drug for review, if available</td>
<td>□</td>
</tr>
<tr>
<td>• Tabulated list of published and unpublished studies (Appendix K)</td>
<td>□</td>
</tr>
<tr>
<td>• Signed declaration that all unpublished studies have been disclosed (Appendix L).</td>
<td>□</td>
</tr>
<tr>
<td>• Search Strategies</td>
<td>□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Economic and Epidemiologic Information</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pharmacoeconomic Evaluation</td>
<td>□</td>
</tr>
<tr>
<td>• Indirect treatment comparison documentation, if applicable</td>
<td>□</td>
</tr>
<tr>
<td>• Economic Model and Supporting Documentation</td>
<td>□</td>
</tr>
<tr>
<td>• Structured Summary of Economic Information for Disclosure</td>
<td>□</td>
</tr>
<tr>
<td>• One non-specific BIA (from the perspective of Canada as a whole, and includes the perspective of each participating province jurisdiction in the pCODR program)</td>
<td>□</td>
</tr>
<tr>
<td>• Supporting Documentation for the BIAs</td>
<td>□</td>
</tr>
<tr>
<td>• Documentation of all market research information used in BIAs</td>
<td>□</td>
</tr>
<tr>
<td>• Copies of documents cited in the BIAs.</td>
<td>□</td>
</tr>
<tr>
<td>Disease Prevalence and Incidence Data With Required Breakdown Where Available</td>
<td>☐</td>
</tr>
<tr>
<td>Details of dose preparation, dose stability and wastage, if appropriate</td>
<td>☐</td>
</tr>
</tbody>
</table>

**Pricing and Availability Information**

| Submitted pricing reported as price per smallest unit to four decimal places | ☐ |
| Method of distribution | ☐ |

**Letter Authorizing Unrestricted Sharing of Information**

**Companion Diagnostics (if applicable)**

☐
APPENDIX I2: Pre-NOC or Pre-NOC/c Submission Requirements Checklist

Category 1

*Note: It is the responsibility of the Manufacturer to advise Health Canada of the intent to file a Pre-NOC or Pre-NOC/c Review Submission with the pCODR Program.*

<table>
<thead>
<tr>
<th>Signed Cover Letter</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Description of Submission being filed</td>
</tr>
<tr>
<td>• Confirmation of intention to provide Category 2 requirements at time of NOC.</td>
</tr>
<tr>
<td>Category 2 information must be provided to the pCODR Program as soon as the NOC or NOC/c has been issued, and must be provided at least six Business Days prior to the targeted pERC meeting date. Please note that any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda</td>
</tr>
<tr>
<td>• Clarification if submitted price is the current market price or intended disclosable price that may become effective and disclosed following release of the pERC Initial Recommendation</td>
</tr>
<tr>
<td>• Names of primary and back-up contacts regarding Submission</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Health Canada Screening Acceptance Letter</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Summary Table Identifying Submitted Non-Disclosable Information (in Word format)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Updated Pre-submission information</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Supporting references for specified listing when requested by Sponsor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product Monograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Draft Health Canada Product Monograph (Microsoft Word copy)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Efficacy, Effectiveness and Safety Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinical Overview and Clinical Summary, including Synopses of Individual Studies (Common Technical Document, Modules 2.5, 2.7.1, 2.7.3, 2.7.4 and 2.7.6) OR Clinical Studies section of Comprehensive Summary in hard copy and Microsoft Word or searchable PDF format on CD/DVD.</td>
</tr>
<tr>
<td>• Copies of critical studies that address key clinical issues (published and unpublished)</td>
</tr>
<tr>
<td>• Protocol of pivotal studies that address key clinical issues (published and unpublished)</td>
</tr>
<tr>
<td>• Statistical Analysis Plan</td>
</tr>
<tr>
<td>• Diagrams following CONSORT reporting standards or similar diagrams documenting flow of patients through studies</td>
</tr>
<tr>
<td>• Copies of editorial articles and errata relating to published studies</td>
</tr>
<tr>
<td>• New data generated since the last date that data were reported in studies included in Submission</td>
</tr>
<tr>
<td>• Copies of references supporting validity of outcome measure OR statement confirming that a search did not identify any</td>
</tr>
<tr>
<td>• Copies of published and unpublished studies that addresses sequencing of therapies in relation to the submitted Drug for review, if available</td>
</tr>
<tr>
<td>• Tabulated list of published and unpublished studies (Appendix K)</td>
</tr>
<tr>
<td>• Signed declaration that all unpublished studies have been disclosed (Appendix L)</td>
</tr>
<tr>
<td>• Search strategies</td>
</tr>
</tbody>
</table>
### Economic and Epidemiologic Information
- Pharmacoeconomic Evaluation
- Indirect treatment comparison documentation, if applicable
- Structured Summary of Economic Information for Disclosure (in Word format)
- Unlocked Economic Model and Documentation
- One non-specific BIA (from the perspective of Canada as a whole, and includes the perspective of each participating province jurisdiction in the pCODR program)
- Supporting Documentation for the BIA
- Documentation of all market research information used in BIA
- Copies of documents cited in the BIA
- Disease Prevalence/Incidence Data With Required Breakdown Where Available
- Details on dose preparation, dose stability and wastage, if appropriate

### Pricing and Availability Information
- Submitted pricing reported as price per smallest unit to four decimal places
- Method of distribution

### Companion Diagnostics (if applicable)

<table>
<thead>
<tr>
<th>Letter Authorizing Unrestricted Sharing of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letter of Authorization allowing Health Canada to share information with pCODR</td>
</tr>
<tr>
<td>Table of Clarifaxes that have been provided</td>
</tr>
<tr>
<td>Copies of Clarifaxes</td>
</tr>
</tbody>
</table>

### Category 2

*To be provided as a single package as soon as NOC or NOC/c is issued*:

<table>
<thead>
<tr>
<th>Signed Cover Letter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Canada NOC or NOC/c (dated and signed)</td>
</tr>
<tr>
<td>Letter of Undertaking (if NOC/c)</td>
</tr>
</tbody>
</table>

| Final Health Canada Product Monograph |

*Sponsors must provide this information as soon as NOC or NOC/c is issued, and at least six Business Days prior to the targeted pERC meeting date. Please note that any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by pCODR and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the Drug review is placed on the pERC agenda.*
## APPENDIX I3: Resubmission Requirements Checklist

| pCODR Resubmission Eligibility Form | □ |
| Signed Cover Letter | □ |
| • Justification for Resubmission | □ |
| • Clarification if submitted price is the current market price or intended disclosable price that may become effective and disclosed following release of the pERC Initial Recommendation | □ |
| • Names of primary and backup contacts to be contacted regarding Submission. | □ |
| Updated Pre-submission Information | □ |
| • Supporting references for specified listing when requested by Sponsor | □ |
| Summary Table Identifying Submitted Non-Disclosable Information (in Word format) | □ |
| New Information | □ |
| • List of all New Information not previously submitted | □ |
| • Copies of New Information | □ |
| • Diagrams following CONSORT reporting standards, documenting flow of patients through studies | □ |
| • Updated tabulated list of published and unpublished studies (Appendix K) | □ |
| • Signed declaration that all unpublished studies have been disclosed (Appendix L) | □ |
| • Search strategies | □ |
| If New Information is new clinical information supporting efficacy or safety: | □ |
| • randomized controlled trial, unless it is not available then non-randomized study(s) may be provided. New Information must address the specific issues identified in the pERC recommendation. | □ |
| • new pharmacoeconomic evaluation | □ |
| • structured summary of economic information for public disclosure (in Word format) | □ |
| • One non-specific BIA (from the perspective of Canada as a whole, and includes the perspective of each participating province jurisdiction in the pCODR program) | □ |
| If New Information is new cost information: | □ |
| • new pharmacoeconomic evaluation | □ |
| • structured summary of economic information for public disclosure | □ |
| • One non-specific BIA (from the perspective of Canada as a whole, and includes the perspective of each participating province jurisdiction in the pCODR program) | □ |
| Status of confirmatory studies for Resubmissions of Drug with NOC/c | □ |
| Most recent interim analysis of confirmatory studies for Drug with NOC/c | □ |
| Drug Notification Form (Copy of Most Recent Form) | □ |
| Letter Authorizing Unrestricted Sharing of Information | □ |
| Pricing and Availability Information | □ |
| • Submitted pricing reported as price per smallest unit to four decimal places | □ |
| • Method of distribution. | □ |
| Companion Diagnostics (if applicable) | □ |
| List of Federal Drug Plans, P/T Ministry of Health and/or Provincial Cancer Agency funding decisions | □ |
## APPENDIX I4: General Requirements Checklist

Depending on the Submission type, the content is organized in the order outlined in sections 5.2, 5.3, or 5.4 of this document or the content of the Resubmission is organized in the order outlined in section 6 of this document.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>✔️</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each file submitted electronically is labelled with the brand name of the drug in the Submission or Resubmission and the type of file (e.g., Brand Name X-product monograph)</td>
<td></td>
</tr>
<tr>
<td>Submission (including submitted studies) is provided in English</td>
<td></td>
</tr>
<tr>
<td>Only Non-Disclosable Information, as defined in the pCODR Disclosure of Information Guidelines, and is highlighted</td>
<td></td>
</tr>
<tr>
<td>A table with a summary of all Non-Disclosable Information is provided, as per pCODR Disclosure of Information Guidelines</td>
<td></td>
</tr>
<tr>
<td>A structured summary of economic information that may be publicly disclosed is provided, as per pCODR Disclosure of Information Guidelines</td>
<td></td>
</tr>
</tbody>
</table>

All required information is included with unpublished studies, under the following headings:

- Objective and rationale of study
- Intervention
- Study population (eligibility criteria, baseline characteristics, and sample size)
- Methods (including randomization, blinding, handling of withdrawals/drop-outs, allocation concealment, and outcome measurement)
- Results (all beneficial and harmful patient effects, including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs with reasons; measure of dispersion such as standard deviation or standard error must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)
- Data analysis
- Conclusions
- Clinical Information for Disclosure (a structured summary as outlined in the pCODR Disclosure of Information Guidelines, when applicable)
APPENDIX J: CONSORT Reporting Standard for Documenting Patient Flow

Note: This is an example of the type of information that is required. It can be provided in a different format as long as all of the information shown in the flowchart below is provided. Any questions regarding this requirement can be sent to the pCODR.

CONSORT Flowchart

Flow Diagram of the progress through the phases of a randomized trial (i.e., enrolment, intervention allocation, follow-up, and data analysis)

Assessed for eligibility (n = …)

Excluded (n = …)
- Not meeting inclusion criteria  (n = …)
- Declined to participate  (n = …)
- Other reasons  (n = …)

Randomized (n = …)

Allocated to intervention (n = …)
- Received allocated intervention  (n = …)
- Did not receive allocated intervention (give reasons)  (n = …)

Lost to follow up (n = …) (give reasons)

Discontinued intervention (n = …) (give reasons)

Allocated to intervention (n = …)
- Received allocated intervention  (n = …)
- Did not receive allocated intervention (give reasons)  (n = …)

Lost to follow up (n = …) (give reasons)

Discontinued intervention (n = …) (give reasons)

Analyzed (n = …)
- Excluded from analysis (give reasons)  (n = …)

**APPENDIX K: Template for Listing Canadian and International Published and Unpublished Studies**

*Note: An example is included to illustrate the level of detail required. This table may be expanded. All parts of the template must be completed as per instructions in footnotes.*

List of Canadian and International Published and Unpublished Studies for [Name of Drug in Submission]

<table>
<thead>
<tr>
<th>Study ID*</th>
<th>Alternate Study IDs</th>
<th>Sponsor†</th>
<th>Description‡</th>
<th>Phase**</th>
<th>Start Date</th>
<th>End Date††</th>
<th>Abstracts and Publications‡‡</th>
<th>Location in Submission*** and PDF§</th>
</tr>
</thead>
</table>

*Study ID: Provide the combination of numbers and/or letters assigned by the sponsoring organization to identify the study.
†Sponsor = Sponsor of the study.
‡Briefly describe the study design [e.g., randomized, blinded (double or single), controlled, open label, extension, long-term safety, etc.], number of patients, objective(s), description of each treatment arm (drugs and doses); outcomes specified in protocol; duration of treatment; condition or disease; the summary/description should be concise and brief. Include study title. All information, requested in this bullet, must be included.
**Indicate if Phase 2, 3, or 4 (do not include Phase 1 studies).
††Indicate when the study is scheduled to end or the date completed or stopped.
‡‡Provide complete citations of all abstracts or publications (e.g., published report on interim findings) related to the included unpublished studies. Include editorials and errata related to included published studies.
***Indicate the name of the section under which the included study is located.
§When available, insert a PDF copy of the abstract or publication.
†††Include Phase 3 studies described in the Common Technical Document.
‡‡‡Contact the pCODR Program for guidance if Drug has been available for more than 10 years in Canada or internationally.
APPENDIX L: Template for Confirming Disclosure of All Known Unpublished Studies

[Manufacturer’s letterhead]

[Date]

Director
pan-Canadian Oncology Drug Review
154 University Avenue, suite 300
Toronto, ON
M5H 3Y9

Dear Director:

Reference: [Brand name, generic name]

This letter confirms that [name of Manufacturer] has disclosed all unpublished studies, known to this manufacturer, including those undertaken by other companies that distribute, market, and license this drug in Canada or in other countries and those undertaken by other groups or individuals as of [date of submission].

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX M: Letter Template for Authorizing Unrestricted Sharing of Information

Note: Only letters free of any restrictions are accepted by the pCODR Program. The letter should authorize the pCODR Program to access from, and to disclose to, the bodies named in the letter any information pertaining to the Drug product at any time. A letter with any restrictions will render the Submission incomplete.

[Manufacturer’s letterhead]

[Date]

Director
ap-Canadian Oncology Drug Review
154 University Avenue, suite 300
Toronto, ON
M5H 3Y9

Dear Director:

Reference: [Brand name, generic name]

This letter authorizes the unrestricted communication with respect to the product within CADTH and with:

- Participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies
- F/P/T governments, including their agencies and departments
- P/T health authorities, including regional health authorities
- Canadian Association of Provincial Cancer Agencies
- Pan-Canadian Pharmaceutical Alliance Office
- Health Canada
- Patented Medicine Prices Review Board

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX N: Guidance on Pharmacoeconomic Information for pCODR Program

The information below provides additional guidance and suggested content for pharmacoeconomic submissions to the pCODR program. The following are examples of the types of economic information that may be requested by the pCODR program during the review of drug submissions. These are examples for illustrative purposes only, do not constitute advice or recommendations from pCODR, and are not a part of economic requirements for reviews.

**APPENDIX A: Suggested Content for Submission**

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modeling</strong></td>
<td>- Probabilistic analysis: Provide ability to include or exclude parameter(s) from analysis in model. Also include table of all parameters used in analysis including distributions and sources of distributions.</td>
</tr>
<tr>
<td></td>
<td>- Time horizon: Completely modifiable to user inputs without select options.</td>
</tr>
<tr>
<td></td>
<td>- Model outputs: Provide both observed and predicted estimates (e.g., median/mean overall survival, progression-free survival, treatment duration, proportion of patients alive at specified time points) for submitted base case. Ability of the model to provide these outputs with modifications.</td>
</tr>
<tr>
<td></td>
<td>- Comparator: If appropriate (e.g., no standard of care) ability to modify distribution of treatment mix, provide justification of included/excluded treatments in treatment mix.</td>
</tr>
<tr>
<td></td>
<td>- Body surface area: Ability of the model to modify this parameter.</td>
</tr>
<tr>
<td></td>
<td>- Subsequent treatments: Justification of inclusion or exclusion, sources of therapies, effectiveness data, distribution of therapies, and anticipated treatment pathway.</td>
</tr>
<tr>
<td></td>
<td>- Scenario analyses: When appropriate, for the full population in Health Canada Indication(s).</td>
</tr>
<tr>
<td><strong>Effectiveness</strong></td>
<td>- Parametric models: These analyses should follow the Survival Model Selection Process Algorithm.</td>
</tr>
<tr>
<td></td>
<td>- Extrapolation: Ability to select: 1) observed Kaplan-Meier survival curve only; 2) Kaplan-Meier survival curve with parametric tail; 3) fully parametric curve; and 4) hazard ratio = 1 after trial period.</td>
</tr>
<tr>
<td></td>
<td>- Duration of treatment effect: Ability to select: 1) intervention effect only for duration for which data available; 2) effectiveness declines over time; or 3) effectiveness continues for duration of the intervention in model.</td>
</tr>
<tr>
<td></td>
<td>- Use of surrogate outcome: Provide clinical justification and data between surrogate and final outcome.</td>
</tr>
<tr>
<td></td>
<td>- Others: Provide options to select investigator versus independent-review committee assessment, adjusted versus unadjusted for cross-over or other relevant factors (e.g., potential effect modifiers), use of multiple data cut-off periods (e.g., interim, final, latest), as well as justification of use.</td>
</tr>
<tr>
<td><strong>Measurement and Valuation of Health</strong></td>
<td>- Canadian patient population: Justification and generalizability if Canadian sources are not used.</td>
</tr>
<tr>
<td></td>
<td>- Utility data: Provide table outlining number of responders at each time point, tariffs used, methods used for handling missing data.</td>
</tr>
<tr>
<td></td>
<td>- Disutilities: Inclusion of significant adverse events that result in permanent quality of life reduction.</td>
</tr>
<tr>
<td></td>
<td>- Minimally important difference: Consideration and supporting references.</td>
</tr>
<tr>
<td><strong>Resource Use and Costs</strong></td>
<td>- Wastage: Justification if excluded. Provide rationale and methods used to calculate if included.</td>
</tr>
<tr>
<td></td>
<td>- Drug regimen costs for intervention and comparator: Provide detailed data on calculations, pricing structure, use of generic or brand prices, dosing schedule, sources, and date accessed.</td>
</tr>
<tr>
<td></td>
<td>- Dose: Ability to modify dose intensity and/or adjustment (interruption, reduction).</td>
</tr>
<tr>
<td></td>
<td>- Duration of treatment: Justification of use of progression-free survival versus treatment discontinuation data. Ability to modify time on treatment (e.g., until progression, fixed treatment duration, beyond progression).</td>
</tr>
<tr>
<td></td>
<td>- Adverse events (AE): All grade 3+ AE s incorporated, cost of AE (incidence of AE, probability of AE, proportion treated as inpatient or outpatient, cost of treating AE [frequency of resource utilization, unit cost and sources, detailed calculations], total AE cost applied to each treatment group by cycle), justification if AE considered only in first cycle.</td>
</tr>
<tr>
<td></td>
<td>- Supportive medications, if any (e.g. neutropenia prophylaxis).</td>
</tr>
<tr>
<td></td>
<td>- Additional resources for monitoring not already in use with current treatments (e.g. CT scans, bloodwork, EKG).</td>
</tr>
</tbody>
</table>
### Reporting / Other Considerations

- Dynamic tables/figures in economic model to align with pharmacoeconomic evaluation, allowing EGP to re-create figures/tables based on scenario analyses.
- Recent (within three months of submission date) updated search of relevant economic evaluations and budget impact analyses in major indexed databases.
- Clinical rationale for assumptions in model: e.g., post-progression benefit, resource utilization.
- Discussion on equity considerations.
- Provide $\Delta C/\Delta E$ by health state, life-years and quality-adjusted life years gained, and cost categories.
- Inclusion of 95% confidence or credible intervals, where possible.
- Alignment of model cycle length with treatment cycle.
- Alignment between inputs in pharmacoeconomic evaluation and budget impact analysis.