pan-Canadian Oncology Drug Review
Submission Guidelines for Biosimilars

August 2018
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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
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1 Purpose

The purpose of the pan-Canadian Oncology Drug Review Submission Guidelines for Biosimilars is to:

- provide guidance to Submitters in the preparation of Submissions for a Biosimilar.
- ensure Submissions for a Biosimilar meet the needs of the pan-Canadian Oncology Drug Review (pCODR)

2 Introduction

2.1 About the pCODR Program

The pCODR, a program of CADTH, is an evidence-based, cancer drug review process. pCODR evaluates clinical effectiveness, cost-effectiveness information and patient perspectives on cancer drugs and uses this evaluation to provide cancer drug funding recommendations to federal drug plans, provincial/territorial (P/T) Ministries of Health (excluding Quebec), and provincial cancer agencies. These recommendations are used by jurisdictions to guide their drug funding decisions.

2.2 Overview of the pCODR Biosimilar Review Process

A biosimilar is a drug demonstrated to be highly similar to a biologic drug (known as the reference biologic drug) that was already authorized for sale by Health Canada. Health Canada has developed a robust, regulatory framework for biosimilars. Within this framework, biosimilars are approved based on having no clinically meaningful differences compared with the reference biologic drug product in terms of safety, purity, and efficacy and may enter the market after the expiry of reference biologic drug patents and data protection.1

Biosimilar manufacturers must provide information to Health Canada comparing the biosimilar with the reference biologic drug. Similarity is demonstrated using a step-wise approach beginning with structural and functional studies and continuing with human clinical studies. Because the purpose of these studies is to demonstrate similarity, the type of data required to support biosimilar authorization differs from that required for a stand-alone biologic drug. Health Canada may authorize a biosimilar for use in more than one indication if similarity between the biosimilar and the reference biologic drug is demonstrated rigorously. Since a biosimilar is theoretically similar in structure and function to a reference biologic drug with well-established safety and efficacy, in many cases clinical studies do not need to be repeated for each indication.

For a Biosimilar, the pCODR review process is initiated when a Biosimilar Drug Submission is made to the pCODR program for an active treatment of cancer. Submissions of Biosimilars 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, a program of CADTH. More information on the Common Drug Review can be found at www.cadth.ca/cdr.

An overview of the pCODR Biosimilar review process is presented in Figure 1. For each ongoing Biosimilar Submission, the details regarding the submission that will be made publicly available on the pCODR section of the CADTH website are presented in Figure 2. Notwithstanding the foregoing, in the event of a Biosimilar Submission being reviewed by pCODR that is a Pre-NOC or Pre-NOC/c

Submission under review by Health Canada, pCODR will not post product strength, product format, and NOC date until such time as regulatory approval has been issued.

3 Definitions

See Appendix A for definitions.

All references to number of days in this document are in pCODR Business Days, as defined in Appendix A, unless otherwise specified.
Figure 1. pCODR Biosimilar Review Process

1. Conduct pre-submission planning activities including getting input from PAG and notifying Patient Group(s)/Registered Clinician(s)

2. Prepare and submit request for a Biosimilar Drug

3. Screen submission and initiate biosimilar review process

4. Collect Patient Group(s)/Registered Clinician(s) Input

5. Prepare/synthesize information/confer with clinical/economic experts

6. Clarification period (Submitter and Health Canada)

7. Summarize evidence, findings, and implications for decision-making

8. Prepare and publicly post dossier

End

*Includes Clinical and Economic Experts and Provincial Advisory Group (PAG)

Estimated
61 – 66 Business Days
For ongoing Biosimilar Submissions, the review process information set out in Figure 2 will be made publicly available on the pCODR section of the CADTH website as it becomes available.

**Figure 2: Biosimilar Review Process Information Posted on the pCODR Section of the CADTH Website** ([www.cadth.ca/pcodr](http://www.cadth.ca/pcodr))

<table>
<thead>
<tr>
<th><strong>Brand Name</strong></th>
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<tr>
<td><strong>Generic Name</strong></td>
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<tr>
<td><strong>Tumour Type</strong></td>
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<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td><strong>Funding Request</strong></td>
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<tr>
<td><strong>Review Status</strong></td>
</tr>
<tr>
<td><strong>Pre-NOC Submission</strong></td>
</tr>
<tr>
<td><strong>NOC Date</strong></td>
</tr>
<tr>
<td><strong>Strength</strong></td>
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<tr>
<td><strong>Manufacturer</strong></td>
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<tr>
<td><strong>Submitter</strong></td>
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<tr>
<td><strong>Submission Date</strong></td>
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<td><strong>Submission Deemed Complete Date</strong></td>
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<tr>
<td><strong>Submission Type</strong></td>
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<tr>
<td>*<strong>Stakeholder Input Deadline</strong></td>
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<tr>
<td><em>Patient groups (or individual patients and caregivers when there is no patient group) and clinicians who are registered with pCODR are eligible to provide input. Deadlines for input are by the end of the pCODR business day (5 p.m. Eastern Time) of the date noted.</em></td>
</tr>
<tr>
<td><strong>Final Biosimilar Summary Dossier Issued</strong></td>
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<tr>
<td><strong>Clarification (where applicable)</strong></td>
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4 The Biosimilar 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 this document.

While the *pCODR Submission Guidelines for Biosimilars* describe the information that pCODR requires to conduct the review of the Biosimilar, the federal drug plans, individual participating P/T Ministries of Health and provincial cancer agencies may require more information to be submitted for decision-making purposes. Submitters may need to work with the participating jurisdictions to determine if additional requirements must be met for completeness of the submission.

4.1 Inquiries

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

The pCODR program will provide the Submitter with the name of the pCODR Program staff member who will be the contact regarding the Biosimilar Submission.

The pCODR program reserves the right to waive Submission Requirements as needed in exceptional circumstances.

4.2 Pre-submission Requirements

The pCODR process requires that Pre-submission Information (Appendix B) be provided at least 120 calendar days before a complete Submission for a Biosimilar is filed. If the anticipated submission received date falls on a weekend or statutory holiday, the following business day will be applied. The pCODR program will monitor this requirement for all Pre-submission Information submitted to pCODR. Detailed Pre-submission Information requirements are outlined in the *pCODR Pre-submission Guidelines*, which can be found on the pCODR section of the CADTH website ([www.cadth.ca/pcodr](http://www.cadth.ca/pcodr)). At the time of filing a complete Biosimilar Submission, updated Pre-submission Information is required. Pre-submission meetings are not typically offered for a Biosimilar Submission. Submitters who have questions regarding a pending Biosimilar Submission should contact the pCODR program by email at pcodrinfo@cadth.ca.

Submitters should confirm the targeted date of filing the complete Biosimilar 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 of the submission date may result in a delay in the processing and review of a Biosimilar Submission by pCODR.

4.3 Stakeholder Input

Registered patient groups (or individual patient or caregiver in cases where there is no patient group), registered clinician(s) and the Provincial Advisory Group (PAG) are invited to submit information related to a Biosimilar Submission under review by pCODR. All eligible stakeholders are required to use the designated biosimilars submission templates,
including the conflict of interest declaration form on the pCODR section of the CADTH website to submit their input.

Patient group (or individual patient or caregiver in cases where there is no patient group) and registered clinician conflict of interest declarations providing input on a Biosimilar Submission will be publicly posted on the pCODR section of the CADTH website. Conflict of interest declarations of PAG members are publicly posted on the pCODR section of the CADTH website and updated on an annual basis or as needed, in accordance with the pCODR Conflict of Interest Guidelines.

All eligible stakeholders must submit input by the posted deadline date (within 10 business days of the pCODR program receiving a Biosimilar Submission) in order that the information to be included in the review.

4.4 Submissions

4.4.1 Eligible Submissions

Eligible submissions may or may not already have an NOC or NOC/c. A Biosimilar that has an NOC or NOC/c at the time of the submission is referred to in the pCODR review process as a “post-NOC or post-NOC/c submission”. A Biosimilar that has a pending NOC or NOC/c or for which an application has not been submitted to Health Canada for review is referred to in the pCODR review process as a “Pre-NOC or Pre-NOC/c submission”. Following are descriptions for each of these types of eligible submissions:

4.4.1.1 Post-NOC or Post-NOC/c Submissions

A Post-NOC or Post-NOC/c Biosimilar Submission that has a NOC or NOC/c and that has not been marketed in Canada, regardless of when the NOC or NOC/c was issued.

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

- has received an NOC or NOC/c for the indication;
- has defined funding criteria by one or more of the federal drug plans, P/T Ministries of Health, or provincial cancer agencies and the P/T Ministries of Health, or provincial cancer agencies or PAG have agreed that it should be submitted for review by pCODR;
- is not funded by any of the federal drug plans, P/T Ministries of Health or provincial cancer agencies and the P/T Ministries of Health, provincial cancer agencies or PAG 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 Biosimilar with New Indication(s).

4.4.1.2 Pre-NOC or Pre-NOC/c Submissions

A Pre-NOC or Pre-NOC/c Biosimilar Submission is one for which Health Canada is highly likely to issue a NOC or NOC/c within six (6) months of the Submitter filing a Submission with the pCODR. In the case of Pre-NOC or Pre-NOC/c Submissions for Biosimilars, the only Submitter that is allowed to make a submission is the Manufacturer. This is because the
Manufacturer is the only Submitter that is likely to have the needed information on product price or anticipated product price to conduct an appropriate cost comparison.

Pre-NOC or Pre-NOC/c Submissions for Biosimilars with a New Indication may be filed by any Submitter type (see Appendix A for definition of Submitter).

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

All Biosimilars 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 of Biosimilars 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.

Whenever there is uncertainty about whether a Biosimilar Submission should be made to the pCODR, Submitters 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 Biosimilars do not clearly fall into a category described above.

Note: pCODR reserves the right to request that a Biosimilar Submission undergo a standard review in limited cases. Please contact the pCODR program for further guidance.

4.4.2 Commencement of Process

The pCODR Biosimilar process is initiated by one of the following filing a submission with the pCODR program:

- by the Manufacturer,
- a provincially recognized clinician-based Tumour Group, or
- the PAG

Note: If the Biosimilar Submission is being made by a provincially recognized clinician-based Tumour Group or the PAG, please see Appendix C for further guidance and/or contact the pCODR program for additional clarity.

4.4.3 Filing of Submissions

Submitters should file a Biosimilar Submission through the CADTH Collaborative Workspaces; however, a Submitter must first register on the pCODR section of the CADTH website. 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 D). If sent by mail or courier, Biosimilar Submissions are to be provided on CD or DVD or on a memory stick and not in hard copy. See Appendix E for the format and naming of the files.

At the same time as filing a Biosimilar Submission with pCODR, Submitters should contact individual federal drug plans, P/T Ministries of Health/provincial cancer agencies to determine whether additional information is required.

4.4.4 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 the pCODR Submission Guidelines for Biosimilars.

If the Biosimilar Submission is incomplete, the pCODR program sends a notice to the Submitter advising what information is needed to complete the Submission.

When the Biosimilar Submission is complete, the pCODR program sends an acknowledgement to the Submitter and publicly posts the date it was deemed complete. Only complete Biosimilar Submissions satisfying all of the requirements are entered in the review queue.

4.4.5 Tracking

Biosimilar submissions are accepted on an ongoing basis, and 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 Biosimilar Submission is considered day zero (0) for the purpose of calculating targeted time frames for reviewing the Submission, and this date is posted on the pCODR section of the CADTH website. The pCODR program posts the status of the review of all Biosimilar Submissions including target dates in the review process.

In general, approximately one month prior to the anticipated submission date the pCODR program will post details of a Pending Submission including the Submitter and the target submission date. Stakeholders will also be notified of the funding conditions and/or criteria being requested by the Submitter. This posting is essential to adequately notify stakeholders who may provide input into the pCODR review process. The posted information will be based on details provided in the Pre-submission Information Requirements Form - Submissions (see the pCODR Pre-submission Guidelines), unless pCODR is otherwise notified by the Submitter. The deadline date for receiving stakeholder input and other details are confirmed when the Submission is received (see Figure 2).

4.4.6 Disclosure of Information

CADTH is committed to providing an open and transparent drug review process for Biosimilars. To ensure that the Biosimilar review process is transparent and accountable, pCODR considers it essential that the evidence used to support the Biosimilar Submission, including the information submitted in the CADTH Biosimilar Summary Dossier template is made fully disclosable. All disclosable information may be publicly disclosed at the absolute discretion of pCODR. If a Submitter has
included non-disclosable information, pCODR will not use the information. Care should be taken when submitting information relating to individuals. Personal identifiers and sensitive information will be removed.

4.4.7 Clarification

Throughout the Biosimilar review, the pCODR reviewers are able to ask questions of the Submitter in writing. Responses to the questions posed during the Biosimilar review process must be made disclosable and may be included in the Final CADTH Biosimilar Summary Dossier.

The pCODR and Health Canada may communicate as required regarding the Pre-NOC or Pre-NOC/c Biosimilar Submission. The Manufacturer has the responsibility of communicating to the pCODR program any relevant issues raised by Health Canada or changes in direction that occur in the Health Canada review as soon as the Manufacturer is aware that a decision has been made during the time that a pre-NOC or NOC/c Biosimilar Submission is under review by pCODR.

If the Review Team considers that Additional Information is required, the pCODR program will contact the Manufacturer and/or Health Canada.

4.4.8 Verification of Information

Prior to the posting of the Final CADTH Biosimilar Summary Dossier, the Submitter will be provided with the opportunity to identify any discrepancies or errors. A Submitter must respond in writing within three (3) Business Days of the date of receipt from pCODR, and must submit the response through the CADTH Collaborative Workspaces. pCODR will have three (3) Business Days to consider the proposed discrepancies and errors and make revisions to the CADTH Biosimilar Summary Dossier as deemed necessary by the pCODR program and prior to public posting of this document. Discrepancies and errors should be documented in a table using the format provided in Appendix K.

4.4.9 Withdrawal and Application Fees

An application fee will apply to a drug manufacturer submitting an application for a Biosimilar Submission. Please refer to the CADTH Guidelines for Manufacturers on Application Fees for Pharmaceutical Reviews for additional information about the Application Fee Schedules, milestones for payments and payment methods. CADTH’s Finance Department will issue an invoice for the application fee owing. All CADTH application fees are due within 30 calendar days of receipt of an invoice. If fee payment for a Biosimilar Submission is not received within 30 days, a reminder will be provided indicating that payment is past due. It is the sole responsibility of the manufacturer to pay any fees by the due date and although it is CADTH’s intention to send subsequent reminders of unpaid fees, it shall not be obligated to do so. If payment remains outstanding after 45 calendar days, all work on the Biosimilar drug review will be temporarily suspended. Once payment in full is received, CADTH will resume its work on the suspended application as soon as it can be reasonably accommodated based on available resources and submission volumes.
Anytime after a Biosimilar Submission is deemed complete, and before a Final CADTH Biosimilar Summary Dossier is posted on the pCODR section of the CADTH website, a Biosimilar Submission may be withdrawn from the pCODR review process.

The Submitter must submit a dated written Request for Withdrawal to the pCODR program that contains the following information:

- the name and signature of the Submitter
- the reason that the Request for Withdrawal is being made
- whether or not the Submitter expects to submit the withdrawn Biosimilar Submission again, and if so, the anticipated time frame.

The pCODR program will stop its review of the Biosimilar Submission and will post this information on the pCODR section of the CADTH website.

If Health Canada withdraws market authorization for the Biosimilar under review by the pCODR program at any time during the review process, the Manufacturer must advise the pCODR program, in writing, within five (5) Business Days and must provide the following information:

- the date on which the market authorization was withdrawn
- the reason why the market authorization was withdrawn

The pCODR program will stop the review of a Biosimilar Submission immediately upon being notified of, or learning about, the withdrawal of market authorization for the Biosimilar under review. The pCODR program will advise the Submitter, the Manufacturer of the drug under review (if not the Submitter) and PAG, in writing, that the review has been stopped, and will also post this information on the pCODR section of the CADTH website. The pCODR program will retain one complete copy of the Biosimilar Submission on file.

No refunds will be issued for a withdrawal after the Biosimilar Submission has been deemed complete. Please refer to the CADTH Guidelines for Manufacturers on Application Fees for Pharmaceutical Reviews for more information.

If a Submitter wishes to re-initiate a review of a withdrawn Biosimilar Submission (voluntary withdrawal or withdrawal of market authorization by Health Canada), the Submitter is required to refile a Biosimilar Submission in accordance with this guideline in order for the review to proceed.

4.5 Post-NOC or Post-NOC/c Submission Requirements

These requirements outline information that the pCODR program needs in order to undertake the Clinical and Economic Reviews of Biosimilars that have received an NOC or NOC/c.

To expedite the screening of Submissions for completeness and to facilitate the efficient use of documents, Submitters must provide the information prescribed (sections 4.5.1 and 4.5.2) and in accordance with the electronic file requirements (see Appendix E). Submission requirements must be submitted to the pCODR program only electronically via online submission through the CADTH Collaborative Workspaces of the pCODR section of the CADTH website) and not as hard copies.
4.5.1 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 Submitter, 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 Pre-NOC or Pre-NOC/c Biosimilar Submission)
- the updated or new information that was not provided in the Pre-submission Information
- the New Indication when filing a Biosimilar Submission with a New Indication
- the names of the primary and backup contact(s) that the pCODR program can contact regarding the Submission. Note: The Submitter 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 the pCODR Pre-submission Guidelines as provided on the pCODR section of the CADTH website (www.cadth.ca/pCodr). 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
- 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) Letter Confirming Disclosure of Submitted Information for Biosimilar Review
A signed letter from the Submitter indicating that all submitted information in the CADTH Biosimilar Summary Dossier is disclosable. This letter is provided in Appendix J. The template may also be downloaded from the CADTH Collaborative Workspaces of the CADTH website.

d) Health Canada NOC or NOC/c
A copy of the NOC or NOC/c, dated and signed by Health Canada. If the Biosimilar 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:

- copies of published studies that address key clinical issues, including switching studies; head-to-head comparison clinical trials between the submitted biosimilar drug product and principal reference drug product comparators are of particular interest.
- a list of all completed published studies, including editorial articles and errata relating to them, 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.
- a list of all completed published and unpublished studies not included in the Submission (Note: For Biosimilars 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 oncology indications.

In consultation with PAG, CADTH may conduct a review of evidence for switching from the reference product or another Biosimilar to the Biosimilar under review. These reviews will be conducted using the CADTH Rapid Response process and will be posted on the CADTH website.

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

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

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

g) Cost Comparison Information

The following are required:

Completed section 5.1 of the CADTH Biosimilar Summary Dossier Template. Include details of dosing and wastage, if appropriate.

The submitted price is the price per smallest unit to four decimal places and per smallest dispensable unit for all dosage forms, strengths, and package sizes submitted to CADTH that must be made available to all the participating public drug programs and cancer agencies following the completion of a Biosimilar review and is disclosed following the release of the CADTH Biosimilar Summary Dossier.

Note: If applicable, the disclosable price for a companion diagnostic(s) must also be provided.
h) 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 the pCODR 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
- Pan-Canadian Pharmaceutical Alliance Office
- Health Canada
- Patented Medicine Prices Review Board

This letter template is provided in Appendix H. The template may also be downloaded from the CADTH 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.

i) 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.

j) Completed CADTH Biosimilar Summary Dossier Template

The Submitter must submit a completed CADTH Biosimilar Summary Dossier template in addition to providing the above listed submission requirements.

- Complete all sections of the CADTH Biosimilar Summary Dossier with the exception of sections 5.2, 6.2, 6.3, and 6.4.
- Do not write in sections labelled “To be completed by CADTH reviewers.”
- References must be provided in the following format:
  - In-text citations must be numbered in order of appearance.
  - A numbered reference list must be provided in the Citing Medicine format at the end of the document in the References section.
4.5.2 Additional Information

Additional information may be requested by the pCODR program, and is assessed on a case-by-case basis. Depending on the volume or complexity of material to be reviewed, extension of the review time frame deadlines may be required. The Submitter will be notified of any extensions, and reasons for the extensions.

The Submitter 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 Biosimilar Submission is under review. This may include any communiqués (e.g. “Dear Doctor” letters regarding harm and safety) and any confirmed labelling changes agreed to with international regulatory agencies (e.g. FDA, EMA) relevant to the Biosimilar Submission while the Biosimilar Submission is under review by pCODR.

All Additional Information provided to the pCODR program will be considered disclosable.

4.6 Pre-NOC or Pre-NOC/c Submission Requirements

These requirements outline information that the pCODR program needs to undertake the Clinical and Economic Reviews of Biosimilars Submissions that are Pre-NOC or Pre-NOC/c.

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

a) Signed Cover Letter (see section 4.5.1)
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 4.5.1)
d) Letter Confirming Disclosure of Submitted Information for Biosimilar Review (see section 4.5.1)
e) 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.
   
   Note: Information posted from the product monograph will be based on the final product monograph.
f) Efficacy, Effectiveness, and Safety Evidence (see section 4.5.1)
g) Cost Comparison Information (see section 4.5.1)
h) Letter Authorizing Unrestricted Sharing of Information (see section 4.5.1)
i) Letter of Authorization for Pre-NOC or Pre-NOC/c Submissions
   A Letter of Authorization from the Manufacturer, applying for an NOC or NOC/c, printed on company letterhead and signed by an appropriate senior official (an electronic signature is acceptable), allowing Health Canada to share information with the pCODR.
This letter template is provided in Appendix I. The template may also be downloaded from the CADTH Collaborative Workspaces of the pCODR section of the CADTH website.

j) Companion Diagnostics (see section 4.5.1)
k) Completed CADTH Biosimilar Summary Dossier Template (see section 4.5.1)

4.6.2 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. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared with the draft Product Monograph will be deemed to be significant by pCODR and may result in the delay of the posting target date for the CADTH Biosimilar Summary Dossier. Depending on the nature, extent and complexity of the information, pCODR may need to adjust the timelines for the review.

Note: In the case of a pre-NOC Biosimilar Submission, the Submitter is required to provide an updated CADTH Biosimilar Summary Dossier at the time the NOC or NOC/c is issued by Health Canada. Category 2 requirements must be satisfied before the CADTH Biosimilar Summary Dossier is posted on the CADTH website.

4.6.2.1 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 Submitter, 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;
- the remaining category 2 requirements, for Pre-NOC/c submissions, must be provided as soon as the NOC or NOC/c has been issued to allow the review to be completed without delay. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared with the draft Product Monograph will be deemed to be significant by pCODR and may result in the delay of the posting target date for the CADTH Biosimilar Summary Dossier. 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 CADTH Biosimilar Summary Dossier is posted on the CADTH website.

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.

4.6.3 Additional Information (see section 4.5.2)

4.7 Disposition of Biosimilar Submission Documents

The posting of the CADTH Biosimilar Summary Dossier by the pCODR program signals the completion of the Biosimilar review process. The pCODR program undertakes the steps detailed in this section regarding the disposition of documents associated with the Biosimilar review. The pCODR program follows the same steps in the disposal of documents associated with a withdrawn Submission.

The pCODR program retrieves all paper and electronic copies of the Biosimilar Submission documents from the Review Team.

The pCODR program retains one (1) complete electronic copy of the Biosimilar Submission, where available, and one (1) complete set of all electronic documents associated with the review of a Biosimilar on file in secure storage for as long as there may be a need to consult the documents.

The pCODR program disposes of any paper documents associated with the Biosimilar Submission by confidential shredding. Any additional CD or DVD sets provided in the Biosimilar Submission are destroyed.
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 that 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 they can monitor clinical response to optimally guide treatment adjustments. Companion diagnostics detect specific biomarkers that predict more favourable responses to particular therapeutic products.

CDR: CADTH Common Drug Review

Disclosable Information: 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 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 pCODR 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 and 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: 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: The pCODR program staff person hired by CADTH to provide leadership, development, and delivery of pCODR.

pCODR Program: The Director and staff make up the pCODR program. The Director is responsible for the leadership, development, and delivery of pCODR. 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.

PMPRB: Patented Medicine Prices Review Board. 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 Submitter filing a Submission with the pCODR. In the case of Pre-NOC or Pre-NOC/c Submissions for New Drugs, the only Submitter 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 Submitter type may file the Submission.

Pre-submission Guidelines: The guidelines that have been adopted by pCODR provide guidance to Submitters on the information required by pCODR prior to a Submission being filed and to provide guidance around pre-submission meetings between pCODR and the Submitter.

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. Submitters 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 Withdrawal: A written request by a Submitter to withdraw a Biosimilar Submission from the pCODR review process.

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 CADTH Collaborative Workspaces of the pCODR section of the CADTH website) provided by the Submitter 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.

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

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: pCODR Pre-submission Information Requirements for Biosimilars

<table>
<thead>
<tr>
<th>SUBMITTER/MANUFACTURER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Name of submitter/manufacturer:</td>
</tr>
<tr>
<td>*Primary contact for submission:</td>
</tr>
<tr>
<td>*Back-up/secondary contact for submission:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DRUG INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Name of drug (non-proprietary and brand):</td>
</tr>
<tr>
<td>Is the brand name to be kept confidential until Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) is issued? Yes ☐ No ☐ Not applicable ☐</td>
</tr>
<tr>
<td>*Indication to be reviewed:</td>
</tr>
<tr>
<td>State if the indication is approved or under review by Health Canada</td>
</tr>
<tr>
<td>Dosing (schedule and duration) and route of administration:</td>
</tr>
<tr>
<td>Available strengths:</td>
</tr>
<tr>
<td>*Requested reimbursement criteria:</td>
</tr>
<tr>
<td>A copy of the product monograph is included with this advance notification: Yes ☐ No ☐</td>
</tr>
<tr>
<td>Type of submission (check as appropriate):</td>
</tr>
<tr>
<td>☐ New drug</td>
</tr>
<tr>
<td>☐ New indication</td>
</tr>
<tr>
<td>☐ Biosimilar</td>
</tr>
</tbody>
</table>

* Required Field that must be completed

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2 Manufacturers are asked to provide a PDF copy of the current approved product monograph (not required for submissions filed on a pre-NOC basis, or if not yet available from Health Canada for submissions to be filed on a post-NOC basis).
**COMPANION DIAGNOSTIC**

*Please indicate if there is a companion diagnostic test associated with the identification of the eligible patient population for the proposed drug submission: Yes ☐ No ☐

**HEALTH CANADA REVIEW TYPE**

*The drug is undergoing review by Health Canada through an expedited pathway:
☐ N/A (standard review pathway)
☐ Priority review
☐ Notice of Compliance with conditions (NOC/c) filed at the outset
☐ Other expedited pathway (please specify)

**HEALTH CANADA CONSENT LETTER**

As described in *Notice to Industry: Aligned Reviews Between Health Canada and Health Technology Assessment Organizations*, manufacturers can consent to Health Canada sharing information and documents with CADTH. Please indicate below if you are willing to participate in the information sharing process between Health Canada and CADTH. **Note:** Submitters are required to provide Health Canada with a completed [consent form](#) to participate in this process.

☐ Yes, Health Canada will be or has been provided with a completed consent form.
☐ No, Health Canada will not be provided with a completed consent form.

**KEY DATE INFORMATION (DAY-MONTH-YEAR)**

Date drug accepted for review by Health Canada: DD-MM-YYYY
*Date of NOC (issued or anticipated): DD-MM-YYYY
*Anticipated date of filing this submission with CADTH: DD-MM-YYYY

**CANADIAN TRIALS & PATIENT ACCESS PROGRAMS**

- *Provide the total number of Canadian patients and the number of patients per province who participated in the trials submitted for review.*
- *Provide total number of Canadian patients and the number of patients per province acquiring the drug through Health Canada's Special Access Program (SAP) and/or compassionate programs.*

**CLINICAL OVERVIEW**

*This section should not exceed ONE page and should include:*
• place in therapy (e.g., first-line, niche), current standard of care (including best supportive care), and treatment algorithm used in Canada
• a brief overview of key trials including outcomes, relevant data, trial design, limitations, mean number of treatment cycles per patient or duration of treatment, doses used
• citations and hyperlinked URLs to main articles or pivotal trial, if clinical data are published, or to an abstract or poster.
• NCI clinical trial number and URL

ECONOMIC OVERVIEW

This section should not exceed ONE page and should include:

• a brief overview, description of model parameters (outcomes, comparators and rationale for choice, doses [% intensity], dosing schedule, number of cycles, etc., as applicable)

• a cost comparison table for the biosimilar under review, the reference product and other biosimilars for the same indication(s) requested (if applicable)

INTERNATIONAL COMPARISONS

• Please provide a direct URL link to the respective regulatory and reimbursement decisions. The following template example below may be used:

  *Regulatory status of [Drug Name and Indication] in the following countries:

<table>
<thead>
<tr>
<th>Country/Regulatory Body</th>
<th>Regulatory Status &amp; Date</th>
<th>Direct URL to drug approval decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td></td>
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<tr>
<td>UK</td>
<td></td>
<td></td>
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<tr>
<td>EMA</td>
<td></td>
<td></td>
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<tr>
<td>Australia</td>
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</tbody>
</table>

  *Health Technology Assessment decision in the following countries/organizations:

<table>
<thead>
<tr>
<th>Country/HTA organization</th>
<th>Recommendation &amp; Date or Review Status</th>
<th>Direct URL to HTA recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quebec INESSS</td>
<td></td>
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<td>UK NICE</td>
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<td>Scotland SMC</td>
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<tr>
<td>Germany IQWiG</td>
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<tr>
<td>France HAS</td>
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<tr>
<td>Australia PBAC</td>
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</tbody>
</table>
- For submissions to pCODR, provide hyperlinked URLs to the following international guidelines for the drug and indication(s) under review, if available:
  - NCCN
  - ASCO
  - ESMO

* Required Field that must be completed
APPENDIX C: Guidance to PAG and Tumour Group 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 Submitters can be found in the pCODR Procedures document on the pCODR section of the CADTH website (www.pcodr.ca).

a) Signed Cover Letter

Provide as per section 4.5.1(a). In addition, outline any Submission Requirements that may have been waived in consultation with the pCODR program.

b) Updated Pre-submission Information

All Submitters should complete the Pre-submission Information Requirement Form as outlined in the pCODR Pre-submission Guidelines on the pCODR section of the CADTH website.

In addition, PAG and Tumour Group Submitters 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 conflict of interest declaration form

c) Letter Confirming Disclosure of Submitted Information for Biosimilar Review (see section 4.5.1)

A letter confirming that the submitted information in the CADTH Biosimilar Summary Dossier is disclosable is disclosable (see Appendix J).

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 4.5.1(e).

Health Canada approved product monographs are publicly available and can be found in the Health Canada Drug Product Database: http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp

f) Efficacy, Effectiveness and Safety Evidence

A tabulated list of all published 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 Submitter 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 4.5.1(f).
g) Cost Comparison Information (see section 4.5.1)
h) Letter Authorizing Unrestricted Sharing of Information (see section 4.5.1)
i) Companion Diagnostics (see section 4.5.1)
j) Completed CADTH Biosimilar Summary Dossier Template (see section 4.5.1)
APPENDIX D: 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 E: Electronic File Format Requirements

Specifications:

- Submitters should file a Biosimilar Submission through the CADTH Collaborative Workspaces; however, a Submitter must first register on the pCODR section of the CADTH website. Details on registration can be found at: https://www.cadth.ca/pcodr/registration
- Documents must be provided in MS WORD or PDF format that is unlocked, searchable and printable. 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

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 are required to meet the same format and naming conventions for the electronic files but follow the order for including the information as specifically outlined for these submission types.

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 Presubmission Information
  - 01.03_Brand Name_Health Canada NOC or NOC/c
  - 01.04_Brand Name_Product Monograph

02_Brand Name_Condition_Clinical Information
  - 02.01_Brand Name_Condition_Switching Studies
    - 03. Brown et al.poster.2010.pdf
02.02_Brand Name_Condition_New data generated after NDS
(See Note 1 above for recommendation on labelling references.)

02.03_Brand Name_Condition_Editorial articles and errata
(See Note 1 above for recommendation on labelling references.)

02.04_Brand Name_Condition_Table-Published studies
- Brand Name_Table of studies

02.05_Brand Name_Condition_Search strategies
- Brand Name_Search strategy

03_Brand Name_Condition_Pricing, Sharing of Information
- 03.03.01_Brand Name_Cost Comparison Information
- 03.03.02_Brand Name_Letter Confirming Disclosure of Information
  - 03.03.03_Brand Name_Letter of Authorization (Pre-NOC or Pre-NOC/c)
  - 03.03.04_Brand Name_Letter-Unrestricted Sharing of Information

04_Brand Name_Condition_CADTHBiosimilarSummaryDossier
- 04.01_Brand Name_CADTHBiosimilarSummaryDossierTemplate

Brand Name_Generic Name_Condition_Category 2 (applies to Pre-NOC submissions)

05_Brand Name_Condition_Additional Regulatory and Other Information
### APPENDIX F: Biosimilar Submission Requirements Checklist

**Category 1 & 2**

<table>
<thead>
<tr>
<th>Requirement</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signed Cover Letter</strong></td>
<td></td>
</tr>
<tr>
<td>• Names of primary and backup contacts to be contacted regarding Submission</td>
<td></td>
</tr>
<tr>
<td><strong>Updated Pre-submission Information</strong></td>
<td></td>
</tr>
<tr>
<td>• Supporting references for specified listing when requested by Submitter</td>
<td>□</td>
</tr>
<tr>
<td><strong>Letter Confirming Disclosure of Information</strong></td>
<td>□</td>
</tr>
<tr>
<td><strong>Completed CADTH Biosimilar Summary Dossier Template</strong></td>
<td>□</td>
</tr>
<tr>
<td><strong>Health Canada NOC or NOC/c</strong></td>
<td>□</td>
</tr>
<tr>
<td>• Letter of Undertaking (if NOC/c)</td>
<td>□</td>
</tr>
<tr>
<td><strong>Product Monograph</strong></td>
<td>□</td>
</tr>
<tr>
<td>• Draft Product Monograph (for Pre-NOC Submission)</td>
<td>□</td>
</tr>
<tr>
<td>• Final Product Monograph</td>
<td>□</td>
</tr>
<tr>
<td><strong>Efficacy, Effectiveness, and Safety Evidence</strong></td>
<td>□</td>
</tr>
<tr>
<td>• Critical studies that address key clinical issues</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>• Tabulated list of published and unpublished studies (Appendix G)</td>
<td>□</td>
</tr>
<tr>
<td><strong>Cost Comparison Information</strong></td>
<td>□</td>
</tr>
<tr>
<td>• Submitted pricing reported as price per smallest unit to four decimal places</td>
<td>□</td>
</tr>
<tr>
<td>• Method of distribution</td>
<td>□</td>
</tr>
<tr>
<td><strong>Letter Authorizing Unrestricted Sharing of Information</strong></td>
<td>□</td>
</tr>
<tr>
<td><strong>Letter of Authorization for Pre-NOC or Pre-NOC/c Submissions</strong></td>
<td>□</td>
</tr>
<tr>
<td><strong>Companion Diagnostics (if applicable)</strong></td>
<td>□</td>
</tr>
</tbody>
</table>

*Note: For pre-NOC Submissions, Submitters must provide this information as soon as NOC or NOC/c is issued. Please note that any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared with the draft Product Monograph will be deemed to be significant by pCODR and may result in the delay of the posting target date for the CADTH Biosimilar Summary Dossier. 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 CADTH Biosimilar Summary Dossier is posted on the CADTH website.*
APPENDIX G: 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.
†††Contact the pCODR Program for guidance if Drug has been available for more than 10 years in Canada or internationally.
APPENDIX H: 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
pan-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 the pCODR Program 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
- 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 I: Letter of Authorization Template for Pre-NOC or Pre-NOC/c Submissions Only

[Manufacturer’s letterhead]

[Date]

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

Bureau Director
[Bureau]
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada

Dear Bureau Director [TPD and pCODR]

Re:  [Product Name], [Health Canada Submission No.]

This letter serves to authorize the pan-Canadian Oncology Drug Review (pCODR) program to request that Health Canada provide the pCODR with information submitted by [submission sponsor] to Health Canada regarding the above-noted drug submission. This authorization shall only apply to information submitted up to and including the date of the decision by Health Canada regarding market authorization.

This letter also serves to authorize Health Canada to release the requested information set out above, with the restrictions noted, to the pCODR. Health Canada may also respond to inquiries from the pCODR regarding the information provided pursuant to this letter of authorization. Please note that any reports resulting from the information submitted by your organization prepared by, or on behalf of, Health Canada in consideration of your submission, may also be shared with pCODR subject to any applicable restrictions.

[Signature]

[Name and title of authorizing officer]

[Submission manufacturer corporate name]
APPENDIX J: Letter Confirming Disclosure of Submitted Information for Biosimilar Review

[Manufacturer’s letterhead]

[Date]

Director
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] agrees that all submitted information provided in the CADTH Biosimilar Summary Dossier for [drug name and indication(s)] is fully disclosable.

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX K: Verification of Information for Biosimilar Review

If during the review of the dossier, the Submitter and/or Manufacturer of the Biosimilar under review identify any discrepancies or errors, these discrepancies or errors should be submitted in writing to pCODR within the **three (3) Business Day period** through the [CADTH Collaborative Workspaces](https://www.cadth.ca/cdhc-cadth-collaborative-workspaces).

pCODR will consider the proposed discrepancies and errors and make revisions to the [CADTH Biosimilar Summary Dossier](https://www.cadth.ca/cadth-biosimilar-summary-dossier) as deemed necessary by the pCODR program and prior to public posting of this document. Discrepancies and errors should be documented in a table using the format provided below:

<table>
<thead>
<tr>
<th>Verification of Discrepancies or Errors for Biosimilars</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gross Factual Errors</strong></td>
</tr>
<tr>
<td>Report Location (page number)</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
