CADTH

pan-Canadian Oncology Drug Review Disclosure of Information Guidelines

August 2019

RECORD OF UPDATES

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INQUIRIES

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1 Purpose

CADTH's pan-Canadian Oncology Drug Review (pCODR) program has developed the following Disclosure of Information Guidelines to ensure appropriate steps and procedures are in place so that the disclosure of information obtained through the pCODR review process is handled and managed in a consistent manner. These Guidelines, together with the pCODR Pre-Submission, Submission and Resubmission Guidelines and pCODR Procedures, provide clarity to the pCODR program and Sponsors/Contributors on how to both appropriately protect and disclose information, allowing for a drug review process that is transparent and accountable.

2 Use

The pCODR program complies with these guidelines when handling information, as part of the pCODR review process. By filing a 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 application of the Disclosure of Information Guidelines. The Disclosure of Information Guidelines constitute an agreement between CADTH and the Sponsor/Contributor.

The pCODR Disclosure of Information Guidelines are applicable to information received as part of a pCODR Submission or Resubmission; they are not applicable to Pre-Submission Information that is received by the pCODR program. The pCODR program will treat all Pre-submission Information provided by the Sponsor as Non-Disclosable, subject to the information that may be posted for a Pending Submission as set out in the pCODR Procedures.

3 Definitions

For the purposes of these guidelines:

3.1 A **Contributor** is 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 and, registered clinician(s) and patient groups.

3.2 A **Sponsor** is the person, corporation or entity submitting a drug to the pCODR program for review and may include the manufacturer of the drug product, a provincially-recognized clinician-based Tumour Group, or the Provincial Advisory Group.

3.3 **Disclosable Information** is any information that falls into either of the following two categories:

a) All information included in a Submission or Resubmission, or anything received by the pCODR program related to the product after a Submission or Resubmission has been filed to the pCODR program unless such information has been clearly identified by a Contributor or Sponsor as Non-Disclosable Information (see definition of Non-Disclosable Information); or

b) Any information that has been identified by a Sponsor or Contributor as Non-Disclosable where such information falls into any one of the following categories:

i) the information has been put into the public domain, in written or electronic form, anywhere in the world;

ii) the information is comprised of a structured summary of evidence from clinical trials provided by the Sponsor/Contributor where such information has not been put into the public domain, in written or electronic form, anywhere in the world. This summary should follow a recognized format for a full trial report, such as that provided by the CONSORT statement. See: www.consort-statement.org;

iii) the information is comprised of an unpublished structured summary or clinical report which the Sponsor/Contributor has agreed to put in the public domain where such summary or report has not been put into the public domain prior to the expiry of the time frame for disclosure agreed upon by the Sponsor with the pCODR program, which shall be no greater than 6 to 12 months from the date of posting of a pERC Initial Recommendation; notwithstanding, if the Sponsor/Contributor requests for a time frame of greater than 6 months, the Sponsor/Contributor must provide a confirmation letter (e.g., acceptance letter from a publication) that the information has been submitted and will be put into the public domain;

iv) the information is comprised of a description of the design, methods and results of the economic model and the design, methods and overview of results of the budget impact analysis used in the Submission or Resubmission (see Appendix C for a structured summary of required economic information for disclosure and Appendix D for an example of this structure summary);

v) the information is comprised of the list price of a drug after the drug has been made available for sale and marketing in Canada (i.e., after launch); for greater clarity, a Sponsor must provide a disclosable price or market price at the time that the submission is made to the pCODR program for each Submission or Resubmission;

vi) the information is comprised of the list price of the relevant comparator(s) included in a Submission or Resubmission;

vii) the information is comprised of the disclosable price or market price for companion diagnostic(s) at the time that the submission is made to the pCODR program for each Submission or Resubmission (if applicable);

viii) the information was already in the possession of pCODR Review Participants (pCODR staff and partners, pCODR Advisory Committee, pERC members, clinical and economic guidance panel members, tumour groups, registered clinician(s), patient groups, Provincial Advisory Group (PAG), cancer agencies, Federal, P/T governments, P/T health authorities, Health Canada, Patented Medicine Prices Review Board (PMPRB), Canadian Association of Provincial Cancer Agencies (CAPCA) or Pan-Canadian Pharmaceutical Alliance (PCPA)) without restriction as to its use or disclosure; or

ix) the information is rightfully disclosed to pCODR Review Participants by a third party who is not under any obligation as to confidentiality or non-disclosure.

3.4 Subject to the exceptions noted in subsection 3.3b) above, **Non-Disclosable Information** is information that is any one of the following:

a) Scientific, clinical, or technical information supplied by a Sponsor/Contributor in a document that is clearly marked “non-disclosable”, “not disclosable”, or “confidential”;

b) Marked “non-disclosable”, “not disclosable”, or “confidential” due to the commercially sensitive nature of the information, including the executable form of the health economic and budget impact analysis models, market research data, manufacturer drug market share forecasts, assumptions on competitor market share projections, and budget impact analysis results; or

c) Scientific, technical or commercial information not previously put into the public domain, in written or electronic form anywhere in the world, received as a result of the exchange of information described in the section on Access to Information and Freedom of Information Legislation and that relates to a manufacturer’s business or a manufacturer’s drug product.

4 Principles

4.1 To ensure that the pCODR review process is transparent and accountable, the pCODR program considers it essential that the evidence upon which pERC’s recommendations are based be publicly available.

4.2 When circumstances warrant public posting of information by the pCODR program regarded by the owner as Non-Disclosable or in accordance with these guidelines, both parties will negotiate in good faith to seek to find a mutually acceptable solution, recognizing the need for the pCODR program to support its recommendations with evidence available in the public domain and the information owner’s right to determine a global publication strategy.

4.3 The pCODR program recognizes that the information owner retains the right to make a final decision in relation to the release of information into the public domain. The pCODR program reserves the right to determine how Non-Disclosable Information is used in the pCODR review process, including pERC deliberations, if at all. Under certain circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information, once it has been agreed mutually by the pCODR program and the Sponsor to be Non-Disclosable (see subsection 3.4). In other circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information for a defined time-limited period [see subsection 3.3b)iii)]. The pCODR program will always strive for the shortest time period of non-disclosure possible.

4.4 All Disclosable Information may be publicly disclosed in the absolute discretion of the pCODR program.

5 Procedure for Determining if Information is Non-Disclosable Information

5.1 Information identified by the Sponsor as Non-Disclosable Information is not Non-Disclosable Information until such information is confirmed as such through the procedure outlined below and in Appendix A.

a) During the submission process, the Sponsor and the pCODR program will have a checkpoint meeting (as indicated in the pCODR Procedures document; see also Appendix A), at which point the information identified as Non-Disclosable Information by the Sponsor will be discussed. If agreement on how to manage the disclosure of information in the Submission cannot be reached at the meeting, the Sponsor will have 5 Business Days to propose a resolution such as, but not limited to, acceptable wording for public disclosure, use of alternative information that is in the public domain and conveys the same intent or time-limited non-disclosure.

b) The pCODR program will have 5 business days to review the proposed resolution and determine whether or not it is acceptable, whether there may be delay in the review to allow for further discussion with the Sponsor on mutually acceptable approaches to disclosure and whether or not to refrain from using the information in the Clinical Guidance Report and/or Economic Guidance Report.

c) If agreement cannot be reached, the pCODR program will not use the information in the Clinical Guidance Report and/or Economic Guidance Report or pERC deliberations. Only in rare circumstances, where the pCODR program is of the view that the inclusion of such information in the Clinical and/or Economic Guidance Reports is necessary for the integrity of pERC recommendations (e.g., important safety/harms information), the pCODR program reserves the right to use such information and pCODR will note that while the Sponsor refused to propose a means of disclosure of the information that was acceptable by the pCODR program, the information was nonetheless used to preserve the integrity of the pERC recommendations.

6 pCODR Structure and Access to Information and Freedom of Information Legislation

6.1 pCODR Structure

pCODR is a program of CADTH that is designed to assess the clinical evidence and cost effectiveness of new cancer drugs and patient and clinician perspectives, and uses this information to make recommendations to the federal, provincial and territorial governments to help guide their cancer drug funding decisions.

6.2 Application of Freedom of Information and Protection of Privacy Legislation to CADTH

Given its nature, pCODR, a program of CADTH, is not subject to federal or provincial freedom of information and protection of privacy legislation. CADTH is a private, not-for-profit organization and is therefore not subject to either federal access to information or provincial/territorial freedom of information statutes. However, many of the P/T health authorities and other partner organizations of CADTH are subject to such legislation. Each P/T health authority and other partner is responsible for interpreting and complying with the applicable legislation, including with regard to third party notification. Any Freedom of Information or Access to information request should be

made through the appropriate P/T health authorities or partner organization and not to CADTH or the pCODR program.

Sponsors are asked to consent to the information in their Submission or Resubmission being shared with federal, P/T governments, P/T health authorities, Drug Plans, Health Canada, PMPRB and the PCPA by signing a letter in the form available in the pCODR Pre-Submission, Submission and Resubmission Guidelines. Each of these bodies has their own disclosure of information procedures and are subject to provincial and federal access to information and freedom of information legislation. CADTH has no jurisdiction or control over these procedures and statutory requirements. Sponsors/Contributors should be aware of these procedures and requirements when including Non-Disclosable Information in a Submission or Resubmission.

6.3 Information Received by pCODR through Access to Information or Freedom of Information Legislation

When information is received by the pCODR program through access to information or freedom of information legislation, it is treated in the same way as a Submission or Resubmission, according to these guidelines. Any Non-Disclosable Information received by the pCODR program through access to information or freedom of information legislation is treated as Non-Disclosable Information pursuant to these guidelines.

7 Handling Non-Disclosable Information

7.1 Responsibilities of the pCODR program

a) The pCODR program is responsible for ensuring that the review process is transparent and accountable. As such, the pCODR program considers it essential that the evidence upon which pERC's recommendations are based be publicly available.

b) The pCODR program will request the Sponsor to reconsider any restrictions on disclosure of information if there appears to be no obvious reason for the restrictions, or when such restrictions would make it difficult or impossible for the pCODR program to show the evidence on which a recommendation is based.

c) The pCODR program will provide an opportunity to the Sponsor, prior to pERC deliberations, to create a common understanding between the pCODR program and the Sponsor of the Non-Disclosable Information in the Submission or Resubmission, as defined by these guidelines, and to understand the management of information not previously put into the public domain.

d) The pCODR program will not put any review documents into the public domain before the product has received Canadian regulatory approval even though a Submission or Resubmission may start before Canadian regulatory approval has been granted.

e) The pCODR program will use reasonable care to prevent the unauthorized use, disclosure, publication or dissemination of Non-Disclosable Information in a Submission or Resubmission. The pCODR program is responsible for redacting and/or removing information that has been agreed to be Non-Disclosable Information by both the Sponsor and the pCODR program.

f) The pCODR program will provide an opportunity to the Sponsor to review the Clinical and Economic Guidance reports, after these reports have been reviewed by the pERC but before they are put into the public domain. The purpose of this opportunity is for

the Sponsor to verify that the pCODR program has adhered to the management of information not previously put into the public domain, as agreed to by the pCODR program and the Sponsor in section 5 and to understand the disposition of information further provided by the Sponsor after the checkpoint meeting.

g) The pCODR program will not disclose Non-Disclosable Information in a Submission or Resubmission to any third party except as permitted by these Disclosure of Information Guidelines, or as required by law or by order of a legally qualified court or tribunal.

h) The pCODR program will use the Non-Disclosable Information in a Submission or Resubmission solely for the purpose of carrying out its responsibilities with respect to pCODR

i) The pCODR program has in place secure filing and storage, a password protected web portal and processes for tracking Submissions and Resubmissions which may contain Non-Disclosable Information

j) The pCODR program has in place internal processes for dealing with Non-Disclosable Information in a Submission or Resubmission as described in this guideline.

7.2 Responsibilities of the Sponsor/Contributor

a) Material identified as Non-Disclosable Information within a Submission or Resubmission is expected to be kept to a minimum. It is not acceptable to mark an entire Submission or Resubmission as Non-Disclosable. When the Sponsor/Contributor believes that part of a Submission or Resubmission or statement should be treated as Non-Disclosable, they must clearly state the reason for this.

b) If a Submission or Resubmission, or anything received by the pCODR program related to the product after a Submission or Resubmission has been filed contains Non-Disclosable Information, it is the responsibility of the Sponsor/Contributor to clearly identify through highlighting that information which they consider to be Non-Disclosable information. Highlighted information shall also be listed in the summary table described below (see also Appendix B).

c) A summary table listing submitted Non-Disclosable Information (see Appendix B) must also be completed with a general justification for considering any highlighted information as potentially Non-Disclosable. The justification shall identify which subsection of the definition of Non-Disclosable Information in Section 3.4 of these Disclosure of Information guidelines is being applied and how the information meets the definition. This table shall also provide a proposed timeframe for when the potentially Non-Disclosable information may be put into the public domain by the Sponsor or a third party. This table shall be included as part of Submission or Resubmission that is filed with the pCODR program. If the pCODR program does not receive a completed table with a Submission or Resubmission or submitted document, none of the information will be considered Non-Disclosable Information. It is only this table and its contents which shall form the basis of confirming Non-Disclosable Information as outlined in the procedures of section 5.

d) The Sponsor will commit to putting into the public domain, any clinical or economic information that was determined to be relevant to pERC deliberations, and which was agreed to be redacted from Clinical or Economic Guidance Reports or pERC recommendations due to the Non-Disclosable nature ascribed to the information at that point. This redaction shall be time-limited, for the duration that was agreed to by pCODR and the Sponsor or for up to 6 to 12 months from the time of the posting of

the pERC Initial Recommendation, whichever is the lesser. As outlined in subsection 3.3(b)(iii) of this Guideline, if the Sponsor/Contributor requests for a time frame of greater than 6 months, the Sponsor/Contributor must provide a confirmation letter (e.g., acceptance letter from a publication) that the information has been submitted and will be put into the public domain.

e) Care should be taken when submitting information relating to individuals. Personal identifiers and sensitive information will be removed.

f) Sponsors submitting a drug for review must sign a statement declaring that all unpublished studies known to the Sponsor have been disclosed to the pCODR program, as outlined in Appendix L of the pCODR Pre-Submission, Submission and Resubmission Guidelines.

7.3 Sharing of Information

a) A Submission or Resubmission, which may include Non-Disclosable Information, may be shared in whole or in part with the following (the Authorized Recipients)

- CADTH Staff
- Clinical Guidance Panel members including applicable ad hoc clinical panel members, Economic Guidance Panel members and Methods Team
- pERC Members
- PAG and pCODR Advisory Committee members
- Canadian Association of Provincial Cancer Agencies (CAPCA)
- Participating P/T Ministries and Provincial Cancer Agencies
- Federal, P/T governments and drug plans, including their agencies and departments
- P/T health authorities, including regional health authorities
- Pan-Canadian Pharmaceutical Alliance (PCPA) Office
- Health Canada
- PMPRB

b) All persons described above (with the exception of staff of Cancer agencies, Federal, P/T governments, P/T health authorities, Health Canada, PMPRB, CAPCA, PCPA) are required to sign a Confidentiality agreement requiring them to comply with these Guidelines.

c) The Submission or Resubmission, which may include Non-Disclosable Information, may be discussed amongst any or all of these groups and any of the bodies name in the letter signed by the Sponsor/Contributor authorizing unrestricted communication about the Drug. The form of this letter is outlined in the pCODR Pre-Submission, Submission and Resubmission Guidelines.

d) In the case of a Pre-NOC Submission, information regarding the manufacturer's product, including Clarifaxes and other relevant information, may be shared between Health Canada and CADTH as authorized in a signed letter from the manufacturer. As described in the *Notice to Industry: Aligned Reviews Between Health Canada and Health Technology Assessment Organizations*, an optional information sharing process has been established to permit Health Canada and CADTH to exchange information regarding the drug under review, for submissions filed with CADTH on a pre-NOC basis. Participation in this process could ensure that CADTH has advance notice of any issues that have the potential to impact CADTH's review of the drug (e.g., changes to

the indicated patient population), potentially avoiding delays in the issuance of CADTH's recommendation.

e) CADTH Staff, the Methods Team, Clinical and Economic Guidance Panel members, PAG and pCODR Advisory Committee members must abide by the confidentiality clauses contained in their Code of Conduct and/or Conflict of Interest Guidelines.

f) Submission or Resubmission documents may be shared by organizations, in whole or in part, to third parties when it is necessary to enable the organization to contribute to the pERC's deliberations and recommendation and the third party has seen and agreed to be bound by the terms of a Confidentiality agreement.

7.4 Documents and Information that May Be Shared

a) The following documents and the information contained in them, including Non-Disclosable Information may be shared with the Authorized Recipients and may be posted on a secure, password protected web portal, accessible only by persons authorized according to these Disclosure of Information Guidelines:

- Drug Submission or Resubmission
- Clinical and Economic Guidance Reports
- pERC Initial and Final Recommendations
- pERC Brief and Reconsideration Brief
- other review related documents that are generated through the pCODR review process

b) The following documents listed in the table below will be posted on the pCODR section of the CADTH website. After the pCODR program has posted these documents on its website they are considered in the public domain and Disclosable Information.

Document	Earliest Estimated Timeline for Public Posting by pCODR*
Clinical Guidance Report	80 business days
Economic Guidance Report summary	80 business days
pERC Initial Recommendation	80 business days
Sponsor Feedback on pERC Initial Recommendation	90 business days
PAG Feedback on pERC Initial Recommendation	90 business days
pERC Final Recommendation	90 business days

** For the purposes of calculating these timelines, Day 0 is the day the Submission or Resubmission is deemed complete and assuming market authorization has been issued.*

c) In addition, tracking information indicating the status of a Submission in the review queue will be publicly posted on the CADTH website, as outlined in the pCODR Procedures document, General Information section. Notwithstanding the foregoing, in the event of a Submission being reviewed prior to regulatory approval for the drug product, pCODR will not post product strength, product format and NOC date, until such time as regulatory approval has been issued.

d) It is the responsibility of Authorized Recipients and any other party that has signed a Confidentiality agreement for the review to treat all review documents listed in subsection 7.4b) that are not in the public domain as Non-Disclosable Information until pCODR puts those documents into the public domain. Authorized recipients which are organizations that have signed a non-disclosure or confidentiality agreement are required to bind the individuals of their organization to the requirements of the agreement.

7.5 Referring to Non-Disclosable Information in pCODR Documents That are Publicly Available

a) In its Clinical and Economic Guidance reports and pERC recommendation briefs, pCODR reserves the right to use any material submitted during the review process that is not marked as "non-disclosable", "not disclosable," or "confidential", or unpublished information which the Sponsor/Contributor has agreed with the pCODR program may be put into the public domain.

b) If the Sponsor/Contributor identifies Non-Disclosable Information in the Submission, Resubmission or other information provided to pCODR after the Submission or Resubmission has been filed, and pCODR has agreed to allow for its use in the review process and consideration by pERC, pursuant to the procedures outlined in these guidelines, the pCODR program will redact the Non-Disclosable Information prior to posting on the public website. In the case of redactions, the pCODR program will 'black out' the Non-Disclosable Information. The pCODR documents may make reference to and indicate the type of information that was redacted (e.g. harms, efficacy, economic evidence) and that the Sponsor requested this Non-Disclosable Information be redacted, pursuant to the pCODR Disclosure Guidelines. The pCODR program may also make reference to the name of the study or such relevant information. The pCODR program may make reference to any time-limit to redaction that has been agreed to by the Sponsor and the pCODR program.

c) The pCODR program expects that Non-Disclosable Information referred to or redacted from the Clinical and Economic Guidance reports or pERC recommendations will be published upon notification by the Sponsor that it can be publicly disclosed or in accordance with the date that the information may be disclosed agreed to by the Sponsor and the pCODR program, whichever is earlier.

7.6 Archiving of Non-Disclosable Documents

In addition to the details outlined in the pCODR Procedures document regarding the disposition of Submission or Resubmission documents, the pCODR program undertakes the following steps regarding the retrieval, archiving and disposal of Non-Disclosable Information:

- all paper and electronic copies of the Submission or Resubmission documents are retrieved from the pCODR Review Team at the completion of the review.
- one (1) complete CD/DVD set of the Submission and one complete set of all documents (paper and/or electronic) associated with the review of a Drug are retained on file in secure storage for as long as there may be a need to consult the documents.
- all other extra copies of paper and electronic documents associated with a review are disposed of as described below.

- regular reviews of archived material are undertaken by the pCODR program. Any material that is no longer required is disposed of as described below.

7.7 Disposal of Non-Disclosable Documents

The pCODR program will dispose of any paper documents associated with the Submission or Resbumission by confidential shredding. Any additional CD/DVD sets provided in the Submission are destroyed.

The pCODR program will advise the Sponsor, in writing, that it has disposed of the extra copies of documents at the completion of the review of the Submission or Resubmission.

Appendix A: pan-Canadian Oncology Drug Review Checkpoint Meeting

1. Purpose of Checkpoint Meeting

The purpose of the pCODR Checkpoint Meeting with the Sponsor is: (1) to directly clarify information in the Submission and any Additional Information being provided with members of the pCODR Review Team and (2) to discuss the management of Non-Disclosable Information included in the Submission. The Checkpoint Meeting is not for the purposes of confirming information that the pCODR Review Team will include in the report or to solicit the pCODR Review Team's interpretation of the Submission.

The pCODR Checkpoint Meeting with the Sponsor will be conducted as outlined in the *pCODR Procedures*, which is available on the pCODR section of the CADTH website, www.cadth.ca/pcodr. Information and details provided in this document, the pCODR Checkpoint Meeting Template, give additional guidance around the conduct of the Checkpoint Meeting with the Sponsor and any required follow-up actions resulting from the Checkpoint Meeting.

If procedures relating to the Checkpoint Meeting are not followed as outlined below or as outlined in the *pCODR Procedures*, the review of the Submission may be delayed or suspended.

2. General Format of the Checkpoint Meeting

The Checkpoint Meeting will occur in two parts and the conduct of each part of the meeting differs. Part one of the Checkpoint Meeting will be to clarify information in the Submission/Resubmission and any Additional Information being provided. Part two of the Checkpoint Meeting will be to discuss the management of Non-Disclosable Information included in the Submission or Resubmission. Part one and part two of the Checkpoint Meeting will be scheduled consecutively with a short break in between.

If the Sponsor is not the manufacturer of the drug under review and the manufacturer has contributed substantive clinical or economic information to the review, the manufacturer may be invited to attend the Checkpoint Meeting with the Sponsor.

Sponsor and manufacturer attendees are required to attend the Checkpoint Meeting with pCODR in-person.

The Checkpoint Meeting will occur, in part, as a teleconference or in a webinar format to maintain the anonymity of the Submission-specific Review Team members. (Note: the pCODR program will disclose a general list of individuals involved in pCODR reviews but does not divulge Submission specific Review Teams as outlined in section B3.1.10 of the *pCODR Procedures*.) The anonymity of the Review Team is preserved by the pCODR program in order to protect pCODR participants from undue influence, to maintain the integrity of assessments without fear of reprisal and to limit the potential for harassment and intimidation of Review Team members in their professional capacity. The Sponsor must not attempt to identify members of the Review Team during the interactive meeting.

Both part one and part two of the meeting will be recorded by the pCODR program and a record of the meeting will be retained on file at CADTH.

There is a maximum of four Sponsor attendees for each part of the Checkpoint Meeting. Sponsor attendees may differ for part one and part two of the meeting. No legal representation is permitted at the Checkpoint Meeting. A list of all attendees must be provided to the pCODR

program at least 5 business days in advance of the meeting, otherwise the meeting may be cancelled. If a Checkpoint Meeting is not held by the target date, the pCODR program cannot guarantee the review will be completed within the posted timelines and/or the review may be temporarily suspended.

3. Clarification of Information – Part One of the Checkpoint Meeting

The procedures outlined below relate to part one of the Checkpoint Meeting.

- At part one of the Checkpoint Meeting, the Sponsor will have an opportunity to provide, directly to the pCODR Review Team, responses to the clarifying questions and the request for Additional Information, which were sent to the Sponsor ten (10) Business Days in advance.
- An electronic version of the Sponsor responses to the clarifying questions and requests for Additional Information must be provided to pCODR at least **one (1) business day** in advance of the scheduled Checkpoint Meeting so that these can be provided to the pCODR Review Team prior to the interactive meeting.
- The duration of part one of the Checkpoint Meeting will be a maximum of one hour. Sponsors will be provided with approximately 30 minutes to present responses to the submitted questions. The remainder of the meeting will allow for further clarifications based on the submitted questions and presented responses.
- Sponsors should limit questions for the Review Team to topics raised in the list of submitted questions. Questions outside the scope of the Checkpoint Meeting will not be addressed at the meeting.
- Sponsor attendees should include individuals with clinical and economic content expertise who will be able to provide adequate clarification on the content of the Submission to the pCODR Review Team.
- Attendees from the pCODR program can include CADTH staff, Clinical Guidance Panel members, Economic Guidance Panel members and individuals with methodological expertise who are assigned to the Review Team.
- Anonymous communication during the meeting between the pCODR Review Team and the Sponsor will be facilitated by the pCODR program.

4. Review of Non-Disclosable Information - Part Two of the Checkpoint Meeting

The procedures outlined below relate to part two of the Checkpoint Meeting.

- At part two of the Checkpoint Meeting, the pCODR program and the Sponsor will discuss the management of Non-Disclosable Information included in the Submission.
- The duration of part two of the Checkpoint Meeting will be a maximum of one hour. At the meeting, the pCODR program and the Sponsor will go through the submitted Summary of Non-Disclosable Information tables and any submitted structured summaries of economic and clinical information, focusing on relevant information that may be included in the pCODR Clinical Guidance Report and the pCODR Economic Guidance Report.
- If new Non-Disclosable Information is provided in part one of the meeting, an Addendum to the Summary Table of Non-Disclosable Information an electronic version must be provided by the Sponsor at least **one (1) business day** in advance of the scheduled Checkpoint Meeting. No additional meeting materials are required.

- Sponsor attendees should include at least one senior representative with the authority to make decisions regarding disclosure of information.
- Attendees from pCODR will include only CADTH staff.

5. Checkpoint Meeting Decisions

The pCODR program will write a *Record of Decisions* for the Checkpoint Meeting. Decisions will include both those related to Additional Information and clarification of the Submission as well as the review of Non-Disclosable Information in the Submission. Both pending decisions and decisions agreed upon at the Checkpoint Meeting will be documented.

The *Record of Decisions* will be provided to the Sponsor and/or Manufacturer within two (2) business days of the Checkpoint Meeting via secure electronic transmission. An email notification will be sent to the Submission contact with a unique, time-limited and user-specific link to the Record of Decisions. The Submission contact is the individual identified as the contact by the Sponsor when the Submission was filed with pCODR.

Decisions made at the meeting will not be open for further negotiation and discussion following the Checkpoint Meeting.

Upon receipt of the Record of Decisions, the Sponsor will have five (5) Business Days to submit proposed resolutions to items noted as pending decisions. The Sponsor should provide the resolution to pCODR through the secure Collaborative Workspaces.

The pCODR program will have five (5) Business Days to review the proposed resolutions. If agreement cannot be reached, pCODR will not use the information in the Clinical Guidance Report or the Economic Guidance Report provided to the pCODR Expert Review Committee (pERC).

An *Addendum to the Record of Decisions* will be written by pCODR and provided to the Sponsor via secure electronic transmission, within five (5) Business Days of receiving the proposed resolutions from the Sponsor. The *Addendum* will outline pCODR's final decisions on the management of Non-Disclosable Information in the review. An email notification will be sent to the Submission contact with a unique, time-limited and user-specific link to the *Addendum to the Record of Decisions*.

The pCODR program may share the *Record of Decisions* and *Addendum to the Record of Decisions* with Authorized Recipients, as defined in the *pCODR Disclosure of Information Guidelines*.

6. Verification of Handling Non-Disclosable Information Following the Checkpoint Meeting

Three (3) days prior to the posting of the pERC initial recommendation and the pCODR guidance reports, the Sponsor will be provided with the opportunity to verify that Non-Disclosable Information was handled in the manner agreed upon at the Checkpoint Meeting, and as documented in the *Record of Decisions* and the *Addendum* to the Record of Decisions.

The Clinical Guidance Report and Economic Guidance Report to be publicly posted will be made available to the Sponsor via secure electronic transmission. An email notification will be sent to the Submission contact with a unique, time-limited and user-specific link to the Clinical Guidance Report and Economic Guidance Report.

If during the review of the report, the Sponsor and/or Manufacturer of the drug under review identify any discrepancies or errors, they should be submitted in writing to pCODR within the three (3) Business Day period through the secure Collaborative Workspaces. pCODR will consider the proposed discrepancies and errors and make revisions or additional redactions to the Clinical Guidance Report, the Economic Guidance Report and the pERC Initial Recommendation as deemed necessary by the pCODR program and prior to public posting of these documents. Discrepancies and errors should be documented in a table using the format provided below:

Verification of Non-Disclosable Information in Guidance Reports			
Discrepancies or Errors in Handling Non-Disclosable Information			
Report Location (EGR or CGR, page number)	Statement	Agreed upon handling of Non-Disclosable Information as per Checkpoint Meeting *Record of Decisions* & *Addendum*	Proposed Handling of Information
Gross Factual Errors			
Report Location (EGR or CGR, page number)	Statement	Correct Information and Location in Submission	Proposed Handling of Information

CGR: Clinical Guidance Report; EGR: Economic Guidance Report

Appendix B: Template for Summary Table Listing Submitted Non-Disclosable Information

[Date]

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

Dear Director:

Reference: **[Brand name, generic name]**

[name of Manufacturer/Sponsor] confirms that the information included in the Table below has not been put into the public domain, in written or electronic form, anywhere in the world (e.g., FDA report, EMA report, etc.) or falls within the definition as set out in clause 3.3(b) of this *pCODR Disclosure of Information Guidelines*, known to this sponsor, 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]**.

Row Number	Type of Info (Economic/Clinical)	Description	Location in Submission (Folder or tab name, page number)	Definition of Non-Disclosable Information being applied, pursuant to subsection 3.4 and the exceptions outlined in subsection 3.3b) of pCODR Disclosure of Information Guidelines	Estimated Date Info will be put into Public Domain
1.					
2.					
3.					
4.					

[Name and Title of Senior Company Official of Manufacturer of Product]

Appendix C: Template for pCODR Structured Summary of Economic Information for Disclosure

Part 1: Economic Evaluation Structured Summary Template

Reporting of economic studies should follow best reporting practices and be guided by the structure outlined below, which has been adapted from the NHS Economic Evaluation Database (NHS EED), http://www.crd.york.ac.uk/CMS2Web/AboutNHSEED.asp. Other examples of structured economic summaries can also be found in this database. Please see Appendix B for an example from this database, which has been adapted to follow the outline below.

Information provided in this summary may be publicly disclosed as per the pCODR Disclosure of Information Guidelines. In addition, the pCODR Economic Guidance Panel's interpretation and evaluation of the economic information provided in the pCODR Submission will be made publicly available.

STUDY DESIGN AND METHODS
Type of economic evaluation
Study Objective
Perspective
Disclosable Price of Drug Under Review
Disclosable price for companion diagnostic(s) associated with Drug Under Review (if applicable)
Disclosable Price of Relevant Comparator(s)
Interventions and Comparators
Patient population (e.g. cancer type, disease stage, treatment-experience/line)
Analytical Approach
Key model inputs and data sources (clinical and economic) Note: In cases where an indirect treatment comparison applies, a Sponsor should include the objective, methodology (including the inclusion/exclusion criteria, included studies) and a summary statement on the conclusion of the results of the indirect comparison conducted.
Time Horizon
Model Assumptions (e.g., include drug wastage)
Analysis of Uncertainty
RESULTS
Base-Case Analysis (ICER, ΔC, ΔE)*
Key Sensitivity Analyses (ICER, ΔC, ΔEs)*
SUBMITTED CONCLUSIONS

**** Quantitative values for ICERs, incremental costs and incremental effects, life years and life years gained must be included in the structured summary. ICERs are based on the list or disclosable price.***

Part 2: Budget Impact Analysis Structured Summary Template

STUDY DESIGN AND METHODS
BIA Objective
BIA Methods
Overview of BIA Results and Sensitivity Analyses

Appendix D: Example of pCODR Structured Summary of Economic Information for Disclosure

The following are examples of the types of economic summaries Sponsors will be asked to provide pCODR in order to facilitate the disclosure of economic information reviewed as part of the pCODR review process. These are examples for illustrative purposes only and do not constitute advice or recommendations from pCODR.

Part 1: Example of a pCODR Economic Evaluation Structured Summary

STUDY DESIGN AND METHODS	
Type of economic evaluation	Cost-effectiveness analysis.
Study Objective	The objective was to assess the cost-effectiveness of palliative chemotherapy using bevacizumab in combination with paclitaxel for patients with human epidermal growth factor receptor 2-negative metastatic breast cancer.
Perspective	Swiss health care system
Disclosable Price of Drug Under Review	$600.0000 per 100mg vial
Disclosable price for companion diagnostic(s) associated with Drug Under Review (if applicable)	N/A
Disclosable Price of Relevant Comparator(s)	$8.25 per 25 mL vial / $16.50 per 50 mL vial
Interventions and Comparators	Bevacizumab plus paclitaxel was compared with paclitaxel alone as primary chemotherapy. All patients received 90mg per m^2 of paclitaxel on days one, eight, and 15 of a 28-day cycle. The intervention group also received 10mg per kg of bevacizumab on days one and 15.
Patient population (e.g. cancer type, disease stage, treatment-experience/line)	Typical patients with metastatic breast cancer. The modeled patient population was based on patients from study E2100. Patients were included in study E2100 if they had histologically or cytologically proven metastatic breast cancer and had not received previous cytotoxic therapy for metastatic disease. Previous hormonal treatment for metastatic disease or adjuvant cytotoxic chemotherapy and concurrent bisphosphonate administration were allowed. Exclusion criteria were ECOG performance status P2 or central nervous system involvement. HER-2 positive metastatic breast cancer was not a formal exclusion criterion but was hardly represented in this trial.
Analytical Approach	A Markov model was used to synthesise the published data from various sources, including a key randomised controlled trial, Study E2100. The study population was a hypothetical cohort of

	Swiss women with an average height of 1.64m and body weight of 65kg, receiving out-patient care. The model time horizon was five years. The analysis was over a patient's lifetime, which is less than one year for patients with metastatic breast cancer.
Key model inputs and data sources (clinical and economic)	Effectiveness data: The effectiveness data were primarily from a clinical trial entitled the E2100 study (Miller, et al. 2007). The clinical data for the efficacy of bevacizumab included progression-free survival and overall survival. Major adverse events, such as hypertension, infections, and cerebrovascular ischaemia, were included. Monetary benefit and utility valuations: The preference-based utility values were from a Canadian published study that used the time trade-off technique (Leung, et al. 1999) and data collected in the E2100 study. Measure of benefit: The measure of benefit was quality-adjusted life-years (QALYs). These benefits were not discounted due to the short life expectancy of the population. Cost data: The direct medical costs were included for medications, laboratory tests, management of disease progression, and adverse events. The resource use was based on patient-level data from the E2100 study and another study. The unit costs were from Swiss national drug prices and tariffs. All costs were reported in 2008 Euros (EUR) and an exchange rate of 1.62 Swiss francs equals EUR 1.00 was applied, where necessary. The costs were not discounted due to the short life expectancy of the patients.
Time Horizon	A life-long time horizon of 15 years was applied in the base-case analysis.
Model Assumptions	The effect of different bevacizumab doses on the ICER was assessed under the simplifying assumption of no change in clinical effectiveness. This assumption is supported by the interim data of a phase III trial showing a comparable disease free survival in patients receiving 7.5 mg q2w or 15 mg q3w of bevacizumab per kg body weight. It was assumed that the treatment duration and treatment dose was defined by the actual duration and dosing in the trial without vial sharing (wastage was included).
Analysis of Uncertainty	The uncertainty was measured in one-way sensitivity analyses on the key parameters. No confidence intervals were available for most of the parameters, so the base-case values were varied by ±30%. The median time to progression and the median time from progression to death were varied by ±50%. Probabilistic sensitivity analyses, using second-order Monte Carlo simulations, were undertaken, with triangular distributions for all parameters. Scenario analyses were performed to assess subgroups by age; patients with different body weights; an assumption of equal time to progression in both arms; and a reduction in the dosage of bevacizumab while assuming the same efficacy. The results were

	expressed in cost-effectiveness scatter plots and tornado diagrams.
RESULTS	
Base-Case Analysis **ICER, ΔC, ΔE**	In the base-case for all ages, the mean undiscounted cost per patient was EUR 69,042 for bevacizumab plus paclitaxel and EUR 28,673 for paclitaxel alone; an incremental cost of EUR 40,369 with bevacizumab. Bevacizumab plus paclitaxel was associated with mean undiscounted QALYs of 0.90 compared with 0.69 for paclitaxel alone. The gain in QALYs was 0.21 with bevacizumab. The incremental cost per QALY gained for bevacizumab plus paclitaxel compared with paclitaxel alone was EUR 189,427 and by age group it ranged from EUR 152,894 in 27- to 49-year-olds to EUR 1,226,615 in 65- to 85-year-olds.
Key Sensitivity Analyses **ICER, ΔC, ΔEs**	The univariate analysis found that the factors having the strongest impact on the results were progression-free survival and post-progression survival. The scenario analyses found that lowering the dosage of bevacizumab from 10 to 2.5mg per kg could produce an incremental cost per QALY of approximately EUR 60,000, with an incremental cost of EUR 12,000 and a gain in QALYs of 0.2.
SUBMITTED CONCLUSIONS	
The authors concluded that bevacizumab in addition to paclitaxel was not cost-effective, but further studies were needed as there were limited data available and one clinical trial primarily contributed to this conclusion.	

Note: *Adapted from the NHS EED structured summary and the following publication: http://www.ejcancer.info/article/S0959-8049(08)01032-0/abstract.*

Part 2: Example of a pCODR Budget Impact Analysis Structured Summary

STUDY DESIGN AND METHODS	
BIA Objective	The aim of this study was to determine the budget impact of adding erlotinib to a US health plan insurer's formulary as a combination therapy with gemcitabine for the treatment of nonresectable pancreatic cancer.
BIA Methods	An Excel-based budget impact model was developed to evaluate the costs for National Comprehensive Cancer Network guideline-recommended treatment options for patients with locally advanced, nonresectable or metastatic pancreatic cancer from the perspective of a US managed care plan. The model compared treatment with gemcitabine alone and in combination with erlotinib, including the costs of treatment, adverse events (AEs), and administration. Inputs for the model were derived from the Surveillance, Epidemiology and End Results Cancer Registry,

	clinical trials, and publicly available sources and were varied in sensitivity analyses to identify influential inputs. The model addressed first-line use in a single indication and assumed that the proportion of patients aged >or=65 years in a managed care organization was the same as in the general population. The model did not account for patient copayments for oral medications, a factor that could lower a plan's overall cost further than estimated herein.
Overview of BIA Results and Sensitivity Analyses	The relatively low incidence of pancreatic cancer and the assumption of treating only 23% of these patients with erlotinib were likely the principal reasons for the low budgetary impact of erlotinib. In this model and using these assumptions, the results suggested that the incremental cost impact on a per member per month basis may be small. The results of the analysis were relatively insensitive to drug costs, drug administration costs, and costs of treatment of AEs based on sensitivity analyses.

Note: *Adapted from Danese MD, Reyes C, Northridge K, Lubeck D, Lin CY, O'Connor P. Budget impact model of adding erlotinib to a regimen of gemcitabine for the treatment of locally advanced, nonresectable or metastatic pancreatic cancer. Clin Ther. 2008 Apr;30(4):775-84.*