Procedure for Common Drug Review

July 25, 2005
# RECORD OF UPDATES

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<td>Original</td>
<td>June 2003</td>
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Inquiries:

Inquiries and correspondence about the Common Drug Review should be directed to:

CDR Directorate
Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600
Ottawa, Ontario
K1S 5S8

Telephone: (613) 226-2553
Fax: (613) 226-5392
Email: cdrinfo@ccohta.ca
Web: www.ccohta.ca
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PROCEDURE FOR COMMON DRUG REVIEW (CDR)

The purpose of this document is to describe the CDR procedures and steps.

Introduction

The CDR is an initiative undertaken by all Canadian, publicly-funded federal/provincial/territorial (F/P/T) Drug Plans, with the exception of Quebec. The goals of the CDR process are to reduce duplication, to maximize the use of limited resources and expertise and to enhance the consistency and quality of Drug reviews. Clinical and pharmacoeconomic reviews are generated using an evidence-based approach. The CDR is managed and overseen by the CDR Directorate, Canadian Coordinating Office for Health Technology Assessment (CCOHTA) in Ottawa.

Clinical and pharmacoeconomic Drug reviews are prepared by expert scientific Reviewers, based on material submitted by Manufacturers and studies identified through independent, systematic literature searches.

The Canadian Expert Drug Advisory Committee (CEDAC), an appointed, national, independent body of physicians, pharmacists and other professionals, uses the clinical and pharmacoeconomic reviews to make common formulary listing recommendations to participating F/P/T Drug Plans.

Each of the participating F/P/T Drug benefit Plans makes its own listing decisions based on CEDAC recommendations and other factors, including the Plan’s mandate, priorities and resources. Each Plan is responsible for independently advising the Manufacturer of its listing decision and the coverage status of the Drug.

Definitions

In this document, unless otherwise provided, the capitalized terms shall have the meanings as set out in Appendix 1 attached hereto.

CDR Process

The procedural steps may be summarized as follows:

Phase I – Secretariat

1.1 Filing of Submission and Supporting Material
1.2 Appointment of Submission Coordinator
1.3 Initial Screening for Completeness
1.4 Review Process
1.5 Distribution of Reviewers’ Reports
1.6 Compilation of File for CEDAC
Phase II – CEDAC

2.1 CEDAC Deliberations
2.2 CEDAC Recommendation
2.3 Request for Clarification
2.4 Reconsideration of CEDAC’s Recommendation

Phase III – Notice of Final Recommendation

3.1 Notice of Final Recommendation

CDR Directorate may amend, from time to time, the CDR process and all matters related to the CDR in consultation with the Advisory Committee on Pharmaceuticals (ACP). Amendments to, and clarifications of, the process and all related documents may be effected through Directives issued by CCOHTA through the CDR Directorate from time to time.

Confidentiality Guidelines

CCOHTA has developed Confidentiality Guidelines to protect Confidential Information obtained for the CDR (see Appendix 2). These Confidentiality Guidelines ensure that appropriate steps and procedures are in place to protect Confidential Information and that this information will be handled in a consistent manner. CCOHTA will comply with these Confidentiality Guidelines when handling information as part of the CDR process. A Manufacturer will be deemed to have consented to the Confidentiality Guidelines when it files a Submission or supplies other information to the CDR Directorate. The Confidentiality Guidelines will constitute an agreement between CCOHTA and the Manufacturer.
1. **PHASE I – SECRETARIAT**

1.1 **Filing of Submission and Supporting Material**

1.1.1 **Commencement of Process**

The CDR process is initiated either

(i) by the Manufacturer, the ACP, or one or more Drug Plans filing a Submission with the CDR Directorate; or

(ii) by the ACP, or one or more Drug Plans, filing a Request for Advice with the CDR Directorate.

Initially, and until further notice, Submissions from Manufacturers will be limited to New Chemical Entities and New Combinations.

1.1.2 **Content of the Submission**

A Submission from a Manufacturer must adhere to the content, format and organization guidelines stipulated by the CDR Directorate in the Submission Guidelines for Manufacturers.

1.1.3 **Filing of Submissions**

a) Submissions must be delivered to the CDR Directorate by mail or courier. Submissions cannot be filed electronically at this time.

b) When making the initial filing of a Submission, the Manufacturer should deliver only one complete copy of the Submission to the CDR Directorate for review.

c) In the case of a Submission or Request for Advice from the ACP or Drug Plans, only one copy of the Submission or Request for Advice should be filed, together with such other relevant supporting materials as the ACP or the Drug Plan(s) may decide.

1.1.4 **Order of Review**

a) The Submission or Request for Advice will be logged when it is received, so that there is a record of the time of receipt. An acknowledgement of receipt will be sent. Each Submission and Request for Advice will also be given a file number so that it can be tracked as it goes through the system.

b) All applications made to the CDR Directorate (i.e., Submissions, Requests for Reconsideration and Requests for Advice) will be assigned to a tiered queue for review and placement on the CEDAC agenda as follows:
• Submissions assigned a Priority Review status
• Reconsiderations
• Regular Submissions
• ACP/Drug Plan-initiated reviews
• Requests for Advice

c) The assignment to a tiered queue for review and placement on the CEDAC agenda will be made by the CEDAC Chair and the CDR Directorate staff, with ACP consultation as required.

1.1.5 Priority Review

a) Manufacturers may request Priority Review status at the time of making a Submission.

b) Submissions may be considered for Priority Review if the Drug is:
   • A New Chemical Entity that is effective for the treatment of an immediately life-threatening disease or other serious disease for which no comparable Drug is marketed in Canada; or
   • A New Chemical Entity that will have a significant impact in reducing the Drug expenditures of the Drug Plans. The total combined annual savings to the CDR Drug Plans must be projected to be at least $2.5 million dollars.

c) Submissions designated for Priority Review will be placed ahead of other Submissions in the review queue and will be given a preferred status on the CEDAC agenda.

d) Submissions that do not contain adequate justification for a Priority Review designation will be scheduled as per the tiered queue for review and for the CEDAC agenda (see item 1.1.4b).

e) Priority Review status will be determined by the CEDAC Chair in consultation with the CDR Directorate staff and expert and ACP consultation as required.

f) If a Manufacturer requests a Priority Review of a Submission, Budget Impact Analyses (BIAs) for the named CDR Drug Plans (see CDR Submission Guidelines for Manufacturers) must be provided to support the New Chemical Entity’s impact on Drug expenditures.

g) Drugs given Priority Review status must undergo all of the steps in the review process.

1.2 Appointment of Submission Coordinator

a) A Submission Coordinator from within the CDR Directorate will be appointed to ensure that the Submission or Request for Advice undergoes a timely review in accordance with the CDR Procedure.
1.3 Initial Screening for Completeness

1.3.1 Initial Screening
An initial screening of the Submission or Request for Advice will be conducted by the applicable Submission Coordinator within five (5) days of receipt to ensure that it is complete.

1.3.2 Manufacturer's Submission
a) In the case of a Manufacturer’s Submission, the Submission Coordinator will verify whether the Submission is complete in accordance with the Submission Guidelines for Manufacturers.

b) If the Submission is incomplete, the Submission Coordinator will send a notice to the Manufacturer advising what information is needed to complete the Submission.

c) When the Manufacturer’s Submission is complete, the Submission Coordinator will send an acknowledgement to the Manufacturer and will advise the ACP/Drug Plans. Upon receipt of such acknowledgement, the Manufacturer ensures:
   i) that the CDR Directorate is provided with four (4) complete copies of the Submission; and
   ii) that each Drug Plan is provided with one or more copies of the Submission or part thereof as directed by the Drug Plans in Appendix 1 of the CDR Submission Guidelines for Manufacturers.

d) Upon receipt of a Manufacturer's Submission, the ACP/Drug Plans may identify questions to be addressed in the review process and submit these to the CDR Directorate for directing to Reviewers.

1.4 Review Process

1.4.1 Initiation of Review by CDR Directorate:
The CDR Directorate initiates a review of each Submission and Request for Advice within ten (10) Business Days of receiving complete documents and:

a) it identifies issues, if any, related to the Submission or Request for Advice;

b) it determines the critical path of the Submission or Request for Advice;

c) it collates questions raised by the ACP/Drug Plans and forwards these to the Reviewer(s)

d) in the case of a Submission, it selects Reviewers from a pre-approved panel of experts and/or CDR Directorate staff; and

e) it screens Reviewers for Conflicts of Interest (based on COI Guidelines).
1.4.2 In the case of a Manufacturer’s Submission:

a) CDR Directorate assigns the Submission Coordinator, an internal Clinical Reviewer, an internal Pharmacoeconomic Reviewer plus external Reviewers for the Clinical and Pharmacoeconomic Reviews. The names of the Reviewers will not be disclosed to the Manufacturer.

b) For each Submission, Manufacturers will be provided with a contact name within the CDR Directorate to whom all inquiries about that Submission are to be directed.

c) The Information Specialist, in consultation with the Reviewers, has ten (10) Business Days to review the search strategy and findings provided by the Manufacturer and conduct an independent systematic literature search.

d) The internal and external Clinical and Pharmacoeconomic Reviewers and CDR Information Specialist may discuss the Submission with each other.

e) A complete list of the studies to be considered in the Reviews is provided to the Manufacturer for information.

f) The Reviewers critically analyze the information provided to them with the Submission and the additional information provided by the Information Specialist. The Reviewers have twenty (20) Business Days to complete their Reports in accordance with the review templates and Reviewer Guidelines. During this process, they will consider whether they need more information from the Manufacturer. If so, they will notify the Submission Coordinator who will contact the Manufacturer. Any delays in providing such information will result in a corresponding delay in the completion of the review.

g) Reviewers may request an extension of deadlines from the CDR Directorate, depending on the volume or complexity of material to be reviewed. The Manufacturer will be notified of any extensions granted by the CDR Directorate.

h) Once the Reviewers have completed their Reports, the Reports are forwarded to the Submission Coordinator who will have five (5) Business Days to check that the Reports are complete and have been prepared in accordance with the Reviewer Guidelines.

1.4.3 In the case of an ACP or Drug Plan Submission

a) The CDR Directorate determines if the Submission is a request for (i) a review of the listing status of a particular Drug already listed on one or more formularies; (ii) a class review; or (iii) a Drug-related review other than as listed in (i) and (ii).

b) The CDR Directorate then assigns a Submission Coordinator.
c) In the case of a request for **review of the listing status of a Drug already on a formulary**: (i) the review is assigned to a Clinical Reviewer and/or a Pharmacoeconomic Reviewer; (ii) the Manufacturer(s) of the Drug(s) in question are apprised that a review is being undertaken, the reasons for the review and are invited to comment or provide information; and (iii) the Information Specialist, in consultation with the Reviewer(s), conducts a literature search. The studies and material identified through the literature search are supplied to the Reviewer(s) to consider as part of their review.

d) In the case of a **request for a class review**: (i) the review is assigned to Reviewer(s); (ii) the Manufacturer(s) of the Drug(s) to be reviewed is/are apprised that a review is being undertaken, the reasons for the review and is/are invited to comment or provide information; (iii) the Information Specialist, in consultation with the Reviewer(s), conducts a literature search (the studies and material identified through the literature search are supplied to the Reviewers to consider as part of their review); and (iv) the critical path for the class review will need to reflect the number of Drugs in the class and the complexity of the review (i.e., class reviews may require more than twenty (20) Business Days for completion).

e) In every other case (i) appropriate Reviewers will be assigned; (ii) Manufacturer(s) will be apprised as appropriate; and (iii) the Information Specialist, in consultation with the Reviewer(s), conducts a literature search (the studies and material identified through the literature search are supplied to the Reviewer(s) to consider as part of their review).

### 1.4.4 In the case of a Request for Advice

a) Direction on how to proceed with the Request for Advice may be sought from the CEDAC Chair.

b) The CDR Directorate assigns a Submission Coordinator and the appropriate Reviewers.

c) The Information Specialist, in consultation with the Reviewer(s), conducts a literature search. The Reviewer(s) prepares a report in response to the Request for Advice.

### 1.4.5 Reviewers (External and Internal)

a) Reviewers will be assigned by the CDR Directorate, as required, to conduct reviews of a Submission or Request for Advice.

b) Reviewers will be chosen based on their qualifications and area of expertise or specialization and compliance with the Conflict of Interest Guidelines.

### 1.4.6 Reviewers’ Reports

a) Once a Reviewer has completed his/her review, he/she drafts a Report which is submitted to the Submission Coordinator.
b) The Submission Coordinator verifies that each Report is complete and meets the requirements of the templates and Reviewer Guidelines. Five (5) Business Days are allocated for this task.

1.5 Distribution of Reviewers’ Reports

1.5.1 ACP/Drug Plans

The Submission Coordinator forwards the duly completed Reviewers’ Reports to the ACP/Drug Plans for information.

1.5.2 Manufacturer

a) The Submission Coordinator forwards to the Manufacturer the duly completed Reviewers’ Reports of (i) such Manufacturer’s Submission; or (ii) the ACP/Drug Plan Submission in respect of such Manufacturer’s Drug, as applicable.

b) The Manufacturer has seven (7) Business Days following receipt of a Report to review such Report and to submit written comments about the Report to the Submission Coordinator. This will be the Manufacturer’s only opportunity to provide comments.

c) The Manufacturer may waive the opportunity to provide comments.

d) The Manufacturer’s comments should be presented clearly and succinctly in point form whenever possible. The issue(s) should be clearly stated and specific reference should be made to the part of the Report under discussion. Lengthy comments may result in increased time requirements for Reviewers to prepare replies.

e) References should be provided if appropriate.

1.5.3 Reviewers

a) The Submission Coordinator forwards the Manufacturer’s written comments, if any, to the Reviewer who authored the Report.

b) The Reviewer has seven (7) Business Days to address the Manufacturer’s comments and to send his/her reply (the “Reply”) to the Submission Coordinator. (Note: additional time may be allowed if the Manufacturer provides lengthy comments.)

c) In the Reply, the Reviewer should clearly identify the comments to which he/she is responding and address them succinctly in point form whenever possible.

d) References should be provided if appropriate.
1.6 Compilation of File for CEDAC

1.6.1 CEDAC Brief

The Submission Coordinator compiles the CEDAC Brief for delivery to CEDAC. The CEDAC Brief consists of an itemization of the Submission that is prepared by CDR Directorate staff, the Reviewers’ Reports relating to the Submission, the Manufacturer’s written comments about the Reviewers’ Reports, if any, and the Reviewers’ Replies, if any.
2. PHASE II – CEDAC

2.1 CEDAC Deliberations

2.1.1 CEDAC

a) CEDAC is established in accordance with the CEDAC Terms of Reference.

b) All CEDAC Members must comply with the COI Guidelines and Code of Conduct.

2.1.2 Scheduling Review of CEDAC Brief

a) The CEDAC agenda is set by the CEDAC Chair in consultation with the CDR Directorate.

b) The CEDAC Brief will be delivered to CEDAC Members, with copies to ACP Members) at least ten (10) Business Days before the date scheduled for consideration of such CEDAC Brief.

c) While the full Submission will be available at the CEDAC meeting, it will not routinely be sent to CEDAC Members in advance but will be available on request.

2.1.3 CEDAC Meeting

a) At the CEDAC meeting, CEDAC Members consider and discuss each CEDAC Brief on the meeting’s agenda with a view to making a Recommendation.

b) If the CEDAC Brief is complete, CEDAC will consider the material and make a Recommendation.

c) If CEDAC needs more information either from the Reviewers or from the Applicant or from external experts, the matter will be sent back to CDR Directorate to collect the additional information and the matter will be put over to the next CEDAC meeting, pending the collection of such information. (Note: no New Information will be entertained at this time.)

d) CEDAC may invite the Reviewer(s) and/or external experts to provide input in person at a CEDAC meeting. (Note: no New Information will be entertained at this time.)

e) ACP Members may attend the CEDAC meeting as observers only. They are not entitled to participate in the meeting.

f) Manufacturers are not permitted to attend any CEDAC meeting either as observers or to make an oral presentation or submission.
2.1.4 Review of CEDAC Brief

a) In conducting its review of the CEDAC Brief and in making its Recommendation, CEDAC will consider the following Review Criteria for each Drug:

i) Clinical studies, demonstrating the safety and efficacy of the Drug in appropriate populations;

ii) Therapeutic advantages and disadvantages relative to accepted therapy;

iii) Cost-effectiveness relative to accepted therapy.

b) Following its review of the CEDAC Brief, CEDAC makes a Recommendation.

2.2 CEDAC Recommendation

2.2.1 CEDAC Recommendation

a) A Recommendation by CEDAC shall be made in the manner set out in the CEDAC Terms of Reference.

b) Minutes will be taken of the CEDAC deliberations so that there is a record of the meeting, of attendance at the meeting, of Recommendations made, and of the Reasons for Recommendations or decisions.

2.2.2 Reasons for Recommendation

a) CEDAC’s Recommendations will, in every case, be accompanied by Reasons for Recommendation. A CDR Directorate staff member may be tasked with the responsibility of preparing a draft statement of Reasons for Recommendation for approval by CEDAC.

b) The Reasons for Recommendation do not need to be lengthy but they shall contain a sufficient explanation to address key issues and be sufficiently detailed to demonstrate that CEDAC has considered all the material before it.

2.2.3 Releasing Recommendation and Reasons for Recommendation

a) In the case of a Manufacturer’s Submission, the CEDAC Recommendation and Reasons for Recommendation will be sent to the Manufacturer, ACP and Drug Plans within five (5) Business Days following the CEDAC meeting at which the Recommendation was made. Manufacturers are entitled to make a Request for Reconsideration of the CEDAC Recommendation and Drug Plans are entitled to make a Request for Clarification of the CEDAC Recommendation. Until the Notice of Final Recommendation has been issued (see Section 3.1), the Recommendation and Reasons for Recommendation will not be acted on by Drug Plans nor will they be publicly available.
b) In the case of an ACP or Drug Plan Submission, the CEDAC Recommendation and Reasons for Recommendation will be sent within five (5) Business Days following the CEDAC meeting to the ACP, Drug Plan(s) and to the Manufacturer whose Drug is the subject of the CEDAC Recommendation. Manufacturers whose drugs are the subject of an ACP or Drug Plan Submission are entitled to make a Request for Reconsideration of the CEDAC Recommendation and Drug Plans are entitled to make a Request for Clarification of the CEDAC Recommendation. Until the Notice of Final Recommendation has been issued (see Section 3.1), the Recommendation and Reasons for Recommendation will not be acted on by Drug Plans nor will they be publicly available.

2.2.4 Releasing Record of Advice

a) In the case of a Request for Advice, CEDAC’s Record of Advice will be sent within five (5) Business Days following the applicable CEDAC meeting to the ACP and to the Drug Plan(s).

2.3 Request for Clarification

2.3.1 Drug Plan’s Request for Clarification

a) A Drug Plan may file a Request for Clarification of a CEDAC Recommendation and/or the Reasons for Recommendation within ten (10) Business Days of notification of CEDAC’s Recommendation.

b) A Request for Clarification is made by filing a written request with the CDR Directorate.

c) The Request for Clarification will comprise the reason for the Request and a brief description of each point requiring clarification. The Request for Clarification cannot be based on New Information.

d) CEDAC, ACP, the other Drug Plans and the Drug Manufacturer will be notified of the Request for Clarification.

2.3.2 Response to Request for Clarification

a) CDR Directorate will not issue a Notice of Final Recommendation until the Drug Plan has received a written response to its Request for Clarification.

b) The CDR Directorate shall prepare a written response to the Request for Clarification for approval by the CEDAC Chair.

c) In responding to the Request for Clarification, the CDR Directorate will consult, as required, with the CEDAC Chair and CEDAC, and any Reviewer or external expert retained in connection with the Submission.
d) CDR Directorate will distribute the response to the Drug Plan, CEDAC, ACP, the other Drug Plans and the Drug Manufacturer within five (5) Business Days of receiving the Request for Clarification.

## 2.4 Reconsideration of CEDAC’s Recommendation

### 2.4.1 Manufacturer’s Request for Reconsideration (upon request)

a) Every Manufacturer whose Drug is the subject of a CEDAC Recommendation has the right to file a Request for Reconsideration of such Recommendation.

b) A Manufacturer shall only be entitled to have the Recommendation reconsidered once.

c) The Manufacturer has ten (10) Business Days after receiving notification of the CEDAC Recommendation to file, in writing, a Request for Reconsideration.

d) A Request for Reconsideration is requested by filing a written request with the CDR Director. CEDAC, ACP and the Drug Plans will be notified by the CDR Directorate once a Request for Reconsideration is appropriately filed.

e) The Request for Reconsideration will comprise the reason and grounds for the request, the relief sought and supporting evidence. A Request for Reconsideration cannot be made solely because the Manufacturer disagrees with the Recommendation. The Request for Reconsideration must identify the aspect(s) of the Recommendation and Reasons for Recommendation with which the Manufacturer disagrees and state the grounds for the Request.

f) A Request for Reconsideration can be made on one or more of the following grounds:
   i) CEDAC failed to act fairly and in accordance with its Procedures in conducting the review;
   ii) the Recommendation is not supported by the evidence that had been submitted or identified in the Reviewers’ Reports.

g) No New Information will be considered in the Reconsideration.

### 2.4.2 Examination of Request by CDR Directorate

a) The CDR Directorate will examine, within five (5) Business Days, each Request for Reconsideration to determine whether the issues raised can be resolved in discussions with the Manufacturer. It may be that the issue can be clarified and the Manufacturer will accept the Recommendation. It may be that the Manufacturer has New Information, in which case a Resubmission is required. If CDR Directorate is unable to address the issues raised in the Manufacturer’s Request for Reconsideration, then the Request for Reconsideration will be forwarded to CEDAC in accordance with Section 2.4.3.

### 2.4.3 CEDAC Reconsideration
a) The CDR Directorate prepares the Reconsideration Brief comprised of the CEDAC Brief, the CEDAC Recommendation, Reasons for Recommendation and the Request for Reconsideration. Five (5) Business Days are allocated for this task.

b) The Reconsideration Brief is delivered to CEDAC Members (including ACP) at least ten (10) Business Days before the scheduled Committee meeting to consider the Request for Reconsideration.

c) If CEDAC needs clarification either from the Reviewers or from the Manufacturer, or advice from external experts, the matter will be sent back to CDR Directorate staff to collect such clarification or advice and the matter will be put over to the next CEDAC meeting, pending the collection of such information. CEDAC may invite Reviewer(s) and/or external expert(s) to attend the meeting to answer questions from the CEDAC members or to provide input. None of the persons attending the CEDAC meeting may introduce New Information.

2.4.4 Outcomes of CEDAC Reconsideration

a) CEDAC shall review and consider the Reconsideration Brief. It may look at the Submission afresh and consider and decide whether, based on the evidence before it and having regard to the Review Criteria, the original Recommendation should be maintained or changed. The conclusion reached by CEDAC on such Reconsideration is hereinafter referred to as the Recommendation on Reconsideration.

b) CEDAC shall provide reasons for its Recommendation on Reconsideration.

c) The Recommendation on Reconsideration and Reasons for such Recommendation are issued within five (5) Business Days following the CEDAC meeting to the ACP, Drug Plan(s) and the Manufacturer whose Drug is the subject of the CEDAC Recommendation.

d) Manufacturers are not permitted to attend any CEDAC meeting for Reconsideration either as observers or to make any oral presentation or submission.

e) There shall be no right to request a review or reconsideration of the Recommendation on Reconsideration.

f) Notification of the Recommendation on Reconsideration is made as described in Section 3 (Phase III – Notice of Final Recommendation).
3. PHASE III – NOTICE OF FINAL RECOMMENDATION

3.1 Notice of Final Recommendation

3.1.1 Notice of Final Recommendation

A final determination of a Submission shall be deemed to have taken place, when a Recommendation has been made, and:

a) a Manufacturer does not file a Request for Reconsideration of the Recommendation within the specified time or waives the right to file a Request for Reconsideration, and;

b) a Drug Plan has not filed a Request for Clarification of the Recommendation within the specified time;

or, in the event that:

c) a Manufacturer has properly filed a Request for Reconsideration and CEDAC has made a Recommendation on Reconsideration, and/or;

d) one or more Drug Plans have properly filed a Request for Clarification of the Recommendation and a Clarification has been provided.

3.1.2 Issuance of Notice of Final Recommendation

Once a final determination of a Submission shall be deemed to have taken place in accordance with Section 3.1.1, the CDR Directorate shall issue and send the following to the ACP, Drug Plans, CCOHTA’s President and every Manufacturer whose Drug is the subject of the Submission:

a) Notice of Final Recommendation

b) a copy of the Recommendation and Reasons for Recommendation or, in the event that a Recommendation on Reconsideration was made, a copy of such Recommendation on Reconsideration together with a copy of the Reasons therefore.

3.1.3 Drug Plan Decision

Upon receipt of the Notice of Final Recommendation, each of the Drug Plans may proceed to take steps to make a listing decision in respect of the applicable Drug.
## TIMEFRAMES* FOR CDR PROCEDURE

<table>
<thead>
<tr>
<th>Task</th>
<th>Timeframe (in Business Days)</th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>REVIEW PROCESS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Checking Submission for Completeness</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>2. Assignment of Submission Coordinator, Contracting Reviewers</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>3. IS Review of search strategy and research</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>4. Review Time for Reviewers</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>5. Quality Assessment of Reviewers’ Reports by Submission Coordinator</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6. Manufacturers Review of Reviewers’ Reports</td>
<td>7</td>
<td>1.5</td>
</tr>
<tr>
<td>7. Reviewers replies to comments</td>
<td>7</td>
<td>1.5</td>
</tr>
<tr>
<td>8. Preparation of CEDAC Brief</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>9. Placement on CEDAC Agenda</td>
<td>10 – 40</td>
<td>2 – 8</td>
</tr>
<tr>
<td>10. Sending out CEDAC Recommendation &amp; Reasons for Recommendation</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>11. Embargo Period</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>12. Sending out Final Recommendation (No request for reconsideration or clarification)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total Review Time</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>99 – 129 days</td>
<td>20 – 26 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RECONSIDERATION PROCESS (Manufacturers)</th>
<th>CLARIFICATION REQUEST (Drug Plans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Examination of Reconsideration Request</td>
<td>5</td>
</tr>
<tr>
<td>2. Preparation of Reconsideration Brief</td>
<td>5</td>
</tr>
<tr>
<td>3. Placement on CEDAC agenda</td>
<td>Next CEDAC agenda**</td>
</tr>
<tr>
<td>4. Sending out CEDAC Final Recommendation</td>
<td>Providing clarification and sending out CEDAC Final Recommendation</td>
</tr>
</tbody>
</table>

* Timeframes assume that the most expedient method of delivering data is used. See Appendix 3 for delivery times.

**Schedule of CEDAC meetings will be posted on the website.
APPENDIX 1: CDR Definitions

In the document to which this Appendix is appended, the following definitions apply, unless otherwise provided.

ACP – Advisory Committee on Pharmaceuticals

ACP Member – a member of the Advisory Committee on Pharmaceuticals

ACP Terms of Reference – the Terms of Reference established for the ACP by CCOHTA’s Board of Directors.

Applicant – the person, corporation or entity filing a Submission.

Budget Impact Analysis or BIA – an analysis of the impact of a new drug product on drug plan expenditures.

Business Day – any day, other than a Saturday, Sunday, statutory holiday, or company holiday on which the Canadian Coordinating Office for Health Technology Assessment office in Ottawa, Ontario is open for business during normal business hours.

CCOHTA – Canadian Coordinating Office for Health Technology Assessment, a body corporate duly incorporated under the laws of Canada.

CDR – Common Drug Review

CDR Director – the CCOHTA staff person appointed as director of the CDR Directorate.

CDR Directorate – the directorate established within CCOHTA to support the CDR process.

CDR Nominating Committee – the nominating committee established according to the CEDAC Terms of Reference for recommending candidates for appointment to CEDAC.

CEDAC – Canadian Expert Drug Advisory Committee

CEDAC Brief – a brief prepared by CDR Directorate staff for the members of CEDAC consisting of:
   i) An itemization of the Manufacturer’s Submission to CDR
   ii) The Reviewers’ Reports relating to the Submission
   iii) The Manufacturer’s written comments about the Reviewers’ Reports, if any, and
   iv) The Reviewers’ Replies, if any.

CEDAC Member – a member of the Canadian Expert Drug Advisory Committee

CEDAC Terms of Reference – the Terms of Reference established for CEDAC by CCOHTA’s Board of Directors.
Clarification – a written response, approved by the CEDAC Chair, to a Drug Plan’s Request for Clarification of a CEDAC Recommendation.

Clinical Review – the critical appraisal of the published and unpublished information about the safety, efficacy, effectiveness (when available) and use of a Drug in the management of a disease or condition.

Clinical Reviewer – a Reviewer who conducts a Clinical Review.

Code of Conduct – the code of conduct for CCOHTA committees approved by CCOHTA’s Board of Directors.

Conflict of Interest Guidelines or COI Guidelines – the conflict of interest guidelines adopted by CCOHTA’s Board of Directors for CEDAC, Reviewers and external experts.

Confidential Information has the meaning given to it in the Confidentiality Guidelines.

Confidentiality Guidelines – the guidelines respecting confidentiality adopted by the CCOHTA Board in respect of CDR.

Directive – a written directive from CCOHTA amending, interpreting or clarifying any process, procedure, guidelines, terms of reference, code of conduct or document relating to the CDR.

Drug – a substance, considered to be a drug under the Canadian Food and Drugs Act, which is sold for human use.

Drug Plans – the participating, publicly-funded federal, provincial and territorial drug plans.

Final Reasons for Recommendation – the Reasons for Recommendation attached to the Notice of Final Recommendation.

Final Recommendation – the applicable Recommendation, or Recommendation on Reconsideration, attached to the Notice of Final Recommendation.

Formulary – a list of Drugs that are covered as benefits as determined by each Drug Plan.

F/P/T – federal, provincial and territorial

Information Specialist – a CCOHTA staff member who specializes in information retrieval and management in a health sciences research environment.

Manufacturer – a Drug manufacturer

New Chemical Entity – an active moiety that has not been previously approved for sale in Canada by Health Canada and marketed in Canada.

New Combination – consists of two or more active moieties that have not previously been approved for sale in Canada and marketed in Canada in that combination. It may consist of
either two or more new active moieties or two or more old active moieties or a combination of
new and old active moieties.

**New Information** – the new clinical trial(s) or information that will significantly affect cost-
effectiveness and which do not form part of the original Submission.

**NOC or NOC/c** – Notice of Compliance or Notice of Compliance with Conditions issued by
Health Canada, giving authorization to market a drug.

**Notice of Final Recommendation** – the notice issued according to *Section 3.1* of the *Procedure
for Common Drug Review*.

**Participants** – unless otherwise stated, CCOHTA staff, Reviewers, CEDAC Members and any
experts retained to assist in the CDR process.

**Pharmacoeconomic Review** – the critical appraisal of the published and unpublished information
about costs and consequences of Drugs and their impact on individuals, health care systems and
society (i.e. value for money of Drugs).

**Pharmacoeconomic Reviewer** means a Reviewer who conducts a Pharmacoeconomic Review.

**Priority Review** – a preferred status in the review queue and on the CEDAC agenda for drugs
meeting the Priority Review criteria. All steps in the CDR procedure are completed and
timelines are not truncated.

**Reasons for Recommendation** – the detailed, written reasons given by CEDAC regarding
Recommendations, or Recommendations on Reconsideration, made by CEDAC.

**Recommendation** – an evidence-based recommendation, made after consideration of Review
Criteria, by CEDAC in response to a Submission made by a Manufacturer, ACP or by one or
more Drug Plans.

**Recommendation on Reconsideration** – the conclusion reached by CEDAC on reconsideration
of the Submission as described in *Section 2.4.4(a)* of the *Procedure for Common Drug Review*.

**Reconsideration Brief** – the CEDAC Brief, CEDAC Recommendation, CEDAC Reasons for
Recommendation. Manufacturer’s Request for Reconsideration.

**Record of Advice** – the detailed advice given by CEDAC in reply to a Request for Advice.

**Reply** – a response by a Reviewer to a Manufacturer’s comments about a Clinical or
Pharmacoeconomic Review conducted by that Reviewer.

**Report** – a report produced by a Reviewer in accordance with Reviewer Guidelines.

**Request for Advice** – a written request made by ACP or by one or more Drug Plans to CEDAC
for advice on specific therapeutic, clinical or pharmacoeconomic issues.
Request for Clarification – a written request from a Drug Plan for clarification of a CEDAC Recommendation.

Request for Reconsideration – a written request from Manufacturers to have a CEDAC Recommendation reconsidered.

Resubmission – the request by a Manufacturer, Drug Plan or the ACP to have an original Submission reviewed again via the CDR process on the basis of New Information that was not previously provided in the original Submission.

Review Criteria – the following criteria are considered by CEDAC in making a listing recommendation:
   i) Clinical studies, demonstrating the safety, efficacy and effectiveness compared to alternatives
   ii) Therapeutic advantages and disadvantages relative to accepted therapy
   iii) Cost-effectiveness relative to accepted therapy.

Reviewer – an expert selected to conduct a clinical or pharmacoeconomic review in accordance with Reviewer Guidelines established by the CDR Directorate.

Reviewer Guidelines – the CCOHTA guidelines adopted by the CDR Directorate that set out how a Reviewer must conduct, and report on, a Clinical Review or a Pharmacoeconomic Review.

Rules of Procedure – the rules of procedure established by CCOHTA’s Board of Directors for CCOHTA’s committees.

Submission – A submission to the CDR consisting of:
   i) A written application made by a Manufacturer, together with supporting documentation, to have a Drug listed on the Drug Plans’ formularies; or
   ii) A written request made by ACP or by one or more Drug Plans, together with supporting documentation, if any, to consider the listing status of Drugs already on formularies, to conduct Drug class reviews or to undertake any other Drug-related review(s) as required. Submission includes a Resubmission.

Submission Coordinator – a CDR Directorate staff person assigned to coordinate the activities associated with the review of a Submission or Request for Advice.

Submission Guidelines – the guidelines adopted by CCOHTA that outline how Submissions from Manufacturers must be prepared and submitted.

Submission Requirements – information the CDR Directorate needs to perform the clinical and pharmacoeconomic reviews of drugs and additional information the Drug Plans use in making listing decisions. The Submission Requirements consolidate the requirements for the CDR and the Drug Plans.
APPENDIX 2: Confidentiality Guidelines

CCOHTA and the CDR Directorate have developed the following Confidentiality Guidelines to ensure the protection of Confidential Information obtained under the CDR program. These Guidelines ensure appropriate steps and procedures are in place and that Confidential Information will be handled in a consistent manner. CCOHTA and the CDR Directorate will comply with these Confidentiality Guidelines when handling information as part of the CDR process. A Manufacturer will be deemed to have consented to the Confidentiality Guidelines when it files a Submission or supplies other information to the CDR Directorate. The Confidentiality Guidelines will constitute an agreement between CCOHTA and the Manufacturer.

A. DEFINITION

Confidential Information means information supplied by a Manufacturer in a document that is clearly marked with the word “confidential” or other similar language and any other non-public scientific, technical or commercial information about a Manufacturer’s business or a Manufacturer’s product received as a result of the exchange of information described in paragraph B below, but does not include information that:

a) was already in the possession of CDR Directorate Staff, External Reviewer(s) assigned to review the Submission, CEDAC Members, External Experts (when contracted to provide specific information in relation to the Submission), ACP Members, F/P/T governments, F/P/T health authorities, Drug Plans, Health Canada or Patented Medicine Prices Review Board (PMPRB) without restriction as to its use or disclosure;

b) is or becomes available to the general public (other than as a result of a breach of the procedures contained herein); information available to the general public includes but is not limited to published articles, Drug prices and product monographs; or

c) a third party who is not under any obligation as to confidentiality or non-disclosure rightfully discloses to CDR Directorate Staff, External Reviewer(s) assigned to review the Submission, CEDAC Members, External Experts (when contracted to provide specific information in relation to the Submission), ACP Members, F/P/T governments, F/P/T health authorities, Drug Plans, Health Canada or Patented Medicine Prices Review Board (PMPRB) without restriction as to its use or disclosure.

Manufacturers who supply Confidential Information are responsible for clearly identifying it as such. Only information that has not previously been made public and is confidential should be labelled or identified as such.
B. ACCESS TO INFORMATION AND FREEDOM OF INFORMATION LEGISLATION

CCOHTA is a private, non-profit organization and is therefore not subject to either federal access to information or provincial/territorial freedom of information statutes. However, Manufacturers will be asked to consent to their information being exchanged with F/P/T governments, F/P/T health authorities, Drug Plans, Health Canada and the Patented Medicine Prices Review Board by signing a letter in the form available in the Manufacturers’ Submission Guidelines. These bodies have their own confidentiality procedures and are subject to provincial or federal freedom of information and access to information legislation. CCOHTA and the CDR Directorate have no jurisdiction or control over these procedures and statutory requirements. Manufacturers should satisfy themselves as to the content of these procedures and requirements before including Confidential Information in a Submission. When information is received by the CDR Directorate as authorized under this paragraph, it will be treated in the same way as a Manufacturer’s Submission is treated pursuant to these Guidelines and any Confidential Information received by the CDR Directorate as authorized under this paragraph will be treated as Confidential Information pursuant to these Guidelines.

C. HANDLING CONFIDENTIAL INFORMATION

1. Responsibilities of the CDR Directorate
a) The CDR Directorate will use reasonable care to prevent the unauthorized use, disclosure, publication or dissemination of Manufacturers’ Submissions and Confidential Information.

b) CDR Directorate will not disclose Manufacturers’ Submissions or Confidential Information, to any third party except as permitted herein or required by law or order of a competent court or tribunal;

c) CDR Directorate will use the Manufacturer’s Submission and Confidential Information solely for the purpose of carrying out its responsibilities with respect to the Common Drug Review;

d) CDR Directorate has in place secure filing/storage and websites and processes for tracking Manufacturers’ Submissions and confidential documents;

e) CDR Directorate has in place internal processes for dealing with Manufacturers’ Submissions and Confidential Information as set out below.

2. Release of Manufacturers’ Information
a) A Manufacturer’s Submission, including the Manufacturer’s Confidential Information may be released to the following (the “Authorized Recipients”):
• CDR Directorate Staff
• External Reviewer(s) assigned to review the Submission
• CEDAC Members
• External Experts when contracted to provide specific information in relation to the Submission
• ACP Members
• F/P/T governments and Drug Plans
• F/P/T health authorities
• Health Canada
• Patented Medicine Prices Review Board (PMPRB)

b) All persons described in the preceding paragraph, including ACP members, but excluding Drug Plans, F/P/T governments, F/P/T health authorities, Health Canada and the PMPRB, are required to sign a non-disclosure agreement requiring them to comply with these Guidelines. (Note: F/P/T health authorities, Drug Plans, Health Canada and PMPRB have their own processes and statutory requirements to address confidentiality issues, as described above.)

c) The Manufacturer’s Submission or parts of it, including Confidential Information, may be discussed amongst any or all of the bodies, named in the letter signed by the Manufacturer authorizing unrestricted communication about the Drug.

CDR Directorate Staff and all Reviewers, CEDAC Committee members, ACP Committee members and Expert Advisors must abide by the confidentiality clauses contained in their Code of Conduct and/or Conflict of Interest Guidelines.

3. Documents That May Be Shared

a) The following documents and the information contained in them, including Confidential Information, may be shared with the Authorized Recipients and may also be posted on a confidential web site accessible only by persons authorized according to these Confidentiality Guidelines:
• Manufacturer’s Submission
• Reviewers’ Reports
• Manufacturer’s Comments About Reviewers’ Reports
• Reviewers’ Replies to Manufacturer’s Comments
• CEDAC Recommendation
• CEDAC Reasons for Recommendation
• CEDAC Brief
• CEDAC Reconsideration Brief
• CEDAC Recommendation on Reconsideration
• CEDAC Reasons for Recommendation on Reconsideration

b) The following documents are shared with a Manufacturer regarding Submissions made with regard to a ACP or Drug Plan Submission that affects its Drug:
• Reviewers’ Reports
• CEDAC Recommendation
• CEDAC Reasons for Recommendation
• CEDAC Recommendation on Reconsideration
• CEDAC Reasons for Recommendation on Reconsideration

c) The following documents are shared on the public web site:
• Tracking document indicating the status of a drug in the review queue
• CEDAC Final Recommendation
• CEDAC Final Reasons for Recommendation with Confidential Information removed

4. Referring to Manufacturer’s Confidential Information in the CEDAC Reasons for Recommendation

The CDR Directorate and the CEDAC may use unpublished studies supplied by the Manufacturer to make listing recommendations. Often the Reasons for Recommendation are based on information that is included in the unpublished studies, deemed and identified as Confidential Information by the Manufacturer.

a) The CDR Directorate will request the Manufacturer’s permission to include information from unpublished studies (deemed Confidential) in the Reasons for Recommendation if required to explain the Recommendation. The information will be included in the “CEDAC Recommendation and Reasons for Recommendation, Confidential and Embargoed” document. The Manufacturer will advise CDR Directorate if permission is granted.

b) In those instances when the Manufacturer does not grant permission to include information from the unpublished study(ies) in the Final Recommendation and Reasons for Recommendation or in the Final Recommendation on Reconsideration and Reasons for Recommendation, the CDR Directorate will replace the information with a statement that, at the request of the manufacturer, the information has been removed pursuant to the Confidentiality Guidelines of the Procedures for CDR.

c) If the unpublished study is mentioned in any public document, the CDR Directorate may make reference to the name of the study and such relevant information as may be publicly available.
5. **CEDAC Minutes**

Minutes of the CEDAC meetings will be released only to CEDAC Members and President of CCOHTA.

6. **Archiving of Confidential Documents**

All documents, including confidential ones, that are associated with the review of a Drug will be kept on file in secure storage for as long as there is or may be a need to consult them. CDR Directorate Staff will undertake regular reviews of archived material and any material they determine is no longer required will be disposed of in accordance with paragraph 6.

7. **Disposal of Confidential Documents**

Confidential documents, supplied by Manufacturers will be disposed either by shredding or by returning to the Manufacturer for disposal (at the Manufacturer’s expense), as directed by the Manufacturer.
APPENDIX 3: Delivery Of Mail/Documents

1. Process/Means

Any notice, request, document or other communication (collectively “Communications”) to be given in connection with the CDR procedure shall be, except as otherwise provided in these procedures, given in writing and shall be given by personal delivery, by registered mail or by facsimile or other electronic means of communication addressed to the recipient as follows:

To CDR Directorate:

CDR Directorate
Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600
Ottawa, ON K1S 5S8

To an Applicant:

The address set out in the Submission or Request for Advice or to such other address or electronic communication number as may be designated by notice given in accordance herewith.

To Other Person or Corporation:

The address or electronic communication number as may be designated by notice given in accordance herewith.

2. 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.