# RECORD OF UPDATES

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<tr>
<th>Update</th>
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<th>Reported in CDR Update</th>
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<tr>
<td>Original</td>
<td>June 2003</td>
<td>No. 3 — June 20, 2003</td>
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<td>August 2003 (Revised August 22, 2003)</td>
<td>No. 4 — August 22, 2003</td>
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<td>September 2003 (Revised September 16, 2003)</td>
<td>No. 6 — September 17, 2003</td>
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<td>3</td>
<td>November 12, 2003 (Revised November 12, 2003)</td>
<td>No. 7 — November 19, 2003</td>
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<td>4</td>
<td>November 12, 2003 (Only Appendix 1 was updated on April 19, 2004. No other changes were made to the November 12, 2003 version.)</td>
<td>No. 9 — April 23, 2004</td>
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<td>July 2007</td>
<td>No. 38 — June 29, 2007</td>
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INQUIRIES

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

CDR Directorate
Canadian Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Telephone:    (613) 226-2553
Fax:          (613) 226-5392
E-mail:       cdrinfo@cadth.ca
Web site:     www.cadth.ca

Submissions should be sent to:

CDR Directorate
Canadian Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Telephone:    (613) 226-2553
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1. PURPOSE

The purpose of the *Common Drug Review Submission Guidelines for Manufacturers* is two-fold.

- They provide guidance to Manufacturers in preparation of Submissions for New Drugs, New Combination Products and Drugs with New Indications and for Resubmissions. The Submissions and Resubmissions must meet the needs of the CDR Directorate and participating federal/provincial/territorial (F/P/T) Drug Plans.

- They provide information about the CDR processes. [Further detail about the CDR process is available in the *Procedure for Common Drug Review* in the CDR section of the Canadian Agency for Drugs and Technologies in Health (CADTH) web site, www.cadth.ca.]

2. INTRODUCTION

The CDR is an initiative undertaken by all Canadian, publicly funded F/P/T Drug Plans, with the exception of Québec (Appendix 1 lists participating plans). The goals of the CDR process are to reduce duplication in the performance of reviews, to maximize the use of limited resources and expertise and to provide consistent and rigorous Drug reviews. The CDR Drug reviews reflect an evidence-based approach. The CDR is managed and overseen by the CDR Directorate of the CADTH in Ottawa.

CDR reviews consist of an evidence-based review of the available clinical evidence and a critique of Manufacturer-submitted pharmacoeconomic studies and Budget Impact Analyses (BIAs).

The Canadian Expert Drug Advisory Committee (CEDAC) – an appointed, national independent body of physicians, pharmacists, other health care professionals and public members – uses Clinical and Pharmacoeconomic Drug Reviews to evaluate the comparative benefits and costs of the drugs under consideration and make common formulary listing recommendations to participating F/P/T Drug Plans.

Each of the participating F/P/T Drug Plans makes its own listing decisions based on CEDAC recommendations plus 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.

An overview of the CDR review process is presented in Figure 1.

3. DEFINITIONS

The capitalized terms in this document are defined in Appendix 2.
Figure 1: CDR Process

Complete submission received

Submission plus information retrieved through independent literature search reviewed by clinical and pharmacoeconomic reviewers

Reviews sent to manufacturer for comments

Manufacturer's comments sent to reviewers for replies

Reviews, comments and replies sent to CEDAC and participating drug plans

CEDAC deliberation

CEDAC recommendation and reasons for recommendation issued to drug plans and manufacturer. Final CDR reviews sent to manufacturer for information.

Embargo period

Request for reconsideration by manufacturer

YES

Request discussed by CDR Directorate and manufacturer

Clariﬁed/Resolved

YES

Final recommendation issued

NO

Drug plans make listing decisions

Recommendation reconsidered by CEDAC

Original recommendation upheld

Final recommendation issued

Recommendation changed

Final recommendation issued

NO

Request for clarification by drug plans

YES

Clarification provided and final recommendation issued

NO

Drug plans make listing decisions
4. THE SUBMISSION PROCESS

A Submission to the CDR Directorate at CADTH represents a Submission to all participating F/P/T Drug Plans. A Submission from a Manufacturer must adhere to the content, format and organization guidelines stipulated by the CDR Directorate in this document.

The *Common Drug Review Submission Requirements for Manufacturers* consolidate the requirements of the participating F/P/T Drug Plans and the requirements of the CDR. While the CDR does not require all of the information in the Submission Requirements to conduct the Clinical and Pharmacoeconomic Reviews of a product, the CDR has agreed to collect the additional information that individual Drug Plans have deemed necessary.

A Drug can undergo only one type of CDR Review during a period. For example, if a Drug is at any stage of the review process as a Submission, the CDR Directorate will not review the Drug concurrently as a Resubmission. An exception to this may be made when the basis for the Resubmission is a new indication; CDR will assess this situation on a case-by-case basis considering factors such as: where in the CDR review process the previous submission is, how distinct the new indication is from the indication under review, and the resources required for the CDR to review the new indication.

4.1 Submissions

4.1.1 Commencement of Process

The CDR process is initiated either:

- by the Manufacturer, the Advisory Committee for Pharmaceuticals (ACP), or one or more Drug Plans filing a Submission with the CDR Directorate; or
- by the ACP, or one or more Drug Plans, filing a Request for Advice with the CDR Directorate; or
- by the Manufacturer, the ACP, or one or more Drug Plans filing a Resubmission with the CDR Directorate.

4.1.2 Eligible Submissions from Manufacturers

Submissions from Manufacturers are limited to New Drugs, New Combination Products and Drugs with New Indications that have received a Notice of Compliance (NOC) or a Notice of Compliance with Conditions (NOC/c) from Health Canada.

- New Drugs are New Active Substances that have not been marketed in Canada, regardless of when the NOC or NOC/c was issued. New Drugs include new salts of marketed products, but do not include the following variations of existing products (line extensions) containing the same Active Substance(s):
  - New dosage forms with the same route of administration and similar pharmacokinetic characteristics (e.g., tablets versus capsules);
  - New strength of the same dosage form (e.g., 100 mg tablet versus 200 mg tablet).
• New Combination Products consist of two or more Drugs that have not been marketed in Canada in that combination. They may consist of either two or more New Drugs or two or more marketed Drugs or a combination of New Drug(s) and marketed Drug(s).

• Drug with New Indication(s) is a Drug either previously reviewed by CDR or marketed prior to the establishment of CDR that has received a NOC or NOC/c for a New Indication(s) and:
  o The Drug has a restricted listing in one or more Drug Plan Formularies and the Drug Plans have agreed that it should be submitted; or
  o The Drug is not listed in any of the Drug Plan Formularies and the Drug Plans have agreed that it should be submitted; or
  o The Drug Plans have requested the review of the Drug with New Indications.

All New Drugs, New Combination Products and Drugs with New Indications, including HIV/AIDS agents and “hospital” Drugs that may be potentially funded by one or more of the participating Drug Plans, should be submitted by Manufacturers to the CDR for review to be eligible for consideration for coverage by participating Drug Plans.

While most of the participating Drug Plans cover HIV/AIDS Drugs, there are some exceptions, and guidance regarding Submissions for these agents, and also for cancer agents, can be found in Appendix 3.

Note: Effective March 1, 2007 and for the duration of the interim Joint Oncology Drug Review, CDR will not accept submissions for oncology drugs.

Whenever there is doubt whether a Submission should be made to the CDR, Manufacturers are invited to contact the CDR Directorate for direction. The CDR Directorate may consult with the participating Drug Plans in those cases where Drugs do not clearly fall into a category described above.

Note: Submissions should continue to be made directly to Drug Plans for the following items until further notice:

• new single source products that do not contain New Drugs
• line extensions of existing products, including: new dosage forms with the same route of administration and similar pharmacokinetic characteristics; and new strengths of the same dosage form. For other line extensions, contact CDR for direction.
• generic products
• resubmissions for products reviewed prior to CEDAC.

The ACP may request that the CDR Directorate undertake the review of Submissions, including Drugs that are not New Drugs, New Combination Products or Drugs with New Indications. In these cases, the CDR Directorate will contact the Manufacturers for clinical and pharmacoeconomic data.

4.1.3 Filing of Submissions

• Submissions must be delivered to the CDR Directorate by mail or courier (Appendix 4). Submissions cannot be filed electronically at this time.
• When filing a Submission, the Manufacturer should deliver only one complete copy of the Submission to the CDR Directorate. The Manufacturer should wait until the Submission has
been deemed complete by the CDR Directorate before submitting the required number of copies to the CDR Directorate and participating Drug Plans.

4.1.4 Screening of Submission for Completeness; Required Number of Copies

- An initial screening of the Submission is conducted by the CDR Directorate within five (5) days of receipt to ensure that it is complete.
- The CDR Directorate verifies whether the Submission is complete in accordance with the Common Drug Review Submission Guidelines for Manufacturers.
- If the Submission is incomplete, the CDR Directorate sends a notice to the Manufacturer advising what information is needed to complete the Submission.
- When the Manufacturer’s Submission is complete, the CDR Directorate sends an acknowledgement to the Manufacturer and advises the ACP/Drug Plans. Upon receipt of the acknowledgement, the Manufacturer must ensure:
  - that the CDR Directorate is provided with six (6) complete copies of the Submission; and
  - that each Drug Plan is provided with one or more copies of the Submission, or part of it, as directed by the Drug Plans in Appendix 1.

4.1.5 Order of Review

- All applications made to the CDR Directorate (i.e., Submissions, Requests for Reconsideration, and Resubmissions) are assigned to a tiered queue for review and placement on the CEDAC agenda. The assignment to the review queue and placement on the CEDAC agenda are made by the CDR Directorate staff and CEDAC Chair, with ACP consultation as required.
- Submissions are accepted on an ongoing basis. The CDR Directorate publishes, on the CADTH web site, targeted CEDAC meeting dates on which Submissions may be considered, if they are received by a given date. In certain circumstances, CDR may need to schedule the placement of a Submission/Resubmission on a CEDAC meeting agenda other than the posted targeted CEDAC meeting date.
- Submissions are logged when they are received, so that there is a record of the date of receipt. An acknowledgement of receipt is issued. The date of receipt of a Submission is considered day zero (0) for the purpose of calculating targeted timeframes.
- Only complete Submissions, satisfying all of the Submission Requirements, are entered in the review queue.
- While Submissions are generally reviewed in the order received, Manufacturers may request a Priority Review when they file a Submission.
- The review queue is as follows:
  - Submissions or Resubmissions assigned a Priority Review status
  - Reconsiderations, Drug Plan Requests for Clarification
  - Regular Submissions for New Drugs, New Combination Products containing a New Active Substance or Drugs with New Indications
  - ACP- or Drug Plan-initiated drug-related reviews or Requests for Advice
  - New Combination Products containing existing Drugs; “Me-too” New Drugs such as those that are structurally very similar to existing drugs and that largely duplicate the action of the existing drugs
  - Resubmissions.
4.1.6 Priority Review

- Manufacturers may request Priority Review status in writing when they file a Submission. Manufacturers must provide justification supporting the request.
- Submissions may be considered for Priority Review if the Drug is:
  - a New Drug or Drug with New Indication 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 Drug or Drug with New Indication 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.
- Submissions or Resubmissions designated for Priority Review are placed ahead of other Submissions or Resubmissions in the review queue and are given a preferred status on the CEDAC agenda.
- Submissions or Resubmissions that do not contain adequate justification for a Priority Review designation are scheduled as per the tiered queue for review and for the CEDAC agenda (Section 4.1.5).
- Priority Review status is determined by the CDR Directorate staff in consultation with the CEDAC Chair, clinical experts and ACP as required.
- If a Manufacturer requests a Priority Review of a Submission or Resubmission based on cost savings, BIAs for the Drug Plans, named in Section 4.2.1 (f), Economic and Epidemiologic Information, must be provided when the Submission or Resubmission is filed to support the impact of the New Drug on drug expenditures.
- Manufacturers are advised by the CDR Directorate whether or not a Priority Review has been granted.
- Submissions or Resubmissions given Priority Review status must undergo all of the steps in the review process; however, they will be processed as quickly as possible.

4.1.7 Inquiries

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

The CDR Directorate will provide the Manufacturer with the name of the CDR Directorate staff member who will be the contact regarding the Submission.

Drug Plan-specific inquiries should continue to be directed to the Drug Plan contacts.

4.1.8 Communications and Conflict of Interest

Direct contact between a Manufacturer and CEDAC Members, in their capacity as members of the committee, or CDR Reviewers is not permitted during the Submission review process. Direct approaches in any form to CEDAC Members or CDR Reviewers may be viewed as introducing conflict of interest and may create an appearance of bias or unfairness. Direct contact by a Manufacturer of a CEDAC Member or CDR Reviewer may result in a significant delay in the Submission review process because additional steps may be required to obtain an unbiased recommendation on the product.
4.1.9 Confidentiality

CADTH and the CDR Directorate have developed guidelines to protect confidential information obtained for the CDR. The Confidentiality Guidelines document is found in Appendix 5. These guidelines ensure that appropriate steps and procedures are in place to protect confidential information and to ensure that this information is handled in a consistent manner. CADTH complies with these guidelines when handling information as part of the CDR process. A Manufacturer is deemed to have consented to the guidelines when it files a Submission or Resubmission, or supplies other information to the CDR Directorate. The guidelines constitute an agreement between CADTH and the Manufacturer.

4.2 Submission Requirements for New Drugs, New Combination Products and Drugs with New Indications

The CDR Submission Requirements listed in this section consolidate the requirements of the CDR and the participating F/T/P Drug Plans. These requirements include information that the CDR Directorate needs to undertake the clinical and pharmacoeconomic reviews of Drugs and other information, such as BIAs, that Drug Plans use in making listing decisions. Participating Drug Plans have requested that the CDR Directorate assume responsibility for ensuring that Manufacturers’ Submissions are complete. The Submission Requirements are subdivided into Category 1, Category 2, and Additional Information.

Submissions for Drugs with New Indications are to contain clinical and pharmacoeconomic information relating to the New Indication only.

- **Category 1** information must all be included when the Submission is filed in order for the review to proceed.

- **Category 2** information must be provided as a single package within 20 Business Days of filing the initial Submission. Category 2 requirements must be satisfied before the Drug review is placed on the CEDAC agenda. The Category 2 requirements may be submitted concurrently with Category 1 requirements.

- **Additional Information** includes information the CDR Directorate requires for completion of the review. The CDR may request additional information from Health Canada or the Manufacturer. The Manufacturer also has the responsibility of advising the CDR Directorate regarding any harm or safety issues that may arise during the time that the Submission is under review.

To expedite the screening of Submissions for completeness and to facilitate the efficient use of documents, Manufacturers must organize the information in the order prescribed (Sections 4.2.1,
4.2.2, and 4.2.3) and clearly tab it (Appendix 6). A copy of the Submission Checklist used by the CDR Directorate is also attached for reference (Appendix 7).

### 4.2.1 Category 1 Requirements

One copy of all Category 1 requirements must be submitted to the CDR Directorate. When deemed complete, the Manufacturer and Drug Plans are apprised and the CDR review is initiated. Category 1 requirements include:

**a) Cover Letter**

An original signed covering letter from the Applicant, confirming that all the required information has been provided in each copy of the Submission. It should also indicate:

- whether the Submission includes Category 1, Category 2 or both Category 1 and 2 requirements
- notification that a Priority Review is being requested for the product and justification for the request
- justification for not providing a BIA for any of the 10 participating Drug Plans, listed in Section 4.2.1, (f) Economic and Epidemiologic Information
- statement clarifying whether the submitted price is the current marketed price or the Confidential Price that may become effective following the release of the CEDAC Final Recommendation [Section 4.2.1 (g)].
- the names of the primary and back-up contact(s) that the CDR Directorate can contact regarding the Submission. [Note: the Manufacturer may designate the consultant(s) preparing the Submission as primary and/or back-up contact(s).]

**b) Executive Summary**

A high-level summary of the Submission, including a brief description of the Drug and its place in therapy, a summary of the clinical and pharmacoeconomic evidence, requested listing criteria and the rationale (five pages maximum) – in hard copy and as an electronic copy (Microsoft Word or PDF format on CD). When a Manufacturer has specified a restricted listing recommendation (e.g., for a specific population), supporting references should be clearly identified in the Executive Summary.

**c) Health Canada NOC or NOC/c**

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

**d) Product Monograph**

- The Product Monograph should show the date it was approved by Health Canada and the company and product names that correspond to the NOC.
- A hard copy and an electronic copy (Microsoft Word or PDF format on CD) of the Health Canada-approved Product Monograph are required.
- Product Profile (a template is available on CADTH's web site, www.cadth.ca):
  - A hard copy and an electronic copy (in Microsoft Word format on CD) are required.
  - The Product Profile is an abridged version of the Product Monograph, containing the following information (three pages maximum):
### Generic Drug name

<table>
<thead>
<tr>
<th>Brand name and Manufacturer</th>
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</table>

<table>
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<tr>
<th>Date of NOC or NOC/c</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>American Hospital Formulary Service (AHFS) classification and description, and Anatomical Therapeutic Chemical (ATC) classification and description</th>
</tr>
</thead>
</table>

<table>
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<tr>
<th>Dosage form(s) and Drug Identification Number (DIN).</th>
</tr>
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<tbody>
<tr>
<td>(this section may be expanded to include all dosage forms and strengths)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dosage form and strength</th>
<th>DIN</th>
</tr>
</thead>
</table>

- Indication(s) (approved by Health Canada)
- Mechanism of action
- Pharmacokinetics and pharmacodynamics (be brief)
- Dose, treatment duration and dose equivalency estimates
- Adverse reactions and their frequencies
- Warnings and precautions
- Contraindications
- Drug interactions.

#### Efficacy, Effectiveness and Safety Evidence

Note: A template, used by CDR reviewers for Clinical Reviews, can be found in the Common Drug Review section of the CADTH web site at www.cadth.ca. Manufacturers may wish to refer to this document to see how information is used and reported in the review.

The following are required:

- A copy of the Clinical Overview (Module 2.5) and Clinical Summary (Modules 2.7.1, 2.7.3, 2.7.4, and 2.7.6) from Module 2 of the Common Technical Document in hard and electronic format (Microsoft Word format on CD); OR
- A copy of the Clinical Studies section of the Comprehensive Summaries or equivalent documentation accepted by Health Canada (as described in Health Canada’s New Drug Submission Guideline) in hard and electronic format (Microsoft Word format on CD) if the Submission is not filed with Health Canada in the Common Technical Document format; and
- Copies of published and unpublished studies that address key clinical issues (double blind, randomized controlled trials are given most weight; head-to-head comparison clinical trials between the proposed product and principal comparators are of particular interest). Note: Phase 1 studies and letters from clinicians should be omitted.

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

- Objective and rationale of study
- Interventions
- Study population (including eligibility criteria, baseline characteristics, and sample size)
- Methods (including randomization method, blinding method, handling of withdrawals and drop-outs, allocation concealment, and outcome measurement)
- Information about pre-planned extension of trial (if relevant)
• Results (all beneficial and harmful patient effects, including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs with reasons; measures of dispersion, such as standard deviation or standard error, must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)
  • Data analysis
  • Conclusions.
• New data, generated since the last date that data was reported in the studies included in the Submission. (Typically, the studies submitted to CDR are the same as those submitted to Health Canada and sometimes these studies are ongoing, with data collected after submission to Health Canada. The data resulting after the study has been submitted to Health Canada is required.) This data will be accepted in a variety of formats, including late draft, Clinical Study Report, synopsis, abstract, or conference proceedings.
• Copies of references supporting the validity of outcome measures in studies (if available). If no references are provided, a statement is required to confirm that a search has been undertaken but no references have been located.
• A tabulated list of Canadian and international published and unpublished clinical trials. The table should be provided in hard copy and as an electronic copy in Microsoft Word format on disk or on CD. (See Appendix 8 table template.) The template can be downloaded from the CADTH web site at www.cadth.ca. The list should include:
  o A list of all completed published and unpublished studies included in the Submission and where they are located in the Submission, including the section in the Submission and the Submission page number.
  o A list of all completed published and unpublished studies not included in the Submission
  o A list of all ongoing studies.
  Upon review of this information, the CDR Directorate may request more details or copies of the studies.
• Search strategies used to locate published studies in medical literature databases (e.g., Medline®, EMBASE®, Cochrane). Search results are not required.
• A signed declaration that all known, unpublished clinical trials have been disclosed (Appendix 9 letter template). The template may be downloaded from the CADTH web site at www.cadth.ca.

f) Economic and Epidemiologic Information
Note: A pharmacoeconomic template for use by CDR Reviewers can be found in the CDR section of the CADTH web site, www.cadth.ca. Manufacturers may wish to refer to this document to see how information is used and reported in the review.

The following are required:
• An appropriate pharmacoeconomic evaluation — required for all Submissions. Refer to Appendix 12 for guidance on the type of economic analyses and what to submit. Please also refer to the CADTH document, Guidelines for the Economic Evaluation of Health Technologies: Canada
• Three (3) copies of the economic model in unlocked (or executable) format and documentation detailing the methods used in the modeling exercise, as well as basic user information. The CDR reviewer must be able to vary individual parameters, view the calculations, and run the model to generate results. The following table identifies the type of
information that the CDR requires for its examination of the model and the preferred format for receiving it:

<table>
<thead>
<tr>
<th>Table 1: CDR Pharmacoeconomic Information Requirements</th>
</tr>
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<tbody>
<tr>
<td><strong>Information Elements</strong></td>
</tr>
<tr>
<td>Basis for the pharmacoeconomic study (model, spreadsheet)</td>
</tr>
<tr>
<td>Media</td>
</tr>
<tr>
<td>Software requirements</td>
</tr>
<tr>
<td>Basic user guide to the model</td>
</tr>
<tr>
<td>Model documentation (manuscripts or a summary of the model report may be submitted)</td>
</tr>
<tr>
<td>Description of the statistical analyses included in the model (data sources, methods and results)</td>
</tr>
</tbody>
</table>

Note: The model will be examined by internal and external CDR reviewers. The model will not be released to any third parties.

In addition, if statistical analyses of data sets are included in the model, the Manufacturer should provide a description of the data sources and analyses conducted, and results from the analyses.

- BIASs — must be provided as a Category 1 requirement if a Priority Review based on cost savings is requested — for each of the following Drug Plans in accordance with their requirements: Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia, and Non-Insured Health Benefits Program (waivers may be granted upon submission of appropriate justification). When data specific to Prince Edward Island is unavailable, the BIA for Prince Edward Island is to be based on Nova Scotia data. The following supporting documentation is required:
  - all market research information used in BIASs
  - copies of documents cited in the BIASs.
- Number of patients accessing the New Drug, pre-NOC and post-NOC up to the time of the Submission, either as compassionate supply from the Manufacturer, under the Special Access Program, or as part of a clinical trial
- Disease prevalence — the prevalence or incidence of the disease(s) or condition(s) for which the Drug is approved by Health Canada should be provided for the Canadian population, with a breakdown by participating province, territory and First Nations’ population where available (must be referenced). This information must be provided as a Category 1 requirement and as well as in the BIASs.

**g) Pricing and Availability Information**

- Submitted prices, reported as price per smallest unit to four decimal places and per smallest dispensable unit for all dosage forms, strengths and package sizes. *(Note: the submitted price is the price that is effective for all CDR participating drug plans. It can be:*
  - the current market price in Canada; or
• If the submitted price is a Confidential Price that may become effective following release of the CEDAC Final Recommendation, the Manufacturer must provide a signed commitment to honour this price for all CDR participating drug plans (Appendix 10 letter template).
• Only one current or Confidential Price per unit is to be submitted.
• The submitted price must be used in the pharmacoeconomic evaluation and in the BIAs, included in the Submission.
• Method of distribution to pharmacies (wholesale, direct, or other arrangements).

h) **Letter Confirming Ability to Supply**
A letter providing assurance of a Manufacturer’s ability to meet the anticipated demand for the product at the time of filing the Submission. (See Appendix 10 letter template. The template may also be downloaded from the CADTH web site, www.cadth.ca.)

i) **Letter Authorizing Unrestricted Sharing of Information**
This letter from the holder of the NOC or NOC/c, printed on company letterhead and signed by an appropriate senior official, should permit unrestricted sharing of information regarding the Drug product between and within CDR and:
• Participating F/P/T Drug Plans
• F/P/T governments, including their agencies and departments
• F/P/T health authorities, including regional health authorities
• Health Canada
• Patented Medicine Prices Review Board.
(Appendix 11 letter template. The template may also be downloaded from the CADTH web site, www.cadth.ca.)

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

### 4.2.2 Category 2 Requirements

All Category 2 information must be provided as a single package to the CDR Directorate within 20 Business Days of filing the Submission for the Drug to be placed on the CEDAC agenda. When advised that Category 1 and 2 requirements are deemed complete, Manufacturers should provide the Drug Plans with copies of the Submission as described in Appendix 1.

**a) Drug Notification Form**
A completed, dated and signed copy [also known as the Drug Identification Number (DIN) notification form].

**b) Economic and Epidemiologic Information**
• BIAs – if not already filed with Request for Priority Review based on cost savings — for each of the following Drug Plans in accordance with their requirements: Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia, and Non-Insured Health Benefits Program (waivers may be granted upon submission of appropriate justification). When data specific to
Prince Edward Island is unavailable, the BIA for Prince Edward Island is to be based on Nova Scotia data. The following supporting documentation is required:

- all market research information used in BIAs
- copies of documents cited in the BIAs

- Number of patients accessing the New Drug, pre-NOC and post-NOC up to the time of the Submission, either as compassionate supply from the Manufacturer, under the Special Access Program, or as part of a clinical trial
- Disease prevalence – the prevalence/incidence of the disease(s)/condition(s) for which the Drug is approved by Health Canada should be provided for the Canadian population, with a breakdown by participating province, territory and First Nations’ population where available (must be referenced).

c) **Compendium of Pharmaceuticals and Specialties (CPS) listing**
A letter indicating the current or intended inclusion of the product monograph in the CPS.

d) **Pharmaceutical Advertising Advisory Board (PAAB)-approved promotional materials – or a draft copy of material submitted to PAAB**
If a Manufacturer does not intend to produce and use promotional material for the product, the Manufacturer may request that this requirement be waived. A letter, signed by a senior company official, stating the rationale and period of time (month and year) for which no promotional material will be used, must be provided.

e) **Certified Product Information Document (CPID)**
A completed and approved copy. In lieu of the CPID, the Master Formula and Final Product Specifications must be provided.

f) **Product Patent Expiration Date**

4.2.3 Additional Information

The following information may be requested by the CDR Directorate.

a) **Harm and Safety Information**
The CDR Directorate may request harm and safety information; however, the Manufacturer has the responsibility of advising the CDR Directorate of all data on harm related to the Drug under review, including harm and safety issues that may arise during the time that the Submission is under review.

b) **Health Canada Reviewer’s Report**
The summary of the assessment of the New Drug Submission by Health Canada reviewers.

c) **Periodic Safety Update Reports (PSURs)**
CDR Directorate may contact the Manufacturer for this information.
5. RESUBMISSIONS

5.1 Resubmissions

Manufacturers may file Resubmissions when they have New Information that was not provided in the original Submission.

New Information is new clinical information (not previously submitted or published) or new cost information that significantly impacts the cost-effectiveness of the Drug.

If the New Information is in support of improved efficacy, it must be from a randomized controlled trial. If the New Information is in support of improved safety, case-control or cohort studies will be accepted if randomized controlled trials are not available.

Note: Information requested by the CDR Directorate to clarify a Submission is not considered New Information and does not affect the place of a Submission in the review queue.

5.1.1 Eligible Resubmissions

Resubmissions from Manufacturers, the ACP or Drug Plans are limited to New Drugs, New Combination Products and Drugs with New Indications that are undergoing review through the CDR process or for which a Notice of Final Recommendation has been issued by the CDR Directorate. The CDR Directorate may accept Resubmissions under the following circumstances:

- New Information becomes available during the review process before the Notice of Final Recommendation has been issued; or
- New Information becomes available after Notice of Final CEDAC Recommendation has been issued; or
- New Information becomes available that affects coverage criteria recommended by CEDAC and accepted by the Drug Plans in their decisions to list a drug in their formularies.

5.1.2 Filing of Resubmissions

- Resubmissions must be delivered to the CDR Directorate by mail or courier (Appendix 4). Resubmissions cannot be filed electronically at this time.
- When filing a Resubmission, the Manufacturer should deliver only one complete copy of the Resubmission to the CDR Directorate. The Manufacturer should wait until the Resubmission has been deemed complete by the CDR Directorate before submitting the required number of copies to either the CDR Directorate and or participating Drug Plans.

5.1.3 Screening of Resubmission for Completeness; Required Number of Copies

- An initial screening of the Resubmission is conducted by the CDR Directorate within ten (10) days of receipt to ensure that it is complete.
- The CDR Directorate verifies whether the Resubmission is complete in accordance with this document.
• If the Resubmission is incomplete, the CDR Directorate sends a notice to the Manufacturer advising what information is needed to complete the Resubmission.
• When the Manufacturer’s Resubmission is complete, the CDR Directorate sends an acknowledgement to the Manufacturer, and advises the ACP or Drug Plans. Upon receipt of the acknowledgement, the Manufacturer must ensure that:
  ▪ when the Resubmission is based on new clinical information, that the CDR Directorate is provided with six (6) complete copies of the Resubmission or, when the Resubmission is based on new cost information, that the CDR Directorate is provided with three (3) complete copies of the Resubmission; and
  ▪ each Drug Plan is provided with one or more copies of the Resubmission, or part of it, as directed by the Drug Plans in Appendix 1.

5.1.4 Deadlines and Order of Review

Contained in Section 4.1.5 of this document. The information for Submissions applies to Resubmissions as well.

5.1.5 Priority Review

Contained in Section 4.1.6 of this document. The information for Submissions applies to Resubmissions as well.

5.1.6 Inquiries

Contained in Section 4.1.7 of this document. The information for Submissions applies to Resubmissions as well.

5.1.7 Communications and Conflict of Interest

Contained in Section 4.1.8 of this document. The information for Submissions applies to Resubmissions as well.

5.1.8 Confidentiality

Contained in Section 4.1.9 of this document. The information for Submissions applies to Resubmissions as well.

5.2 Resubmission Requirements

The following table identifies the type of information that the Manufacturer must provide in filing a Resubmission, depending on when the Resubmission is being filed relative to the status of the Drug in the CDR process and the reason why the Manufacturer is resubmitting. Explanations for the symbols in superscript in Table 2 can be found on pages 16 and 17.
### Table 2: Guidance for Filing Resubmission

<table>
<thead>
<tr>
<th>When in the Review Process, the Resubmission is Filed</th>
<th>Reason For Filing Resubmission</th>
<th>What the Manufacturer Must Submit to the CDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Resubmission is filed before Notice of Final Recommendation is issued*</td>
<td>New clinical information, supporting improved efficacy</td>
<td>New randomized controlled clinical trial(s) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New clinical information, supporting improved safety</td>
<td>New case-control or cohort study(ies) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New cost information</td>
<td>New pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td>2. Resubmission is filed after Notice of Final Recommendation is issued*</td>
<td>New clinical information, supporting improved efficacy</td>
<td>New randomized controlled clinical trial(s) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New clinical information, supporting improved safety</td>
<td>New case-control or cohort study(ies) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New cost information</td>
<td>New pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td>3. Resubmission is based on New Information that affects coverage criteria being filed after Notice of Final Recommendation is issued*</td>
<td>New clinical information, supporting improved efficacy</td>
<td>New randomized controlled clinical trial(s) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New clinical information, supporting improved safety</td>
<td>New case-control or cohort study(ies) and new pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td></td>
<td>New cost information</td>
<td>New pharmacoeconomic evaluation and BIAs</td>
</tr>
<tr>
<td>4. Resubmission is filed after withdrawn market authorization has been re-instated</td>
<td></td>
<td>Resubmission requirements are determined by the type of New Information. Refer to the column Reason for Filing Resubmission to determine CDR information requirements</td>
</tr>
<tr>
<td>5. Resubmission is filed after voluntary withdrawal</td>
<td></td>
<td>Resubmission requirements are determined by the type of New Information. Refer to the column Reason for Filing Resubmission to determine CDR information requirements</td>
</tr>
</tbody>
</table>

#### Explanations for Table 2:

*When a Resubmission is filed as described in Items 1 to 3 in Table 2, New Information, data and reference material that were not included in the original Submission are required. The following information must be supplied when making a Resubmission, and organized in the Resubmission binder with clearly labelled tabs identifying the sections.*

**a) Signed Cover Letter**

An original signed covering letter from Applicant, confirming that the information is new and stating the anticipated change or outcome. The letter should also provide:

- justification for the Resubmission – the rationale for why the Resubmission is being made
- whether a Priority Review is being requested for the product and justification if requested
- justification for not providing a BIA for any of the ten (10) participating Drug Plans listed in Economic and Epidemiologic Information, in Section 4.2.1 of this document (if relevant)
- statement clarifying whether the submitted price is the current marketed price or the Confidential Price that may become effective following release of the CEDAC Final Recommendation [Item (f) in this section]
- the names of the primary and back-up contact(s) the CDR Directorate can contact regarding the Resubmission. (Note: the Manufacturer may designate the consultant(s) preparing the Submission as primary and/or back-up contacts.)

**b) Product Monograph**

A copy of the most recent product monograph, showing the date it was approved by Health Canada, and the company and product names that correspond to the NOC.
c) **New Information**
   - A list of all New Information not included in the original Submission, or previous Resubmissions, which is being included in the Resubmission
   - Copies of all New Information and supporting documentation.

d) **Drug Notification Form** [also known as Drug Identification Number (DIN) notification form].
   A completed, dated and signed copy of the most recent form. If no changes have been made to the original form, it should be submitted.

e) **Letter Authorizing Unrestricted Sharing of Information**
   This letter from the holder of the NOC or NOC/c, printed on company letterhead and signed by an appropriate senior official, should permit unrestricted sharing of information regarding the Drug product between and within CDR and:
   - Participating F/P/T Drug Plans
   - F/P/T governments, including their agencies and departments
   - F/P/T health authorities, including regional health authorities
   - Health Canada
   - Patented Medicine Prices Review Board.
   (See Appendix 11 letter template. The template may be downloaded from the CADTH web site at www.cadth.ca.)

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

f) **Pricing Information**
   - Submitted prices reported as price per smallest unit to four decimal places and per smallest dispensable unit for all dosage forms, strengths and package sizes. *(Note: the submitted price is the price that is effective for all CDR participating drug plans. It can be:
     - the current market price in Canada; or
     - the Confidential Price effective for all CDR participating drug plans following the release of the CEDAC Final Recommendation.)*
   - If the submitted price is a Confidential Price that may become effective following release of the CEDAC Final Recommendation, the Manufacturer must provide a signed commitment to honour this price for all CDR participating drug plans. (Appendix 10 letter template).
   - Only one current or Confidential Price per unit is to be submitted.
   - The submitted price must be used in the pharmacoeconomic evaluation and in the BIAs, included in the Resubmission.
   - Method of distribution to pharmacies (wholesale, direct, or other arrangements).

g) **List of Decisions by Participating F/P/T Drug Plans**
   A summary of the benefit status of the Drug product in all participating F/P/T/ Drug Plans at the time of the Resubmission, including all criteria for coverage if applicable.
## APPENDIX 1: Participating F/T/P Drug Plans

*Note: Manufacturers should send copies of Submissions to participating F/P/T Drug Plans AFTER receiving confirmation from the CDR Directorate that the Submission is complete — i.e., that both Category 1 and 2 requirements are satisfied.*

<table>
<thead>
<tr>
<th>Plan</th>
<th>Contact/Send Submission to:</th>
<th>What to Send</th>
</tr>
</thead>
</table>
| British Columbia* | Senior Pharmacist  
PharmaCare  
Ministry of Health Services  
3-2, 1515 Blanshard Street  
Victoria, BC V8W 3C8  
T: (250) 952-1183 | One Complete Submission† |
| Alberta*     | Marilyn Thornton  
Director  
Pharmaceuticals and Life Sciences  
Strategic Directions Division  
Alberta Health and Wellness  
10025 Jasper Avenue, 18th Floor,  
P.O. Box 1360, STN Main  
Edmonton, AB T5J 2N3  
T: (780) 422-1344 | One Complete Submission† |
| Saskatchewan | Dr. Lorne Davis  
Pharmacologist  
Department of Pharmacology  
College of Medicine  
University of Saskatchewan  
107 Wiggins Road  
Saskatoon, SK S7N 5E5  
T: (306) 933-5599  
Director, Pharmaceutical Services  
Drug Plan and Extended Benefits Branch  
Saskatchewan Health  
3475 Albert Street, 2nd Floor East  
Regina, SK S4S 6X6  
T: (306) 787-3305 | Two Complete Submissions†  
(Note: one each for L. Davis and Director, Pharmaceutical Services) |
| Manitoba     | Kathy McDonald  
Secretary  
Drug Standards & Therapeutics Committee  
1014-300 Carleton Street  
Winnipeg, MB R3B 3M9  
T: (204) 786-7317 | Two Complete Submissions† |
| Ontario*     | Director  
Ontario Public Drug Programs  
Ministry of Health and Long-Term Care  
5700 Yonge Street, 3rd Floor  
Toronto, ON M2M 4K5  
T: (416) 327-8109 | Three Complete Submissions in hard copy format† |
<table>
<thead>
<tr>
<th>Plan</th>
<th>Contact/Send Submission to:</th>
<th>What to Send</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Brunswick</td>
<td>Leanne Jardine&lt;br&gt;Director&lt;br&gt;NB Prescription Drug Program&lt;br&gt;Department of Health&lt;br&gt;P.O. Box 5100&lt;br&gt;520 King Street, 3rd Floor&lt;br&gt;Fredericton, NB E3B 5G8&lt;br&gt;T: (506) 453-3884</td>
<td>One Complete Submission†</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>Manager&lt;br&gt;Nova Scotia Department of Health&lt;br&gt;Joseph Howe Building&lt;br&gt;1690 Hollis Street&lt;br&gt;Halifax, NS B3J 2R8&lt;br&gt;T: (902) 424-1596</td>
<td>Executive Summary&lt;br&gt;(two copies), NOC, Product Monograph, Pivotal Clinical Trials, BIA, and Prices</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>Patrick Crawford&lt;br&gt;Pharmacy Consultant&lt;br&gt;PEI Drug Programs&lt;br&gt;Department of Social Services and Seniors&lt;br&gt;P.O. Box 2000, 16 Fitzroy Street&lt;br&gt;Charlottetown, PE C1A 7N8&lt;br&gt;T: (902) 368-6711</td>
<td>Executive Summary, NOC, Product Monograph, BIA, and Prices</td>
</tr>
<tr>
<td>Newfoundland and Labrador</td>
<td>Colleen Janes&lt;br&gt;Director&lt;br&gt;Pharmaceutical Services Division&lt;br&gt;Department of Health and Community Services&lt;br&gt;57 Margaret’s Place&lt;br&gt;St. John's, NL A1C 3Z3&lt;br&gt;T: (709) 729-6507</td>
<td>One Complete Submission†</td>
</tr>
<tr>
<td>Northwest Territories</td>
<td>Manager&lt;br&gt;Health Services Administration&lt;br&gt;Territorial Services&lt;br&gt;Department of Health and Social Services&lt;br&gt;Bag Service #9&lt;br&gt;Inuvik, NT X0E 0T0&lt;br&gt;T: (867) 777-7412</td>
<td>Product Monograph, NOC, and Prices</td>
</tr>
<tr>
<td>Yukon Territory</td>
<td>Dianne Tait&lt;br&gt;Manager, Extended Benefits and Pharmaceutical Services&lt;br&gt;Insured Health and Hearing Services (H-2)&lt;br&gt;Government of Yukon&lt;br&gt;4th Floor, 204 Lambert Street (Box 2703)&lt;br&gt;Whitehorse, YT Y1A 2C6&lt;br&gt;T: (867) 667-5628</td>
<td>Executive Summary, NOC, Product Monograph, and Prices</td>
</tr>
<tr>
<td>Nunavut Territory</td>
<td>Brooke Fulmer&lt;br&gt;Territorial Pharmacist&lt;br&gt;2 Ring Road&lt;br&gt;Iqaluit, Nunavut X0A 0H0&lt;br&gt;T: (867) 979-7368</td>
<td>None</td>
</tr>
<tr>
<td>Plan</td>
<td>Contact/Send Submission to:</td>
<td>What to Send</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
</tbody>
</table>
| Non-Insured Health Benefits (NIHB)           | Federal Pharmacy and Therapeutics Committee Secretariat  
|                                               | c/o Director, Benefit Management  
|                                               | Non-Insured Health Benefits  
|                                               | First Nations and Inuit Health Branch  
|                                               | Health Canada  
|                                               | Room 1913A, Jeanne Mance Building  
|                                               | Tunney’s Pasture, Locator 1919A  
|                                               | Ottawa, ON K1A 0L3  
|                                               | T: (613) 954-9876                          | One Complete Submission† |
| Department of National Defence (DND) ‡       | LCol Susan Groves  
|                                               | Pharmacy Clinical Practice Leader  
|                                               | Pharmacy Policy and Standards  
|                                               | Department of National Defence  
|                                               | 1745 Alta Vista Drive, Room 207  
|                                               | Ottawa, ON K1A 0K6  
|                                               | T: (613) 945-6904                          | One Complete Submission† |
| Veterans Affairs Canada (VAC)‡               | Mike Duffy  
|                                               | Program Policy Analyst  
|                                               | Veterans Affairs Canada  
|                                               | Box 041, DJ MacDonald Building  
|                                               | P.O. Box 7700  
|                                               | Charlottetown, PE C1A 8M9  
|                                               | T: (902) 566-8665                          | One Complete Submission† |
| Royal Canadian Mounted Police (RCMP)‡        | Rockie Palmer  
|                                               | Pharmaceutical Consultant  
|                                               | Federal Healthcare Partnership  
|                                               | 66 Slater Street, Suite 200  
|                                               | Ottawa, ON K1A 0P4  
|                                               | T: (613) 992-4236                          | One Complete Submission†  
|                                               | (Note: one only for joint use by RCMP and CSC)                                             |                    |

* Refer to the Drug Plan web site for Drug Plan requirements  
†Complete Submission means that all of the Category 1 and Category 2 requirements are supplied; manufacturers must prepare and provide BIAs for each of the participating provincial plans and NIHB when they have the potential to list the particular product. The following Drug Plans have waived the requirement for a BIA: Northwest Territories, Yukon Territories, DND, VAC, RCMP and CSC.  
‡Although these Drug Plans have waived the requirement for a BIA to be prepared for them, each has requested copies of the BIAs prepared for other Drug Plans. Manufacturers should supply copies of all prepared BIAs to these federal Drug Plans.  

**Note:** When BIAs are not supplied for plans that have not waived the requirement, justification must be provided. In these cases, the CDR Directorate reviews the information and determines whether the Submission is complete. The Manufacturer is advised accordingly.  

When sending the Complete Submissions to the participating provincial Drug Plans and NIHB, Manufacturers have the option of including the BIAs for each of the different plans in the document (for example, Alberta would receive not only the BIA for Alberta but for the other plans as well) OR the Manufacturers may include only the plan – specific BIA in the Submission (e.g., Alberta would receive only the Alberta BIA).  

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**Common Drug Review Submission Guidelines For Manufacturers**  
Revised July 2007
APPENDIX 2: CDR Definitions

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

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 CADTH’s Board of Directors.

Additional Information – any information (excluding New Information) that is requested by the Review Team, CEDAC or CDR Directorate and required to complete the review of the Submission or Resubmission, or to explain or clarify information related to the Submission or Resubmission. Providing this information does not affect the review queue; however, if there is a delay in providing it or if the quantity and complexity of the requested information is significant, there may be a consequent delay in completion of the review.

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

Appropriate comparator(s) – currently accepted therapy.

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 Agency for Drugs and Technologies in Health (CADTH) office in Ottawa, Ontario is open for business during normal business hours.

CADTH – Canadian Agency for Drugs and Technologies in Health, a body corporate duly incorporated under the laws of Canada.

CDR – Common Drug Review.

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

CDR Directorate – the directorate established within CADTH 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 but not limited to:
- the Manufacturer’s Executive Summary of the Submission or Resubmission
- a list of unpublished studies known to the Manufacturer
- the Reviewers’ Reports relating to the Submission or Resubmission
- the Manufacturer’s written comments about the Reviewers’ Reports, if any
• 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 CADTH’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 review of published and unpublished information about the comparative 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 CADTH committees approved by CADTH’s Board of Directors.

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

Confidentiality Guidelines – the guidelines respecting confidentiality adopted by the CADTH Board regarding CDR.

Confidential Price – a price per unit (generally lower than the listed current market price) that is submitted as part of the CDR submission requirements and that is not publicly disclosed by CDR without permission from the Manufacturer. If the Confidential Price becomes effective, it must be available to all CDR-participating drug plans.

Conflict of Interest Guidelines or COI Guidelines – the conflict of interest guidelines adopted by CADTH’s Board of Directors for CEDAC, Reviewers and External Experts.

Directory – written information from CADTH amending, interpreting, updating or clarifying any process, procedure, guideline, terms of reference, code of conduct or document relating to the CDR.

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

Drug Plans – the participating publicly funded federal/provincial/territorial drug plans.

Embargo Period – refers to a period of time [ten (10) Business Days following the issuance of the Recommendation and Reasons for Recommendation] during which the Recommendation and Reasons for Recommendation are neither acted on by Drug Plans, nor are publicly available. During this period, the Manufacturer may submit a Request for Reconsideration or ACP, or Drug Plans may submit a Request for Clarification.
**External Expert** – an individual with appropriate qualifications and expertise required for some aspect of the review of the Submission or Resubmission, and whose services are obtained on a contract basis, as required.

**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 covered as benefits, as determined by each Drug Plan.

**F/P/T** – federal, provincial and territorial.

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

**Manufacturer** – a Drug manufacturer.

**New Active Substance** – a therapeutic substance that has never before been approved for marketing in any form. It may be:
- a chemical or biological substance not previously approved for sale in Canada as a drug
- an isomer, derivative or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy
- a biological substance previously approved for sale in Canada as a drug, but differing in molecular structure, nature of the source material or manufacturing process.

**New Combination Product** – consists of two or more Drugs that have not been previously marketed in Canada in that combination. It may consist of either two or more New Drugs, or two or more previously marketed Drugs, or a combination of New Drug(s) and previously marketed Drug(s).

**New Drug** – a New Active Substance that has not previously been marketed in Canada.

**New Indication** – a condition or disease that has not previously been approved for the use of the Drug.

**New Information** – new clinical information (not previously submitted or published) or new cost information that significantly impacts on the cost-effectiveness of the Drug and which does not form part of the original Submission or Resubmission. If the New Information is in support of improved efficacy, it must be in the form of a randomized controlled trial. If the New Information is in support of improved safety, case-control or cohort studies will be accepted if randomized controlled trials are unavailable.

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

**Notice of Final Recommendation** – the notice issued according to Section 7 of the *Procedure for Common Drug Review*. 
Old Drug – any Drug that is not a New Drug.

Participants – unless otherwise stated, CADTH 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 – a Reviewer who conducts a Pharmacoeconomic Review.

PMPRB – Patented Medicine Prices Review Board.

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. The Reasons for Recommendation are released to the Manufacturer and Drug Plans only and are not publicly available during the Embargo Period.

Recommendation – an evidence-based recommendation made by CEDAC, after consideration of Review Criteria, in response to a Submission or Resubmission made by a Manufacturer, ACP or by one or more Drug Plans, or in response to a Request for Advice regarding a CEDAC recommendation or Reasons for Recommendation made by ACP or by one or more Drug Plans. The Recommendation is released to the Manufacturer and Drug Plans only and is not publicly available during the Embargo Period.

Recommendation on Reconsideration – the conclusion reached by CEDAC on reconsideration of the Submission or Resubmission, as described in Section 6.4.4(a) of the Procedure for Common Drug Review.

Reconsideration Brief – the CEDAC Brief, CEDAC Recommendation, CEDAC Reasons for Recommendation, and 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 to by ACP or by one or more Drug Plans to CEDAC for advice on specific therapeutic, clinical or pharmacoeconomic issues, or regarding a CEDAC Recommendation or Reasons for Recommendation.

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.

**Request for Withdrawal** – a written request by an Applicant to withdraw a Submission or Resubmission from the review process.

**Resubmission** – the request by a Manufacturer, Drug Plan or the ACP to have an original Submission, that is under review or has received a Notice of Final Recommendation, reviewed again through the CDR process on the basis of New Information that was not previously provided in the original Submission or considered by CEDAC. The Resubmission goes to the end of the review queue.

**Review Criteria** – the following criteria are considered by CEDAC in making a listing recommendation:
- clinical studies, which assess safety and/or efficacy of the Drug in appropriate populations (when available, effectiveness data will be compared with accepted therapy)
- therapeutic advantages and disadvantages relative to accepted therapy
- cost-effectiveness relative to current accepted therapy.

**Review Team** – a team of individuals – including CDR Staff Reviewers, Contracted Reviewers and External Experts (clinical experts, methodologists, or other experts) with appropriate qualifications and expertise – assembled by the CDR Directorate to undertake the review of a Submission or Resubmission, or to prepare a Report in response to a Request for Advice.

**Review Template** – a template developed by the CDR Directorate for use by Reviewers to prepare Review Reports that are consistent in type of content and format.

**Reviewer** – an expert selected to conduct a Clinical or Pharmacoeconomic Review in accordance with Reviewer Guidelines established by the CDR Directorate.

**Reviewer Guidelines** – the CADTH 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 CADTH’s Board of Directors for CADTH’s committees.

**Submission** – a submission to the CDR consisting of:
- a written application made by a Manufacturer, together with supporting documentation, to have a Drug listed on the Drug Plans’ Formularies; or
- a written request, together with supporting documentation, if any, made by ACP or by one or more Drug Plans, 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 Guidelines** – the guidelines adopted by CADTH that outline how Submissions from Manufacturers must be prepared and submitted.

**Submission Requirements** – information that is required by the CDR Directorate to undertake the Clinical and Pharmacoeconomic Reviews of Drugs and other information that is required by the Drug Plans in making listing decisions. The Submission Requirements consolidate the requirements for the CDR and the Drug Plans. The Requirements apply to Submissions and Resubmissions.
**Systematic Review** – involves a review of a clearly formulated question using systematic and explicit methods to identify, critically appraise and summarize relevant studies (published and unpublished) according to predetermined criteria. Reported outcomes can be synthesized either quantitatively or narratively to summarize the results of included studies.
APPENDIX 3: Clarification of Where Submissions for Specialty Drugs Should Be Filed [Cancer or HIV/AIDS Drugs]

Many of the participating Drug Plans review and consider coverage for specialty products, such as HIV/AIDS Drugs, and therefore, a complete Submission to the CDR Directorate is required. However, some provinces have separate review and reimbursement agencies for specialty products. For example, the BC Centre of Excellence for HIV/AIDS reviews all HIV/AIDS drugs for British Columbia, and therefore, documentation for the BC Drug Plan is not required in the CDR Submission.

Note: Effective March 1, 2007 and for the duration of the interim Joint Oncology Drug Review, CDR will not accept submissions for oncology drugs. All Submissions for oncology drugs should be sent to the Ontario Drug Programs Branch (Appendix 1).

The following summary provides general guidelines for Manufacturers about where Submissions for HIV/AIDS Drugs (New Drugs and New Combination Products) should be sent.

Note: these are general guidelines only; whenever there is doubt about whether a Submission should be made to the CDR, Manufacturers are asked to contact the CDR Directorate for direction.

<table>
<thead>
<tr>
<th>Province</th>
<th>Oral HIV/AIDS Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>Send to Centre of Excellence in HIV/AIDS</td>
</tr>
<tr>
<td>Alberta</td>
<td>Send to Alberta Health and Wellness</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Manitoba</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Ontario</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Newfoundland and Labrador</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Northwest Territories</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Yukon Territories</td>
<td>Send to CDR</td>
</tr>
<tr>
<td>Federal – Participating Drug Plans</td>
<td>Send to CDR</td>
</tr>
</tbody>
</table>
APPENDIX 4: Delivery of Mail and Documents

a) Process and 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 Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON  K1S 5S8

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

To Another Person or Corporation:
The address or electronic communication number as may be designated by notice given in accordance herewith.

b) 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.

c) Determining Timeframes
The date on which the Submission or Resubmission is received is considered day zero (0) for the purpose of calculating timeframes.
APPENDIX 5: Confidentiality Guidelines

CADTH 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 is handled in a consistent manner. CADTH and the CDR Directorate comply with these Confidentiality Guidelines when handling information, as part of the CDR process. A Manufacturer is deemed to have consented to the Confidentiality Guidelines by filing a Submission or by supplying other information to the CDR Directorate. The Confidentiality Guidelines constitute an agreement between CADTH and the Manufacturer.

Definition

Confidential Information (including Confidential Price) is 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 the following section (Access to Information and Freedom of Information Legislation), but which does not include information that:

a) was already in the possession of CDR Directorate Staff, External Reviewer(s) assigned to review the Submission or Resubmission, CEDAC Members, External Experts (when contracted to provide specific information in relation to the Submission or Resubmission), 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 or Resubmission, CEDAC Members, External Experts (when contracted to provide specific information in relation to the Submission or Resubmission), ACP Members, F/P/T governments, F/P/T health authorities, Drug Plans, Health Canada or 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.
Access to Information and Freedom of Information 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, Manufacturers are asked to consent to their information being exchanged with F/P/T governments, F/P/T health authorities, Drug Plans, Health Canada and the PMPRB 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. CADTH and the CDR Directorate have no jurisdiction or control over those procedures and statutory requirements. Manufacturers should be aware of those procedures and requirements when including Confidential Information in a Submission or Resubmission. When information is received by the CDR Directorate through access to information or freedom of information legislation, it is treated in the same way as a Manufacturer’s Submission or Resubmission is treated according to these Guidelines. Any Confidential Information received by the CDR Directorate through access to information or freedom of information legislation is treated as Confidential Information pursuant to these Guidelines.

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 Resubmissions and Confidential Information;

   b) The CDR Directorate will not disclose Manufacturers’ Submissions or Resubmissions, or Confidential Information, to any third party except as permitted by these Confidentiality Guidelines or required by law or by order of a legally qualified court or tribunal;

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

   d) The CDR Directorate has in place secure filing and storage, web sites, and processes for tracking Manufacturers’ Submissions or Resubmissions and confidential documents;

   e) The CDR Directorate has in place internal processes for dealing with Manufacturers’ Submissions or Resubmissions and Confidential Information as set out below.
2. **Release of Manufacturer’s Information**

a) A Manufacturer’s Submission or Resubmission, including the Manufacturer’s Confidential Information, may be released to the following “Authorized Recipients”:

- CDR Directorate Staff
- Review Team
- CEDAC Members
- ACP Members
- F/P/T governments and Drug Plans
- F/P/T health authorities
- Health Canada
- 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 governments, F/P/T health authorities, Drug Plans, Health Canada and PMPRB have their own processes and statutory requirements to address confidentiality issues, as previously described.)

c) The Manufacturer’s Submission or Resubmission, 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 be posted on a confidential web site accessible only by persons authorized according to these Confidentiality Guidelines:

- Manufacturer’s Submission or Resubmission
- 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, with respect to Submissions or Resubmissions by it or in respect to an ACP or Drug Plan Submission or Resubmission 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 or Confidential Price supplied by the Manufacturer to make listing recommendations. Often the Reasons for Recommendation are based on information that is included in the unpublished studies, identified as Confidential Information by the Manufacturer, and, from time to time, on Confidential Price information. In such cases, the following provisions shall apply:

a) if any of the Reasons for Recommendation are based on unpublished Confidential Information and/or the Confidential Price, this information will be included in the Recommendation and Reasons for Recommendation document; however, this will be brought to the Manufacturer’s attention and the Manufacturer will be asked for permission to use this information in the Final Recommendation and Reasons for Recommendation.

b) if the Manufacturer instructs that the unpublished Confidential Information and/or the Confidential Price be deleted from the Final Recommendation and Reasons for Recommendation, CDR may indicate that unpublished Confidential Information and/or the Confidential Price was used by CEDAC to make its listing Recommendation and may indicate that the Manufacturer requested that the unpublished information be kept confidential, pursuant to the CDR Confidentiality Guidelines.

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

Minutes of the CEDAC meetings are released only to CEDAC members and the President of CADTH.

6. **Archiving of Confidential Documents**

All documents, including confidential ones, associated with the review of a Drug are kept on file in secure storage for as long as there is or may be a need to consult them. CDR Directorate Staff undertake regular reviews of archived material and any material they determine is no longer required is disposed of as outlined in paragraph 7.

7. **Disposal of Confidential Documents**

Confidential documents supplied by Manufacturers are disposed of either by shredding, or by returning them to the Manufacturer for disposal (at the Manufacturer’s expense), as directed by the Manufacturer.

8. **Drug Plan Information**

The CDR Directorate shall protect the confidential nature of any information provided by a Drug Plan and clearly marked “confidential”, and shall not share such information with Manufacturers or others except as may be permitted by the applicable Drug Plan(s).
APPENDIX 6: Format of Submissions and Resubmissions

The Manufacturers’ Submission Requirements for New Drugs, New Combination Products and Drugs with New Indications and the Resubmission Requirements have been developed to assist Manufacturers in providing the information, required by the CDR and participating Drug Plans.

Manufacturers are invited to use the Submission and Resubmission Checklists (for CDR Directorate Use) in Appendix 7 of this document to ensure that each Submission or Resubmission is complete. An incomplete Submission or Resubmission leads to delays in the process and may be returned to the Manufacturer at the discretion of the CDR Directorate staff, at the Manufacturer’s expense. An incomplete Submission or Resubmission does not enter the CDR process until all of the required Category 1 information is received by the CDR Directorate. A Submission is not placed on the CEDAC agenda until all of the Category 2 information is received.

Various letter templates, review templates and worksheets are contained within this document as appendices to assist with the completion of the Submission and Resubmission. This document and the templates are also available on the CADTH web site, www.cadth.ca.

The following guidelines are provided to assist Manufacturers in the preparation and organization of Submissions and Resubmissions:

- Submissions and Resubmissions must be provided in hard copy at this time.
- All Category 1 requirements must be included in the Submission and Resubmission (if applicable) so that the review may proceed.
- If a Manufacturer requests a Priority Review based on cost savings, BIAs must be submitted at the time of filing a Submission and Resubmission.
- The Clinical Studies section of the Comprehensive Summary will be accepted by the CDR Directorate during the transition to the Common Technical Document for New Drug Submissions made to Health Canada. Synopses of individual studies must also be included.
- All Category 2 information must be provided as a single package within 20 Business Days of filing the initial Submission and Resubmission (if applicable).
- Submissions must be organized in the order outlined in the “CDR Submission Requirements for New Drugs and New Combination Products” (Section 4.2 of this document) while Resubmission must be organized as described in Resubmission Requirements (Section 5.2 of this document).
- All pages of the Category 1 requirements in the Submission and Resubmission (if applicable) should be numbered consecutively from beginning to end. All pages of the Category 2 requirements should be numbered separately (i.e., starting at page 1 again) from beginning to end. It is also acceptable to number the pages consecutively within each section but the section and page number must be clearly identified on each page.
- Binders should be sturdy and not overfilled. The maximum thickness of binders should not exceed seven (7) centimetres [three (3) inches].
- Each binder should be clearly labelled.
- Double-sided pages should be used.
- Each section of the Submission and Resubmission must be identified with large tabs that are clearly labeled with the section name.
• The Submission or Resubmission is to be provided in English. All submitted articles should be in English. Unpublished data may be submitted. To be appraised, the unpublished studies should include the following:
  ▪ Objective and rationale of study
  ▪ Study population (including eligibility criteria, baseline characteristics and sample size)
  ▪ Methods (including blinding, handling of withdrawals and drop-outs, allocation concealment and outcome measurement)
  ▪ Results (all beneficial and harmful patient effects including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs, with reasons; measure of dispersion such as standard deviation or standard error must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)
  ▪ Data analysis
  ▪ Conclusions.

Although it is preferred that unpublished data be submitted in manuscript format, manuscript format is not a requirement. When unpublished data is not submitted in manuscript format, the information listed above should be included in clearly labelled sections. Only information that is truly confidential should be labelled as such. (See Confidentiality Guidelines, Appendix 5.)

Submissions and Resubmissions should be sent to:

  CDR Directorate  
  Canadian Agency for Drugs and Technologies in Health (CADTH)  
  600-865 Carling Avenue  
  Ottawa, ON  
  K1S 5S8

  Telephone: (613) 226-2553
APPENDIX 7: Submission and Resubmission Checklists

Drug Name: _________________________________________________________________

Manufacturer: _______________________________________________________________

**Category and Designation**

<table>
<thead>
<tr>
<th>Category</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>New Drug</td>
<td></td>
</tr>
<tr>
<td>New Combination</td>
<td></td>
</tr>
<tr>
<td>Drug with New Indication</td>
<td></td>
</tr>
<tr>
<td>ACP Request</td>
<td></td>
</tr>
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</table>

**Submission Type**

<table>
<thead>
<tr>
<th>Type</th>
<th></th>
<th>File number:</th>
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</thead>
<tbody>
<tr>
<td>First review</td>
<td></td>
<td>____________</td>
</tr>
<tr>
<td>Resubmission</td>
<td></td>
<td>____________</td>
</tr>
</tbody>
</table>

**Priority Review Submission**

<table>
<thead>
<tr>
<th>Request</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Priority Review</td>
<td></td>
</tr>
<tr>
<td>Justification provided</td>
<td></td>
</tr>
</tbody>
</table>

**Administrative Issues**

- Complete set of Category 1 Submission Requirements provided __________
  *(See list of Submission Requirements)*

- Number of binders that make up Submission set __________
## Category 1: Submission Requirements

### Signed Cover Letter
- Priority Review request and justification (if applying for Priority Review)
- Justification for intention not to provide a Budget Impact Analysis (BIA) for a specific jurisdiction (if relevant)
- Clarification if submitted price is current market price or Confidential Price.
- Names of primary and back-up contacts to be contacted regarding Submission

### Executive Summary (Hard Copy and Electronic Copy)
- Supporting references for specified listing when requested by Manufacturer

### Health Canada NOC or NOC/c (dated and signed)
- Letter of Undertaking (if NOC/c)

### Product Monograph
- Product Monograph (hard copy and Microsoft Word or PDF copy)
- Product Profile (hard copy and Microsoft Word copy)

### Efficacy, Effectiveness and Safety Evidence
- Clinical Overview and Clinical Summary, including Synopses of Individual Studies (Common Technical Document, Modules 2.7.1, 2.7.3, 2.7.4 and 2.7.6) OR Clinical Studies section of Comprehensive Summary in hard copy and Microsoft Word format on CD
- Critical studies that address key clinical issues (published and unpublished)
- New data generated since last date that data was reported in studies included in Submission
- Copies of references supporting validity of outcome measures OR statement confirming that a search did not identify any
- Tabulated list of published and unpublished studies (Appendix 8)
- Search strategies
- Signed declaration that all unpublished studies have been disclosed

### Economic and Epidemiologic Information

### Pharmacoeconomic Evaluation

### Three copies of economic model and documentation
- BIAs Provided with the Initial Submissions if Priority Review requested based on cost savings
- Newfoundland and Labrador
- Prince Edward Island
- Nova Scotia
- New Brunswick
- Ontario
- Manitoba
- Saskatchewan
- Alberta
- British Columbia
- Non–Insured Health Benefits Program
### Supporting Documentation for the BIAs

- Documentation of all market research information used in BIAs
- Copies of documents cited in the BIAs.

### Number of Patients Accessing Drugs Pre-NOC and Post-NOC Until Submitted

### Disease Prevalence and Incidence Data With Required Breakdown Where Available

### Pricing and Availability Information

- Submitted pricing reported as price per smallest unit to four decimal places
- Signed commitment if submitted price is Confidential Price
- Method of distribution

### Letter Confirming Ability to Supply

### Letter Authorizing Unrestricted Sharing of Information
## Category 2: Submission Requirements

*(To be provided as a single package within 20 Business Days of filing the initial Submission)*

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Notification Form (Drug Identification Number Notification Form) Dated and Signed</td>
<td></td>
</tr>
<tr>
<td>Economic and Epidemiologic Information</td>
<td></td>
</tr>
<tr>
<td>BIAs (If Not Provided With the Initial Submission)</td>
<td></td>
</tr>
<tr>
<td>• Newfoundland and Labrador</td>
<td></td>
</tr>
<tr>
<td>• Prince Edward Island</td>
<td></td>
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<tr>
<td>• Nova Scotia</td>
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<td>• New Brunswick</td>
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<td>• Ontario</td>
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<td>• Manitoba</td>
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<tr>
<td>• Saskatchewan</td>
<td></td>
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<tr>
<td>• Alberta</td>
<td></td>
</tr>
<tr>
<td>• British Columbia</td>
<td></td>
</tr>
<tr>
<td>• NIHB</td>
<td></td>
</tr>
<tr>
<td>Supporting Documentation for the BIAs:</td>
<td></td>
</tr>
<tr>
<td>• documentation of all market research information used in BIAs</td>
<td></td>
</tr>
<tr>
<td>• copies of documents cited in the BIAs.</td>
<td></td>
</tr>
<tr>
<td>Number of Patients Accessing Drugs Pre-NOC and Post-NOC Until Submitted</td>
<td></td>
</tr>
<tr>
<td>Disease Prevalence and Incidence Data With Required Breakdown Where Available</td>
<td></td>
</tr>
<tr>
<td>Compendium of Pharmaceuticals and Specialties Listing Intention Letter</td>
<td></td>
</tr>
<tr>
<td>Pharmaceutical Advertising Advisory Board (PAAB)-Approved Promotional Materials (Or Draft Copy of Material Submitted to PAAB) Or Letter Requesting Waiver</td>
<td></td>
</tr>
<tr>
<td>Certified Product Information Document (CPID)</td>
<td></td>
</tr>
<tr>
<td>Product Patent Expiration Date</td>
<td></td>
</tr>
</tbody>
</table>
# Resubmission Checklist

## Signed Cover Letter
- Justification for Resubmission
- Priority Review request and justification (if applying for Priority Review)
- Justification for intention not to provide a BIA for a specific jurisdiction (if relevant)
- Clarification if submitted price is current market price or Confidential Price.
- Names of primary and back-up contacts to be contacted regarding Submission

## Product Monograph

## New Information
- List of all New Information not previously submitted
- Copies of New Information.

If New Information is new clinical information supporting efficacy:
- new randomized controlled trial(s)
- new pharmacoeconomic evaluation
- BIAs.

If New Information is supporting improved safety:
- new case control or cohort study(ies)
- new pharmacoeconomic evaluation
- BIAs.

If New Information is new cost information:
- new pharmacoeconomic evaluation
- BIAs.

## Drug Notification Form (Copy of Most Recent Form)

## Letter Authorizing Unrestricted Sharing of Information

## Pricing and Availability Information
- Submitted pricing reported as price per smallest unit to four decimal places
- Signed commitment if submitted price is Confidential Price
- Method of distribution

## List of Participating Drug Plan Listing Decisions
### General Requirements Checklist

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submission is organized in the order outlined in Section 4.2 of this document or Resubmission is organized in the order outlined in Section 5.2 of this document.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Each section of the Submission is labelled with large tabs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The pages are numbered consecutively from the beginning to end of the Submission, or consecutively within each section with clear identification of section and page number.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Category 1 and Category 2 requirements are numbered separately.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binders are sturdy and not overfilled (maximum thickness 7 centimetres or 3 inches).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binders are clearly labelled.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double-sided pages are used.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Submission (including submitted studies) is provided in English.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only Confidential information is labelled as “Confidential.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All required information is included with unpublished studies, under the following headings:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Objective and rationale of study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Study population (eligibility criteria, baseline characteristics and sample size)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Methods (including randomization, blinding, handling of withdrawals/drop-outs, allocation concealment and outcome measurement)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Results (all beneficial and harmful patient effects, including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs with reasons; measure of dispersion such as standard deviation or standard error must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Data analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Conclusions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 8: Table Template for Listing Canadian and International Published and Unpublished Studies

Note: An example is included to illustrate the level of detail required. This table may be expanded. A copy of this table should be submitted in hard copy and as an electronic copy (Microsoft Word format on CD).

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

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

List of All Completed Published and Unpublished Studies NOT INCLUDED in Submission

List of All Ongoing Studies

*Study ID: provide the combination of numbers and/or letters, assigned by the sponsoring organization to identify the study
** Sponsor=Sponsor of the study
†Study title and/or description: briefly describe the study design [e.g., randomized, blinded (double or single), controlled, open label, extension, long-term safety, etc.], number of patients, objective(s), description of each treatment arm (Drugs and doses); outcomes specified in protocol; duration of treatment; condition or disease; the summary/description should be concise and brief
‡Study phase: indicate if phase 2, 3 or 4 (do not include phase 1 studies)
***End date: indicate when the study is scheduled to end, or the date completed or stopped
††Abstracts or publications: provide complete citations of all abstracts or publications (e.g., published report on interim findings) related to the unpublished study
‡‡Location in Submission: indicate the name of the tab under which the included study is located
APPENDIX 9: Letter Template for Confirming Disclosure of All Known Unpublished Studies

[Manufacturer’s letterhead]

[Date]

Director of CDR
CDR Directorate
Canadian Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Dear Director

Reference: [Brand name, generic name]

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

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX 10: Letter Template for Confirming Ability to Supply

[Manufacturer’s letterhead]

[Date]

Director of CDR
CDR Directorate
Canadian Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Dear Director

Reference: [Brand name, generic name]

This letter confirms that [name of Manufacturer]
   i) will supply the Drug at the submitted price, as provided elsewhere in this Submission, to all CDR participating drug plans;
   ii) is currently able (i.e., at the time of filing this submission) to supply the above drug product at the submitted price in a quantity sufficient to meet the anticipated national demands for this product.

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX 11: Letter Template for Authorizing Unrestricted Sharing of Information

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

[Manufacturer’s letterhead]

[Date]

Director of CDR
CDR Directorate
Canadian Agency for Drugs and Technologies in Health (CADTH)
600-865 Carling Avenue
Ottawa, ON
K1S 5S8

Dear Director:

Reference: [Brand name/generic name]

This letter authorizes the unrestricted communication with respect to the product within the CDR Directorate at the Canadian Agency for Drugs and Technologies in Health (CADTH) and with:

- Participating F/P/T Drug Plans
- F/P/T governments, including their agencies and departments
- F/P/T health authorities, including regional health authorities
- Health Canada
- Patented Medicine Prices Review Board.

[Signature]

[Name and Title of Senior Company Official of Manufacturer of Product]
APPENDIX 12: Guidelines for the Type of Economic Analysis to be Submitted

This appendix provides guidance for the type of economic analysis to submit to the Common Drug Review (CDR). Users of this document should refer to Section 4.2.1 (f), Economic and Epidemiologic Information. For methodological details, see the CADTH document, *Guidelines for the Economic Evaluation of Health Technologies: Canada*. If the clinical claims in the pharmacoeconomic evaluation are unsupported, the CDR Pharmacoconomic Review Report will report this finding and provide CDR cost comparison information only.

Based on the type of drug being submitted and its expected place in therapy, specific guidance has been provided.

Where it is unclear by which category(ies) the submitted Drug is best represented, the Manufacturer may contact the Common Drug Review (CDR). The CDR will only be able to provide clarification based on the information provided by the Manufacturer, which should include the name of the Drug, indication, dosage, pharmacologic classification, clinical trial information, and cost.

**Figure 1: Summary of the Guidelines for Type of Economic Analysis to Submit**

CEA=cost-effectiveness analysis; CCA=cost-consequence analysis; CUA=cost-utility analysis; Final Clinical Outcome= an event that is relevant and noticeable to patients; Intermediate Clinical Outcome=includes subjective clinical measures where extrapolation of health benefits to life-years or quality-adjusted life-years (QALYs) is more difficult (migraine pain score, urinary symptom scale), non-clinical endpoints or surrogate endpoints.
1. The Drug is the First Available for Treatment of the Disorder or Disease

Drugs that fall under this category include Drugs indicated for the treatment of diseases or disorders for which there are currently no drugs approved in Canada, or Drugs that establish a new therapeutic class for the treatment of a disease or disorder.

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Final</th>
<th>Intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Analysis</td>
<td>CEA/CUA</td>
<td>CEA/CUA CCA</td>
</tr>
<tr>
<td>Acceptable</td>
<td>- Cost per LYG</td>
<td>Cost consequence analysis:</td>
</tr>
<tr>
<td>Pharmacoeconomic</td>
<td>- Cost per QALY</td>
<td>- Cost analysis</td>
</tr>
<tr>
<td>Outcomes</td>
<td>- Cost per event avoided</td>
<td>- Cost per event avoided</td>
</tr>
<tr>
<td></td>
<td>(Section 1.1.1 of this appendix)</td>
<td>- Cost per additional response</td>
</tr>
<tr>
<td>Comparator</td>
<td>Standard or current care (Section 1.1.2 or 1.2.2 of this appendix)</td>
<td></td>
</tr>
<tr>
<td>Details of Cost Estimates</td>
<td>Price comparison table and health care cost tables (Section 1.1.3 or 1.2.3 of this appendix)</td>
<td></td>
</tr>
</tbody>
</table>

CEA=cost-effectiveness analysis; CCA=cost-consequence analysis; CUA=cost-utility analysis; LYG=Life-year gained; QALY=Quality-adjusted life-year.

The preferred clinical outcomes for CDR are Final Clinical Outcomes. If Final and Intermediate Outcomes are available, the submitted analysis should be based on Final Clinical Outcomes. Where possible, the Manufacturer should provide clinical evidence detailing the implications of the submitted treatment on Final Clinical Outcomes. Where this information is not available, surrogate outcomes shown to be valid surrogates for Final Clinical Outcome may be used. If data is not available to support the relationship between surrogate and Final Clinical Outcome, a cost-consequence should be provided.

1.1 Final Clinical Outcomes

A Final Clinical Outcome is defined as an event that is relevant and noticeable to patients. Outcomes may include:
- survival (overall)
- non-subjective clinical outcome measures, or disease or condition-related events that enable health benefits to be expressed in life-years, QALYs or events (e.g., myocardial infarction, stroke, or fracture).

1.1.1 Primary Type of Analysis

The primary type of analysis should be presented as a cost-utility analysis or cost-effectiveness, reporting:
- cost per life-year gained or cost per QALY gained
• cost per clinical event avoided (only for “non-subjective clinical outcome measures” when extrapolation to life years or QALYs is inappropriate).

Other analyses may be provided in the appendix of the Manufacturer’s Submission. CDR will assess whether the additional information is relevant and whether the details will be included in the CDR Pharmacoeconomic Report.

1.1.2 Comparator

In all cases, the new therapy should be compared with the accepted therapy (existing practice), where accepted treatment would either be the single most prevalent clinical practice (if there is one that is dominant). Where generic versions of the accepted therapies exist, this price should be used. All other reasonable alternative therapies should be at least discussed in the report.

See the CADTH document, Guidelines for the Economic Evaluation of Health Technologies: Canada for further guidance.

1.1.3 Requirements for Cost Data

Companies should submit a price comparison table (Table 3 in this appendix) and cost tables (Tables 4 and 5 in this appendix) outlining all appropriate costs, identifying source and assumptions for the costs included in each category.

1.2 Intermediate Clinical Outcomes

These include subjective clinical measures where extrapolation of health benefits to life-years or QALYs is more difficult (migraine pain score, urinary symptom scale), non-clinical endpoints or surrogate endpoints. A surrogate endpoint is an endpoint that is intended to relate to a clinically important outcome but does not in itself measure a clinical benefit. Surrogate endpoints, may be used as primary endpoints when appropriate (when the surrogate is reasonably likely or well known to predict clinical outcome). (Health Canada, http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ich/efficac/e8_e.html).

1.2.1 Primary Type of Analysis

The primary type of analysis should be presented as a cost-consequence analysis. Since the clinical data will be taken from the CDR Clinical Review for the Submission under review, only the cost tables will need to be completed (Suggested Format of Cost Information of this appendix).

Where appropriate, companies may choose to present the analysis as a cost per event avoided or cost per additional response. Companies should only present a cost per QALY (or cost per life-year) gained analysis if the surrogate endpoint has been shown to be a valid surrogate for true clinical outcomes. In such a case, the company should present, in a succinct fashion, the quantitative evidence justifying the surrogate as a valid predictor of clinical outcomes. Other analyses may be provided in the appendix of the Manufacturer’s Submission and referred to in the main text of the report. CDR will assess whether the Additional Information is relevant and whether the details will be included in the CDR Pharmacoeconomic Report.
1.2.2 Comparator

In all cases, the new therapy should be compared against current practice (Final Clinical Outcomes, Comparator Section of this appendix).

1.2.3 Requirements for Cost Data

Companies should submit a price comparison table (Table 3 in this appendix) and cost tables (Tables 4 and 5 in this appendix) outlining all appropriate costs, identifying source and assumptions for the costs included in each category.

1.3 Suggested Content for Submission

Companies should include the following information when submitting an economic evaluation to the CDR:
- Description of the study treatment
- Description of, and justification of, comparator(s) (i.e., reflects current management)
- Description of indication or treatment population
- Perspective
- Time horizon and justification
- Discount rates and justification (if applicable)
- Target audience
- Type of economic analysis and justification
- Appropriate and clear description of research methodology
- Clear description of data sources: effectiveness, cost and resource use, and other data
- Inclusion of pertinent outcome parameters (if applicable)
- Description of any assumptions used in the analysis
- Identification and definition of the key cost drivers
- Report of total and incremental costs and effects
- Description, justification and comprehensive reporting of sensitivity analyses (if applicable)
- Discussion of limitations
- Discussion of equity considerations
- Discussion of transferability of results across different jurisdictions.

For more detailed information on reporting structure, companies should refer to the CADTH document, Guidelines for the Economic Evaluation of Health Technologies: Canada (3rd edition, 2006).

2. The Drug Is Not the First Available Treatment for the Disorder or Disease

Drugs that fall under this category include Me-Too Drugs, such as those Drugs which largely duplicate the action of existing drugs, and combination products (for which all constituent Drugs are funded). Table 2 shows the analysis required.
Table 2: Guidelines for economic analyses conducted for subsequent drugs available for the disorder or disease

<table>
<thead>
<tr>
<th>Submitted Drug: Drug is Not the First Available for the Disorder or Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other available treatment(s) listed?</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

If other available treatments are listed as benefits by any of the participating publicly funded federal/provincial/territorial (F/P/T) Drug Plans in Canada, the Manufacturer needs to indicate whether a randomized trial has been conducted comparing the new therapy with either the first available drug or other available drugs (as defined above) for the disorder or disease.

2.1 Head-to-head trials have been conducted versus other available drugs*

*Other available drugs for the disorder or disease that are listed as benefits by any of the participating Drug Plans

Do the results of the trial(s) show no difference in safety and efficacy?

“No difference in safety and efficacy” is defined as: the lack of any statistically significant differences between the intervention and alternatives. This decision should be based on a high quality clinical assessment of the intervention.

Beyond treatment effects, the submitted Drug may differ from alternatives in terms of compliance or convenience of use (e.g., due to less frequent drug administration). These differences should only be considered as relevant for claiming clinical benefits if they have been linked to changes in clinically meaningful outcomes.

Note: Inappropriate assumptions of clinical equivalence compared to existing available drugs for treatment of this disease or disorder may compromise the ability to fully review the submitted Drug.

2.1.1 Results from the head-to-head trial(s) show no difference in safety and efficacy (non-inferiority or non-superiority)

Requirements for Cost Data – Companies should submit a price comparison table (Table 3 of this appendix) and cost tables (Tables 4 and 5 of this appendix) outlining all appropriate costs, identifying source and assumptions for the costs included in each category.
2.1.2 Results from the head-to-head trial show difference(s) in safety and/or efficacy

Follow submission process for first available drug (Section 1 of this appendix).

2.2 No head-to-head trial(s) have been conducted versus another available drug*

*Other available drugs for the disorder or disease that are listed as benefits by any of the participating Drug Plan

Requirements for Cost Data – Companies should submit a price comparison table (Table 3 of this appendix) and cost tables (Tables 4 and 5 of this appendix) outlining all appropriate costs, identifying source and assumptions for the costs included in each category.

2.3 Suggested Content for Submission

Companies should include the following information when submitting economic information to the CDR in support of a drug for which similar drugs are currently available:

- Description of the study treatment
- Description of, and justification of, comparator(s)
- Description of indication or treatment population
- Perspective
- Time horizon considered in cost table(s) and justification
- Discount rates and justification (if considering time horizons beyond one year)
- Justification for approach to economic submission (cost table(s)) – this may include reference to specific studies or sections in the submission binder.
- Clear description of data sources: effectiveness/efficacy, safety, cost and resource use, and other data
- Appropriate and clear description of research methodology (if applicable)
- Description of any assumptions used in the analysis
- Cost table(s) (Tables 3, 4, and 5 of this appendix)
- Description, justification and reporting of sensitivity analyses (if applicable)
- Discussion of limitations.

3. Suggested Format of Cost Information

CDR has suggested a possible approach to reporting the cost data. Manufacturers are strongly urged to consider all potentially relevant costs that may be applicable to their Drug; the cost components listed here by no means reflect a comprehensive list of all possible costs. Also, Manufacturers may provide tables that are more specific to their submitted Drug. The following tables are examples intended to assist those submitting economic information.
<table>
<thead>
<tr>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
<th>Column 4</th>
<th>Column 5</th>
<th>Column 6</th>
<th>Column 7</th>
<th>Column 8</th>
<th>Column 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>Strength</td>
<td>Form</td>
<td>List Price Per Unit (Specify) ($)</td>
<td>Average Daily Use</td>
<td>Average Daily Drug Cost Per Patient</td>
<td>Typical Annual Drug Cost*</td>
<td>Range of Plausible Costs</td>
<td>Extra Columns May Include: Daily Pill Burden, Daily Frequency of Use</td>
</tr>
<tr>
<td>Submitted Drug</td>
<td>XX mg</td>
<td>Tablet or Caplet</td>
<td>$Y</td>
<td>Z mg daily, twice daily, etc.</td>
<td>SA</td>
<td>(Consider actual market use of Drug)</td>
<td>(Consider other patient weights, possible wastage scenarios)</td>
<td></td>
</tr>
<tr>
<td>Comparator 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparator 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparator x (previous standard of care)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Where the typical duration of treatment is less than one year, the typical cost for a full course of treatment should be considered.

**Note:** Data sources and assumptions must be clearly stated by Manufacturer. As necessary, it is recommended that the company include sections detailing the calculations resulting in the value reported in each of these boxes.

Included within this table should be a detailed comparison of cost for the submitted Drug with all other available drugs for the treatment of the disease or disorder (if applicable) and with any previous Drugs that were considered standard of care.

A description of the submitted Drug and relevant comparators must be provided in columns 1 through 3. The list price of the treatment per unit, and the intended dosing and use should be described in columns 4 to 6. In addition, the typical price of each Drug, as used in clinical practice, should also be addressed in this table. “Typical Annual Drug Cost” should account for the actual doses used, wastage (where partial vials cannot be re-used), etc. The components included in this figure should be clearly detailed, and details of how this number was derived should be provided. These details should be provided in a footnote to this table, or if necessary in an appendix to the pharmacoeconomic submission. Factors that may affect the cost of the treatment should be detailed in column 8, “Range of Plausible Costs.” These factors might include: patient weight, possible wastage, treatment resistance. Additional columns may be included if necessary; justification must be provided for the inclusion of additional information. For example (column 9), where complex dosing or treatment regimens are being considered, the number of pills per day or the frequency of use may be relevant.
Table 2 details the direct health care costs associated with the submitted Drug. For each category, the costs provided should be reported as mean total cost per patient (i.e., taking into account the frequency of an event and its cost).

Note: Data sources and assumptions must be clearly stated by the Manufacturer. As necessary, it is recommended that the company include sections detailing the calculations resulting in each of these boxes.

Relevant cost items should be detailed in the rows, under the appropriate heading – examples have been provided of possible cost items. Other comparators may be included in this table, include columns as necessary.

Costs incurred during treatment
The costs to be included under this subheading are those incurred by individuals during, for instance, the course of the clinical trial. These might include the cost of administering the Drug, such as clinic time, visits to the physician and supplies. Induced costs of treatment may include items such as: additional time required to monitor patients receiving treatment, lab tests, treatment-related complications (which may include the need for additional Drugs, outpatient visits, hospitalizations, etc). Costs that may be impacted by the use of a Drug for a condition should also be included in this subsection, which might include the treatment of disease-related complications, hospitalizations, ER visits. Where the costs have not been collected alongside the clinical trial, it should be indicated that the costs were derived by the economic model and specific sources and assumptions should be stated in the last column.

Costs incurred beyond treatment
Based on extrapolation beyond the clinical trial, these are the expected costs for patients receiving the submitted Drug and appropriate comparators during the specified, extended, time horizon. This would include the costs of complications caused or prevented by the administration of the New Drug. These costs tend to be more important when performing full economic evaluations.

<table>
<thead>
<tr>
<th>Category</th>
<th>Submitted Drug</th>
<th>Comparator A</th>
<th>Comparator B</th>
<th>(Other Appropriate Comparator)</th>
<th>Time-Frame</th>
<th>Data Source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug — List price†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug — Typical cost†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs incurred during treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administration of Drug (Specify clinic time, outpatient visit, supplies, where relevant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other costs induced through use of the Drug (Specify treatment of adverse events or complications, concomitant drugs, etc.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs that may be impacted by treatment (Specify surgery, in-hospital stay)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs incurred beyond treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical costs (Specify cost of treating disease, complications with treatment)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Specify timeframe: monthly, annual or lifetime, etc.
† As detailed in Table 3.
Table 5: Non-Health Care Resources and Costs

<table>
<thead>
<tr>
<th>Category</th>
<th>Submitted Drug</th>
<th>Comparator A</th>
<th>Comparator B</th>
<th>Other Appropriate Comparator</th>
<th>Time Frame</th>
<th>Data Source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s time (total)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lost productivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Out-of-pocket costs (total)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Specify individual items: travel expenses, child care, modifications to home)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Specify timeframe: monthly, annual or lifetime, etc.

Table 3 details the non-health care costs associated with the submitted treatment compared to the appropriate comparators. Where non-health care costs are relevant in the economic evaluation, this table must be completed.

Note: Data sources and assumptions must be clearly stated by Manufacturer. As necessary, it is recommended that the company include sections detailing the calculations resulting in each of these boxes. Where assumptions or modeling have been conducted to determine the estimates for this table, the validation process for these estimates must be described and results of the validation reported.

Cells should be completed with respect to the expected cost for each item. The costs are derived by the expected number of hours spent multiplied by the wage or cost per hour. These data should be reported separately, and the sources of this information should be presented clearly.

Patient’s time should be reported in terms of the time spent receiving medical care and the lost productive time due to the disease or disability, multiplied by the mean wage or expected cost per hour. Patient and caregiver time must be converted to costs. The values used for this calculation must be provided. Calculations should be provided if the estimate is not transparent. The patient’s, or caregiver’s, out-of-pocket costs should be detailed. These items might include travel expenses, child care or modifications to the home.