

## **GUIDELINES FOR RAPID REVIEW SUBMISSIONS**

On June 20, 2006, Bill 102, "*The Transparent Drug System for Patients Act*", received Royal Assent. One of the resulting changes to the Ontario Drug Benefit Act allows for a submission from the manufacturer prior to receiving Health Canada Notice of Compliance (pre-NOC submission) for a product if specific criteria are met, where previously, submissions for products were only accepted after NOC had been issued.

The new Rapid Review mechanism encompasses both pre-NOC and post-NOC submissions. The previous "Fast Track" mechanism has been replaced by the new Rapid Review process.

For pre-NOC submissions that meet the criteria, the Minister has indicated that the Ministry will endeavour to come to a listing decision 30 days after the manufacturer receives NOC. Submissions that are received by the Ministry at least 60 days in advance of issuance of NOC and that qualify for Rapid Review will be subject to the 30-day post-NOC timeline. If NOC is issued within 60 days of receipt of a submission that qualifies for Rapid Review, the submission will be reviewed as quickly as possible.

For products that are submitted post-NOC, no timeline commitment has been made.

### **REGULATION:**

Further to Bill 102, the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96* states that,

**12. (1) A strength and dosage form of a drug product shall not be designated as a listed drug product unless the manufacturer of the drug product submits to the Executive Officer,**

- (a) either,
  - i. evidence that Health Canada has approved the product for sale in Canada, a copy of the product's drug notification form issued by Health Canada and, subject to subsection (2), a copy of the product monograph approved by Health Canada, or
  - ii. evidence that an application has been made to Health Canada to approve the product for sale in Canada, and evidence satisfactory to a panel of experts established for the purpose that the product meets at least one of the following criteria :
    - A. the product is a new chemical entity that is effective for the treatment of an immediately life-threatening disease or other serious disease for which it offers substantial improvements on significant outcomes, including improved efficacy, safety and tolerability and quality of life over other available drug therapies in Canada, or for which no treatment or no other effective drug therapy is currently available in Canada,
    - B. the product is a new chemical entity that if designated as a listed drug product, would have the effect of saving or creating efficiencies for the Government of Ontario, an average of at least \$2,500,000 per year for the first three years the product is marketed in Ontario,
    - C. the product is a new chemical entity that would have, if designated as a listed drug product, the effect of saving the Ontario Drug Benefit Program an average of at least \$250,000 per year for the first three years the product is marketed in Ontario.

### **SUBMISSION REQUIREMENTS:**

### **Pre-NOC Rapid Review Submissions:**

**Pre-NOC** submissions for Rapid Review consideration may be made by a manufacturer on or about the time that product monograph (PM) negotiations with Health Canada begin. Submissions will not be accepted more than 90 days from date of NOC. Submissions received less than 60 days from date of NOC will be unable to meet the 30-day post-NOC decision timeline.

1. Written evidence (letter or e-mail) of initiation of PM negotiations with Health Canada must be included with the Rapid Review submission request.
2. Pre-NOC submissions for Rapid Review consideration must fulfil **ALL** ODBA regulatory requirements at the time of the submission, with the exception of:
  - i. The final Pristine Product Monograph (PPM)
  - ii. The NOC or NOC/c.
  - iii. The completed Drug Notification Form (DNF)
  - iv. Proof of ability to supply
3. For pre-NOC submissions, manufacturers are required to provide the outstanding items (above) to meet regulatory requirements within 10 calendar days of issuance of NOC. In addition, if a NOC/c is issued, the manufacturer is required to provide a copy of the conditions and the plan to address the conditions within 10 calendar days of issuance of NOC/c.

Submissions that do not fulfil the regulatory requirements within 10 calendar days of issuance of the NOC or NOC/c would not be subject to Rapid Review commitments made by the Ministry, ie, to render a listing decision by 30 days post NOC. These submissions will move to the regular stream for post-NOC submissions.

**IN ADDITION**, pre-NOC Rapid Review submission requests would need to be accompanied by the following documentation:

1. **IF** the pre-NOC Rapid Review request is based on clinical considerations (**criteria “A” above**) under Section 12(1)(a)(ii) of the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96*,
  - i. Copy of the Health Canada letter of Acceptance for Priority Review, if available.
  - ii. Copy of the Clinical Assessment Package (CAP) and all accompanying correspondence between Health Canada and the Manufacturer relevant to the review of the CAP.
  - iii. Copy of the correspondence (e-mail OR letter) from Health Canada requesting the Manufacturer to begin PM negotiations
  - iv. 3 original executed copies of the specific pre-NOC consent letter allowing Health Canada and the Ministry to exchange information regarding the product. (See Appendix III.)

**Note that submissions qualifying for Priority Review under Health Canada provisions will NOT necessarily qualify for Rapid Review under the Ontario MOHLTC provisions. In addition, the review of a “Rapid Review” submission by the CED panel is not dependent upon a positive decision by Health Canada for a “Priority Review.”** However, the information contained in the CAP is relevant to the deliberations of the panel.

If the manufacturer feels that their request for Rapid Review merits consideration due to a specific clinical circumstance and a CAP is not available, they are invited to contact the Ministry for further discussion.

2. **IF** the pre-NOC Rapid Review request is based on economic considerations (**criteria “B” and “C” above**) under Section 12(1)(a)(ii) of the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96*,
  - i. An unlocked (or executable) copy of the pharmacoeconomic model which can be manipulated; details of the methods used in the modelling exercise; basic user information to enable manipulation of the model including the ability to vary individual parameters, view the calculations and run the model to generate results.
  - ii. An unlocked (or executable) copy of the budget impact analysis (BIA) model which can be manipulated; details of the methods used in the modelling exercise; basic user information to enable manipulation of the model including the ability to vary individual parameters, view the calculations and run the model to generate results

**Note that unlocked (or executable) copies of both the pharmacoeconomic model and BIA will be required for ALL submissions in future. This change will be reflected in the new Ontario Guidelines for Drug Submission and Evaluation, expected in the Spring/Summer of 2007.**

***Post-NOC Rapid Review Submissions:***

**Post-NOC** submissions for Rapid Review consideration will be considered if the criteria under Section 12(1)(a)(ii) of the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96* are met. However, these products are **NOT** subject to the 30-day post-NOC CED recommendation timeline.

**Post-NOC** submissions will continue to be required to fulfil ALL ODBA regulatory requirements at the time of submission and prior to review.

**IN ADDITION**, post-NOC Rapid Review submission requests would need to be accompanied by the following documentation:

1. **IF** the Rapid Review request is based on clinical considerations (**criteria “A” above**) under Section 12(1)(a)(ii) of the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96*,
  - i. Copy of the Health Canada letter of Acceptance for Priority Review, if available.
  - ii. Copy of the Clinical Assessment Package (CAP) and all accompanying correspondence between Health Canada and the Manufacturer relevant to the review of the CAP.

**Note that submissions qualifying for Priority Review under Health Canada provisions will NOT necessarily qualify for Rapid Review under the Ontario MOHLTC provisions. In addition, the review of a “Rapid Review” submission by the CED panel is not dependent upon a positive decision by Health Canada for a “Priority Review.”**

However, the information contained in the CAP is relevant to the deliberations of the panel. If the manufacturer feels that their request for Rapid Review merits consideration due to a specific clinical circumstance and a CAP is not available, they are invited to contact the Ministry for further discussion.

2. **IF** the Rapid Review request is based on economic considerations (**criteria “B” and “C” above**) under Section 12(1)(a)(ii) of the *Ontario Drug Benefit Act (ODBA) O. Reg. 201/96*,

- iii. An unlocked (or executable) copy of the pharmacoeconomic model which can be manipulated; details of the methods used in the modelling exercise; basic user information to enable manipulation of the model including the ability to vary individual parameters, view the calculations and run the model to generate results.
- iv. An unlocked (or executable) copy of the budget impact analysis (BIA) model which can be manipulated; details of the methods used in the modelling exercise; basic user information to enable manipulation of the model including the ability to vary individual parameters, view the calculations and run the model to generate results

**Note that unlocked (or executable) copies of both the pharmacoeconomic model and BIA will be required for ALL submissions in future. This change will be reflected in the new Ontario Guidelines for Drug Submission and Evaluation, expected in the Summer of 2007.**

**Manufacturers may make a Conditional Listing proposal at any time after the submission is made, or with the submission. Possible conditions to listing are within the scope of discussions at the CED. Manufacturers may be invited to begin negotiations for pricing or conditional listing with the DSS at any time after receipt of the proposal or after the CED recommendation is issued.**

**A Conditional Listing is defined as:**

A new Formulary listing category, intended to provide access to new and existing drugs under specific conditions and based on the recommendations of the Committee to Evaluate Drugs (CED).

These conditions may include but are not limited to:

- commitment to promote appropriate use where there may be concerns about inappropriate use or “off-label” use
- use in specific subgroup of patients
- requirement for outcomes data
- requirement for other, specific evidence to meet identified gaps in clinical or economic information
- mechanism to monitor and enforce conditions
- requirement for the Committee to Evaluate Drugs to further review the drug in a specific timeframe

Conditional listings are set up through partnership agreements between manufacturers and the Executive Officer.

***SUBMISSION PROCESS:***

1. Products will be screened against submission requirements as well as the Rapid Review criteria in parallel, within 2 weeks. The screening process will include liaising with the manufacturer within the 2-week timeframe to provide any deficient documents before the end of the 2-week screening period. If the manufacturer cannot provide the required documentation within the 2-week timeframe, a “Notice of Drug Submission Status “ (NDSS) letter will be issued to indicate that the Rapid Review submission is incomplete and the submission will be placed on hold.
2. The submission will be sent to an external clinical reviewer and/or an external pharmacoeconomic (PE) reviewer based on the rationale for the Rapid Review request.

3. The reviewer reports are provided to the Rapid Review Panel (consisting of the CED Chair and two CED expert members) to render a decision on whether or not the product qualifies for rapid review.
4. If the product qualifies for rapid review, the submission reviews and reports will be sent to the CED in approximately 4 – 6 weeks (includes time to identify and assign a reviewer).
5. For **Pre-NOC** products for which a complete submission is received between **60 and 90 days** prior to NOC and qualify for the Rapid Review process, the Ministry will endeavour to make a listing decision within 30 days of receipt of NOC.
6. **Pre-NOC** products for which a complete submission is received **less than 60 days** prior to receipt of NOC and qualify for the Rapid Review process will be reviewed as quickly as possible, but minimum required review times may preclude the ability to meet a 30-day post NOC listing decision.
7. **Pre-NOC** submissions reviewed through the Rapid Review stream must provide the outstanding documentation within 10 calendar days of issuance of NOC. The additional requirements will be screened and a final NDSS letter issued. If final documentation is not provided within the 10-calendar day timeframe, the submission will move to the regular review stream and will not be subject to the 30-day post NOC CED recommendation timeline.
8. **Post-NOC** product submissions that meet all regulatory requirements that qualify for the Rapid Review process are NOT subject to the 30-day post-NOC CED recommendation timeline. The products will be reviewed as quickly as possible and placed on the CED agenda as a priority item.
9. **Cancer products** that qualify for Rapid Review will be subject to review through a joint CED/CED-CCO subcommittee meeting to minimize delay. However, cancer products reviewed for the ODB and/or the NDFP include an evidence based review through the CCO's Program in Evidence Based Care (PEBC) and the development of a guideline which must go forward with the review before a recommendation is made through the CED-CCO joint review process. Timing of a final recommendation by CED is dependent upon the receipt of the PEBC guideline. This process can begin at the time of receipt of the Rapid Review submission and every effort will be made to target a CED recommendation within 30 days from the receipt of NOC or NOC/c. It is the responsibility of the Manufacturer to notify the CCO of the status of their product and request a PEBC guideline.
10. The final CED recommendation and rationale will be shared with the manufacturer per the current process as well as publicly through the new transparency process.
11. Recommendations will go forward for approval by the Executive Officer. Final listing decisions of the EO will also be publicly available with the new transparency process.
12. Manufacturers are encouraged to provide a resubmission to the CED and update their Product Monograph information when new evidence becomes available, such that the CED may revisit their recommendation.

**ONTARIO RAPID DRUG REVIEW PROCESS:  
Letter of Authorization to Collect and Disclose Pre-NOC Information**

[Manufacturer's letterhead]

[Date]

Director  
Ontario Public Drug Programs  
Ministry of Health and Long-Term Care  
3rd Floor, 5700 Yonge Street  
Toronto, ON M2M 4K5

Dear Director:

**RE: Rapid Review of <product name/generic name, strength, and dosage form> (the "Product") manufactured by <name of manufacturer> ("the Manufacturer")**

**BACKGROUND:**

- The Manufacturer has made a submission to Health Canada seeking authorization to market and sell the Product in Canada ("Drug Submission") but has not, as of yet, been issued a Notice of Compliance ("NOC") in respect of the Product;
- The Manufacturer has also submitted the Product for designation as a listed drug product on the Ontario Formulary under the expedited review process established by s.12(1)(a)(ii) of O.Reg 201/96 made under the *Ontario Drug Benefit Act* (the "Rapid Review Process"), which permits Her Majesty the Queen in right of Ontario as represented by the Executive Officer for Ontario Public Drug Programs ("Ontario") to commence review of drug products prior to the issuance by Health Canada of a NOC;
- As a condition of being considered for designation as a listed drug product on the Ontario Formulary through the Rapid Review Process, the Manufacturer must authorize Ontario to obtain information in respect of the Product from Health Canada prior to the potential issuance by Health Canada of a NOC for the Product ("Pre-NOC Information").
- For the purposes of this Letter of Authorization, Pre-NOC Information:
  - (a) includes:
    - (i) information provided to Health Canada by the Manufacturer as part of the Drug Submission and any other information obtained by Health Canada in connection with the Drug Submission;
    - (ii) any information, documents or reports, including reviewer reports, created by Health Canada in the course of its review of the Drug Submission; and
    - (iii) any information pertaining to the Product or the Manufacturer in the possession of the government of any province or territory in Canada, the Patented Medicine Prices Review Board (PMPRB), the Canadian Agency for Drugs and Technology in Health (CADTH), or Cancer Care Ontario.
  - (b) excludes:

- (i) third party proprietary information in the possession of Health Canada which Health Canada has agreed with that third party to hold in confidence; and
- (ii) any pricing information in respect to the Product which the Manufacturer has supplied to Ontario as confidential information.

AUTHORIZATION OF MANUFACTURER:

The Manufacturer, both during and after the Rapid Review Process, authorizes Ontario to:

- (a) collect and use any and all Pre-NOC Information in the possession of Health Canada, the government of any province or territory in Canada, the PMPRB, the CADTH, or Cancer Care Ontario;
- (b) disclose in confidence any and all Pre-NOC Information in the possession of Ontario to Health Canada, the government of a province or territory in Canada, the PMPRB, the CADTH, or Cancer Care Ontario; and
- (c) if the Product is a cancer drug, disclose in confidence any pricing information in respect of the Product to Cancer Care Ontario.

The Manufacturer further authorizes Health Canada to:

- (a) disclose in confidence any and all Pre-NOC Information in its possession to Ontario for use by Ontario, and
- (b) respond to any inquiries made by Ontario in respect of Pre-NOC Information disclosed to Ontario pursuant to this Letter of Authorization.

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Name:

Title:

I have authority to bind the Manufacturer

**Appendix V**

**PRE-NOC RAPID REVIEW PROCESS**

