Health Canada Santé Canada

February 6, 2009

NOTICE

Our file number: 09-101263-867

Administrative Corrections to Health Canada`s Priority Review Documents

Administrative changes were made to the French and English versions of the following Health Canada documents:

- *Policy: Priority Review of Drug Submissions/ Politique: Évaluation prioritaire des présentations de drogues*
- *Guidance for Industry: Priority Review of Drug Submissions/ Ligne directrice à l'intention de l' industrie: Évaluation prioritaire des présentations de drogues*

On December 20, 2007, administrative changes were made to the English and French versions of Priority Review Policy and Guidance documents to ensure consistent messaging for both official languages. However, in the process of making these administrative changes, errors were inadvertently introduced in the documents. Health Canada has therefore made the subsequent corrections to ensure consistent application of terminology.

Questions or concerns related to the policy and guidance documents should be directed to:

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Canada
Holland Cross, Tower B,
Address Locator 3102C3
1600 Scott Street
Ottawa, Ontario
K1A 0K9

Tel: (613) 948-4623
Fax: (613) 941-1812
E-mail: Policy_Bureau_Enquiries@hc-sc.gc.ca

Canada

Health Canada Santé Canada

GUIDANCE FOR INDUSTRY

Priority Review of Drug Submissions

Published by authority of the
Minister of Health

Date Adopted	2002/09/16
Revised Date	2005/11/30
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Administrative Changes Date	2008/12/18

Health Products and Food Branch

Canada

Our mission is to help the people of Canada maintain and improve their health. *Health Canada*	The Health Products and Food Branch's mandate is to take an integrated approach to the management of the risks and benefits to health related products and food by: • minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and, • promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. *Health Products and Food Branch*

Également disponible en français sous le titre : Ligne directrice à l'intention de l'industrie
Évaluation prioritaire des présentations de drogues

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with the policies and governing statutes and regulations. They also serve to provide review and compliance guidance to staff, thereby ensuring that mandates are implemented in a fair, consistent and effective manner.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate scientific justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this guidance documents, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

Document Change Log		
Change Date	**Location (section, paragraph)**	**Nature of and/or Reason for Change**
2002/09/16		Date of Original Adoption
2006/03/01	Section 3.6	Reflecting necessary changes resulting from finalization of the guidance document *Reconsideration of Final Decisions Issued for Human Drug Submissions*
2007/12/20	Throughout document	Address updates Consistent application of terminology
2008/12/18	Throughout document	Consistent application of terminology

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1.0 INTRODUCTION

1.1 Purpose

This guidance is intended to provide assistance to sponsors in the interpretation of the Priority Review policy and in preparing and submitting a request for Priority Review status. It should be read in conjunction with the *Priority Review of Drug Submissions Policy*.

All therapeutic products sold in Canada must meet safety and effectiveness requirements outlined in Part C of the *Food and Drug Regulations*. Special consideration relating to drug submissions qualifying under the Notice of Compliance with Conditions (NOC/c) policy, or those sold under C.08.010 and C.08.011 of the *Food and Drug Regulations* for Special Access purposes, may be warranted. For additional information on the NOC/c policy, refer to "*Guidance for Industry; Notice of Compliance with Conditions (NOC/c)*". Information on Health Canada's Special Access Program is available on the Health Canada Web site.

This guidance aims to articulate Health Canada's expectations and generate a level of consistency regarding the interpretation of the *Priority Review of Drug Submissions* policy and the filing of a Priority Review request. Additional clarification of the process by which the Priority Review request is assessed is provided.

1.2 Background

On December 13, 1996, the former Therapeutic Products Programme issued a policy statement entitled ***Priority Review of Drug Submissions***. The policy, replacing Information Letter, number 804, provided for the "fast-tracking" of eligible New Drug Submissions (NDS) and Supplemental New Drug Submissions (SNDS) intended for the treatment, prevention or diagnosis of serious, life-threatening or severely debilitating diseases or conditions.

A reassessment of this policy was prompted in December 1999 by concerns communicated through industry and the HIV/AIDS community. These groups questioned the criteria used to assign priority review status to submissions and expressed a desire for increased transparency of the drug review process. In particular, concerns related to an increase in the current submission backlog within Health Canada, confusion with respect to eligibility criteria for Priority Review status and a desire to ensure that relevant breakthrough therapies would be captured within the scope of Priority Review.

Assigning shorter review time-frames to a selected group of submissions impacts on Health Canada's ability to meet performance targets for other submission types. In providing additional clarification for both eligibility criteria and the process by which Priority requests are assessed, Health Canada aims to increase the consistency of the Priority Review process while continuing to satisfy the intent of the policy in providing an expedited review of critical new drugs and breakthrough therapies under the identified scope.

1.3 Definitions

CLINICAL BENEFIT: outcomes that have an overall positive impact on the treatment of a disease[1].

SIGNIFICANT INCREASE/DECREASE: statistically significant and clinically relevant increase (or decrease) identified through well controlled clinical trials.

1.4 Scope

This policy applies to a New Drug Submission (NDS) or Supplemental New Drug Submission (S/NDS) for a serious, life-threatening or severely debilitating disease or condition for which there is substantial evidence of clinical effectiveness that the drug provides:

- effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada; or

- a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada.

1.5 Time frames

Priority Review status allows for the insertion of eligible drug submissions into Health Canada's submission workload on the basis of a shortened review target of 180 calendar days. As such, qualifying submissions may undergo review in advance of non-eligible submissions in accordance with approaching target dates.

Submission workload consists of all submission types, differentiated across biological, pharmaceutical and medical device product lines. Specific therapeutic expertise within the Biologics and Genetic Therapies Directorate (BGTD) and the Therapeutic Products Directorate (TPD) is directed towards the review of corresponding submission types where required. As such, the review of a priority submission will commence before the review of other pending submissions of the same therapeutic area, which have a target completion date after that of a priority submission. The review of submissions with a target review date preceding the target review date of the priority submission, will not be disrupted.

[1] Quality of Life (QOL) factors may be admissible in support of clinical outcomes, however QOL will not be considered sufficient on its own to establish clinical benefit.

Once priority review status has been granted, there is a stated expectation that the submission will:

1) be filed within 60 calendar days;

2) contain the information and material for the purposes of Division 8 , Part C of the *Food and Drug Regulations*; and

3) be subject to the *Guidances for Industry Management of Drug Submissions*.

The performance target for the screening and review of the original submission is 215 calendar days (10 days processing within the Submission and Information Policy Division (SIPD), 25 days screening with the Submission Management Division (SMD) of the appropriate Directorate, 180 days submission review) and for the subsequent screening and review of the response to a Priority Submission Notice of Non-compliance, 125 calendar days (10 days SIPD, 25 days SMD screening, 90 days review).

Priority Review is utilized to establish review priorities. Both Priority Review requests and submissions will be subject to established Performance Standards. Although every attempt is made to commence review of the priority submission in an expedited manner, the policy does not preclude staff from working on other projects.

2.0 CRITERIA FOR QUALIFICATION AS A PRIORITY REVIEW SUBMISSION

To be considered for Priority Review status, a drug submission must first meet Health Canada criteria outlined in Section 1.4 above.

As with similar programs in other international jurisdictions, Priority Review designation applies to a combination of the product and specific indication(s) for which it is being studied and not the product alone. Therefore, it applies to a specific drug for specific indications where indication includes both the condition for which the drug is intended and the anticipated or established benefits of use.

In order to qualify for Priority Review status, the product must not only be intended for patients suffering from a serious, life-threatening or severely debilitating disease or condition but must also be indicated to treat, prevent or diagnose a serious symptom or manifestation of the condition. For example, a product indicated for alleviating a minor skin irritation in a patient with cancer would not be eligible for Priority Review status although the condition (cancer) itself is clearly life-threatening.

Sponsors seeking Priority Review status are encouraged to deliver a brief presentation to Directorate review staff, prior to submitting a written request for Priority Review status. The sponsor may, at this time, discuss details of the submission, as well as the potential eligibility of

the submission for Priority Review status. For additional information on pre-submission meetings, refer to Section 3.1.

For the purposes of establishing Priority Review eligibility, the following section provides guidance regarding how Health Canada determines whether a condition meets the 'serious' criterion. All life-threatening conditions would also be considered 'serious' diseases and as such, separate distinction will not be provided. In the following discussion, all references to serious conditions will include life-threatening diseases.

2.1 Serious/Life-Threatening Disease

In defining whether a condition is 'serious', Health Canada believes that a matter of discretionary judgement is required. Factors such as survival, day-to-day functioning or the likelihood that the disease if left untreated, will progress from a less severe condition to a more serious one are all taken into account. The latter includes, but is not limited to:

Acquired immunodeficiency syndrome (AIDS);
All other stages of human immunodeficiency virus (HIV) infection;
Alzheimer's dementia;
Amyotrophic Lateral Sclerosis (ALS);
Angina Pectoris;
Heart Failure;
Cancer; and
Other diseases that are clearly serious in their full manifestations.

'Serious' conditions are generally associated with morbidity with a substantial impact on day-to-day functioning. Reversible persistent or recurrent morbidity outcomes may also be sufficient to qualify a product for Priority Review status should all additional criteria be met. Alternatively, examples of insufficient morbidity would normally include short-lived and/or self-limiting morbidity.

2.2 Severely Debilitating Disease

Priority Review eligibility extends to drug submissions indicated for the treatment of a severely debilitating disease or condition wherein there exists an unmet medical need or for which a substantial improvement in the benefit/risk profile of the therapy is demonstrated. Many chronic diseases that may be generally well-managed by available therapy may have severely debilitating outcomes. Examples of the above include inflammatory bowel disease, asthma, rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, depression and psychoses. Once again, discretion on the part of Health Canada will be exercised.

2.3 *"Effective Treatment, Prevention or Diagnosis of a disease ..." (Section 1.4)*

Serious, life-threatening or severely debilitating diseases or conditions, for which no drug therapy is presently marketed in Canada, represent an obvious medical need. A new therapy effective in the treatment, prevention or diagnosis of an eligible condition would therefore meet this criterion for Priority Review status.

The term 'marketed' implies that sale of the product has commenced, pursuant to C.01.014 and that the product continues to be available for sale (i.e. has not been discontinued or removed from the market). Note: The above criterion does not provide for eligibility due to drug shortage scenarios. For further information on drug shortages, refer to the Health Canada Web site.

Products approved, but not yet not marketed, at the time a Priority Review request is assessed will have no bearing on the decision to accept or reject Priority Review status. Similarly, the existence of a submission undergoing review in Health Canada does not affect the decision for acceptance or rejection of a Priority Review request by another sponsor for the same indication. The decision for acceptance or rejection will be based solely on whether the conditions for Priority Review status have been met at the time of request and are accurately reflected in the Clinical Assessment Package (Section 3.2).

2.4 "Significant Increase in Efficacy and/or Significant Decrease...". (Section 1.4)

For the above Priority Review criterion to be met, the sponsor should be able to demonstrate that the therapy provides a statistically significant and clinically relevant improvement in efficacy or decrease in risk such that the overall benefit/risk profile is improved over existing therapies on the Canadian market. Priority Review request packages will be assessed based on products and information available at the time the request is reviewed and within the context of the disease for which the therapy is indicated. Packages will not be assessed based on comparator therapies at the time the pivotal trials were initiated.

The benefit/risk evaluation is consistent with Health Canada's approach to submission review and may include any of the following aspects:

- Improvement in one or more of the serious outcomes of the condition on which the effect is claimed;
- A favourable effect on a serious symptom or manifestation of the condition for which there is no existing therapy;
- A clinical benefit for individuals unable to tolerate, or unresponsive to, existing therapies;

- Demonstration of effectiveness in combination with other critical agents, where no information is available or where combined use with existing therapy(ies) is not feasible due to safety or efficacy considerations;

- Demonstration that the new agent is able to provide clinical benefits that are similar to existing therapies while a) avoiding serious toxicity present in existing therapies and/or b) avoiding less serious toxicity, common to the therapy, which results in the discontinuation of treatment of a serious disease; and,

- The ability to provide similar benefit to existing therapies while demonstrating improvement in a factor that has been shown to be significant during the conduct of the pivotal trial[2].

2.5 Substantial Evidence of Clinical Effectiveness

The evolution of science and the practice of drug development and clinical evaluation has implications for the quantity and type of data required to support effectiveness in certain instances.

In general, Health Canada views substantial evidence of clinical effectiveness as evidence consisting of at least two adequate and well controlled clinical studies, each convincing on its own to establish effectiveness of the drug involved. The effectiveness of the therapy would be assessed by experts qualified by scientific training and experience to evaluate the effect of the drug in treating the represented indication under the conditions of use prescribed, recommended or suggested in the labeling or proposed labeling thereof.

In some instances, clinical evidence consisting of a single, large-scale, adequate and well controlled study or one pivotal trial and additional clinical evidence may be deemed "substantial". Sponsors seeking Priority Review status are encouraged to deliver a brief presentation to Directorate review staff, prior to submitting a written request for Priority Review status, at which time additional clarification may be provided.

"Promising" clinical evidence including the use of non-validated surrogate markers, or Phase II studies is further addressed within the scope of the NOC/c policy and clarified in associated guidance. Specific shortened timeframes for NOC/c submissions are addressed within. For further information on NOC/c policy and guidance, refer to the Health Canada Web site.

The following sources may be consulted for additional guidance:

- *"Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products", Food and Drug Administration, May 1998*; and

[2] Factors such as compliance or convenience will not be considered sufficient on their own to establish clinical benefit however may be used in support of a rationale for Priority Review status.

- *"Points to Consider on Application with 1. Meta-Analyses; 2. One Pivotal Study", European Agency for the Evaluation of Medicinal Products, May 31, 2001.*

3.0 APPLYING FOR PRIORITY REVIEW STATUS

3.1 Pre-Submission Meetings

Prior to filing a request for Priority Review status, sponsors are encouraged to deliver a pre-NDS or pre-S/NDS presentation to the appropriate Directorate within Health Canada outlining the evidence of effectiveness to be provided in the submission.

Pre-submission meetings:

- familiarize Health Canada review staff with the pending submission, prior to its arrival;

- provide an opportunity for the sponsor to discuss details of the submission with the Regulator and obtain direction regarding any areas of concern based on current experience and regulatory requirements, as well as the potential eligibility of the submission for Priority Review status; and,

- provide the affected Directorate the opportunity to re-align its resources to accomodate the arrival of the submission.

Sponsors should submit a pre-submission meeting information package to the Submission Management Division/Unit of the appropriate Directorate in advance of the meeting. For further information, sponsors are advised to contact the Submission Management Division/Unit of the appropriate review Directorate.

3.2 Request Packages for Priority Review Status

The sponsor is required to submit, **in advance of the filing of the drug submission**, a written request for Priority Review status to the Director of the appropriate Bureau within Health Canada and a completed Clinical Assessment Package (CAP) in a format similar to that outlined in Appendix 1. See Section 4.0 for further guidance on completing the CAP. Incomplete packages and requests received subsequent to, or concurrent with, the arrival of the submission will not be accepted.

If the request is accepted, the sponsor will submit the full drug submission to Health Canada within 60 calendar days of, **but not prior to**, the date of issuance of the acceptance letter. Information regarding filing of the Priority submission is contained within Section 3.3.

Priority Review Requests are to be sent to the appropriate Directorate below:

Biologic and Genetic Therapies Directorate *(choose one)*

For biotherapeutic and radiopharmaceutical submissions:

Director, Centre for the Evaluation of Radiopharmaceuticals and Biotherapeutics
Regulatory Affairs Division - Biotherapeutics and Quality
Biologics and Genetic Therapies Directorate
Health Canada
Building # 7, Address Locator 0701A
200 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 0L2
Fax: 613-946-9520

For blood products and vaccine submissions:

Director, Centre for Biologics Evaluation
Regulatory Affairs Division - Blood, Tissue, Organs and Vaccines
Biologics and Genetic Therapies Directorate
Health Canada
Building # 7, Address Locator 0701A
200 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 0L2
Fax: 613-941-1708

OR

Therapeutic Products Directorate *(choose one)*

Director, Bureau of Metabolism, Oncology and Reproductive Sciences (BMORS)
Regulatory Project Management Division servicing BMORS
Therapeutic Products Directorate
Health Canada
Finance Building # 2, Address Locator 0202D2
101 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 1B9
Fax: 613-941-1365

Director, Bureau of Gastroenterology, Infection and Viral Diseases (BGIVD)
Regulatory Project Management Division servicing BGIVD
Therapeutic Products Directorate
Health Canada
Finance Building # 2, Address Locator 0202B1
101 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 1B9
Fax: 613-941-1183

Director, Bureau of Cardiology, Allergy and Neurological Sciences (BCANS)
Regulatory Project Management Division servicing BCANS
Therapeutic Products Directorate
Health Canada
Finance Building # 2, Address Locator 0202A1
101 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 1B9
Fax: 613-941-1668

Director, Bureau of Pharmaceutical Sciences (BPS)
Regulatory Project Management Division servicing BPS
Therapeutic Products Directorate
Health Canada
Finance Building # 2, Address Locator 0201D
101 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 1B9
Fax: 613-957-3989

3.3 Review of the Request, Approval and Filing of the Submission

Upon receipt, the CAP (i.e. request) is vetted by Submission Management to ensure completion of all mandatory sections. The CAP is then forwarded to the appropriate review division for assignment to a clinical evaluator.

The clinical evaluator may, on occasion, request additional supporting information to support and clarify the information provided in the Priority Review request. The sponsor is required to submit, within two (2) business days of a request, any supplementary information needed to assist in the assessment. In the event that supplementary information is not received within the above period, the decision to accept or reject a request for Priority Review status will be based on the information provided in the original request, subject to the interpretation of Health Canada evaluators.

Health Canada will notify the sponsor of the decision to accept or reject Priority Review status within 30 calendar days of receipt of the request. If the request is accepted, the sponsor will submit the full drug submission to Health Canada within 60 calendar days of, **but not prior to**, the date of issuance of the acceptance letter.

Submissions received in advance of the acceptance letter will undergo screening and, if found acceptable, shall enter the review queue as a non-priority submission. The review of a Priority request related to the submission shall cease immediately upon receipt of the submission.

All drug submissions, including Priority Review submissions, should be sent to the following:

Submission and Information Policy Division
Therapeutic Products Directorate,
Health Canada
1st Floor, Finance Building # 2, Address Locator 0202A1
101 Tunney's Pasture Driveway
Ottawa, Ontario
K1A 1B9
Fax: 613-941-0825

3.4 Screening

Where Priority Review status has been granted, the submission will be screened in accordance with a reduced screening target of 25 days.

A submission may be filed with the appropriate review directorate and undergo screening while the Reconsideration of a rejection for Priority Review status is underway. In the event that Priority Review status is granted as a result of a Request for Reconsideration, the review target will be adjusted accordingly from the date upon which screening acceptance was issued.

3.5 Rejection of a Priority Review Request

A request for Priority Review status may be rejected for reasons including, but not limited to, the following:

- failure to provide the records outlined in Sections 3.1 and 4.0;
- failure to demonstrate that the product satisfies the criteria outlined in Section 1.4 above; and,
- failure to adhere to request filing procedures outlined in section 3.2. Specifically, requests received after or concurrent with the submission will not be accepted and will be returned to the sponsor without review.

The following are not acceptable rationales for rejection of a Priority Review request:

- the existence of a submission for a similar indication undergoing review in Health Canada;
- approval of a product for the same indication, where the product is not available for sale in Canada;
- off-label use of the proposed indication for a product already marketed in Canada; and,
- disclosure of a sponsor's inability to market the product in a timely manner following approval (refer to Section 4j).

3.6 Reconsideration Process for Priority Review Requests

In the event that an initial Request for Priority Review is rejected, sponsors may file a Request for Reconsideration of the decision in accordance with the procedure outlined in the Health Canada's Guidance: *Guidance for Industry Reconsideration of Final Decisions Issued for Human Drug Submissions*.

As per section 5.1 of Health Canada's Guidance: *Guidance for Industry Reconsideration of Final Decisions Issued for Human Drug Submissions*, the rejection of either a first or second Rejection of Priority Review Request under the *Priority Review Policy* is eligible for Reconsideration. However, sponsors may only file a Request for Reconsideration of the first rejection *or* file a second Request for Priority Review status - they may not file both.

A submission may be filed with the appropriate review directorate and undergo screening while the Reconsideration of a rejection is underway. In the event that Priority Review status is granted as a result of a Request for Reconsideration, the review target will be adjusted accordingly from the date upon which screening acceptance was issued.

3.7 Re-filing of a Request for Priority Review Status

Instead of filing a Request for Reconsideration, sponsors may choose to file a second request, for additional consideration for the same indication, following a period of 60 days from the date of the original request. New information in support of the Priority Review status of the submission must be evident, i.e. results of ongoing clinical trials. Failure to provide new information will result in rejection of the request. Re-analysis of data to address reasons for the rejection of the original request falls within the scope of the Reconsideration procedure and may not be used as the basis for a second request.

Sponsors re-filing Priority Review requests are required to adhere to procedures outlined in Section 4 b) through f) of the Priority Review policy. In the event that the second request for Priority Status is rejected, for the same indication, no further requests will be accepted. In the event that the second Request for Priority Review status is rejected, sponsors may file a Request for Reconsideration of the second decision.

4.0 COMPLETING THE CLINICAL ASSESSMENT PACKAGE (CAP)

The Clinical Assessment Package (CAP) should be provided in a format similar to that outlined in Appendix 1. It must be no longer than 20 pages[3] in length and consist of the following elements:

a. *The proper or common name of the drug and brand name of the product*;

b. *The regulatory status of the drug worldwide;*

ELIGIBILITY REQUIREMENTS

c. *The **specific** indication for which Priority Review status is requested.*

In many instances numerous indications for one drug are presented, however Priority status will only be granted on the basis of applicable indications. Sponsors are requested to present the strongest case for Priority Review status and no others, e.g., for antibiotic therapies, the nature of the microorganism and/or disease site against which the antibiotic provides resistance should be indicated. Do not list all indications (e.g. all microorganisms). List only the indication for which Priority Review status is warranted.

Sponsors filing submissions containing multiple related indications or uses should contact the Submission Management Division /Unit of the appropriate review Directorate to discuss the submission filing.

Sponsors of submissions with multiple un-related indications are required to submit a Priority Request for each indication. Sponsors will be requested to remove non-priority indications from the package and submit as a separate NDS, including complete chemistry and manufacturing information.

[3] Excluding references. Volumes of data to support a request will not be accepted.

d. *A brief description of the illness or condition and the clinical context within which the product will be used to support the request for Priority Review of the submission. Indicate how the product will enhance the clinical management of the disease or condition;*

e. *A clear indication that no other drug is available to Canadians which provides the same therapeutic profile (i.e. demonstrating an unmet medical need);*

or

A rationale for the improvement in benefit/risk profile over therapies currently available on the Canadian market;

CLINICAL TRIAL INFORMATION

f. *Concise information on the design of the studies. This information may be presented in point form or tabular format and should indicate the type of study(ies), design, patient population, number of patients withdrawn due to safety or efficacy concerns etc;*

g. *The status of ongoing studies; should they be interim results (e.g. oncology products based on surrogate markers), provide anticipated completion dates;*

h. *Properly tabulated results demonstrating statistically significant and clinically relevant data in support of the claim;*

ADDITIONAL INFORMATION

i. *In a separate binder, up to twelve key references supporting the data/indication as cross-referenced in the CAP. Remaining references must be available on request within one business day; and*

In addition to the key references supplied, all relevant references should be identified in a list/appendix or alternatively within the body of the request.

j. *Indication of the sponsor's intent and capability to market the product in a timely manner following approval.*

An information request concerning time to market is consistent with the expectations of Health Canada and accurately reflects the intent of the

policy. It is for statistical use only and will have no bearing on the acceptance or rejection of the Priority Review request.

It is acknowledged that occasional delays in marketing, particularly for biological products, may result from sourcing delays, lot release issues and other legitimate circumstances.

5.0 DISCONTINUATION OF PRIORITY REVIEW STATUS

Priority Review status will be re-evaluated upon issuance of a Notice of Noncompliance (NON) or Notice of Deficiency (NOD). Sponsors will receive formal notification of Health Canada's decision to continue or reject Priority Review status based on whether the conditions precedent for Priority Review status still apply.

If there is more than one submission for drugs for the treatment, prevention or diagnosis of the same disease or condition and a Notice of Compliance is issued in relation to one of the submissions, the Priority Review status of the remaining submission(s) will continue until such time as a NON or NOD is issued and Priority Review status is re-evaluated.

Due to the impractical nature of ceasing a review once initiated, and in the interests of enhanced transparency, submission review will continue until such time as a NON/NOD is issued, regardless of the issuance of a NOC and subsequent marketing for a product with the same indication.

6.0 RELATED RESOURCES

For more information, please consult the *Priority Review of Drug Submissions Policy (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/pol/prds_tppd_pol-eng.php).*

7.0 APPENDICES

Appendix - 1 - Clinical Assessment Package

Health Canada Santé Canada

Clinical Assessment Package

Date of Request:

Sponsor:

Contact Information:

SECTION 1: GENERAL INFORMATION (Mandatory)

Proper or Common Name:

Specific Indication Sought:

Regulatory Status of the Drug Worldwide:

SECTION 2 : SERIOUS, LIFE-THREATENING, SEVERELY DEBILITATING (Mandatory)

- Provide a brief description of the disease or condition and the clinical context within which the product will be used to support the request. Indicate briefly how the product will add to the clinical management of the disease or condition.

*****SPONSORS MUST COMPLETE EITHER SECTION 3 OR 4*****

SECTION 3: "effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada"

- Provide a statement as to how the drug satisfies an unmet medical need for treatment, prevention or diagnosis of the disease state outlined in Section 2. *Note: the sponsor must clearly indicate that no other drug is available on the Canadian market which provides the same therapeutic profile.

SECTION 4: " significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada."

- Provide a rationale for the overall improvement in benefit/risk profile over therapies currently available on the Canadian market and clearly state that no other drug is available on the Canadian market which provides the same therapeutic profile.

SECTION 5: CLINICAL EVIDENCE (Mandatory)

This section **must** include the following:

I. Concise information on the design of the studies to indicate type of study (ies), design, patient population, number of patients withdrawn due to safety concerns or lack of efficacy, etc. This information may be presented in point form or in a tabular format;

II. Properly tabulated results demonstrating statistically significant and clinically relevant data in support of the claim; a brief discussion and comments on the results is desirable; and

III. The status of ongoing studies. Should they be interim results (e.g. oncology products based on surrogate markers), provide anticipated completion dates.

SECTION 6: ADDITIONAL INFORMATION (Mandatory)

- In a separate binder, provide up to twelve key references supporting the data/indication as cross-referenced in the Clinical Assessment Package. Any remaining references must be available on request within one business day.

  Reference binder included with request package Yes ___ No ___ (check one)

The following question is for information purposes only.

- Do you intend to, and are you capable of, marketing the above product within 30-60 calendar days? **Note: it is expected that a drug for which priority review is granted will be marketed in a timely fashion (i.e. 60 days) should market authorization be granted.*

Appendix - 2 - Frequently Asked Questions/comments (FAQ)

1. ***The Priority Review policy is inconsistent with the Guidance for Industry Management of Drug Submissions.***

   The *Guidance for Industry Management of Drug Submissions*. (MDSG) is updated regularly to reflect ongoing changes in drug policy. Subsequent updates to the MDSG shall reflect all effective changes with respect to the *Priority Review of Drug Submissions* Policy.

2. ***The decision to continue or discontinue priority review status for a given submission should not be tied in with the issuance of a NON or NOD. If an NOC is issued for a product, then all submissions filed and under review to treat a similar condition should be re-evaluated as to whether the rationale for granting priority review still remains valid.***

   The Priority Review policy, effective May 2002, implemented measures to enhance the transparency of process including limiting re-evaluation of Priority Review status to the issuance of a NON or NOD. Due to the impractical nature of ceasing a review once initiated and subsequent re-familiarization at a later date, submission review will continue until such time as a NON/NOD is issued, regardless of the issuance of a NOC and subsequent marketing for a product with the same indication.

3. ***Please explain why it is not possible to have a submission go through screening while the 30 calendar days review of the request for priority status is on-going?***

   The workload of Health Canada drug evaluators consists of a variety of submission types including, but not limited to, New Drug Submissions (NDS), Supplemental New Drug Submissions (S/NDS), Notifiable Changes (NC), DIN applications, Clinical Trial Applications and Amendments. Furthermore, evaluator expertise is often directed specifically towards clinical, chemistry and manufacturing, or label review thus requiring a coordinated effort with numerous individuals. Upon approval of a Priority request, evaluators require between 30-60 days to complete work on ongoing submissions and re-align workload and resources to accomodate the arrival of the priority submission. This is essential in order to ensure that accelerated review targets of 180 days are met.

4. ***For submissions designated Priority Reviews, screening timeframes should be reduced to 10 days.***

   The target assigned to screening of Priority Review submissions has been reduced from 45 to 25 (calendar) days. The 25-day target provides for the allowance of a 15 day clarifax. Health Canada will make every effort to screen priority submissions in a timely manner.

5. ***Can a submission be filed and go through screening while the Reconsideration of the rejection of a request for Priority Review is being evaluated by Health Canada?***

Yes. Should Priority Review status be granted as a result of a Request for Reconsideration, the target review timeframes will be adjusted accordingly, as of the date of screening acceptance.

6. ***Can a request for Priority Review be filed a second time if a first request for Priority review is denied? The sponsor may be able to generate new data or analyse the data in a different way to address the reason(s) for the rejection of the first request for Priority Review.***

In the event that an initial request for Priority Review status is rejected, sponsors may file a Request for Reconsideration of the decision in accordance with the procedure outlined in the Health Canada's Guidance: *Guidance for Industry Reconsideration of Final Decisions Issued for Human Drug Submissions.* Alternately, sponsors may file a second request, for additional consideration for the same indication, following a period of 60 days from the date of the original request. New information in support of the Priority Review status of the submission must be evident, i.e. results of ongoing clinical trials. Failure to provide new information will result in rejection of the request. Re-analysis of data to address reasons for the rejection of the original request falls within the scope of the Reconsideration procedure and may not be used as the basis for a second request.

In the event that the second Request for Priority Review status is rejected, sponsors may file a Request for Reconsideration of the second decision. As per section 5.1 of Health Canada's Guidance: *Guidance for Industry Reconsideration of Final Decisions Issued for Human Drug Submissions,* the rejection of either a first or second Rejection of Priority Review Request under the *Priority Review Policy* is eligible for Reconsideration. However, sponsors may only file a Request for Reconsideration of the first rejection *or* file a second Request for Priority Review status - they may not file both. Sponsors are not permitted to file a third request for the same indication.

Priority Review requests will be subject to applicable fee regulations.

7. ***Please indicate whether a separate meeting to discuss Priority Review eligibility is required or whether the discussion can be included in a standard pre-submission meeting with TPD/BGTD?***

The discussion can be included in a standard pre-NDS or SNDS meeting with TPD/BGTD staff.

8. ***Why are Priority Review request packages limited to 20 pages in length?***

Packages in excess of 20 pages (excluding references) should not be necessary. Sponsors are advised to provide relevant information, limited to one specific indication, in a concise manner consistent with the template design provided in Appendix 1. Larger packages negatively impact on Health Canada's ability to meet 30 day performance targets for review of the Priority Review request.

9. ***Please provide a definition for substantial clinical evidence. Does this mean a certain number of patients or a certain level of response in a specific therapeutic area? How much better do the outcomes have to be than what is currently on the market?***

In defining "substantial clinical evidence", the Regulator takes into account the disease state treated, its epidemiologic considerations as to whether it would qualify as an orphan drug, i.e. the size of the population to be treated, advances in the treatment of the disease and existing therapies. Narrowly defining substantial evidence limits the ability of Health Canada to respond to new and novel developments in health care and provide timely access to critical breakthrough therapies. Individual requests and supporting evidence (including response, trial design and number of patients) will therefore be examined on a case-by-case basis.

In order to qualify for Priority Review status a sponsor would have to demonstrate that the therapy represents a significant improvement in efficacy or decrease in risk over all other therapies with a similar therapeutic profile available on the Canadian market. For further information, refer to Section 2.4.