Health Canada Santé Canada

Therapeutic Products Directorate

Health Products and Food Branch

Direction des produits thérapeutiques

Direction générale des produits de santé et des aliments




Strategies for Filing Efficient Submissions

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Canada

Objective: to provide suggestions and tips for facilitating the processing, screening and review of submissions filed to the Therapeutic Products Directorate in order to help avoid delays and negative decisions.

General/Communication

- The Cover Letter should clearly indicate the reason for the filing and relevant pre-submission correspondence with Health Canada should be referenced (as well as included in Module 1).
  - i.e. pre-submission meeting minutes, email correspondence regarding filing requirements or drug status, communications with the Marketed Health Products Directorate (MHPD), etc.
  - It should be indicated if the submission is being filed in response to an Advisement Letter; a copy of the letter should also be provided in Module 1.0.3.
  - Address a clarifax response to the individual who issued it and include the clarifax date.

- As per C.08.005.1(4) of the Food and Drug Regulations (FDR), the Submission Certification Form must be signed by a senior executive officer of the manufacturer in Canada.

General/Communication *(continued)*

- Indicate the foreign regulatory status of the product/submission, including meetings, filings, review pathways, approvals and/or anticipated decision dates. If available, also include foreign review documents (as well as the accompanying foreign review attestation).
  - Explain if not filed with the United States Food and Drug Administration or the European Medicines Agency.
  - Notify Health Canada of updates as they become available (i.e. filings, decisions, availability of foreign review documents).

- Use Notes to Reviewer to provide explanations and guide the review team through the submission.

- Ensure to clearly indicate where in the submission information requested at a pre-submission meeting (or through other pre-submission correspondence) has been included or addressed.

General/Communication *(continued)*

- Provide confirmation of receipt of clarifaxes.
- Providing courtesy copies of clarifax responses via email will help to expedite screening or review.
  - The electronic copy of the response is still the official/legal copy.
- Ensure that clarifax responses prepared by global affiliates respect the process outlined in Health Canada's *Guidance for Industry: Management of Drug Submissions*
  - i.e. new data cannot be submitted during the review period.
- It is important to notify the Regulatory Project Manager (RPM) and submit a revised *Drug Submission Application Form* (HC-SC 3011) or Regulatory Enrollment Process (REP) document when the regulatory contact information changes.
  - Clarifaxes issued by the various review streams are sent to the individual identified as Contact B on the HC-SC 3011 form.

General/Communication *(continued)*

- Ensure hyperlinks in eCTD documents are functional.
  - Hyperlinks to relevant supporting data in the submission should be included in the annotated PM to facilitate screening and review.

- Be aware of Health Canada's *Notice - Mandatory use of the Electronic Common Technical Document (eCTD) Format* (April 15, 2019)

  https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/activities/announcements/notice-mandatory-use-electronic-common-technical-document-ectd-format.html
  - **January 1, 2018: Mandatory eCTD was limited to NDS, SNDS, ANDS, SANDS**
  - **June 1, 2019: Expanding to remainder of Division 8 transactions (i.e. EU NDS, EU SNDS, SNDS-C, NC, CAPs, UD-RA, Pre-Submission Meetings, PSUR-C, PBRER-C, DSUR)**
  - **September 1, 2019 (to be confirmed):** Expanding to Division 1 for prescription products (i.e. DINA, PDC) and Master Files
  - For further information, please contact hc.ereview.sc@canada.ca

General/Communication *(continued)*

- Concurrent/parallel submissions should be filed strategically.
  - Consider existing target dates as well as varying screening and review timelines by submission type and review pathway.
  - Planning for at least 1 month between submission target dates is ideal (keeping in mind labelling document version control as well as Plain Language Labelling requirements).
  - Discussing in advance with Health Canada to determine the best approach is encouraged.

- Be proactive about submitting updated labelling/documentation following the approval of a concurrently filed/parallel submission.
  - i.e. incorporating approved updates into the Product Monograph, Package Insert, inner/outer label mock-ups, CPID, etc.

General/Communication *(continued)*

- Sponsors interested in opting in to an aligned review between Health Canada and Health Technology Assessment (HTA) organizations should provide a completed *template authorizing sharing of information* in Module 1.2.6 of the submission
  - Available for NDSs and SNDSs for new indications where the sponsor intends to seek a coverage recommendation from the HTAs on a pre-Notice of Compliance (NOC) basis
  - Consent can be provided at the time of filing, during submission screening or review, or up to 30 days after a NOC or NOC/c has been issued
  - Notify the RPM if consent is being provided after the submission has been filed and screened in.
  - In order to help maximize the benefits of alignment between HC and the HTA reviews, sponsors are encouraged to opt in and consent to information sharing as early as possible in the review process
  - Note: As of June 1, 2019, the Canadian Agency For Drugs And Technologies In Health (CADTH) is no longer accepting new biosimilar submissions and has stopped work on any biosimilar reviews that would have been completed after June 1, 2019. At this time, Institut national d'excellence en santé et en services sociaux (INESSS) has indicated that they will continue to review biosimilars.

Administrative Submissions

- For Administrative Submissions, ensure to complete boxes 54-69 on the *Drug Submission Application Form* (HC-SC 3011), including identifying the medicinal ingredient, strength, dosage form, etc.
  - If incomplete, or referencing the parent submission, the submission will be placed on Process Hold until a complete form is provided.
  - Providing a Note to Reviewer will facilitate administrative processing, i.e. a justification for any differences from the Licensor.

Refer to Health Canada's *Guidance Document Administrative Processing of Submissions and Applications: Human or Disinfectant Drugs*

https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-administrative-processing-human-disinfectant-drugs.html

Quality – General

- Include a detailed scientific justification where deviating from guidance documents or common scientific practices.
  - For example, explain why stability batches tested/manufactured are the “worst case scenario” or how the data demonstrates the product was stressed.

- For Quality by Design (QbD), clearly identify in the Quality Overall Summary (QOS) Introduction what is being claimed/supported based on information and data from the QbD approach included in the submission
  - i.e., Design space(s), Proven Acceptable Range(s) (PARs), Omission of test(s) from specifications, Implementation of skip testing, Real Time Release Testing, Process robustness, Other

- Process validation protocol should be included in drug product section 3.2.P.3.5.

Quality – General *(continued)*

- Information on packaging materials should be included in section 3.2.P.7, if it pertains to composition and specifications and in section 3.2.P.2.4 if it pertains to qualification of packaging materials.

- Information on development of the dissolution method should be included in section 3.2.P.5.3, and referenced, wherever relevant, within section 3.2.P.2. Also, when applicable, all raw dissolution data used to generate comparative dissolution profiles should be included in the submission along with corresponding f2 values.

- As of July 22, 2016, a Risk Assessment Summary for Elemental Impurities must be provided with NDS filings.

Quality – Master Files (MFs)

- Refer to Health Canada's *Guidance Document: Master Files (MFs) - Procedures and Administrative Requirements* (Effective February 13, 2019)

  https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-master-files-procedures-administrative-requirements.html

- Any discrepancies between Letters of Access (LoAs) provided in the submission and those provided to the MF Administration Unit may result in delays in the assessment of the submission.
  - i.e. dates on above-mentioned LoAs must be identical
  - The fee for processing a LoA by the MF Administration Unit is applicable each time a LoA is filed (including revisions to LoAs already registered with Health Canada)

Quality – GMP

- Ensure a valid Canadian GMP compliance rating has been issued by the Regulatory Operations and Enforcement Branch (ROEB) for all required sites prior to filing.

Notice: Submission Filing Requirements - Good Manufacturing Practices (GMP)/Drug Establishment Licences (DEL)

http://hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/notice_gmp_el_avis_bpf_le-eng.php

OR

As of February 10, 2017, TPD will also accept submissions where a complete application to amend the Drug Establishment License (DEL) pursuant to C.01A.006 of the FDR for new buildings and activities not currently listed on the drug submission sponsor's DEL has been filed with the Minister at least 90 days prior to the time of filing a drug submission.

  - The *Acknowledgement of Application Acceptance* issued by ROEB must be provided in the submission

Quality – GMP *(continued)*

- Ensure the activities performed by each site are clearly identified
  - For consistency, use the terminology from table in the GMP/DEL Notice when listing the activities that require documentation of a valid DEL and/or DEL application
  - i.e. indicate whether site performs “drug substance release testing”, as opposed to just stating “testing”

- For sterile products, the activities of sterilization of packaging components and/or lyophilization of sterile drug substance (as applicable) should be identified.

Quality – Batch Analysis

Certificates of Analysis (CoAs) or a detailed tabulated summary outlining results of batch analyses should be provided for the following:

- Drug Substance (DS)
  - All batches used in pivotal clinical studies and/or comparative bioequivalence studies (not including food effect), with clear and specific reference to study numbers
  - At least two batches from each proposed commercial manufacturing site
- Drug Product (DP)
  - All batches used in pivotal clinical studies and/or comparative bioequivalence studies (not including food effect), with clear and specific reference to study numbers
  - A minimum of three batches for:
    - Each strength
    - Each dosage form
    - Each proposed manufacturing site of the drug product

Quality – Batch Analysis *(continued)*

- It is extremely helpful to include overall summary tables clearly identifying and linking drug substance and drug product batches to their use in clinical, preclinical, comparative in-vitro and stability studies.
  - Clearly identify and link the API drug substance batches used to manufacture drug product batches used in pivotal clinical studies, with reference to the manufacturing site(s) and study numbers.
  - Where different batch numbers are assigned to drug product intermediates or where a manufacturing batch is assigned a different number when used in a clinical study, the tabulated summary should include and link together these data.
  - Clearly indicate the location of CoAs in the submission, if provided.

Quality – Batch Analysis *(continued)*

- RPMD has developed the following *Summary of Batch Analyses for Clinical Studies* table to facilitate screening and review. This is the preferred format to represent this information.

Appendix 1: Summary of Batch Analyses for Clinical Studies for [Brand Name] ((S)(A)NDS, Control No. XXXXXX)

Reference: Guidance Document: Quality (Chemistry and Manufacturing) Guidance: New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs) (Effective date: 2018/01/30)

Study Number	Is the study considered pivotal? *(Yes/No)*	Drug Product Description *(Strength/dosage form/formulation)*	Drug Product			Drug Substance *(repeat if necessary)*		
			Lot Number	Manufacturing site	Location of Tabulated Summary or CoA within submission	Lot Number	Manufacturing site	Location of CoA within submission

Quality – Stability

- Summaries of stability data could be better presented in many submissions by including groupings to demonstrate what the data is showing rather than just summarizing results for each batch.
  - For example, if all batches show similar impurity trends, group together and list trends and maximum impurity levels.
  - Minimum and maximum assay values across the whole range of batches are illustrative if there are no trends.
  - Highlight different trends across strengths or packaging materials.
- If any stability requirements have not been met, additional supporting data and justification should be provided.
- Effective October 30, 2019, stability data is required for 3 batches (as opposed to 2) for existing drug products (i.e. SNDS)

Quality - Executed Production Documents

- Copies of the executed production documents provided (in English or French) for the batches used in the pivotal clinical and/or comparative bioavailability studies (not including food effect studies) must be provided.
- Documents for a minimum of 2 batches including 1 batch for each proposed strength should be provided.
- Any notations made by operators on the executed production documents should be clearly legible.
- When a batch of a strength which has not been used for a pivotal study is submitted, the executed document for the primary stability batch should be submitted and clearly identified as such.

Quality - Executed Production Documents
(continued)

- When there are multiple pivotal batches (i.e. 2 or more), executed production documentation submitted can be limited to 1 pivotal batch per strength as long as executed documents are provided for a minimum of 2 batches that cover the range of strengths.

- When 2 or more pivotal batches have been manufactured and a suitable matrixing/bracketing approach is proposed, a minimum of 2 pivotal executed batches per product should be provided and executed documents from a minimum of the highest and lowest strength per manufacturing site should be included.

Quality - Master Production Documents (MPDs)

- Copies of master production documents (in English or French) provided for each proposed strength, commercial batch size, and manufacturing site?
  - Note: batch records should include formulation, manufacturing and packaging
  - Where there is significant redundancy (i.e., common blend compressed to different tablet sizes), reduced documentation can be provided (i.e., complete MPD for one strength and compression steps for remaining strengths), as long as it is ensured that each variation in manufacturing is fully described.

Toxicology

- Be aware of Health Canada's *Notice: ICH M7(R1): Genotoxic Impurities - Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk* (April 26, 2018)

  https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/multidisciplinary/m7r1-notice.html

Consider whether you have impurities (for either DS or DP) that fall within the scope of ICH M7, and if yes, indicate whether you have complied with, and provided all of the requirements outlined in, the above-mentioned Notice.

Clinical – Safety & Efficacy

- Ensure all study reports (clinical and non-clinical) are provided in a .pdf format, with copy-paste functionality.

- Avoid "data dumping" – ensure that all information provided supports the purpose (or a component) of the submission.
  - Relevance of information provided can be explained in a Note to Reviewer and/or Clinical Overview and Summary documents.

- It is helpful for initial submission scoping and assignment to include a summary table listing all study numbers, titles and location within the submission (clinical and non-clinical).
  - Currently, when these sorts of tables are provided, several of the smaller studies are often omitted (biopharmaceutics, PK, etc.).

Clinical – Safety & Efficacy *(continued)*

- Clearly identify which studies are considered pivotal and indicate whether the batches from these studies were developed according to the proposed method of manufacture.
  - Be explicit when explaining how every indication, strength and dosage form is being supported by the data package (i.e., if bridging, waivers or extrapolation are being relied upon).
- Ensure to include appendices for clinical trial data.
- If pivotal studies are not conducted in proposed patient population and with proposed dosage form and strengths, ensure a biostudy, biowaiver or scientific rationale been included in the submission to address this.

Clinical – Safety & Efficacy *(continued)*

- For NDSs, if a QT prolongation study has not been provided in the submission, ensure a rationale has been provided.

- Ensure to provide references that were used to assemble the data to substantiate the proposed changes (i.e. references cited in the Clinical Overview, etc.), that have not already been provided in a previously approved submission.
  - Ensure to use hyperlinking capability.
  - Providing a URL to access a reference online is not sufficient; a website address is not reliable as it may change or the document may get removed or updated over time.

Clinical – Biopharmaceutics

- A completed Comprehensive Summary: Bioequivalence (CS:BE) in Word format (Module 1.4.2), as well as electronic copies of the PK data files (.inf and .dat) in ASCII format (Module 1.6.1) are required for all for pivotal bioequivalence (BE) and bioavailability (BA) studies.
  - If not provided at filing, PK data files and CS:BE are requested by **Screening Deficiency Notice (SDN)**.
  - In order to expedite responding to the SDN the Sponsor may respond with PK data files and then **written commitment** to provide the completed CS:BE document **within two weeks of the submission being accepted in to review**.

- To avoid an automatic screening clarifax, the Sponsor can indicate at filing, for all pivotal BE/BA studies, whether they comply with Health Canada's *Notice: Clarification of bioanalytical method validation procedures* (October 8, 2015).

  http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/announce-annonce/notice_avis_mthd_validation-eng.php
  - Confirmation of the above, or location of this confirmation within the submission, should be provided in a Note to Reviewer; if not in compliance with the Notice, a justification should be provided in lieu of.

Clinical – Biopharmaceutics *(continued)*

Pivotal bioequivalence/bioavailability studies:

1. Comparing to a Canadian Reference Product to support a generic submission
   - considered pivotal

2. Bridging between formulations
   - considered pivotal when comparing the formulation used in the pivotal trial(s) (usually Phase III) and the formulation intended for market. Where a comparative bioavailability study is included to bridge to the formulation used in an earlier development study (e.g. phase I or II), consultation with clinical about the pertinence of the trial (to determine whether it will be considered pivotal) may be required.

Clinical – Biopharmaceutics *(continued)*

Pivotal bioequivalence/bioavailability studies *(continued)*:

3. Food effect studies
   - Criteria for determining a food effect study to be pivotal at screening:
     (a) All NAS submissions for products that are orally administered
     (b) New combination products
     (c) New formulations, especially modified-release
     (d) The study results in specific numbers or wording describing a food effect anywhere in the Product Monograph, for example, an impact on PK parameters (AUC, Cmax), absorption is affected by food, etc.

4. Required by the Post NOC Changes guidance
   - considered pivotal (i.e. to support a change in manufacturing site for a modified release product).

Clinical – Biopharmaceutics *(continued)*

Biopharmaceutics Classification System (BCS) Based Biowaiver:

If a BCS based biowaiver has been provided, the Sponsor should make reference (in Module 1.6.1) to Health Canada's *Guidance Document: Biopharmaceutics Classification System Based Biowaiver* (BCS Guidance) and the eligibility criteria described within.

- If no reference made to the BCS Guidance, a rationale should be provided.

Labelling

- Ensure to use the current Product Monograph (PM) template
  http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/pm-guid-ld-mp-eng.php
  - New 2016 PM format for NDS came in to effect June 9, 2017.
  - As of June 2019, all subsequent filings are encouraged to adopt the new format

- Take note of the new Recent Major Label Changes component of the 2016 PM format
  - List the section headings above the table of contents in the product monograph where any major label changes related to safety and efficacy have been made within the past 24 months, under the following sections:
    - *Serious Warnings and Precautions Box;*
    - *Indications;*
    - *Contraindications;*
    - *Dosage and Administration;*
    - *Warnings and Precautions;*
  - All label changes (not only those deemed “major”, as indicated above) made in the last 24 months should be indicated within the body of the product monograph where they occur, by a vertical line on the left edge of the page.

Labelling *(continued)*

- Ensure that proposed PMs contain only information relevant to the Canadian dossier (i.e., no dosage forms or indications that are not part of the submission).

- Since Health Canada revised its PM finalization process back in December 2014 (to remove the requirement for the Pristine PM to be submitted prior to decision issuance), every clean/non-annotated PM provided (at filing or in response to a clarifax) *could* be deemed the approved PM for the submission.
  - Avoid watermarks or “draft” markings anywhere in the clean PM (including on the cover page and within the headers/footers).

- Use a Note to Reviewer (Module 1.3.2) to provide any necessary explanations to accompany the completed *Mock-Up Packages and Labels Certification Form for Prescription Products.*

Labelling *(continued)*

- It is helpful to keep a “running annotated PM”, as the submission could be worked on by multiple reviewers/review streams.
  - Ensure to keep existing annotations and comments/rationales when providing a new/updated version.
- During PM negotiations, ensure that revisions made to Parts I and II of the PM are also reflected in Part III, as applicable.
- Be proactive about updating the contents of the Package Insert (PI) throughout review.
  - Once PM negotiations commence, revisions made to PM should also be reflected in the PI, as applicable.
  - An updated PI can also be provided in response to a clarifax from another review stream.

Post-NOC Changes

- It is helpful if the reason for the submission is well-described in the cover letter.
- Substantial evidence is required to support labelling changes/updates. Providing only a Company Core Data Sheet to support revisions to the PM is not considered to be sufficient.
  - Also provide the relevant documentation and/or data to support the proposed changes to the PM.
- Ensure there are no implied claims (efficacy or safety) being filed within Notifiable Change submissions.
- Any Level III changes included within a submission should be clearly marked as such, and annotated in the affected documents (i.e. Product Monograph/Package Insert and/or CPID).
  - Supporting data for Level III changes should not be included in the submission

Post-NOC Changes *(continued)*

- Use the *Summary of Post-NOC Quality Changes* table to provide an explicit indication of how the proposed changes link to the Guidance (i.e. type of change, condition fulfillment, supporting data, etc.)

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Example: Summary of Post-Notice of Compliance Quality Changes

Reference: Post-Notice of Compliance (NOC) Changes: Quality Document (Effective date: 2016/10/14)

Post-NOC quality change according to guidance document (Please indicate the number for each change)	Description of change	Conditions to be fulfilled for this change and reporting category based on Health Canada guidance document	Explanation of how each condition is, or is not, fulfilled	Based on fulfilment of the conditions, what is the corresponding reporting category? (i.e. Supplement or Annual Notification)	Supporting data required	Location of required supporting data within submission or reason for omission
33. Replacement or addition of a primary container closure system for: **a)** sterile drug products	Change in the primary container closure system from blisters to bottles	None – This change is for a sterile product	N/A – No conditions to be met	Supplement	**1.** (1.3) Product Monograph [e.g., Where applicable, Title Page, Storage and Stability (Part I), Dosage Forms, Composition and Packaging (Part I)] and Inner and Outer Labels.	Module 1.3.1, Module 1.3.2
					2. (P.2) Data demonstrating the suitability of the container closure system (e.g., extractable/leachable testing, permeation testing, light transmission). For changes to functional packaging, data to demonstrate that the functioning of the new packaging is equivalent to that previously approved.	Module 2.2, Module 3.2.P.8.1, Module 3.2.P.8.3
					3. (P.3.5) For sterile products, process validation and/or evaluation studies. Evidence of process validation for sterilization processes for the container/closure.	Module 3.2.P.3.5
					4. (P.7) Information on the proposed container closure system (e.g., description, materials of construction of primary packaging components, specifications, including results of transportation studies, if appropriate).	Module 3.2.P.2, Module 3.2.P.7
					5. (P.8.1) Stability Summary and Conclusions, results of a minimum two (2) pilot scale, of three (3) months of accelerated (or intermediate as appropriate) and three (3) months of long term testing and, where applicable, results of photostability studies; (bracketing and matrixing for multiple strengths and packaging components could be applied, if scientifically justified).	Module 3.2.P.8.1
					6. (P.8.2) Updated post-approval stability protocol and stability commitment to place the first commercial scale batch of each strength of the proposed product into the long term stability programme (bracketing and matrixing for multiple strengths and packaging components could be applied, if scientifically justified).	Module 3.2.P.8.2

Post-NOC Changes – Generics

- Generic Sponsors should monitor the Product Monograph Brand Safety Updates table to ensure timely labelling updates.
  http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/pm_saf_mp_innoc/lab_safety_rep_rap_eval_etiq-eng.php

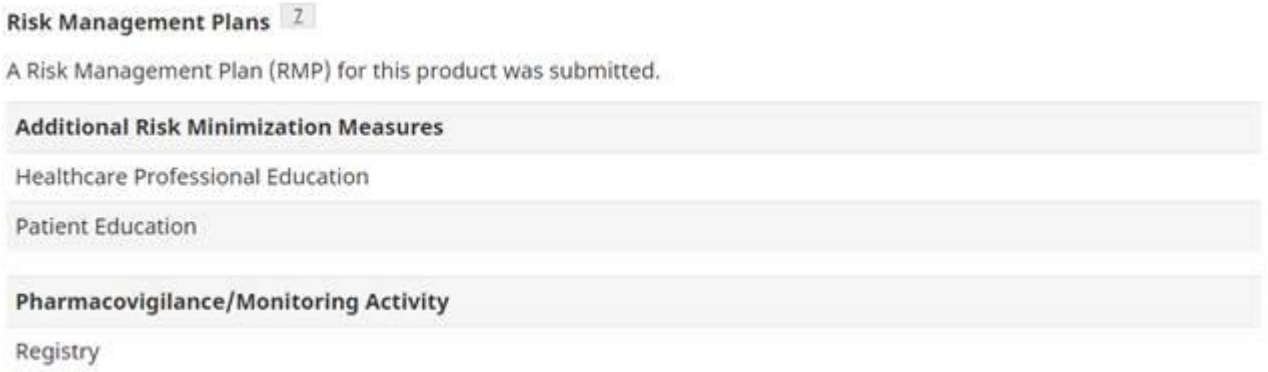
- Fully complete all sections of the *Label Safety Assessment Update – Sponsor Attestation* (i.e. the document comparison summary tables).
  http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/pm_saf_mp_innoc/lab_safety_att_eval_etiq-eng.php

- Ensure to properly annotate PMs (against the Canadian Reference Product (CRP) and previously approved generic PM):
  - Different/new information in the PM should be highlighted
  - Information removed should be marked with strikeout

- Check the Drug Product Database (DPD) immediately prior filing to ensure you are comparing against the most recent innovator PM
  http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp

Pharmacovigilance

- Sponsors filing submissions for generic or administrative (cross-licensed) products are encouraged to verify the DPD to confirm whether the CRP or Licensor has additional Risk Management Plan (RMP) measures in place that could apply for them as well



Risk Management Plans 2

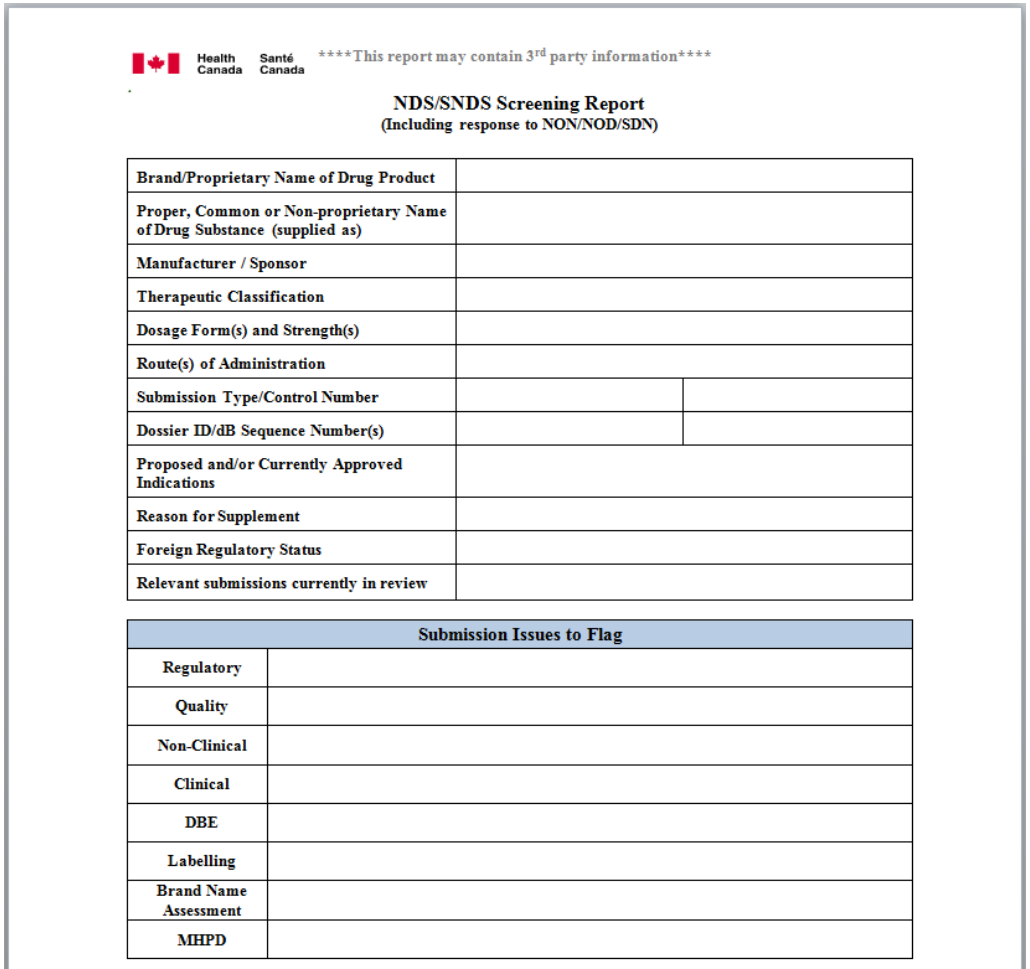
A Risk Management Plan (RMP) for this product was submitted.

Additional Risk Minimization Measures
Healthcare Professional Education
Patient Education
Pharmacovigilance/Monitoring Activity
Registry

- Sponsors can also reach out to MHPD (mpmdb_rpm@canada.ca) prior to filing for information on RMP requirements

Screening Report

- A copy of the *latest* version of the Screening Report has been provided to assist with efficient submission preparation.



Health Canada Santé Canada ****This report may contain 3rd party information****

NDS/SNDS Screening Report
(Including response to NON/NOD/SDN)

Brand/Proprietary Name of Drug Product		
Proper, Common or Non-proprietary Name of Drug Substance (supplied as)		
Manufacturer / Sponsor		
Therapeutic Classification		
Dosage Form(s) and Strength(s)		
Route(s) of Administration		
Submission Type/Control Number		
Dossier ID/dB Sequence Number(s)		
Proposed and/or Currently Approved Indications		
Reason for Supplement		
Foreign Regulatory Status		
Relevant submissions currently in review		

Submission Issues to Flag	
Regulatory	
Quality	
Non-Clinical	
Clinical	
DBE	
Labelling	
Brand Name Assessment	
MHPD	

Questions?

Thank you!