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




Submissions Relying on Third Party Data (from a Regulatory Perspective)

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Objective: to provide information, clarity and recommendations with respect to submissions filed to the Therapeutic Products Directorate that rely on third-party data (a.k.a. SRTDs).

Guidance Document: Drug Submissions Relying on Third-Party Data (Literature and Market Experience)

https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/drug-submissions-relying-third-party-data-literature-market-experience.html

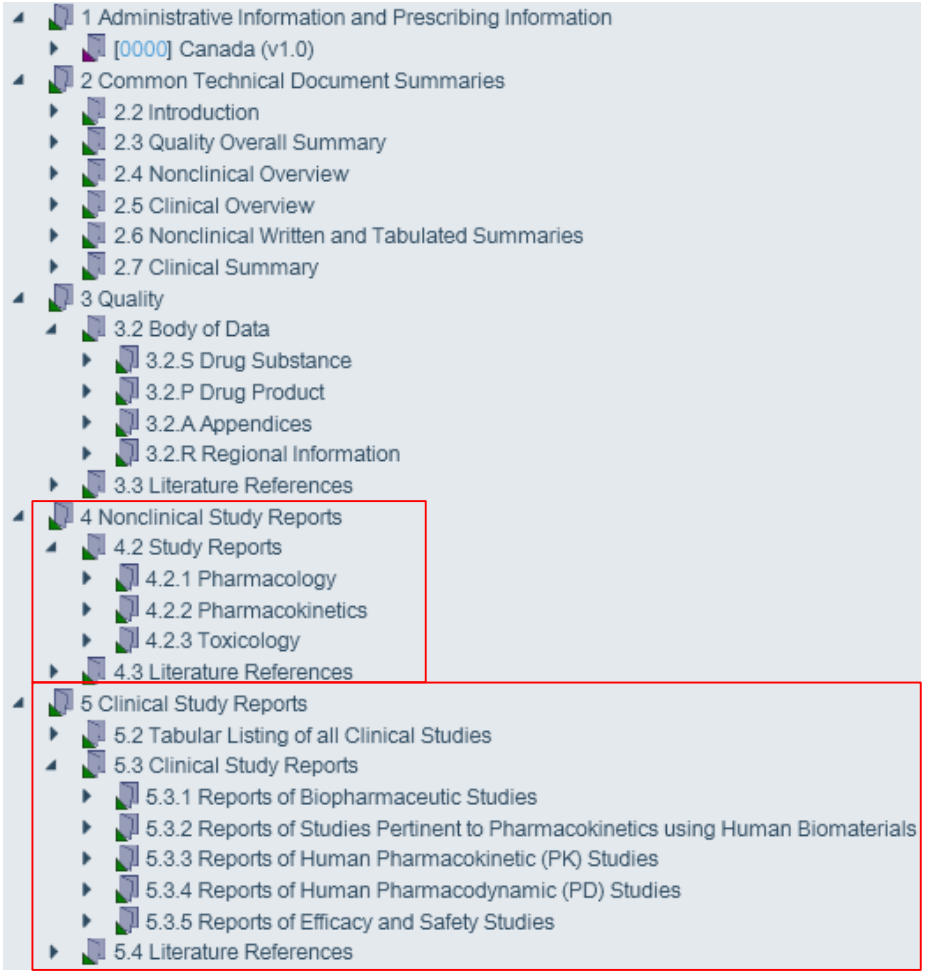
What is an SRTD?

- SRTDs are defined as New Drug Submissions (NDSs) and Supplements to New Drug Submissions (SNDSs) that substantially rely on literature and market experience.
  - i.e. pivotal support for indication is solely based on publically available published data, **in lieu of** clinical study reports of safety and efficacy

- Although SRTDs may differ in the source of information used to support safety and effectiveness, it is of primary importance that it meets the same standards for approval as a conventional submission, i.e., substantial evidence of safety and efficacy, as stipulated in C.08.002(2)(g) and (h) for NDSs and C.08.003(3) for SNDSs.

What is an SRTD? *(continued)*

- SRTDs rely on published literature and/or market experience for Module 5 (clinical) and/or Module 4 (non-clinical).
- However, a full Module 3 (Quality/Chemistry package) is required.
- Only literature provided in the submission will be considered; reviewers will not conduct their own literature search.



Examples of "Third-Party Data"

- Articles in peer-reviewed journals
- Systematic review and/or Meta-analysis of published studies
- Study reports of trials not conducted or sponsored by the applicant
- Current guidelines from professional bodies
- Sections of published books
- Market experience
- Evidence of extent of population exposure and/or information regarding safety profile from domestic and/or foreign markets
  - Relevant domestic (Canadian) product, if available (IMS data, sale data, years marketed, patient populations, conditions of use)
  - Relevant foreign market use
  - Warning letters, safety review, post-market intervention, foreign labelling updates
- ADR info from domestic and foreign authorities
  - Canada Vigilance Adverse Reactions
  - PSURs and PBRERs

Pre-Submission Meetings

- Sponsors intending to file SRTDs are strongly encouraged to request a pre-submission meeting.

- The following information should be included in the pre-submission meeting package and presentation:
  - why clinical studies were not conducted and why any other elements of a conventional submission will not be included;
  - the product being bridged to and product's market experience;
  - an outline of the proposed systematic review methodology (i.e., research question and whether the Cochrane methods or other validated methods are used);
  - the information considered to be pivotal in supporting the proposed claims;
  - what consultation was done with authors of pivotal literature to request additional trial design details and raw data, whenever feasible;
  - The approach to bridging the proposed product formulation to the formulation used in the published studies.

What is the submission class and associated fee* for an SRTD?

New Active Substance (NAS) - $355,579

An SRTD submitted for a drug that contains a medicinal ingredient not previously approved in a drug for sale in Canada, and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph.

- NAS determinations are made by the Office of Patented Medicines and Liaison (OPML)

Clinical or non-clinical data and chemistry and manufacturing data (Clin/C&M) - $180,101

An SRTD submitted for a drug that contains a medicinal ingredient already approved in a drug for sale in Canada.

- As the published data is being provided **in lieu of** clinical study reports of safety and efficacy, the clinical fee still applies (as opposed to the published data fee)

* for submissions filed on or after April 1, 2019

What is unique at screening for an SRTD?

In addition to meeting the C&M and labelling requirements, the following requirements should be addressed in the submission:

1. Has a rationale supporting SRTD filing to explain why a conventional drug submission was not assembled provided in the submission?

2. Has evidence, based on comparative pharmaceutical and/or comparative bioavailability data, to establish that the product used in studies reported in the literature (i.e. reference product) is representative of the proposed commercial product, been provided?

Note: Clinical studies reported in the literature and included in the submission will not be considered sufficient to establish the clinical safety and efficacy required by the Regulations unless it is demonstrated that the proposed commercial product will have the same in vivo performance as the reference product used in the studies reported in the literature.

What is unique at screening for an SRTD?
(continued)

3. Are the proposed indications, route of administration, patient population, and strength on the proposed PM the same as those for the reference product presented in the literature?

- Consider the relevance of literature being provided to the proposed indication, patient population, dosage form(s), dosing range, etc.

4. Has evidence of extensive current foreign market experience with the same medicinal ingredient (for a minimum of 10 years under the same conditions of use), or evidence that the same medicinal ingredient is currently or has previously been marketed in Canada (under the same conditions of use) been provided in the submission?

What is unique at screening for an SRTD?
(continued)

5. Has a systematic review using the methodology outlined in the Cochrane Handbook for Systematic Reviews of Interventions and presented in the form as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement been provided in the submission? (Refer to the Guidance Document: Drug Submissions Relying on Third-Party Data (Literature and Market Experience) for additional information on systematic reviews.

6. Have additional supporting information been provided (e.g., foreign reviews)?

Tips to Facilitate SRTD Screening and Review

- 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.
  - Categorize findings by indications, patient populations, treatment regimen and formulation used.
  - Discuss the literature search inclusion and exclusion criteria.
- Clearly identify which of the information provided is considered pivotal and which is supportive.
  - Be explicit when explaining the extent to which the data supporting the submission mirrors the proposed indication for use in terms of dosing, population, intervention, and outcome measures.

Who reviews SRTDs?

- The lead review group for SRTDs is either medical (BMS) or clinical (BMORS/BCANS/BGIVD).

- The appropriate lead is determined on a case-by-case basis, taking in to account the following considerations:
  - Has the benefit/risk already been established for the active ingredient in a similar indication, i.e. similar target organ or body system or disease state to the one for which the active ingredient's benefit/risk has already been established.
  - Does the indication include pediatric patients and, if so, is this the first time this active ingredient is being reviewed for a similar indication in pediatric patients in Canada?

Questions regarding evidence requirements:

Bureau of Medical Sciences (BMS):
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Bureau of Metabolism, Oncology and Reproductive Sciences (BMORS): HC.bmors.enquiries.SC@canada.ca

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Questions?

Thank you!