



# Guidance Document:

## Management of Drug Submissions and Applications

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Health Canada is responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

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## Document change log

Version	Guidance Document: Management of Drug Submissions and Applications	Replaces	Guidance Document: Management of Drug Submissions and Applications
Date	November 26, 2020 (posted May 21, 2021)	Date	November 8, 2019

Date	Change	Location (Section, paragraph)	Nature of and/or Reason for Change
July 7, 2021	Change to include joint reviews with other regulatory authorities into Pause-the-Clock mechanism	Section 11.1.3	Policy Change
November 26, 2020	Changes were made to reflect the new names of the bureaus in the Marketed Health Products Directorate (MHPD)	Section 2 & Appendix 2	Administrative
	Change to reflect the new Medical Device Directorate (MDD)	Sections 1.1 & 5.1 Appendix 2	Administrative
	Correct the email address for questions about the classification of products at the device-drug interface to hc.drug.device.classification-droque.instrument.sc@canada.ca	Sections 5 & 5.2	Administrative

Date	Change	Location (Section, paragraph)	Nature of and/or Reason for Change
November 8, 2019	<b>Deleted:</b>	Appendix 3	As of April 1, 2020, new fees along with

	<ul style="list-style-type: none"> <li>• Notifiable Changes (NCs) Safety (90 days) and Safety (120 day).</li> </ul> <p><b>New fee categories for:</b></p> <ul style="list-style-type: none"> <li>• Labelling Only (Generic) and Safety Updates to Labelling (each with a 120 day performance standard), and</li> <li>• Labelling Only (Disinfectants) with a 90 day performance standard.</li> </ul> <p><b>Eliminate fee categories for:</b></p> <ul style="list-style-type: none"> <li>• Published Data and Rx to OTC Switch.</li> </ul> <p><b>Revised performance standard for:</b></p> <ul style="list-style-type: none"> <li>• Labelling Only for Div.1 (180 days to 120 days) and for Div.8 (60 days to 120 days),</li> <li>• DINA, DINF, DIND, Labelling Standard (45 days to 60 days), and</li> <li>• Addition of screening 1, 2 and review 2 timelines for existing and new fee categories where none previously existed.</li> </ul> <p><b><u>Added:</u></b></p> <ul style="list-style-type: none"> <li>• Information regarding the Pause-the-Clock mechanism</li> </ul>	Section 11.1.3	a revised fee policy will come into force requiring significant changes to the guidance document.
July 25, 2019	<ul style="list-style-type: none"> <li>• Information was reorganized and reformatted to reflect current procedures</li> </ul>	Whole document	Administrative

(with no change to existing practices).		
<p><b>Added:</b></p> <ul style="list-style-type: none"> <li>• A section on the Classification of a Therapeutic Product,</li> <li>• An Appendix indicating the individual responsible for signing Decision Documents, and</li> <li>• An Appendix listing relevant guidance and policy documents.</li> </ul>	Section 5, Appendices 6 & 7	Addition of new information to assist sponsors in the preparation and filing of drug submissions and applications
<p><b>Deleted:</b></p> <ul style="list-style-type: none"> <li>• Update Notices,</li> <li>• Final Data,</li> <li>• Safety Information,</li> <li>• Advance Notice Letters, and</li> <li>• Issuance of Acknowledgement Letters upon receipt of information by OSIP</li> </ul>	<p>Sections: 5.5.1, 5.5.2, 5.4</p> <p>Sections: 9.1, 9.1.1</p>	Deletion of sections from the previous version because no longer used or applicable
<p><b>Other Changes:</b></p> <ul style="list-style-type: none"> <li>• Amended the existing 15-day standard timeline for response to a Clarification Request during Scientific Review based on the type and performance standards of the submission/application.</li> </ul>	Section 12.1.2	Administrative
Reorganization of the Target Performance Standards Table (Appendix 3) to delete replication of the classes/types of submissions/applications filed.	Appendix 3	

December 19, 2013 (posted December 19, 2013)			Changes were made to the document to reflect an amendment to the Food and Drug Regulations that replaced Schedule F with the Prescription Drug List.
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## Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

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 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.

Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, 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.

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# 1. Introduction

## 1.1 Purpose/overview

The Guidance Document: Management of Drug Submissions and Applications (MDSG) gives sponsors and Health Canada staff from the Therapeutic Products Directorate (TPD), the Biologic and Radiopharmaceutical Drugs Directorate (BRDD), the Medical Device Directorate (MDD), the Non-Prescription Drug Evaluation Division (NDED) of the Natural and Non-prescription Health Products Directorate (NNHPD), the Office of Submission and Intellectual Property (OSIP) within the Resource Management and Operations Directorate (RMOD), and the Marketed Health Products Directorate (MHPD) operational direction and guidance when managing information submitted in accordance with the Food and Drugs Act and its Regulations.

## 2. Scope and application

This guidance document applies to all drug submission/application types<sup>1</sup> including:

- Clinical Trial Application (CTA), Clinical Trial Application - Amendment (CTA-A)<sup>2</sup>
- New Drug Submission (NDS)
- Supplement to a New Drug Submission (SNDS)
- Abbreviated New Drug Submission (ANDS)
- Supplement to an Abbreviated New Drug Submission (SANDS)
- Extraordinary Use New Drug Submission (EUNDS)
- Supplement to an Extraordinary Use New Drug Submission (EUSNDS)
- Abbreviated Extraordinary Use New Drug Submission (EUANDS)
- Supplement to an Abbreviated Extraordinary Use New Drug Submission (EUSANDS)
- Supplement to a New Drug Submission - Confirmatory (SNDS-c)
- Supplement to an Abbreviated New Drug Submission - Confirmatory (SANDS-c)
- New Drug Submission for Disinfectant products (NDS-D)
- Supplement to a New Drug Submission for Disinfectant products (SNDS-D)
- Application for a Drug Identification Number for a pharmaceutical product, including non-prescription products attesting to a Labelling Standard (DINA)
- Application for a Drug Identification Number for a Category IV Monograph Product (DINF)
- Application for a Drug Identification Number for a biological product (DINB)
- Application for a Drug Identification Number for a disinfectant product (DIND)
- Notifiable Change (NC) (for human biologic or radiopharmaceutical drug quality changes)
- Post-authorization Division 1 Change for a pharmaceutical product (PDC)<sup>3</sup>
- Post-authorization Division 1 Change for a biologic drug product (PDC-B)<sup>4</sup>
- Development Safety Update Reports (DSUR)<sup>5</sup>

Post-Market pharmacovigilance monitoring documents

The following documents are not within the scope of this guidance; however, they are part of the post market pharmacovigilance monitoring which is related to a submission. These documents should be sent to the Office of Submissions and Intellectual Property (OSIP) for

processing. Refer to Appendix 2 for contact information. OSIP will notify the appropriate review bureau, or the MHPD of the document(s) submitted:

- Periodic Safety Update Report(PSUR-PV)
- Periodic Safety Update Report - Confirmatory (PSUR-C)
- Risk Management Plans (RMP-PV)
- Periodic Benefit-Risk Evaluation Report (PBRER-PV)
- Periodic Benefit-Risk Evaluation Report - Confirmatory (PBRER-C), and
- Other data Post-Market Vigilance (various types of Undefined Data Post-market Vigilance (UD-PV)

Content-related questions specific to post market pharmacovigilance monitoring should be directed to the Marketed Pharmaceuticals Bureau or the Biologicals, Radiopharmaceutical and Self-Care Products Bureau in the MHPD. Refer to Appendix 2 for contact information.

### 3. Policy objectives

The objective of this document is to ensure consistent application of the handling of submission/application information and procedures related to drug review by providing operational direction and guidance to sponsors and Health Canada staff on:

- the processes and procedures to be followed in the management of a drug submission/application or pharmacovigilance monitoring documents
- the tools available to share information (e.g., pre-submission meetings)
- related guidance documents, policies and other relevant information (e.g., related guidance and policies), and
- the performance standards that ensure predictability of the processes.

### 4. Background

The first major revision to this guidance was in 1993. In 2013, changes were made to reflect an amendment to the Food and Drug Regulations that replaced Schedule F with the Prescription Drug List. In order to maintain consistency and enhance transparency, this guidance was updated in July 2019 to reflect the most current information, processes and procedures to be used by sponsors and Health Canada staff in the management of a drug submission/application or pharmacovigilance monitoring documents. The November 2019 version reflected new fee categories and performance standards due to the coming into force of the Fees in Respect of Drugs and Medical Devices Order on April 1, 2020.

### 5. Classification of a therapeutic product

To proceed with the filing of information for a proposed product, sponsors should know how their product is classified (e.g., as a drug, a biologic, a medical device or a combination product).

Classification of a therapeutic product determines whether a product is regulated as a device or a drug. In most cases, the distinction between drugs and devices is clearly identifiable and these products can be easily classified according to their definitions.

As new technologies and products emerge, it can be increasingly difficult to identify the appropriate framework under which these products should be regulated. When the classification of a product is not clear, members of the Therapeutic Products Classification Committee (TPCC) may be consulted. The committee makes recommendations on the classification of a product as either a drug (pharmaceutical, biological, or natural health product), medical device, or combination product. If a product does not readily meet one of the definitions provided in the Food and Drugs Act, other regulatory areas of Health Canada are asked to participate in the committee's discussion.

Refer to the Classification of Health Products at the Device-Drug Interface (<https://www.canada.ca/en/health-canada/services/drugs-health-products/classification-health-products-device-drug-interface.html>) and the Guidance Document: Factors Influencing the Classification of Products at the Device-Drug Interface (<https://www.canada.ca/en/health-canada/services/drugs-health-products/classification-health-products-device-drug-interface/guidance-document-factors-influencing-classification-products-device-drug-interface.html>) for more information.

For questions about the classification of products at the device-drug interface, please email: [hc.drug.device.classification-droque.instrument.sc@canada.ca](mailto:hc.drug.device.classification-droque.instrument.sc@canada.ca).

## 5.1 Combination products

For a combination product that has not been previously classified, sponsors or manufacturers may submit a written request for a classification decision to the relevant review Centre/Bureau/Office or make a presentation to the TPD, NNHPD, BRDD or the Medical Device Directorate (MDD) (as appropriate) for the purpose of classifying the product in advance of filing a submission/application. Alternatively, sponsors may file a submission/application to the review Centre/Bureau/Office based on their own classification. If the submission/application was filed incorrectly, the sponsor or manufacturer will be notified.

If the receiving Centre/Bureau/Office cannot reach a consensus as to the classification of the combination product, the submission/application will be referred to the TPCC. The TPCC then makes a recommendation to the Review Centre/Bureau/Office.

Submissions/applications for combination products will be handled in accordance with the Drug/Medical Device Combination Products Policy, (November 2005) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/policies/drug-medical-device-combination-products.html>) and subject to either the Medical Devices Regulations or the Food and Drug Regulations based on the principal mechanism of action by which the claimed effect or purpose is achieved. Both principal and ancillary components must meet acceptable standards of safety, efficacy and quality.

For a combination product classified as a drug, a submission or an application should be sent to the OSIP. The submission or application will be managed in accordance with this guidance.

For a combination product classified as a medical device, manufacturers are to submit a device license application to the Medical Devices Directorate. Refer to the Guidance Document: Management of Applications for Medical Device Licenses (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/policies/management-applications-medical-device-guidance-2019/document.html>) for further information.

## 5.2 Other regulations that influence the classification of a drug

Once a product has been classified as a drug and not a device at the level of the Food and Drugs Act (“the Act”), further classification is required to determine whether the product is a drug subject to the Food and Drug Regulations or a natural health product (NHP), a subset of drugs under the Act, subject to the Natural Health Products Regulations (NHPR). This further classification is guided by the definition of a NHP in section 1 of the NHPR, the exclusion of prescription drugs in section 2(2), and the inclusive and exclusive lists of substances set out in Schedules 1 and 2 to the NHPR.

Personal care products may share characteristics of both “cosmetic” and “drug”, as currently defined under the Food and Drugs Act and could fall under one of three sets of regulations: the Cosmetic Regulations, the Food and Drug Regulations or the Natural Health Products Regulations. The Guidance Document: Classification of Products at the Cosmetic-Drug Interface (<https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/industry-professionals/guidance-document-classification-products-cosmetic-drug-interface.html>) identifies criteria in the decision making process in determining the appropriate regulatory regime that applies to a given product at the cosmetic-drug interface.

For questions about which regulatory framework may apply to a particular health product or about the classification of products at the device-drug interface please e-mail: [hc.drug.device.classification-drogeu.instrument.sc@canada.ca](mailto:hc.drug.device.classification-drogeu.instrument.sc@canada.ca)

## 6. Specific submission/application pathways<sup>6</sup>

Information provided below is to inform sponsors of certain submission/application pathways that require the filing of a specific submission/application type or class. Sponsors are encouraged to consult existing guidance/policy documents on the Health Canada website to familiarize themselves with the requirements of each submission/application type or class.<sup>7</sup>

### 6.1 Priority review

A drug submission sponsor requesting priority review of a submission under the Guidance for Industry: Priority Review of Drug Submissions is to request Priority Review status in advance of filing a submission. Requests for Priority Review status of an NDS or SNDS (i.e., PRNDS, PRSNDS) should be sent to OSIP, to the attention of the Director of the appropriate Centre/Bureau/Office. Following the review of the request for Priority Review status, the submission (NDS or SNDS) should be filed. If the drug submission was granted Priority Review, the sponsor must clearly state this in their cover letter and the submission must be filed within 60 calendar days.

For further information and management of Priority Review requests and submissions, including performance standards, refer to the Guidance for Industry: Priority Review of Drug Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html>).

## 6.2 Notice of Compliance with conditions (NOC/c)

Sponsors requesting Advance Consideration to file a submission under the NOC/c Policy, as per the Guidance Document: Notice of Compliance with Conditions (NOC/c) should request a pre-submission meeting with the appropriate review Centre/Bureau/Office (refer to Section 7.1). Submissions should then be filed as a NDS, SNDS, ANDS or SANDS. If the drug submission is deemed eligible for Advance Consideration under the NOC/c Policy, the sponsor must clearly state this in their cover letter and the submission must be filed within 60 calendar days. Where a Notice of Compliance with Conditions (NOC/c) has been issued, results from confirmatory trials outlined in the Letter of Undertaking (LOU) should be filed as a SNDS-c or a SANDS-c.

For further information on eligibility, procedural requirements and the performance standards, refer to the Guidance Document: Notice of Compliance with Conditions (NOC/c) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>).

## 6.3 Extraordinary use new drug

Submissions eligible under the criteria in C.08.002.01 (1) of the Food and Drug Regulations may be filed as an Extraordinary Use New Drug Submission (EUNDS), a Supplement to an Extraordinary Use New Drug Submission (EUSNDS), an Abbreviated Extraordinary Use New Drug Submission (EUANDS) or a Supplement to an Abbreviated Extraordinary Use New Drug Submission (EUSANDS).

For submission requirements, refer to the Guidance Document: Submission and Information Requirements for Extraordinary Use New Drugs (EUNDS) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/submission-information-requirements-extraordinary-drugs-eunds.html>). These submissions have the same performance standards as the corresponding NDS, SNDS, ANDS or SANDS.

## 6.4 Biosimilar biologic drug

Biosimilar biologic drugs, like all new drugs, are subject to Part C, Division 8 of the Food and Drug Regulations for authorization and oversight. Submissions for Biosimilar Biologic drug products should be filed as a NDS/SNDS and have the same performance standards as the corresponding NDS/ SNDS. For submission requirements, refer to the Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs-1.html>).



## 6.5 Administrative processing

Submissions/applications should be filed in accordance to the Guidance Document: Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/administrative-processing-human-disinfectant-drugs-2019/document.html>). All information will be administratively processed to ensure it is complete and of suitable quality for the intended purpose.

## 7. Guidance for implementation

### 7.1 Pre-Submission or pre-application meetings

Pre-submission or pre-application meetings may be requested by sponsors prior to filing a submission/application.

Pre-submission or pre-application meetings may be conducted via a face to face meeting or by teleconference.

Sponsors may request a pre-submission/application meeting with the appropriate Directorate within Health Canada if they have any questions or concerns prior to filing the following:

- a drug submission/application (e.g., NDS, SNDS, ANDS, SANDS, DINA)
- a clinical trial application
- a request for a combination product classification (e.g., medical device-drug, drug-drug)
- a request for a priority review
- a request for advanced consideration of a submission under the Notice of Compliance with Conditions (NOC/c) Policy<sup>8</sup>
- a submission for Extraordinary Use New Drugs (EUNDS)
- a submission/application relying on third party data<sup>9</sup>, or
- a response to a Notice of Deficiency (NOD) or Notice of Non-Compliance (NON)

The purpose of pre-submission/application meetings is for Health Canada and the sponsor to discuss the data in support of the proposed submission/application. In addition, the purpose of such meetings could be to (if applicable):

- familiarize Health Canada review staff with the submission/application prior to its filing, and provide a forum to discuss the data in the submission/application for the purpose of facilitating its review
- identify potential problems or issues and manage disputes early in the submission/application process
- identify studies the sponsor is relying on as adequate and well controlled in establishing the safety and efficacy of the drug
- provide an opportunity for the sponsor to discuss details of the submission/application with Health Canada and obtain feedback regarding areas of concern based on current experience and regulatory requirements
- provide an opportunity to discuss the potential eligibility of the submission for Priority Review or NOC/c consideration

- increase the quality of information submitted, and
- provide the appropriate Directorate the opportunity to re-align resources to accommodate the arrival of the submission/application

Note: While the available data may be a point of discussion at the meeting, the acceptability of the data will only be considered during the scientific review of the proposed submission/application.

For information on Pre-Clinical Trial Application (CTA) Consultation Meetings, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.2) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>). Sponsors should ensure the requested feedback relates to clinical trial information and not market authorization requirements. For example, a meeting request to discuss pivotal clinical trials for market authorization may require a pre-NDS meeting rather than a pre-CTA meeting.

For information related to pre-submission meetings for Priority Review requests or requests for advance consideration of a submission under the Notice of Compliance with Conditions (NOC/c) Policy, refer to the Guidance to Industry: Priority Review of Drug Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html>) and the Guidance Document: Notice of Compliance with Conditions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>) respectively.

For information related to pre-submission/application meetings relying on third party data, refer to the 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>).

#### 7.1.1 Meeting requests

For pre-CTA meeting requests, the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.2.1) provides meeting requirements and contact information.

For all other pre-submission/application meeting requests, sponsors are encouraged to contact the appropriate review Centre/Bureau/Office prior to submitting a formal meeting request. Refer to the Appendix 2 for contact information.

An administrative cover letter (refer to Section 2.1 of the Guidance Document: Preparation of Drug Regulatory Activities in the Electronic Common Technical Document Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>) or Section 2.1 of the Guidance Document: Preparation of Drug Regulatory Activities in the Non-eCTD Electronic-Only Format for further details) ([Guidance Document: Management of Drug Submissions & Applications | 18](https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-</a></p></div><div data-bbox=)

document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html) and a meeting request should be addressed to the Director of the appropriate review Centre/Bureau/Office and sent to OSIP as early as possible, but no less than three months prior to the proposed meeting date in one of the acceptable file formats (refer to Section 8.1).

Meeting requests should be submitted in the form of a separate document (i.e., not included in the cover letter) and include the following information:

- the purpose of the meeting (e.g., pre-NDS, pre-Phase III, pre-response to a NOD/NON, etc.)
- the specific details regarding the product to be discussed (e.g., active ingredient, dosage form and therapeutic classification, etc., including whether the drug is first in class)
- adequate information regarding the product to enable Health Canada to assess the utility of the meeting
- a list of preliminary questions to be addressed during the meeting
- submission/application information (control number, product name, etc.) and a copy of the NOD/NON if the meeting is regarding a response to a NOD/NON
- three possible meeting dates, and whether an afternoon or morning meeting is being requested
- suggestion regarding the review expertise necessary to discuss the proposed issues (e.g., clinical/chemistry/biopharmaceutics reviewers, biostatisticians, etc.), and
- if the drug submission will rely solely on third-party data (as per Guidance Document: Drug Submissions Relying on Third-Party Data) (<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>)

The Regulatory Project Manager (RPM) in TPD and NNHPD, or the Senior Regulatory Affairs Officer (SRAO) in BRDD will contact the sponsor to discuss the request. If Health Canada determines a meeting is warranted, this discussion will include possible meeting dates, the overall content of the pre-submission/application package and confirmation of the number of meeting participants. The meeting request may be declined if the information listed above is not provided with the meeting request.

If Health Canada considers that a formal meeting is not required, a response and rationale will be provided by the RPM/SRAO within a reasonable time period.

#### 7.1.2 Meeting packages

For information on the Pre-Clinical Trial Applications Consultation Information Package, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.2.2) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>).

Sponsors will be requested to submit a pre-submission/application meeting package in one of the acceptable file formats (refer to Section 8.1) at least one month in advance of the meeting. If the sponsor is making a presentation, the slide deck should be submitted one week prior to the meeting. Meeting packages should be as concise as possible and contain only the

information listed below. Please note that hard copy meeting packages may be requested.

Pre-submission/application meeting packages should include, where applicable:

- a cover letter
- a proposed meeting agenda
- a brief slide presentation
- a brief summary of the drug product
- identification of the indication(s) for which approval is sought
- proposed strengths and dosages
- a summary of the clinical development plan for the drug, including identification of clinical trials completed in Canada (if any) and confirmation of which trials are still on-going (if any)
- a summary of the development of the product, including any changes in production process, dosage form, testing methods etc., leading up to a description of the manufacturing process for the product to be marketed
- brief summaries of the safety and efficacy data relating to the drug (e.g. draft of the Product Monograph (PM))
- an overview of the market history of the product including the foreign regulatory status of the drug
- a list of specific issues or questions (grouped by discipline) the sponsor would like to discuss or have addressed, and
- the projected submission/application filing date

### 7.1.3 Post-meeting requirements

For information on Pre-CTA consultation meeting records, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.2.3).

After the pre-submission/application meeting, sponsors are to draft and submit meeting minutes to Health Canada no later than two weeks following the meeting. Final meeting minutes should be submitted in one of the acceptable file formats (refer to Section 8.1).

When filing their submission/application, sponsors should reference the following information in the cover letter:

- the control number of the pre-submission/pre-application meeting as well as a confirmation that the submission/application reflects what was committed to at the meeting, and
- the meeting minutes and any other pre-submission/application correspondence with Health Canada

It is in the sponsor's best interest to file a submission/application within a reasonable time period following the pre-submission/application meeting.

## 8. Filing of information to Health Canada

Sponsors should ensure that their submissions/applications contain the information needed to satisfy the regulatory requirements of Part C of the Food and Drug Regulations. All submitted information and any subsequent information filed (solicited and unsolicited) should accompany the cover letter that indicates the reason for filing the information and the date filed.

## 8.1. Acceptable formats for filing submissions/applications

Currently, Health Canada accepts submissions/applications in the electronic common technical document (eCTD) electronic-only format and in the non-eCTD electronic-only format. Paper documents are no longer accepted by Health Canada for any type of submission/application.

The eCTD Format is the mandatory format for filing a submission/application as per the Notice - Mandatory use of Electronic Common Technical Document (eCTD) Format (<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>). All submissions/applications filed in eCTD format, including subsequent information (e.g., SNDSs, NCs, PSURs, etc.), should be prepared using the requirements provided in the Guidance Document: Preparation of Drug Regulatory Activities in the Electronic Common Technical Document (eCTD) Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>).

The non-eCTD Electronic-Only Format: is the alternative format for filing a submission/application. All submissions/applications that are filed and any subsequent information submitted should be prepared using the requirements provided in the Guidance Document: Preparation of Regulatory Activities in the Non-eCTD Electronic-Only Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>).

If the proposed submission/application will be filed in the eCTD format, the pre-submission/application meeting request and packages should be filed in the same format.

## 8.2 Filing formats and where to file for CTAs and CTA-As

The CTA or CTA-A should be submitted on electronic media and organized in accordance with the Guidance Document: Preparation of Regulatory Activities in the Non-eCTD Electronic-Only Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>).

For additional information, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Sections 2.3.2 and 2.4.4) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>). Sponsors should address the application to the Director of the appropriate review Centre/Bureau/Office and send information to the Office of Regulatory Affairs (ORA) in BRDD or to the Office of Clinical Trials (OCT) in TPD. Refer to Appendix 2 for contact information.

## 8.3 Transmission of electronic data

Electronic data prepared in eCTD format should be provided as prescribed in the transmission section of the Guidance Document: Preparation of Regulatory Activities in the eCTD Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>).

Electronic data prepared in non-eCTD electronic-only format should be provided as prescribed in the transmission section of the Guidance Document: Preparation of Regulatory Activities in the Non-eCTD Electronic-Only Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>).

## 9. Submission/application processing

### 9.1 Processing of an initial submission/application

All information received by OSIP will be processed and sent to the appropriate review Centre/Bureau/Office within 10 calendar days of receipt with the exception of CTAs and CTA-As, which are sent directly to ORA in BRDD or OCT in TPD. Refer to Appendix 2 for contact information.

For details on CTA and CTA-A processing, refer to Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.5) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>).

During the 10-day processing period, OSIP performs the following activities, depending on the submission/application type:

- assigns a control number and Dossier ID (only when applicable) to the submission/application
- enters the initial information into the Drug Submission Tracking System (DSTS) (e.g., medicinal ingredient, dosage form, brand name, date received, etc.
- verifies that the information submitted is administratively complete (e.g., all necessary forms, including those related to cost-recovery have been submitted)
- verifies that the format, structure and attributes of electronic data submitted comply with the CTD format and specifications
- for submissions subject to the provisions of the Patented Medicines (Notice of Compliance) Regulations, verifies that a Patent Form V has been included in the submission/application and ensures that all relevant patents have been addressed through the filing of the Form V, and
- verifies the submission is not subject to data protection under the data protection provisions of section C.08.004.1 of the Food and Drug Regulations<sup>10</sup>

At this stage in processing, the information package may be placed on the following administrative holds:

- Process Hold - Initial
- Cost Recovery Hold
- Patent Form V Hold, or
- Data Protection Refused Hold

Refer to Appendix 5 for a description of the different types of “Administrative Holds.”

When the hold is resolved or the initial information package is considered administratively complete, the following occurs:

- the information package becomes a submission/application
- the filing date is entered into the DSTS (i.e., the date when the submission/application is considered administratively complete)
- the remainder of the submission/application information is entered into the DSTS, if applicable, and
- the appropriate review Centre/Bureau/Office is notified that the submission/application has been processed and can be assigned to a RPM/SRAO for screening.

## 9.2 Cancellation or withdrawal letter during the processing period

If a sponsor wishes to cancel their submission/application during the processing period, a signed letter requesting the cancellation should be sent to OSIP in the same format as the original submission/application. The status of the submission/application would be changed to “Cancelled Admin” in the DSTS, as the scientific review has not started.

For CTAs/CTA-As, a signed letter requesting the withdrawal of an application/amendment should be sent directly to ORA (BRDD) or OCT (TPD). The status of the application/amendment would be changed to “Withdrawn” in the DSTS.

Submissions/applications that are cancelled/withdrawn by the sponsor may be done so without prejudice to a refiling (refer to Section 15.2 of this Guidance for pharmaceuticals/biologics or Section 15.3 for CTAs/CTA-As for refiling information).

## 9.3 Submissions/applications for administrative processing

Submission/Applications for administrative processing are to be submitted to Health Canada when there is a change in manufacturer's name and/or product name such as following a merger, buy-out, other corporate restructuring, or through a licensing agreement.

Submissions/Applications may be processed administratively only if the original manufacturer's cross referenced drug product has received market authorization from Health Canada and has an active Drug Identification Number (DIN).

These types of submissions/applications may be filed for: NDSs/ANDSs including their applicable Supplements, NCs (quality changes for biologics and radiopharmaceuticals) and Applications for a DIN and Post-Authorization Division 1 Changes (PDCs, PDC-Bs).

To be eligible for administrative processing, these submissions/applications should not contain scientific data, or require regulatory review. All aspects of the product, except for the manufacturer name and/or product name, must be identical to those previously authorized for that product. Any deviations from the previously authorized product is not accepted under the administrative pathway.

For additional information on administrative processing, refer to the 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/administrative-processing-human-disinfectant-drugs-2019/document.html>).

Solicited information in a Clarification Request should be submitted within five (5) business days from the date of the request. If the response to a Clarification Request is not satisfactory or not submitted within the specified time to respond, the following may be sent to the sponsor:

- a Deficiency Notice (response should be submitted within 45 days from the date of the request), or
- a Rejection Letter

## 10. Screening of submissions/applications

### 10.1 Screening of a submission/application during the Screening 1 period

For information on the screening process of CTAs and CTA-As, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.5.1) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>).

When the submission/application is received in the Centre/Bureau/Office, the Screening 1 period begins.

The RPM/SRAO<sup>11</sup> will screen all submissions/applications<sup>12</sup> to:

- verify that the type and class of the submission/application has been filed correctly given the intended purpose
- ensure requisite information for the type and class of the submission/application has been provided, and
- verify the fee is appropriate for the submission/application.

Health Canada will screen the original submission/application within the performance standards in Appendix 3 for Screening 1 period.

#### 10.1.1 Cancellation letter during the Screening 1 period

If a sponsor wishes to cancel their submission/application during the screening period before it has been accepted into scientific review, a signed letter requesting the cancellation should be sent to OSIP in the same format of the original submission/application. The status of the



submission/application would be changed to “Cancelled Admin” in the DSTS, as the scientific review has not started.

The SRPM/SRAO<sup>13</sup> will issue a cancellation acknowledgement letter.

Submissions/applications that are cancelled by the sponsor may be done so without prejudice to a refiling (refer to Section 15.2 for refiling of pharmaceuticals/biologics or Section 15.3 for refiling of CTAs/CTA-As).

#### 10.1.2 Screening Acceptance Letter (SAL)

If the information submitted by the sponsor is acceptable at screening and requests for information/clarification are not required (refer to Section 10.2.1 for more information):

- the submission/application or response to solicited information is accepted for scientific review and a Screening Acceptance Letter (SAL) is sent to the sponsor
- the appropriate databases are updated, and
- the relevant review division will be notified that the submission/application has been accepted for review.

Once the submission/application is accepted for scientific review, the RPM/SRAO will continue to be the point of contact for communication with the sponsor, unless otherwise indicated.

### 10.2 Solicited Information

Solicited information is considered any information that is requested by Health Canada during the screening of a submission/application. Examples include but are not limited to: Clarification Requests or Screening Deficiency Notices.

#### 10.2.1 Clarification Requests during the Screening 1 period

For information on the screening requests of CTAs and CTA-As, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.5.1).

The purpose of a Clarification Request is to expand on, seek clarification on specific information or re-analyze existing information in the submission/application during the screening period. For example, Clarification Request may be used to locate misplaced documents, etc.

Clarification Requests should not be used to request missing documents or new data such as, new clinical and/or pre-clinical information, including bioavailability studies or chemistry and manufacturing data not previously submitted.

Requests will be solicited by fax or email and must be responded to in writing (for more information, refer to Section 10.2.2). The screening is not interrupted if a complete response is submitted within the requested timeframe.

#### 10.2.2 Response to a Clarification Request during the Screening 1 period

When responding to a Clarification Request, sponsors should clearly identify the name of the drug, the Dossier ID, the control number of the relevant submission/application and the purpose of the correspondence (i.e. “Response to a Screening Clarification Request”).

Responses to Clarification Requests should be submitted in a Question and Answer format that is referenced to the applicable section(s) in the submission/application.

Sponsors are requested to send their responses to Clarification Requests in accordance with the Guidance Document: Preparation of Drug Regulatory Activities in the Electronic Common Technical Document (eCTD) Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>) or the Guidance Document: Preparation of Regulatory Activities in the Non-eCTD Electronic-Only Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>), as applicable. For sponsors who filed in the non-eCTD electronic-only format, the response should be submitted to OSIP via electronic media (i.e., USB or CD) via courier mail. For the shorter response times to a Clarification Request, sponsors are reminded to take into account the delivery and processing time.

For questions regarding filing submissions/applications electronically, sponsors can contact OSIP. Refer to Appendix 2 for contact information.

The solicited information should be submitted within 15 calendar days from the date of the request or as indicated in the Clarification Request. A response is complete if:

- all clarifications or questions identified in the Clarification Request have been addressed, or
- the sponsor provided a sound scientific rationale as to why the requested information is not necessary.

For submissions/applications that are administratively processed, solicited information in a Clarification Request should be submitted within five (5) business days from the date of the request.

If a Clarification Request is inquiring about the location of data in the submission/application, the response should only include the location of the data or an explanation as to why the data is missing.

To clarify points of the Clarification Request, or the rationale for its issuance, sponsors should contact the RPM/SRAO.

There is no limit on the number of Clarification Requests that may be solicited for one submission. However, no particular issue will be addressed more than once. Acknowledgement letters are not sent upon receipt of information received in response to Clarification Requests.

During the screening of a submission/application, if a response to a Clarification Request is not satisfactory or is not submitted within the specified time to respond, a Deficiency Notice or Rejection letter will be sent for submissions/applications with administrative processing. For all other submission/application types, a Screening Deficiency Notice is sent.

### 10.2.3 Screening Deficiency Notice (SDN)

If deficiencies are identified during the screening of material relating to a submission or application, the sponsor will be sent a Screening Deficiency Notice identifying the deficiencies. This may also include submissions where the drug is filed as a DIN Application but is considered a new drug or where the monograph attestation is found not to reflect the submission content.

The status of the submission/application will change to “inactive 45” in the DSTS. A SDN can be sent to the sponsor without prior issuance of a Clarification Request.

The solicited information is to be submitted within 45 calendar days from the date the SDN was sent.

To clarify points of the SDN or the rationale for its issuance, sponsors should contact the RPM/SRAO.

#### *10.2.3.1 Response to Screening Deficiency Notice (SDN)*

When responding to a SDN, sponsors should clearly identify the name of the drug, the Dossier ID, the control number of the relevant submission/application and the purpose of the correspondence (i.e. “Response to SDN”) in the cover letter. The response is to be submitted in a question and answer format, referenced to the applicable section(s) of the submission/application as appropriate. The response to a SDN should not contain unsolicited information (refer to Section 14.0) unless otherwise specified in the SDN.

The sponsor should send all requested information along with the up-to-date documents (e.g., updated cover letter, Submission Certification form, etc.) in a single package to OSIP for processing. All information received by OSIP will be processed and sent to the appropriate review Centre/Bureau/Office within 10 calendar days. When OSIP begins to process the Response to SDN, the status of the submission would be changed to “Process” in the DSTS. Should OSIP determine that the Response to SDN is administratively incomplete; the submission status will be changed to “Process Hold”.

Once OSIP verifies that the “Response to SDN” is administratively complete, the RPM/SRAO will be notified that the response has been processed.

Acknowledgement letters are not sent upon receipt of responses to SDNs. Upon receipt of the information requested in the Screening Deficiency Notice, a new Screening 1 period will begin (with the associated performance standards), and the requested material and information will be screened for completeness.

#### *10.2.3.2 Acceptance letter following the response to a Screening Deficiency Notice (SDN)*

If the response to the SDN is acceptable, a SAL will be sent to the sponsor and the Review 1 Period will begin immediately (refer to Section 10.1.2 - SAL).

#### *10.2.3.3 Screening Rejection Letter (SRL)*

A SRL will be sent for by the SRPM/SRAO<sup>14</sup> for all drug submissions/applications if the sponsor fails to provide a response to the SDN within 45 calendar days or if the information submitted is incomplete, deficient or contains unsolicited information. A SRL (instead of a SDN) will be sent for a Notifiable Change (NC) or SNDS/SANDS if the proposed changes are Level III changes only<sup>15</sup>.

To clarify points of the SRL or the rationale for its issuance, sponsors should contact the RPM or SRAO.

If a SRL has been issued, the sponsor may refile the submission/application (refer to Section 15.1).

A sponsor may file a Request for Reconsideration following the issuance of a SRL (Refer to Section 16 - Reconsideration of Decisions issued for Human Submissions and Applications).

## 11. Scientific Review of submissions/applications

### 11.1 Scientific Review process

For information on the scientific review process of CTAs and CTA-As, refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (Section 2.5.2) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>).

The Review 1 period begins immediately after the SAL is issued. Health Canada will evaluate the submission/application within the performance standards in Appendix 3. The reviewer will examine and analyse the information submitted to ensure the product meets the requirements set out in the applicable sections of the Food and Drug Regulations.

The RPM/SRAO is responsible for coordinating review timelines and is the initial point of contact for communication with the sponsor. Refer to Appendix 2 for contact information.

#### 11.1.1 Screening solicited and unsolicited information submitted during the Scientific Review

For information on what is considered solicited and unsolicited information, refer to Sections 12.0 and 14.0 respectively.

Solicited and unsolicited information submitted by the sponsor during the scientific review will be screened, where appropriate, to ensure that:

- a cover letter is provided with the information that includes the control number of the relevant submission/application
- the purpose of the correspondence is clearly stated as solicited or unsolicited, and
- the information submitted in an acceptable format (e.g. question and answer, side-by-side comparison), referenced to the applicable section in the electronic submission/application, as appropriate, and the information is complete for the intended purpose

#### 11.1.2 Cancellation letter during the Scientific Review

If a sponsor wishes to cancel their submission/application during the scientific review, but before a decision is made to issue an NOC, NOD, NON, Notice of Compliance with Conditions Qualifying Notice (NOC/c-QN), NOD-Withdrawal (NOD-W) or NON-Withdrawal (NON-W), a signed letter requesting the cancellation should be sent to OSIP in the same format as the original submission/application. The status of the submission/application would be changed to “Cancelled Science” as the scientific review has started.

The SRPM/SRAO will issue a cancellation acknowledgement letter.

Submissions/applications may be cancelled by the sponsor without prejudice to a refiling (refer to Section 15.2 for information on refiling).

### 11.1.3 Pause the Clock during the scientific review

Pause the clock is a tool that allows the review clock to be paused under specified circumstances. When there is a pause, the target date is shifted to account for the amount of time the clock has been paused.

The review clock can pause only during the review period (e.g., Review 1 and Review 2) for cost-recovered submissions/applications. Administrative submissions/applications are excluded from this mechanism.

Pauses can occur with these submissions/applications in the following instances:

#### a) Sponsor request for an extension to respond to a Clarification Request

A sponsor may request an extension to respond to a Clarification Request. The extension request should be submitted as soon as possible in the form of a letter and written rationale. The clock would pause if the following criteria are met:

- the extension request is beyond the number of days allocated to respond to a Clarification Request as indicated in Section 12.1.2 of this guidance document, (i.e., 15 days for submissions with a 180 -300 day performance standard; 10 days for submission/application with a 91-179 day performance standard; 5 days for submissions/applications with a 0 -90 day performance standard),
- the extension request is a minimum of 5 days but not beyond 90 days per Clarification Request, and
- Health Canada approves the extension in writing to the sponsor.

Following Health Canada's approval of the extension and after the standard clarification response time has elapsed, the review clock pauses. The sponsor has the additional time approved by Health Canada to respond to the request, and the target date is changed. Note that there may be situations where Health Canada would not approve an extension or grant an extension to an existing pause. The review clock would resume at the end of the approved extension period. If the response to a Clarification Request is not satisfactory or not submitted within the specified time to respond, a NOD or NON will be issued (refer to Section 12.1.2).

For example, if Health Canada issues a Clarification Request with a 10 day response time for a submission with a 91-179 day performance standard:

- if an 8 day extension is requested beyond the standard 10 day response time and the extension request is approved, the review clock would pause for 8 days beginning on day 11, and the response would be due on day 18,
- if a 2 day extension is requested beyond the standard 10 day response time, and the extension request is approved, the review clock would not pause.

#### b) Seeking Advice from an External Advisory Committee<sup>16</sup>

Health Canada will inform the sponsor if an External Advisory Committee is required during the review period. Health Canada will strive to identify the need for an External Advisory Committee as early as possible in the review. If a pause is required, the sponsor will be notified

of this by Health Canada. The nature of the questions for the External Advisory Committee will be included in the notification. Health Canada's review clock would resume upon receipt of the final recommendation(s) from the committee, at which point the revised performance standard date will be confirmed.

## 12. Solicited information during the Scientific Review

### 12.1 Solicited information

Solicited information is any information requested by Health Canada during the scientific review. Examples include but are not limited to: Clarification Requests, a Notice of Deficiency (NOD) or a Notice of Non-Compliance (NON).

#### 12.1.1 Clarification Request during the Scientific Review

Refer to Section 10.2.1 for information regarding Clarification Requests as the information in this section is also applicable to Clarification Requests solicited during the scientific review. Examples of solicited information during the scientific review may include clarification on a statistical analyses package, the rationale for interim pivotal trials, or changes to proposed labelling material.

#### 12.1.2 Response to a Clarification Request during the Scientific Review

Refer to Section 10.2.2 for information regarding the response to a Clarification Request during the screening period. This information is also applicable to a response to a Clarification Request submitted during the scientific review.

Sponsors are to send their responses to Clarification Requests in accordance with the Guidance Document: Preparation of Drug Regulatory Activities in the Electronic Common Technical Document Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>) or the Guidance Document: Preparation of Regulatory Activities in the Non-eCTD Electronic-Only [1] Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>).

The timeline to respond should be between 2 and 15 calendar days and will be based on the type and the performance standard of the submission/application (see Table 1 below). While the type of submission/application should guide response times, these are guidelines and can be adjusted. Where warranted, Health Canada can adjust the timelines to be longer or shorter based on the complexity of the request, dialogue with the sponsor and/or circumstances of the review.

Table 1: Time to Respond to a Clarification Request during Scientific Review

180-300 day performance standard	15 days
91-179 day performance standard	10 days
0-90 day performance standard	5 days
CTAs and CTA-As	2 days

Note: During the review of a Clinical Assessment Package to request Priority Review status, the solicited information in a Clarification Request should be submitted within two (2) business days from the date of the request. Refer to the Guidance for Industry: Priority Review of Drug Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html>).

The review of the submission/application will not be interrupted if a complete response is submitted within the given time period.

If the response to a Clarification Request submitted during the scientific review is not satisfactory, or not submitted within the specified time to respond, the following may be sent to the sponsor:

- a Notice of Deficiency (NOD) (refer to Section 12.1.3)
- a Not Satisfactory Notice (NSN) (refer to Section 13.4) , or
- a Notice of Non-Compliance (NON) (refer to Section 13.6)

12.1.3 Notice of Deficiency (NOD) - NDS, SNDS, ANDS, SANDS or an Application for a DIN (DINA, DINB, DIND)

A NOD will be sent to the sponsor when:

- during the scientific review of a submission/application<sup>17</sup>, deficiencies and/or significant omissions that preclude continuing the review are identified, or
- during the scientific review of an Application for a DIN (DINA, DINB, DIND), the product is identified as a New Drug and the sponsor is requested to file a NDS, or an ANDS.

At the time of the NOD issuance, all scientific review streams will stop and the submission/application status will change to “Inactive 45” or “Inactive 90” in the DSTS (depending on the submission/application type) even if the review in the other streams has not been completed. Deficiencies identified to date from all review streams will be included in the NOD. Only one NOD is sent per submission/application.

The difference between a NOD and a Notice of Non-Compliance (NON) is that the review of the submission/application is not complete when a NOD is issued.

To clarify points of the NOD or the rationale for its issuance, sponsors should contact the RPM/SRAO.

For NDSs, SNDSs, ANDSs and SANDSs, the Response to a Notice of Deficiency is to be submitted within 90 calendar days (or such time as the Centre/Bureau/Office and sponsor may agree upon) from the date the NOD was sent.

For Applications for a DIN, the Response to a Notice of Deficiency is to be sent within 45 calendar days (or such time as the Centre/Bureau/Office and sponsor may agree upon) from the date the NOD was sent.

If a NOD was issued during an early review, and after a subsequent review, the sponsor may be sent a:

- Notice of Deficiency Withdrawal (NOD-W) (refer to Section 12.1.3.3)
- Notice of Compliance (NOC) (refer to Section 13.2), or
- Notice of Non-Compliance (NON) (refer to Section 13.6).

#### 12.1.3.1 Response to Notice of Deficiency (NOD) - NDS, SNDS, ANDS, SANDS or an Application for a DIN (DINA, DINB, DIND)

A Response to NOD is to be submitted in the same format as the original submission/application. The solicited information is to include a copy of the NOD and should be submitted in a question and answer format and referenced to the applicable section(s) of the submission/application.

Should a sponsor decide it is not necessary to file the solicited information; a sound scientific rationale for this position must be presented in order for the response to be considered complete.

The sponsor should send all of the requested information along with up-to-date documents (e.g., updated cover letter, Submission Certification form, etc.) in a single package to OSIP for processing. All information received by OSIP will be processed and sent to the appropriate review Centre/Bureau/ Office within 10 calendar days. When OSIP begins to process the Response to NOD, the status of the submission would be changed to "Process". Should OSIP determine that the Response to NOD is administratively incomplete; the submission status will be changed to "Process Hold".

Once OSIP verifies that the Response to a NOD is administratively complete, the appropriate Centre/Bureau/Office is notified that the response has been processed.

When the response to the NOD is received, a new Screening 1 period begins (refer to Section 11.1.1 - Screening of Solicited and Unsolicited Information Submitted during the Scientific Review).

Acknowledgement letters are not sent upon receipt of Responses to NODs.

#### 12.1.3.2 Acceptance of a response to a Notice of Deficiency (NOD)

When the Response to a NOD is screened and found acceptable for scientific review, a SAL will be sent to the sponsor (refer to Section 10.1.2 - SAL).

A new Review 1 period begins immediately after the issuance of the SAL.

The RPM/SRAO will serve as the initial point of contact for communication with the sponsor.



### 12.1.3.3 Notice of Deficiency Withdrawal letter (NOD-W<sup>18</sup>)

A NOD-W will be sent to the sponsor if:

- during the screening process the Response to a NOD is found to contain unsolicited information, is incomplete, or is deficient
- the sponsor fails to submit the solicited information (i.e. the Response to the NOD) within the assigned time period. Health Canada will interpret this as a request to withdraw the submission/application, or
- during the scientific review of the Response to a NOD, it is determined that the submission/application remains deficient.

Submissions/applications may be withdrawn without prejudice to a refiling (refer to Section 15.4 for information on refiling).

A sponsor may file a Request for Reconsideration following the issuance of a NOD-Withdrawal Letter (refer to Section 16 - Reconsideration of Decisions Issued for Human Submissions and Applications).

## 13. Completion of the Scientific Review of a submission/application

### 13.1 Processing of the submission/application following completion of the review

Upon completion of a review where a decision has been recommended (either negative or positive), one of the following decision documents is prepared.

### 13.2 Notice of Compliance (NOC) - NDS, SNDS, ANDS, SANDS, EUNDS, EUSNDS, EUANDS, AEUSNDS, NDS-D, SNDS-D, SNDS-c, SANDS-c

When the scientific review of a submission for a Division 8 product is completed and the submission complies with the Food and Drug Regulations, the sponsor may receive the following:

- a Drug Identification Number, in the form of a Drug Notification Form (DNF), in accordance to sub-section C.01.014.2(1) of the Food and Drug Regulations, and
- either a NOC once the requirements of the Patented Medicines (Notice of Compliance) Regulations and the data protection provisions in section C.08.004.1 of the Food and Drug Regulations have been met, or
- a notification that the submission has been placed on Intellectual Property-Hold (IP Hold) until the requirements of the Patented Medicines (Notice of Compliance) Regulations have been met and/or until the term of market exclusivity for an innovative drug in accordance with the data protection provisions in section C.08.004.1 of the Food and Drug Regulations has expired.

Prior to receiving a NOC, submissions may also be placed on a Switch Hold or a Regulatory Hold. For a description of the types of holds mentioned in this section, refer to Appendix 5.

### 13.3 No Objection Letter (NOL) - Application for a DIN (DINA, DINB, DIND), NC, PDC, PDC-B, CTA, CTA-A

When the scientific review of an Application for a DIN (DINA, DINB, and DIND) has been completed and found to be in compliance the sponsor will receive:

- a Drug Identification Number, via a Drug Notification Form (DNF), in accordance to sub-section C.01.014.2(1) of the Food and Drug Regulations,
- a NOL for PDCs and PDC-Bs, or
- an Approval Letter for DIN-Bs

A NOL will also be sent by the responsible review Centre/Bureau/Office for NCs, CTAs or CTA-As when the scientific review of the submission/application has been completed and found to be in compliance.

### 13.4 Not Satisfactory Notice (NSN) - NC, PDC, PDC-B, CTA, CTA-A

When deficiencies are identified during the review of a NC, PDC, PDC-B, or CTA, CTA-A, a NSN will be sent to the sponsor by the responsible review Centre/Bureau/Office specifying the deficiencies. The review of the submission will stop on the date the NSN is sent.

To clarify points of the NSN or the rationale for its issuance, sponsors should contact the RPM/SRAO.

If a NSN has been issued, the sponsor may refile the submission/application (refer to Section 15.5 for information on refiling).

A sponsor may file a Request for Reconsideration following the issuance of a NSN (refer to Section 16 - Reconsideration of Decisions issued for Human Submissions and Applications).

### 13.5 Notice of Compliance with Conditions Qualifying Notice (NOC/c-QN)

This section is not applicable to CTAs and CTA-As

When data submitted has undergone a scientific review and has been determined to qualify under the NOC/c policy, the appropriate Directorate of Health Canada will contact the sponsor to discuss the details of the submission, commitments, and its potential consideration under the NOC/c policy. Following discussions with the sponsor, Health Canada will issue a NOC/c – QN if appropriate.

The NOC/c - QN indicates that the submission qualifies for a NOC under the NOC/c policy and outlines the additional clinical evidence to be provided in confirmatory studies, post-market surveillance responsibilities, and requirements related to advertising, labelling, or distribution. The scientific review of the submission will stop on the date the Qualifying Notice is issued.

The sponsor should submit the appropriate information within 30 calendar days of receipt of the NOC/c-QN. Responses to a NOC/c-QN should reference the submission control number and be sent to OSIP.

Upon receipt of the sponsor's response to the NOC/c - QN, Health Canada will commence a scientific review of the additional information provided, which is subject to a 30 calendar day

performance standard. Should the information be considered acceptable, Health Canada will finalize, with the sponsor, the conditions associated with issuance of the NOC under the NOC/c policy as well as the Letter of Undertaking (LOU). For more information, consult the Guidance Document: Notice of Compliance with Conditions (NOC/c) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>) available on the Health Canada website. If the information is not considered acceptable, a NON may be issued (refer to Section 13.6).

Acknowledgement letters are not sent upon receipt of information received in response to NOC/c-QNs.

### 13.6 Notice of Non-Compliance (NON) - NDS, SNDS, ANDS, SANDS, or an Application for a DIN (DINA, DINB, DIND)

This section is not applicable for CTAs and CTA-As.

If the scientific review of a submission/application has been completed and is found to be incomplete or non-compliant with the requirements outlined in the Food and Drugs Act and its Regulations, a NON will be sent to the sponsor.<sup>19</sup>

The NON will specify the issues from all of the scientific review streams that render the submission as non-compliant. At the time of the NON issuance, the scientific review is completed and the submission/application status will change to “Inactive 45” or “Inactive 90” in the DSTS (depending on the submission/application type). Only one NON per submission/application will be sent.

To clarify points of the NON or the rationale for its issuance, sponsors should contact the RPM/SRAO.

For NDSs, SNDSs, ANDSs and SANDSs, the sponsor must submit the solicited Response to a Notice of Non-Compliance within 90 calendar days (or such time as the Centre/Bureau/Office and sponsor may agree upon) from the date the NON was sent. For Applications for a DIN, the sponsor is required to submit the solicited information within 45 calendar days (or such time as the Centre/Bureau/Office and sponsor may agree upon) from the time the NON was sent.

#### 13.6.1 Response to a Notice of Non-Compliance (NON)

A Response to a NON is to be submitted in the same format as the original submission/application. The Response to a NON is to include a copy of the NON and should be submitted in a question and answer format which references the applicable section(s) in the original submission/application.

Should a sponsor decide it is not necessary to file the solicited information; a sound scientific rationale for this position must be presented in order for the response to be considered complete.

The sponsor should send all the requested information along with up-to-date documents (e.g., updated cover letter, Submission Certification form, etc.) in a single package to OSIP for processing. All information received by OSIP will be processed and sent to the appropriate review Centre/Bureau/ Office within 10 calendar days. When OSIP begins to process the

Response to NON, the status of the submission would be changed to “Process”. Should OSIP determine that the Response to NOD is administratively incomplete; the submission status will be changed to “Process Hold”.

Once OSIP verifies that the Response to a NON is administratively complete, the appropriate Centre/Bureau/Office is notified that the response has been processed.

When the Response to the NON is received, the Screening 2 period begins (refer to Section 11.1.1 - Screening of Solicited and Acceptable Unsolicited Information Submitted during the Scientific Review).

Acknowledgement letters are not sent upon receipt of responses to NONs.

#### 13.6.2 Acceptance of a response to a Notice of Non-Compliance (NON)

When the response to a NON is screened and found to be acceptable for review, a SAL will be sent to the sponsor (refer to Section 10.1.2 - SAL).

A Review 2 period begins immediately after the issuance of the SAL.

The RPM/SRAO will serve as the initial point of contact for communication with the sponsor.

#### 13.6.3 Notice of Non-Compliance Withdrawal letter (NON-W)

A NON-W is sent to the sponsor if:

- during the screening process, the Response to a NON is found to contain unsolicited information that is incomplete or deficient
- the sponsor fails to submit the solicited information (i.e. the “Response to a NON”) within the assigned time period. Health Canada will interpret this as a request to withdraw the submission/application, or
- during the scientific review of the Response to a NON, it is determined that the submission remains non-compliant

Submissions/applications may be withdrawn without prejudice to a refiling (refer to Sections 15.6 and 15.7 for information on refiling).

A sponsor may file a Request for Reconsideration following the issuance of a NON-W (refer to Section 16 - Reconsideration of Decisions Issued for Human Submissions and Applications).

## 14. Unsolicited information

When a sponsor files unsolicited information (as described in Sections 14.1 to 14.6 below), the information should be filed in the same format as the original submission/application (i.e., eCTD or non-CTD electronic only) with a cover letter stating the type of information provided and the reason for the filing and the date of filing. All information should be sent to OSIP for processing and the RPM/SRAO will be notified that unsolicited information has been received.

If unsolicited information, other than what is described below, is filed to Health Canada, the sponsor will be asked to remove those documents from the submission. For submissions filed in the eCTD format, the sponsor will be required to submit a new eCTD sequence to withdraw the unsolicited information as follows:

- Assign operations attribute “delete” on leaves provided as “new,” or
- Assign operation attribute “replace” on leaves provided as replace (using file reuse to reinstate the previous document as the current submission content)

Sponsors should contact Health Canada at [hc.ereview.sc@canada.ca](mailto:hc.ereview.sc@canada.ca) if they require further assistance. If the sponsor wishes to include the unsolicited information in a future drug submission/application, it will need to be resubmitted as a new submission/application, and will be assigned a new control number.

All unsolicited information pertaining to a CTA or CTA-A should be submitted as CTA-Notifications to ORA in BRDD and OCT in TPD, unless otherwise directed. Refer to the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/guidance-clinical-trial-sponsors-clinical-trial-applications.html>).

## 14.1 Safety information

### 14.1.1 Information that may be submitted at any time during the submission process

Sponsors are encouraged to submit, at any time, negative safety findings or risk information collected from animal studies or clinical experience. This information should support the addition or change to the wordings in the ‘Contraindications’, ‘Warnings and Precautions’, and ‘Adverse Reactions’ sections of the PM.

If a revision to the PM is proposed as a result of the unsolicited safety data, a revised PM that appropriately references the original PM with the proposed changes is to accompany any submission of unsolicited data. A mock-up label is also required if changes to the PM result in changes to the label. The new information will not affect the performance standards for review of the submission.

When submitting negative safety information, the cover letter should include: the name of the drug, the Dossier ID, the control number of the relevant submission/application, the purpose of the correspondence, and a statement that information is unsolicited.

### 14.1.2 Information that will not be accepted once the submission has been accepted for review

Unsolicited final reports of safety studies that do not require changes to the “Contraindications”, “Warnings and Precautions”, and “Adverse Reactions” sections of the PM will not be accepted for scientific review. However, sponsors can file this information in response to a NOD, NON, or may include this data with the filing of a SNDS, where applicable, in accordance with the Guidance Document: Post-Notice of Compliance (NOC) Changes: Safety and Efficacy (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-2019/document.html>).

## 14.2 Foreign regulatory information

### 14.2.1 Assessment reports

Health Canada will accept assessment reports prepared by other regulatory authorities within 120 days of receipt of the original submission. If assessment reports are submitted outside the 120-day time period, it is possible that it will not assist the Canadian review and may not be used or considered. Reports that have been summarized will not be accepted if filed.

### 14.2.2 Correspondence

Health Canada will accept copies of correspondence between the sponsor and other regulatory authorities at any time. Summaries of the correspondence will not be accepted. Supporting data or appendices should not be included with the correspondence, but should be available if requested.

## 14.3 Reports from an expert or from expert advisory committees

Reports from an expert or from expert advisory committees will only be accepted at the time of filing or if submitted in a response to a NOD or a NON (refer to Sections 12.1.3.1 or 13.6.1).

## 14.4 Changes in the manufacturer's/sponsor's name and/or product name during the processing, screening or review of a submission/application

During the review of any initial submission/application for a new product that has not yet been issued a Drug Identification Number (DIN), if the sponsor's name or the product's name changes, the following should be submitted to OSIP:

- a letter stating the nature of the change
- a revised Drug Submission Application Form for: Human, Veterinary or Disinfectant Drugs and Clinical Trial Application/Attestation (HC/SC 3011 Form)
- a revised PM, package insert and labels, including mock-up labels
- a brand name assessment and mock-up labels for a product name change
- the Labels and Packages Certification Form
- a revised Certified Product Information Document (CPID), and
- a letter of authorization from the originating sponsor if the product is being transferred from one sponsor to another

If a product has already received market authorization (i.e., has been issued a DIN) and the sponsor's name or the product's name changes during the review of a subsequent submission/application, a submission/application must be filed to make the necessary changes.

Information regarding the requirements for sponsor and product name changes can be found in the following documents:

- 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/administrative-processing-human-disinfectant-drugs-2019/document.html>)

- Guidance Document for Industry: Review of Drug Brand Names (<https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-document-industry-review-drug-brand-names.html>)
- Guidance Document: Questions and Answers: Plain Language Labelling Regulations for Prescription Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/questions-answers-plain-language-labelling-2019/document.html>)
- Frequently Asked Questions – Guidance Document for Industry – Review of Drug Brand Names (<https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/frequently-asked-questions-guidance-document-industry-review-drug-brand-names.html>), and
- Guidance Document: Questions and Answers: Plain Language Labelling Regulations for Non-prescription Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/questions-answers-plain-language-labelling-non-prescription-drugs-2019/document.html>)

### 14.5 Efficacy data

Efficacy data will not be accepted at any point during the review unless it is solicited in a NOD or NON. Efficacy data may be filed as a Supplement to a New Drug Submission, where applicable, in accordance with the Guidance Document: Post-Notice of Compliance (NOC) Changes: Safety and Efficacy (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-2019/document.html>).

If a sponsor has committed to providing additional efficacy data in a Letter of Undertaking prepared in response to a NOC/c Qualifying Notice, this data should be submitted as a SNDS-c or SANDS-c.

### 14.6 Stability data

Updated stability information relating to the quality of the drug substance or drug product should only be submitted when requested.

## 15. Refiled submissions or applications

In all cases, a refiled submission is considered to be a new submission/application and will be assigned a new control number, a new filing date and managed in accordance with this guidance. A refiled submission/application is subject to Health Canada policies, procedures and guidance documents that are in effect at the time of refile; therefore, the sponsor should update the submission accordingly. The performance standards, matters pursuant to intellectual property and fees for the relevant submission/application type and class will be applicable at the time of the refiled submission/application.

Refiled submissions/applications should be sent to OSIP, along with up-to-date documents (e.g., updated cover letter, Submission Certification form) and should indicate the Directorate to

whom the initial submission/application was submitted. For CTAs and CTA-As, refiled applications should be sent to ORA in BRDD or OCT in TPD.

Prior to refiling of a submission/application in eCTD format, the sponsor may contact OSIP for technical advice on how to reference the new information to the original submission/application.

Refer to Appendix 2 for contact information.

A refiled submission/application is a submission/application that a sponsor files following:

- the issuance of a SRL
- the cancellation of a submission/application by a sponsor
- the issuance of a NOD-W, NON-W, or
- the issuance of a NSN

### 15.1 Refiling a submission/application following a screening rejection letter

Should a sponsor wish to refile a submission/application that received a screening rejection letter, the sponsor will be required to resubmit all information for the submission/application. Referencing to the original submission/application will not be acceptable.

### 15.2 Refiling of a submission/application following a cancellation by the sponsor

Should a sponsor wish to refile a submission/application following a cancellation at any point during the processing, screening, Review 1, or following a NOD, the sponsor will be required to resubmit all information for the submission/application. Referencing to the original submission/application will not be acceptable.

For submissions/applications cancelled by the sponsor following the issuance of a NON or NON-W or during Review 2, refer to sections 15.6 and 15.7 for information on the refiling of information.

### 15.3 Refiling of a CTA/CTA-A following the withdrawal by the sponsor

For applications withdrawn by the sponsor, all information for the application should be resubmitted and, if applicable, the information to address any deficiencies previously identified. The refiled information will be considered a new application.

### 15.4 Refiling a submission/application following a Notice of Deficiency (NOD) withdrawal

Should a sponsor wish to refile a submission/application any time following the issuance of a NOD-W, the sponsor is required to resubmit all information for the submission/application along with the information to address the deficiencies identified in the NOD or related Withdrawal Letter. Referencing to the original submission/application will not be acceptable.



## 15.5 Refiling a submission/application in 5 years or less following a Not Satisfactory Notice (NSN)

Should a sponsor wish to refile a submission/application within 5 years or less following the issuance of a NSN, all information should be resubmitted including the information to address the deficiencies identified in the NSN.

Sponsors should provide a rationale to Health Canada as to why the refiled information should be reviewed. Reference should be made to the previous control number of the original submission/application. Sponsors should certify that all other information previously submitted remains unchanged.

Any Level II (for biologic and radiopharmaceutical drug quality changes) or Level III changes according to the Guidance Documents: Post-Notice of Compliance (NOC) Changes, (Safety & Efficacy (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-2019/document.html>) or Quality (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/quality-document/guidance.html>) for Division 8 drugs, or any PDCs in accordance with the Guidance Document: Post-Drug Identification Number (DIN) Changes (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-drug-identification-number-changes.html>) for Division 1 drugs should be incorporated into the appropriate section(s) of the refiled submission/application respectively. The sponsor should provide a summary of the changes that have been included, and reference the supporting data in the submission/application.

To increase the efficiency of the scientific review, sponsors should clearly identify both the new and the original information that is being resubmitted. Appropriate referencing to the original submission/application where applicable should be included.

A complete and properly referenced comprehensive summary is required for refiled submissions/applications, where applicable.

## 15.6 Refiling a submission/application in 5 years or less following a NON-W, a cancellation following the issuance of a NON (prior to the issuance of a NON-W)

Should a sponsor wish to refile a submission/application in five years or less following the issuance of a NON (prior to the issuance of a NON-W) or after receipt of a NON-W, the sponsor is only required to resubmit the information to address the issues identified in the NON or NON-W Letter. The sponsor should provide a rationale to Health Canada as to why the refiled information should be reviewed. Reference should be made to the previous control number of the original submission/application. Sponsors should certify that all other information previously submitted remains unchanged.

Information that would be classified as Level II (for biologic or radiopharmaceutical drug quality changes) or Level III changes according to the Guidance Document: Post-Notice of Compliance

(NOC) Changes (Safety & Efficacy) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-2019/document.html>) or Quality (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/quality-document/guidance.html>) for Division 8 drugs, or any PDCs in accordance with the Guidance Document: Post-Drug Identification Number (DIN) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-drug-identification-number-changes.html>).

Changes for Division 1 drugs should be incorporated into the appropriate section(s) of the refiled submission/application respectively. The sponsor should provide a summary of the changes that have been included and reference the supporting data in the submission/application.

To increase the efficiency of the scientific review, sponsors should clearly identify both the new and the original information that is resubmitted. Appropriate referencing to the original submission/application where applicable should be included.

A complete and adequately referenced comprehensive summary is required for refiled submissions/applications, where applicable.

### 15.7 Refiling of a submission/application more than 5 years after receipt of a NON-W, cancellation following the issuance of a NON (prior to the issuance of a NON-W) or a NSN

Should a sponsor wish to refile a submission/application more than five years after receipt of a NON-W, cancellation following the issuance of a NON (prior to the issuance of a NON-W) or a NSN. The sponsor is required to resubmit all information for the submission/application along with up to date documents (e.g., updated cover letter, Submission Certification form, etc.). Referencing the original information submitted is not acceptable. Information that was previously submitted in the original submission/application and remains unchanged should be clearly identified and certified as such by the sponsor.

## 16. Reconsideration of decisions issued for human submissions and applications

Reconsideration is a dispute resolution process designed to ensure that negative decisions were made in accordance with existing scientific and regulatory standards. The process is designed to look at the information in specific submissions/applications rather than address complaints about perceived systemic issues. Health Canada will try to identify, manage, and resolve disputes at the level at which they take place. Dispute prevention and early resolution will primarily take place through communication between the Directorates and submission/application sponsors.

If mechanisms for early dispute resolution are not successful, sponsors may file a formal Request for Reconsideration of a decision in accordance with the Guidance Document: Reconsideration of Decisions Issued for Human Drug Submissions and Natural Health Products (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/reconsideration-final-decisions/reconsideration-final-decisions-issued-human-drug-submissions.html>).

A sponsor may request a reconsideration following the issuance of one of the following decisions:

- Rejection of Priority Review Request under the Guidance for Industry; Priority Review of Drug Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html>)
- Rejection of Request for Advance Consideration under the Notice of Compliance with Conditions Policy (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>)
- SRL
- NOD/W
- NON/W, or
- NSN for NCs, PDCs, PDC-Bs, CTAs & CTA-As

Issues not eligible for reconsideration are: decisions based on submissions/applications containing documented falsified information, allegations of bias, and complaints about the submission management process. Issues of this nature should be addressed to the Director of the relevant review Centre/Bureau/Office.

## 17. Accessing submission information

### 17.1 Scientific review reports

Sponsors will receive review reports from Health Canada within seven (7) calendar days following the issuance of a NOD, a NOD/W, a NON, or a NON/W for all submissions except DINAs/DINBs. For DINAs/DINBs, sponsors may request reports following receipt of a NOD, NON, NOD/W, or NON/W.

Sponsors may also request review reports following receipt of a NOL, NOC, or NSN.

Requests should be addressed to the Director of the review Centre/Bureau/Office (refer to Appendix 2 for contact information) and provided through the CESG for submissions in eCTD format or on media for submissions in non-eCTD electronic only format. Health Canada aims to provide requested review reports to the sponsor within 30 calendar days of receipt of the request.

## 17.2 Drug Submission Tracking System (DSTS) - industry access

Sponsors are able to access information regarding their own submissions/applications via the Drug Submission Tracking System - Industry Access (DSTS-IA). Sponsors can access the database using their assigned user name and password.

Information available via the DSTS-IA includes:

- submission/application information, i.e. Dossier ID, control number, submission type, class, file number, Lead reviewing Centre/Bureau/Office, filing date
- drug product information (e.g., includes brand name, manufacturer, active ingredient), document history including document type issued or received and document date
- review (assessment) history including the review type (type of assessment e.g. clinical, chemistry and manufacturing, label), the division assigned with status (e.g. pending, active) and date

To obtain a DSTS-IA account, or information about DSTS-IA, sponsors should contact OSIP at [hc.client.information.sc@canada.ca](mailto:hc.client.information.sc@canada.ca).

## 17.3 Status requests

Sponsors should first check the status of their submissions/application via the DSTS-IA; however if there are further questions about the status of their drug submissions/application the following should be contacted:

- for BRDD: the Office of Regulatory Affairs, or
- for TPD and NNHPD: the appropriate Regulatory Project Manager

Refer to Appendix 2 for contact information.

For CTAs and CTA-As, status updates will not be provided given the short performance standards for review.

# Appendix 1

## Definitions

### **Biologic Drug**

A drug listed in Schedule D to the Food and Drugs Act.

### **Biosimilar biologic drug**

A biosimilar biologic drug, or biosimilar, is a biologic drug demonstrated to be similar to a brand name drug already authorized for sale (known as the reference biologic drug). Biosimilars were previously known in Canada as subsequent entry biologics (SEBs). Biosimilars may enter the market after the expiry of reference biologic drug patents and data protections. Biosimilars are regulated as new drugs under the Food and Drugs Act and the Food and Drug Regulations.

### **Combination Product**

A therapeutic product that combines a drug component and a device component (which by themselves would be classified as a drug or a device), such that the distinctive nature of the drug component and device component is integrated in a singular product<sup>20</sup>.

### **Dossier**

A collection of all regulatory activities throughout the life cycle of a product.

### **Dossier Identifier (Dossier ID)**

A number created by Health Canada to uniquely identify the dossier related to a specific drug product.

### **Drug**

Drugs include both prescription and non-prescription pharmaceuticals; biologically-derived products such as vaccines, blood derived products, and products produced through biotechnology; tissues and organs; disinfectants; and radiopharmaceuticals. According to the Food and Drugs Act, "a drug includes any substance or mixture of substances manufactured, sold or represented for use in:

- a. the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state, or its symptoms, in human beings or animals;
- b. restoring, correcting or modifying organic functions in human beings or animals; or
- c. disinfection in premises in which food is manufactured, prepared or kept."

### **Ethical Drug**

A drug that, in accordance with Federal Legislation, does not require a prescription, but is generally prescribed by a medical practitioner. Ethical products are unscheduled non-prescription professional use products (e.g. MRI contrast agents, hemodialysis solutions) and a few emergency use products (e.g. nitroglycerine).

### **Filing Date**

Refers to the date that the submission/application is deemed administratively complete by Health Canada (that is [i.e.] once all elements and forms required for processing are

completed and submitted to Health Canada). This date may differ from the date of original receipt should the submission/application be considered administratively incomplete at that time.

Note: A submission/application received after 5:00 pm Eastern Standard Time, during a weekend, or on a statutory holiday is considered to be received on the next Health Canada business day.

### **Generic Drug**

A generic drug is a copy of a brand name drug. The generic drug is pharmaceutically equivalent to the brand name drug and contains the identical medicinal ingredients, in the same amounts and in a similar dosage form. Generic medications may have different non-medicinal ingredients than the brand name drug, but the company must show that these do not affect the safety, efficacy, or quality of the drug compared to the brand name drug. Generic drugs are approved as Abbreviated New Drug Submissions (ANDSs).

### **Manufacturer/Sponsor**

For drug products, the manufacturer/sponsor is whose name the drug submission is filed under and, where a Drug Identification Number (DIN)/Notice of Compliance (NOC) is to be issued, the company in whose name the DIN/NOC will be registered, (i.e., the DIN/NOC holder) and whose name must be included on the product label and Product Monograph/Package Insert. For CTAs and CTA-As, a sponsor is defined by Division 5, Part C of the Food and Drug Regulations as the individual, corporate body, institution or organization that conducts a clinical trial. Note that the sponsor is not necessarily the company that fabricates the drug product.

For medical devices, the "manufacturer" means a person who sells a medical device under their own name, or under a trade-mark, design, trade name or other name or mark owned or controlled by the person, and who is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the device, or for assigning to it a purpose, whether those tasks are performed by that person or on their behalf. "Person" includes a partnership, firm or association.

### **Medical Device**

"Device" means an instrument, apparatus, contrivance or other similar article, or an in vitro reagent, including a component, part or accessory of any of them, that is manufactured, sold or represented for use in:

- a) diagnosing, treating, mitigating or preventing a disease, disorder or abnormal physical state, or any of their symptoms, in human beings or animals,
- b) restoring, modifying or correcting the body structure of human beings or animals or the functioning of any part of the bodies of human beings or animals,
- c) diagnosing pregnancy in human beings or animals,
- d) caring for human beings or animals during pregnancy or at or after the birth of the offspring, including caring for the offspring, or

- e) preventing conception in human beings or animals; however, it does not include such an instrument, apparatus, contrivance or article, or a component, part or accessory of any of them, that does any of the actions referred to in paragraphs (a) to (e) solely by pharmacological, immunological or metabolic means or solely by chemical means in or on the body of a human being or animal; (Food and Drugs Act).

**Non-prescription Drug**

A drug that can be bought without a doctor's prescription (i.e. not included in the Prescription Drug List), or a drug that is part of a class of drugs that is set out in the Food and Drugs Act.

**Prescription Drug**

A drug that is set out in the Prescription Drug List, as amended from time to time, or a drug that is part of a class of drugs that is set out in it (the Food and Drugs Act).

**Regulatory Activity**

A collection of all regulatory transactions throughout the process of a specific activity which includes, but is not limited to a NDS, ANDS or DIN Application, etc.

**Therapeutic Product**

A drug or device or any combination of drugs and devices, but does not include a natural health product within the meaning of the Natural Health Products Regulations (the Food and Drugs Act).

## Appendix 2

### Review centre/bureau/office responsibilities and contact information

#### **Biologic and Radiopharmaceutical Drugs Directorate (BRDD)**

Centre for Biologics Evaluation (CBE): CBE is responsible for the regulation of biologics, including but not limited to vaccines, blood and blood products, cellular therapies, cells, tissues, organs and xenografts and allergenic extracts. Key functions include the scientific review of submissions/applications provided in support of product quality, safety, and efficacy, development of laboratory standards and methods, pre-approval of on-site evaluations in support of submission/application review and managing the lot-release program for biologics.

Centre for the Evaluation of Radiopharmaceuticals and Bio therapeutics (CERB): CERB is responsible for the regulation of biologics and radiopharmaceuticals, including but not limited to, gene therapies and somatic cell therapies, hormones, monoclonal antibodies, enzymes, allergenic extracts, and cytokine products. Key functions include the evaluation scientific review of submissions provided in support of product quality, safety, and efficacy, development of laboratory standards and methods, pre-approval of on-site evaluations in support of submission review and managing the lot-release program for biologics.

The Office of Regulatory Affairs (ORA) core function is the management of submissions and applications associated with the products that the BRDD regulates and the regulatory review of brand names and labels under the Plain Language Labelling (PLL) Regulations. The ORA serves as the primary contact with sponsors, manages submission/application screening/validation, coordinates and facilitates submission/application meetings with sponsors, provides regulatory/policy guidance to sponsors, manages receipt and issuance of all regulatory correspondence for the Directorate.

Office of Regulatory Affairs

Biologic and Radiopharmaceutical Drugs Directorate (BRDD)

Health Products and Food Branch

Health Canada

100 Eglantine Driveway,

Tunney's Pasture, Address Locator #0601C

Ottawa, ON

K1A 0K9

Tel: 613-957-1722

Fax: 613-946-9520

E-mail: [hc.brdd.ora.sc@canada.ca](mailto:hc.brdd.ora.sc@canada.ca)

#### **Therapeutic Products Directorate (TPD)**

The Therapeutic Products Directorate (TPD) is responsible for the regulation of prescription pharmaceutical (i.e. chemically synthesized) products and medical devices.

Depending upon therapeutic class and the types of studies filed in support of a pharmaceutical submission, the safety and efficacy (clinical and pre-clinical) component may be reviewed by



one or more of the four review Bureaus in the TPD, whose functions are described below. The quality (chemistry and manufacturing) component of all pharmaceutical submissions is reviewed by the Bureau of Pharmaceutical Sciences.

The following is a brief overview of all the Bureaus in the TPD.

**The Bureau of Metabolism, Oncology and Reproductive Sciences (BMORS)** is comprised of the Division of Reproduction and Urology drugs, the Division for Oncology drugs, and the Division of Metabolic and Musculoskeletal drugs.

Responsibilities include, but are not limited to: the clinical, pre-clinical and labelling review of submissions indicated for use in/as: hormone replacement, contraceptive drugs, menopause, erectile dysfunction, oncology (includes hormone based therapies), haematology, diabetes, osteoporosis and musculoskeletal anti-inflammatories.

The Bureau of Metabolism, Oncology and Reproductive Sciences  
Therapeutic Products Directorate

Health Canada

Finance Building #2

101 Tunney's Pasture Driveway,

Tunney's Pasture, Address Locator #0202D2

Ottawa, ON

K1A 0K9

Telephone: 613-941-3171

Fax: 613-941-1365

E-mail: [hc.bmors.enquiries.sc@canada.ca](mailto:hc.bmors.enquiries.sc@canada.ca)

**The Bureau of Gastroenterology, Infection and Viral Diseases (BGIVD)** comprises the Division of Anti-Infective Drugs, the Division of Gastroenterology drugs, and the Division of AIDS and Viral Diseases drugs. Responsibilities include, but are not limited to, the clinical, pre-clinical and labelling review of submissions indicated for use in/as: anthelmintic drugs, anti-fungal drugs, antibacterial drugs, antibiotic drugs, sterile diluents, anti-herpetic drugs, AIDS, influenza, cytomegalovirus, hepatitis B&C, immunosuppressant drugs for transplants and skin disorders, antidiarrheal drugs, antispasmodic drugs, antiulcer drugs, colitis therapy, digestive aids, ophthalmic drugs for macular degeneration and glaucoma, contrast agents and antidotes/poison treatments. BGIVD is also responsible for the administrative review of submissions/applications for changes to manufacturer and/or brand name.

The Bureau of Gastroenterology, Infection and Viral Diseases  
Therapeutic Products Directorate

Health Canada

Finance Building #2

101 Tunney's Pasture Driveway

Tunney's Pasture, Address Locator #0202B

Ottawa, ON

K1A 0K9

Telephone: 613-941-2566  
Fax: 613-941-1183  
E-mail: hc.bgivd.enquiries.sc@canada.ca

**The Bureau of Medical Sciences (BMS)** comprises medical evaluators assigned to one of two Medical Sciences Divisions, modelled and structured to perform reviews as the other review bureaus in the Therapeutic Products Directorate. Responsibilities include: review of first in class submissions; review of Submissions Relying on Third Party Data (SRTD), particularly when the Canadian medical practice context is required; determination of Priority Review submission status; assessment of requests for Advance Consideration of a Notice of Compliance with Conditions review status; conducting all Medical Necessity Determinations for the Directorate; conducting Health Risk Assessments.

The Bureau also provides a medical consultation service to the other review bureaus when requested. To facilitate the Bureau's involvement in these review activities, medical evaluators attend pre-submission meetings across the review bureaus. A third division, the Office of Risk Management, within BMS/TPD, is responsible for the coordination of Health Risk Assessments, Medical Necessity determinations and Drug Shortages files and serves a liaison role with the Regulatory, Operations and Enforcement Branch (ROEB).

The Bureau of Medical Sciences  
Therapeutic Products Directorate  
Health Canada  
5th Floor Holland Cross, Tower B  
1600 Scott Street, Address Locator #3105B  
Ottawa, ON  
K1A 0K9  
Fax: 613-948-8324  
E-mail : hc.bms.enquiries-bsm.sc@canada.ca  
hc.bmsormrisk-bsmbgrrisque.sc@canada.ca (BMS-ORM Risk Division)

**The Bureau of Cardiology, Allergy and Neurological Sciences (BCANS)** comprises the Division for Cardio-Renal drugs, the Division of Allergy and Respiratory drugs and the Division for Central Nervous System drugs. Responsibilities include, but are not limited to, the clinical, pre-clinical, and labelling review of submissions indicated for use in/as: neurology, anaesthesiology, pain management, psychiatry, obesity, substance related disorders, hypertension, vasodilators, myocardial ischemia, stroke, diuretic drugs, antithrombotic drugs, anticoagulant drugs, antiplatelet drugs, plasma expanders, dialysis, immunosuppressant drugs for allergy, asthma and cough and cold.

The Bureau of Cardiology, Allergy and Neurological Sciences  
Therapeutic Products Directorate  
Health Canada  
2nd Floor Holland Cross, Tower B  
1600 Scott Street, Address Locator #3102C  
Ottawa, ON  
K1A 0K9

Telephone: 613-941-1499  
Fax: 613-941-1668  
E-mail: hc.bcansenquiries.sc@canada.ca

**The Bureau of Pharmaceutical Sciences (BPS)** is responsible for the chemistry and manufacturing review as well as the scientific review of clinical comparative bioavailability studies, including but not limited to bioequivalence studies for all submission types of all therapeutic classes of pharmaceutical products. Responsibilities also include the assessment of pharmaceutical product information and labelling of generic product submissions.

The Bureau of Pharmaceutical Sciences  
Therapeutic Products Directorate  
Health Canada  
Finance Building #2  
101 Tunney's Pasture Driveway  
Tunney's Pasture, Address Locator #0201D  
Ottawa, ON  
K1A 0K9

Telephone: 613-941-3184  
Fax: 613-957-3989  
E-mail: hc.bps.enquiries.sc@canada.ca

**The Office of Clinical Trials (OCT)** is responsible for managing and evaluating information related to clinical trial applications for drug products used in Phase I, II, or III clinical trials. This includes but is not limited to receiving and reviewing Clinical Trial Applications, serious unexpected adverse drug reactions, and providing guidance to all relevant stakeholders.

Submission Management Division, Office of Clinical Trials  
Therapeutic Products Directorate  
Health Canada  
5th Floor, Holland Cross, Tower B  
1600 Scott Street, Address Locator #3105A  
Ottawa, ON  
K1A 0K9

Fax: 613- 946-7996  
E-mail: hc.oct\_bec\_enquiries.sc@canada.ca

**The Regulatory Project Management Division (RPMD)** in the Office of Planning, Performance and Review Services includes Regulatory Project Manager (RPMs) assigned to each bureau. These RPMs serve as the key regulatory contact for submissions and applications, and they are responsible for communicating progress internally and externally, coordinating review streams as well as pre-submission meetings, ensures consistent application of policies, guidelines, processes and practices within and between bureaux. They also ensure consistent application by sponsors of minimum requirements during submission screening, and are responsible for monitoring the adherence to review performance standards through the submission life cycle.

The Regulatory Project Management Division  
Therapeutic Products Directorate  
Health Canada  
Finance Building #2  
101 Tunney's Pasture Driveway,  
Tunney's Pasture, Address Locator #0201A1  
Ottawa, ON  
K1A 0K9  
Telephone: 613- 941-1248  
Fax: 613-957-1483  
E-mail: hc.rpmd-dgpr.sc@canada.ca

### **Medical Device Directorate (MDD)**

The Medical Devices Directorate (MDD) is responsible for reviewing scientific information to assess the safety, effectiveness and quality of medical devices, assessing the potential benefits and risks of a medical device and reviewing applications for Investigational Testing Authorizations (ITAs) for medical devices to ensure that studies are well designed and participants will not be exposed to undue risk.

The Bureau of Licensing Services is responsible for authorizing the sale of lower risk Class II medical devices, providing project management services and logistical support related to medical device licence applications and managing stakeholder enquiries regarding medical device classification.

Contact us

Medical Devices Directorate  
Health Products and Food Branch  
11 Holland Avenue, Tower A  
2nd Floor  
Address Locator: 3002A  
Ottawa, Ontario  
K1A 0K9

General Enquiries  
Telephone: 613-957-4786  
Fax: 613-957-6345  
E-mail: hc.meddevices-instrumentsmed.sc@canada.ca

### **The Resource Management and Operations Directorate (RMOD)**

The Resource Management and Operations Directorate is responsible for supporting the Health Products and Food Branch by providing direction, coordination, and advice on financial

management, cost recovery and information technology/information management, as well as ensuring internal governance mechanisms are in place to allow the Branch to deliver effectively on legislated functions. The Office of Submission and Intellectual Property (OSIP) is responsible for the processing of eCTD and non-eCTD electronic-only submissions/applications, including invoicing of fees, and maintaining various databases such as the DSTS, the DPD and the NOC databases. OSIP also administers the Fees in Respect of Drugs and Medical Devices Regulations, is responsible for the issuance of all Drug Identification Numbers (DINs), the application of regulatory requirements for DINs and performance reporting. The Office of Patented Medicines and Liaison (OPML) within OSIP is responsible for the administration of the Patented Medicines (Notice of Compliance) Regulations, data protection under the Food and Drug Regulations, and Certificates of Supplementary Protection under the Patent Act.

Office of Submissions and Intellectual Property  
The Resource Management and Operations Directorate  
Health Canada  
Finance Building #2  
101 Tunney's Pasture Driveway,  
Tunney's Pasture, Address Locator #0201A1Ottawa, ON  
K1A 0K9  
Telephone: 613-941-7281  
Fax: 613-941-0825  
Email: [hc.osip-bppi.sc@canada.ca](mailto:hc.osip-bppi.sc@canada.ca)  
Email for technical advice relating to electronic submissions: [hc.ereview.sc@canada.ca](mailto:hc.ereview.sc@canada.ca)

### **Natural and Non-prescription Health Products Directorate (NNHPD)**

The Natural and Non-prescription Health Products Directorate (NNHPD) is responsible for the regulation of non-prescription drugs and disinfectant drugs as well as natural health products. The Non-Prescription Drug Evaluation Division (NDED) is responsible for, but not limited to, the scientific review of pre-market applications and the management of all issues related to non-prescription drugs (excluding generic Division 8 drugs)<sup>21</sup>, including DIN applications for products subject to Category IV Monographs and to Labelling Standards as well as disinfectant products.

Regulatory Project Management Unit, servicing NDED in NNHPD  
Natural and Non-prescription Health Products Directorate  
Health Canada  
5th Floor, Graham Spry Building  
250 Lanark Avenue, Address Locator #2005A  
Ottawa, ON  
K1A 0K9  
Telephone: 613-946-9315  
Fax: 613-946-9614  
Telephone: 613-946-9315  
613- 957-6801 for the Regulatory Project Management Unit  
Email: [hc.nnhpd-dpsnso.sc@canada.ca](mailto:hc.nnhpd-dpsnso.sc@canada.ca)

## **Marketed Health Products Directorate (MHPD)**

The Marketed Health Products Directorate (MHPD) leads an evidence-based vigilance program for health products in Canada. This is accomplished by using a risk-based approach to make regulatory decisions that are communicated in an open and transparent manner to help Canadians make informed decisions. The MHPD is responsible for functions including, but not limited to, monitoring and collecting adverse reaction and medication incident data for drugs and medical devices; reviewing and analysing marketed health product safety data; conducting risk/benefit assessments of marketed health products; and communicating product related risks to health professionals and the public.

Marketed Pharmaceuticals Bureau  
Marketed Health Products Directorate  
Health Canada  
Address Locator #1912A  
Ottawa, ON  
K1A 0K9  
Telephone: 613-946-5140  
Facsimile: 613-952-6011  
E-mail: [hc.mhpd-dpsc.sc@canada.ca](mailto:hc.mhpd-dpsc.sc@canada.ca)

Biologicals, Radiopharmaceuticals, and Self-Care Products Bureau  
Marketed Health Products Directorate  
Health Canada  
Address Locator #1906A  
Ottawa, ON  
K1A 0K9  
Facsimile: 613-954-2354  
E-mail: [hc.mhpd-dpsc.sc@canada.ca](mailto:hc.mhpd-dpsc.sc@canada.ca)

## Appendix 3

### Performance standards for drug submission/application review

Process: the 10 calendar days for processing by the Office of Submissions and Intellectual Property (OSIP) for all submissions/applications (except CTAs and CTA-As) prior to acceptance into both Screening 1 and Screening 2.

#### Pharmaceuticals, Biologics & Radiopharmaceuticals

Submission		Performance Standards (in calendar days)					
Type	Class	Screening 1 (including response to NOD)	Review 1 (including response to NOD)	CR review*	Screening 2 Response to NON	Review 2 Response to NON	Review of Response to NOC/c-QN
CTA CTA-A <sup>†</sup>	1. Phase I - bioequivalence, Phase I - healthy human	7 (target)	N/A	N/A	N/A	N/A	N/A
	2. All other Phase I, Phase II, Phase III	30 (default)		N/A	N/A	N/A	
NDS SNDS ANDS	1. <b>Priority</b> - NAS, Clin or Non Clin data and C&M, Clin or Non Clin data only,	25	180	300	25	90	0
SANDS	2. <b>NOC/c</b> - NAS, Clin or Non Clin data and C&M, or Clin or Non Clin data only	25	200	300	25	90	30
EUNDS <sup>†</sup> EUSNDS <sup>†</sup>	3. NAS	45	300	300	45	150	0
EUANDS <sup>†</sup> EUSANDS <sup>†</sup>	4. Clin or Non Clin data and C&M	45	300	300	45	150	0
(For NDS-D and SNDS-D Disinfectants see section below)	5. Clin or Non Clin data only	45	300	300	45	150	0
	6. Clin or Non Clin data only, in support of safety updates to the labelling (SNDS/SANDS only)	25	120	120	7	75	0
	7. Comp data and C&M or Comp data only	45	180	180	45	150	0
	8. C&M data only	45	180	180	45	150	0
	9. Labelling only	45	120	120	45	75	0

Submission		Performance Standards (in calendar days)					
Type	Class	Screening 1 (including response to NOD)	Review 1 (including response to NOD)	CR review*	Screening 2 Response to NON	Review 2 Response to NON	Review of Response to NOC/c- QN
	10. Labelling only (Generic) (SNDS/SANDS only)	45	120	120	45	75	0
	11. Administrative	45 Administrative Screening		45	0	0	0
DINA, DINB	1. Labelling Standard	60		60	0	0	0
(For DIND Disinfectants see section below)	2. Clin or Non Clin data and C&M	45	210	210	45	150	0
	3. Clin or Non Clin data only	45	210	210	45	150	0
	4. Comp data and C&M or Comp data only	45	210	210	45	150	0
	5. C&M data only	45	210	210	45	150	0
	6. Labelling only	45	120	120	45	75	0
	7. Administrative	45 Administrative Screening		45	0	0	0
DINF	1. Labelling Standard	60		60	0	0	0
	2. Administrative	45 Administrative Screening		45	0	0	0
NC <sup>+</sup>	1. NC Quality (90 day) for biologics and radiopharmaceuticals	7	90	N/A	0	0	0
PDC <sup>+</sup>	1. Post-authorization Division 1 Change (Pharmaceuticals)	30		N/A	0	0	0
	2. Administrative	45 Administrative Screening		N/A	0	0	0
PDC-B <sup>+</sup>	1. Post-authorization Division 1 Change (Biologics)	45	210	N/A	45	150	0



Submission		Performance Standards (in calendar days)					
Type	Class	Screening 1 (including response to NOD)	Review 1 (including response to NOD)	CR review*	Screening 2 Response to NON	Review 2 Response to NON	Review of Response to NOC/c- QN
	2. Administrative	45 Administrative Screening		N/A	0	0	0

\*The Cost Recovery (CR) Review column defines the applicable performance standard associated with each activity and fee as per the Performance Standards for Fees in Respect of Drugs and Medical Devices Order.

The performance standard is the period from the date of acceptance to date of first decision not including any review clock pauses.

In the event that a drug submission (not including combination products or those subject to a joint/parallel foreign review) is not reviewed within the established CR performance standard, sponsors will be credited 25% of the fee originally paid. Please see the Guidance Document: Fees for the Review of Human or Disinfectant Drug Submissions and Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fees/fees-review-drug-submissions-applications.html>).

† Non cost-recovered submissions/applications

### **Disinfectants**

For more detailed information regarding disinfectants, please refer to the Guidance Document: Management of Disinfectant Drug Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/disinfectants/summary.html>).

Submission		Performance Standards (in calendar days)					
Type	Class	Screening 1 (including response to NOD)	Review 1 (including response to NOD)	CR Review*	Screening 2 Response to NON	Review 2 Response to NON	Review of Response to NOC/c- QN
NDS SNDS	1. Clin or Non Clin data and C&M	45	300	300	45	150	30
	2. Clin or Non Clin data only	45	300	300	45	150	30
	3. Clinical or non-clinical data only, in support of safety updates to the labelling	45	90	90	45	60	0

Submission		Performance Standards (in calendar days)					
Type	Class	Screening 1 (including response to NOD)	Review 1 (including response to NOD)	CR Review*	Screening 2 Response to NON	Review 2 Response to NON	Review of Response to NOC/c- QN
	4. C&M data only	45	300	300	45	150	0
	5. Labelling Only	45	90	90	45	60	0
	6. Administrative	45 Administrative Screening		45	0	0	0
DIND	1. Labelling Standard	60		60	0	0	0
	2. Clin or Non Clin data and C&M	45	210	210	45	150	0
	3. Clin or Non Clin data only	45	210	210	45	150	0
	4. C&M data only	45	210	210	45	150	0
	5. Labelling only	45	90	90	45	60	0
	6. Administrative	45 Administrative Screening		45	0	0	0
PDC-D <sup>†</sup>	1. Post-authorization Division 1 Change (disinfectants)	30		N/A	0	0	0
	2. Administrative	45 Administrative Screening		N/A	0	0	0

\*The Cost Recovery (CR) Review column defines the applicable performance standard associated with each activity and fee as per the Performance Standards for Fees in Respect of Drugs and Medical Devices Order.

The performance standard is the period from the date of acceptance to date of first decision not including any review clock pauses.

In the event that a drug submission (not including combination products or those subject to a joint/parallel foreign review) is not reviewed within the established CR performance standard, sponsors will be credited 25% of the fee originally paid.

Please see the Guidance Document: Fees for the Review of Human or Disinfectant Drug Submissions and Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fees/fees-review-drug-submissions-applications.html>).

† Non cost-recovered submissions/applications

## Appendix 4

Notes for the Performance standards for drug submission/application review table in Appendix 3

Glossary of abbreviations

**CTA**

Clinical Trial Application

**CTA-A**

Clinical Trial Application - Amendment

**NDS**

New Drug Submission

**SNDS**

Supplement to a New Drug Submission

**ANDS**

Abbreviated New Drug Submission

**SANDS**

Supplement to an Abbreviated New Drug Submission

**DIN**

Drug Identification Number

**NC**

Notifiable Change

**PDC**

Post-authorization Division 1 Change (PDC)

**PDC-B**

Post-authorization Division 1 Change for Biologics (PDC-B)

**DINA**

Application for a Drug Identification Number

**DINB**

Application for a DIN - Biological product

**DINF**

Application for a DIN - Category IV product

**DIND**

Application for a DIN - Disinfectant product

**NAS**

New Active Substance

**Clin**

Clinical

**Comp**

Comparative Studies (Bioavailability, Clinical, Pharmacodynamics or Pharmacokinetic)

**C&M**

Chemistry and Manufacturing (i.e. Quality)

**EUNDS**

Extraordinary Use New Drug Submission

**EUSNDS**

Supplement to an Extraordinary Use New Drug Submission

**EUANDS**

Abbreviated Extraordinary Use New Drug Submission

**EUSANDS**

Supplement to an Abbreviated Extraordinary Use New Drug Submission

**NOC**

Notice Compliance

**NON**

Notice of Non-Compliance

**NOD**

Notice of Deficiency

**NOL**

No Objection Letter

**NSN**

Not Satisfactory Notice

**NOC/c-QN**

Notice of Compliance with Conditions - Qualifying Notice

### Notes on terminology

**Class**

Submission class based on information included in submission (except for a NAS which applies a medicinal ingredient not previously approved in a drug for sale in Canada), corresponding to the fee class.

**NOC/c**

Submissions that have been accepted for advance consideration under the Notice of Compliance with Conditions Policy.

**Priority**

Submissions that have been accepted for priority status according to the Priority Review of Drug Submissions policy.

**Process of an Initial submission/application**

The 10-day processing period where OSIP verifies that the information submitted to HC in an initial submission is administratively complete to accept as a submission/application.

**Process**

The 10-day processing period where OSIP verifies that the information submitted to HC as a Response to SDN, Response to NOD, or Response to NON is administratively complete to accept as a submission/application.

**Screening 1**

Period from date of receipt to the date of acceptance, rejection, Screening Deficiency Notice or Withdrawal Unacceptable Response to NOD Screening.

**Review 1**

Period from date of acceptance to:

- a) A No Objection Letter or Not Satisfactory Notice issued for CTAs, CTA-As, NCs and PDC-Bs
- b) a NOD, NOD-Withdrawal, NON, NOC/c-QN or NOC issued for all other submissions

**Screening 2**

Period from date of receipt of response to NON to the date of acceptance or Withdrawal Unacceptable Response to NON Screening.

**Review 2**

Period from date of acceptance of response to the date of NON to NOC or NON-Withdrawal letter.

**Review of Response to NOC/c-QN**

Period from date of acceptance of response to NOC/c-QN sent under the Notice of Compliance with Conditions Policy.

## Appendix 5

### Types of administrative holds

Not applicable to CTA or CTA-As

#### **A. Process Hold - Initial**

OSIP will place the original information on Process Hold- Initial when additional information is required (e.g., a certification form), when the electronic data is not in CTD structure or when a validation report with error is issued. When the reason for the Process Hold - Initial is addressed, the submission then follows the standard submission processing route.

If additional information is required but has not been provided by the company within 10 days, a final letter is sent to the company notifying them that the information initially provided is considered administratively incomplete and the submission will be cancelled without prejudice to refiling.

#### **B. Cost Recovery Hold**

In accordance with the Guidance Document: Fees for the Review of Drug Submissions and Applications, a Drug Submission/Application Fee Form must be included with the information package at the time of filing, when applicable. In the event that the fee form or applicable fee is not provided, OSIP will request the form from the sponsor. Pending receipt of the fee form or the payment fee, the information will be placed on a Cost Recovery Hold. If the fee form is not received in a timely manner, the submission/application will not be accepted.

#### **C. Patent-Form V Hold**

For submissions subject to the provisions of the Patented Medicines (Notice of Compliance) Regulations, Health Canada is required to ensure that all relevant patents have been addressed through the filing of a Form V – Declaration Re: Patent List. OSIP will notify the sponsor when patent requirements are not met and the original information will be placed on Form V Hold. Once all the Form V requirements have been met, the received date will be entered and the submission will be sent to the relevant review Bureau/Centre.

#### **D. Data Protection Refused Hold**

Where a manufacturer seeks a Notice of Compliance (NOC) based on a direct or indirect comparison with an innovative drug, the manufacturer will not be permitted to file the submission for six years from the date of issuance of the NOC for the innovative drug. The manufacturer will be provided with a preliminary decision by letter informing it of the intent to reject the submission and granting a period to make representations in response. If, following consideration of the representations, the OPML remains of the view that the submission cannot be filed, and then the submission will be deleted.

#### **E. Process Hold**

A submission will be placed on Process Hold when the response to a NOD, NON or SDN is administratively incomplete (e.g., missing or incomplete form(s), or a validation report with error is issued).

If additional information is required but has not been provided by the company within 10 days, a final letter is sent to the company notifying them that the response will not be accepted.

When the missing information is received by OSIP, the received date will be entered and the response forwarded to the Review Centre/Bureau/Office.

#### **F. Switch Hold**

Upon approval of an application related to a switch in status from prescription to non-prescription, the submission is placed on switch hold pending the removal of the medicinal ingredient from the Prescription Drug List.

#### **G. Regulatory Hold**

When the scientific review of the submission is complete, and there are outstanding regulatory requirements, the submission will be placed on Regulatory Hold (e.g., completion of an On-Site Evaluation (OSE) related to the review of a biologic). A submission may also be placed on Regulatory Hold when there are pending related regulatory amendments.

#### **H. Intellectual Property Hold**

When the scientific review of a submission for a Division 8 product is complete and the submission is found to be in compliance, the sponsor will receive a notification that the submission has been placed on Intellectual Property Hold until the requirements of the Patented Medicines (Notice of Compliance) Regulations have been met and/or until the term of market exclusivity for an innovative drug in accordance with the data protection provisions at section C.08.004.1 of the Food and Drug Regulations has expired.

While on Intellectual Property Hold, subsequent SNDs, SANDSs, NCs and Post-Market Vigilance Data, will be accepted into review.

Once the above-mentioned regulations and provisions have been satisfied, the original NOC and subsequent NOCs or Letters of No Objection will be sent to the sponsor.

For further information on issues related to intellectual property, refer to the Guidance Document: Patented Medicines (Notice of Compliance) Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/patented-medicines/notice-compliance-regulations.html>) and the Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-data-protection-under-08-004-1-food-drug-regulations.html>).



## Appendix 6

### Issuance of decision documents

The following tables list the submission/application type or category (i.e., Division 1 or Division 8 drugs) and the individual responsible to sign the decision document.

#### Notice of Deficiency (NOD)

Division #	TPD	NNHPD (NDED)	BRDD
Division 8 Drugs	Director General	Director General	Director General
Division 1 Drugs (DINA <sup>22</sup> , DIND, DINB)	Director	Division Manager	Director General

#### No Objection Letter (NOL)

Type	TPD	NNHPD (NDED)	BRDD
CTA/CTA-A	Division Manager	N/A	Senior Regulatory Affairs Officer
Notifiable Changes (NC) (for human biologic or radiopharmaceutical drug quality changes)	N/A	N/A	Senior Regulatory Affairs Officer
Division 1 Drugs (DINA <sup>23</sup> , DIND, DINB <sup>24</sup> )	Director	Division Manager/Reviewer	Director General
PDC- pharmaceuticals	Director	Division Manager/Reviewer	N/A
PDC-biologics	N/A	N/A	Senior Regulatory Affairs Officer

#### Not Satisfactory Notice (NSN)

Type	TPD	NNHPD (NDED)	BRDD
CTA/CTA-A	Director General	N/A	Review Centre Director
Notifiable Changes (NC) (for human biologic or radiopharmaceutical drug quality changes)	N/A	N/A	Review Centre Director

PDC - pharmaceuticals	Director	Division Manager/Reviewer	N/A
PDC - biologics	N/A	N/A	Review Centre Director

#### Notice of Deficiency-Withdrawal (NOD-W)

Division #	TPD	NNHPD (NDED)	BRDD
Division 8 Drugs	Director General	Director General	Director General
Division 1 Drugs (DINA,DIND,DINB)	Director	Division Manager	Director General

#### Notice of Non-Compliance (NON)

Division #	TPD	NNHPD (NDED)	BRDD
Division 8 Drugs	Director General	Director General	Director General
Division 1 Drugs (DINA,DIND,DINB)	Director	Division Manager	Director General

#### Notice of Non-Compliance –Withdrawal (NON-W)

Division #	TPD	NNHPD (NDED)	BRDD
Division 8 Drugs	Director General	Director General	Director General
Division 1 Drugs (DINA,DIND,DINB)	Director	Division Manager	Director General

#### Notice of Compliance (NOC)

Division #	TPD	NNHPD (NDED)	BRDD
Division 8 Drugs	Director General Manager (Generics) Director (Administrative)	Director General	Director General

## Appendix 7

Health Canada has published numerous guidelines and policies to assist sponsors in the preparation and filing of drug submissions/applications. Sponsors of pharmaceutical or biological drug submissions/applications should refer to the Health Canada web site for guidelines and policies relating to a particular submission type of interest.

The following list of guidance documents and policies is not exhaustive and is meant to be read in conjunction with the MDSG.

### Guidance and policy documents on drugs

- 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/administrative-processing-human-disinfectant-drugs-2019/document.html>)
- Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-data-protection-under-08-004-1-food-drug-regulations.html>)
- Guidance Document: Data Requirements for Switching Medicinal Ingredients from Prescription to Non-Prescription Status (<https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/legislation-guidelines/guidance-documents/data-requirements-switching-medicinal-ingredients-prescription-to-non-prescription-status.html>)
- Guidance Document: Development Safety Update Report (DSUR) - International Conference on Harmonisation (ICH) Topic E2F (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/efficacy/guidance-document-development-safety-update-report-dsur-international-conference-harmonisation-topic.html>)
- 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>)
- Guidance Document: Fees for the Review of Human Drugs and Disinfectant Submissions and Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fees/fees-review-drug-submissions-applications.html>)
- Guidance Document for Industry: Review of Drug Brand Names (<https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-document-industry-review-drug-brand-names.html>)
- Guidance Document Questions and Answers: Plain Language Labelling Regulations for Non-prescription Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-questions-answers-plain-language-labelling-regulations-non-prescription-drugs-contact-lens-disinfectants.html>)

- Guidance Document Questions and Answers: Plain Language Labelling Regulations for Prescription Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/questions-answers-plain-language-labelling-2019/document.html>)
- Guidance Document - Management of Disinfectant Drug Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/disinfectants/summary.html>)
- Guidance Document: Non-prescription Drugs Labelling Standards - Drug Product (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/nonprescription-drugs-labelling-standards.html>)
- Guidance Document: Non-prescription Drugs - Category IV Monographs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/non-prescription-drugs-category-iv-monographs.html>)
- Guidance Document: Drug Facts Table for Non-prescription Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/public-involvement-consultations/natural-health-products/guidance-document-drug-facts-table-non-prescription-drugs.html>)
- Guidance Document: Electronic Canadian Drug Facts Table (eCDFT) Technical Standards (<https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-electronic-canadian-drug-fact-table-technical-standards.html>)
- Guidance Document: Notice of Compliance with Conditions (NOC/c) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>)
- Guidance Document on Post-Drug Identification Number (DIN) Changes (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-drug-identification-number-changes.html>)
- Guidance Document: Patented Medicines (Notice of Compliance) Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/patented-medicines/notice-compliance-regulations.html>)
- Guidance Document: Preparation of Drug Regulatory Activities in Electronic Common Technical Document (eCTD) Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html>)
- Guidance Document: Preparation of Regulatory Activities in “Non-eCTD Electronic-Only” Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html>)

- Guidance Document: Preparation of Drug Regulatory Activities in the Common Technical Document (CTD) Format (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/preparation-drug-regulatory-activities-common-technical-document-format.html>)
- Guidance Document: Submission and Information Requirements for Extraordinary Use New Drugs (EUNDS) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/submission-information-requirements-extraordinary-drugs-eunds.html>)
- Guidance for Industry: Priority Review of Drug Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html>)
- Guidance Document - Post-Notice of Compliance (NOC) Changes: Framework (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/framework-document.html>)
- Guidance Document - Post-Notice of Compliance (NOC) Changes: Quality (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/quality-document/guidance.html>)
- Guidance Document - Post-Notice of Compliance (NOC) Changes: Safety and Efficacy (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-document.html>)
- Guidance Document – Regulatory Requirements for Drug Identification Numbers (DIN) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/regulatory-requirements-drug-identification-numbers/document.html>)
- Guidance for Industry, Drug Submission Status Requests (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/drug-submission-status/guidance-industry-drug-submission-status-requests-therapeutic-products-directorate.html>)
- Guidance Document: Reconsideration of Decisions Sent for Human Drug and Natural Health Products Submissions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/reconsideration-final-decisions/reconsideration-final-decisions-issued-human-drug-submissions/guidance-document.html>)
- Notice - New requirements for submitting administrative drug submissions to Health Canada (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/announcements/new-requirements-submitting-administrative-drug-submissions.html>)

- Questions and Answers - Prescription Drug List (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/prescription-drug-list/questions-answers.html>)
- Guidance Document - Development Safety Update Report (DSUR) - International Conference on Harmonisation (ICH) Topic E2F (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/efficacy/guidance-document-development-safety-update-report-dsur-international-conference-harmonisation-topic.html>)
- Guidance Document - Classification of Products at the Cosmetic-Drug Interface (<https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/industry-professionals/guidance-document-classification-products-cosmetic-drug-interface.html>)

### Documents on clinical trials

- Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/clinical-trial-sponsors-applications.html>)

### Documents on medical devices and combination products

- Guidance Document: Management of Application for Medical Device Licenses and Investigational Testing Authorizations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/policies/management-applications-medical-device-guidance-2019/document.html>)
- Guidance Document: Factors Influencing the Classification of Products at the Device-Drug Interface (<https://www.canada.ca/en/health-canada/services/drugs-health-products/classification-health-products-device-drug-interface/guidance-document-factors-influencing-classification-products-device-drug-interface.html>)
- Classification of Health Products at the Device-Drug Interface (<https://www.canada.ca/en/health-canada/services/drugs-health-products/classification-health-products-device-drug-interface.html>)
- Policy on Drug/Medical Device Combination Products (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/policies/policy-drug-medical-device-combination-products-decisions.html>)
  - Policy on Drug/Medical Device Combination Products - Decisions (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/policies/policy-drug-medical-device-combination-products-decisions.html>)

## Documents on biologics

- Guidance Document: Annual update of seasonal influenza vaccines (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/annual-update-seasonal-influenza-vaccines.html>)
- Guidance Document: Blood Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/blood-regulations/guidance-document-blood-regulations-1.html>)
- Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs-1.html>)
- Lot Release - Guidance Documents - Applications and Submissions - Biologics, Radiopharmaceuticals and Genetic Therapies (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/release.html>)
- Yearly Biologic Product Reports: Questions and Answers (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/release/yearly-biologic-product-reports-questions-answers.html>)
- Guidance for Sponsors: Lot Release Program for Schedule D (Biologic) Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/release/guidance-sponsors-program-schedule-biologic-drugs.html>)

## Documents on pharmacovigilance monitoring

- Guidance Document: Submission of Risk Management Plans and Follow-up Commitments (<https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-document-submission-risk-management-plans-follow-commitments.html>)
- Annual Summary Report Checklist (including PSUR and PBRER) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/efficacy/annual-summary-report-checklist-including-psur-pbrer.html>)
- Notice - Adoption of the International Conference on Harmonisation (ICH) Guidance on Periodic Benefit Risk Evaluation Report - ICH Topic E2C (R2) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/efficacy/notice-adoption-international-conference-harmonisation-guidance-periodic-benefit-risk-evaluation-report-topic-march-1-2013.html>).

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- 1 Except for Blood Establishment Submissions and Submissions for annual updates of influenza vaccines. For information on the management of these submission types, refer to the Guidance Document: Blood Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/blood-regulations/guidance-document-blood-regulations-1.html>) and the Guidance Document: Annual update of seasonal influenza vaccines respectively (<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/annual-update-seasonal-influenza-vaccines.html>).
  - 2 Applicable only to clinical trials filed under Division 5 of the Food and Drug Regulations. For clinical trials filed under the Natural Health Product Regulations, refer to the Guidance Document: Clinical Trials for Natural Health Products (<https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/legislation-guidelines/guidance-documents/clinical-trials.html>).
  - 3 Refer to the Guidance Document: Post-Drug Identification Number (DIN) Changes (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-drug-identification-number-changes.html>)
  - 4 Refer to the Guidance Document: Post-Drug Identification Number (DIN) Changes (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-drug-identification-number-changes.html>) and the Guidance Document: Post-Notice of Compliance (NOC) Changes: Quality (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/quality-document/guidance.html>)
  - 5 When provided to TPD, BRDD and NNHPD as a standalone document (i.e. not as part of a submission).
  - 6 Not applicable to CTAs or CTA-As
  - 7 Refer to Appendix 7 for relevant guidance and policy documents.
  - 8 A pre-submission meeting is required as per the Guidance Document: Notice of Compliance with Conditions (NOC/C) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html>).
  - 9 A pre-submission meeting is required as per the Guidance Document: Drug Submissions Relying on Third-Party Data (<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>).
  - 10 Comparative submissions filed within the 6-year no-file period under the data protection provisions of the Food and Drug Regulations will be prevented from filing. Refer to the Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-data-protection-under-08-004-1-food-drug-regulations.html>).
  - 11 In NNHPD, some submissions are screened by the label reviewers.
  - 12 But not PSUR-Cs and PBRER-Cs.
  - 13 In NNHPD, Cancellation acknowledgement letters may be issued by the label reviewer.
  - 14 In NNHPD, Screening Rejection Letters may be issued by the label reviewer.
  - 15 Refer to the Guidance Documents: Post-Notice of Compliance (NOC) Changes (Safety and Efficacy or Quality). (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/safety-efficacy-2019/document.html>)



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(<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/quality-document/guidance.html>)

- 16 Expert Advisory Panels/Committees are convened in accordance with Health Canada's policy on External Advisory Bodies (<https://www.canada.ca/en/health-canada/corporate/about-health-canada/public-engagement/resource-centre/policy-external-advisory-bodies-health-canada-2011.html>)
- 17 Sponsors should note that the evaluation of the submission may not be complete at the time of NOD issuance.
- 18 Sponsors should note that the evaluation of the submission may not be complete at the time of NOD/W issuance.
- 19 Pursuant to sections C.01.014.2 (2) and C.08.004 (1) of the Food and Drugs Regulations.
- 20 Does not apply to combination of drugs and medical devices where the two drug components and/or drug and device components can be used separately (that is, products sold together in procedure packages and trays).
- 21 NNHPD (NDED) does not review Division 8 generic drugs (i.e., ANDSs/SANDSs). Refer to the Bureau of Pharmaceutical Sciences (BPS) for information for these submission types.
- 22 Not applicable to a DINA for a Labelling Standard or a Labelling Standard to a Category IV Monograph.
- 23 Not applicable to a DINF and a DINA for a Labelling Standard.
- 24 Approval Letters signed by the Director General are issued for all DIN-Bs.