Health Canada Santé Canada

Guidance Document

Preparation of regulatory activities in non-eCTD format

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Canada

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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Note about guidance documents in general

Guidance documents provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. They also provide guidance to Health Canada staff on how mandates and objectives should be met fairly, consistently and effectively.

Guidance documents are administrative, not legal, instruments. This means that flexibility can be applied. However, to be acceptable, alternate approaches to the principles and practices described in this document must be supported by adequate justification. They should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As always, Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, to help us adequately assess the safety, efficacy or quality of a therapeutic product. We are committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read along with the relevant sections of the Regulations and other applicable guidance documents.

Document change log

Date	Description
November 27, 2025	Revision required to update section 1.4 Scope and application to add biocides, 2.1 cover letter requirements, Appendix E to add examples of folder structures, to remove Appendix F Electronic Submission Gateway and minor revisions to improve clarity throughout the document.
May 08, 2024	Revision required to update the Appendix F: Electronic Submission Gateway, remove of the Appendix E: UDRA Table and revisions to improve clarity throughout the document.
June 09, 2023	Revision required to update the Appendix G Electronic Submission Gateway, mandatory use of web-based Master File Application form and minor revision to improve clarity throughout the document.
October 1, 2022	Revisions required for mandatory use of Regulatory Enrolment Process (REP) for veterinary drugs, transmission and top level folder requirements for Developmental Safety Update Reports (DSUR), cover letter changes for Master files, directorate name change to Pharmaceutical Drugs Directorate (PDD), new Electronic Submission Gateway (ESG) Accounts Management Portal and minor revision to improve clarity throughout the document.
February 28, 2022	Medical Device information has been removed, information for regulatory activities that are mandatory in eCTD format has been removed, and updated information has been provided for revised processes and requirements
October 31, 2016	Updates to Medical device and Veterinary Drugs
February 29, 2016	Div.1, Div.5, Div.8, DSUR, Post-market Vigilance, Level III, DNF and MF
September 25, 2015	Guidance Document: Preparation of Drug Regulatory Activities in non-eCTD Format
June 15, 2015	Notice: Health Canada's requirements for filing a regulatory activity in "non-eCTD electronic-only" format

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1. Introduction

1.1 Purpose and background

This document defines the filing requirements and provides guidance on the structure, content and transmission of regulatory transactions filed in the non-electronic common technical document (non-eCTD) format.

Health Canada has published requirements for the mandatory filing of specified regulatory activities in eCTD format. Refer to the Filing submissions electronically (FSE) information page for more comprehensive requirements on filing in electronic common technical document (eCTD) format.

Filing submission electronically (FSE) URL: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/filing-submissions-electronically.html

The non-eCTD guidance document was first published in 2015 and has been revised several times to reflect the onboarding of additional product lines to the non-eCTD format. This revision prescribes changes that have resulted since the previous version, stemming from various process implementations, such as the mandatory use of the eCTD format and the mandatory use of Regulatory enrolment process (REP).

Regulatory enrolment process (REP) URL: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/regulatory-enrolment-process.html.

1.2 Policy objectives

The objective of this document is to provide operational direction and guidance to sponsors and Health Canada staff on the requirements for the preparation of:

- Regulatory activities for human drugs and disinfectants* pursuant to Part C - Division 1 and Division 5 of the *Food and Drug Regulations*
- Regulatory activities for veterinary drugs pursuant to Part C - Division 1 and Division 8 of the *Food and Drug Regulations*
- Master files (MFs)
- Biocides

*Disinfectants authorized under the *Food and Drug Regulations* with DIN that have not yet transitioned to *Biocides Regulations*: https://www.canada.ca/en/health-canada/services/drugs-health-products/biocides/guidance/transition-to-regulations.html

1.3 Policy statements

Health Canada has established the following options that are available for filing regulatory activities in scope of this document and their related subsequent transactions:

Drugs and disinfectants for human use (Division 1)

- Health Canada accepts regulatory activities for Division 1 human drugs in non-eCTD format.
- Use of the Regulatory enrolment process (REP) is mandatory. Refer to the Regulatory enrolment process information page for detailed information.

- Regulatory activities for Division 1 human drugs can also be filed in eCTD format. Refer to the Filing submissions electronically page for detailed information related to the eCTD format.

Drugs for clinical trials involving human subjects (Division 5)

- Health Canada accepts clinical trial regulatory activities in non-eCTD format.
- Use of the REP is not available.
- Regulatory activities for clinical trials can also be filed in eCTD format. Refer to the Filing submissions electronically page for detailed information related to the eCTD format.

Positron-emitting radiopharmaceuticals (PERs) used in basic clinical research studies (Division 3)

- Health Canada accepts basic research applications: positron-emitting radiopharmaceuticals (BRAP) regulatory activities filed in non-eCTD format.
- Use of the REP is not available.

Veterinary drugs

- Health Canada accepts veterinary drug regulatory activities in non-eCTD format.
- Use of the REP is mandatory (except for Experimental studies certificates (ESC), Investigational new drugs (IND) and their amendments). Refer to the Regulatory enrolment process information page for detailed information.

Medical devices

- Health Canada accepts regulatory activities for medical devices in the IMDRF ToC format. Refer to the page of Guidance documents - Medical devices for detailed information.
- Use of REP is available for regulatory activities for medical devices. Refer to the Regulatory enrolment process information page for detailed information.

Master files

- Health Canada accepts regulatory transactions for existing master files in non-eCTD format where the master file number has already been assigned.
- Use of the web-based Master file application form is mandatory. https://health-products.canada.ca/mf-fm/en/master-file-form.html#def-top
- All new master files must be filed in eCTD format. Refer to the Filing submissions electronically information page for detailed information related to the eCTD format.

Biocides

- Health Canada accepts regulatory activities for biocides in non-eCTD format.
- Use of company and dossier enrolment of the REP is mandatory. Refer to the Regulatory enrolment process information page for detailed information.
- Use of the biocide application form (BAF) https://nnhpd-baf-fab-dpsnso.hc-sc.gc.ca/baf-fab/ is mandatory.
- Refer to the Biocides web page https://www.canada.ca/en/health-canada/services/drugs-health-products/biocides.html.

1.4 Scope and application

The following regulatory activities and related regulatory transactions are in scope for filing in non-eCTD format.

Human drugs and disinfectants - including administrative regulatory activities

Division 1

- Application for drug identification number (DINA)
- Application for drug identification number - biologic (DINB)
- Application for drug identification number - disinfectant (DIND)
- Application for drug identification number - category IV product (DINF)
- Post-authorization division 1 change (PDC)
- Post-authorization division 1 change - biologic (PDCB)
- Post-DIN notification
- Level 3 - Notice of change (for DINB only)
- Yearly biologic product report (YBPR) - biologic products
- Pre-submission meeting information (MPDIN)
- Undefined regulatory activity (UDRA)
- Post-market vigilance data when provided to the Marketed Health Products Directorate (MHPD)
    - Periodic safety update report (PSUR-PV)
    - Periodic benefit risk evaluation report (PBRER-PV)
    - Risk management plan (RMP-PV)
    - Post-authorization commitments (PA-PV)
    - Post-authorization act and regulations (REG-PV)
    - Issue related summary report (IRSR-PV)
    - Risk communication (RC-PV)
    - Patient safety/advertising ad-hoc post market request (PSA-PV)
    - Notification of foreign action (NFA-PV)

Division 5

- Clinical trial application (CTA)
- Clinical trial application - amendment (CTA-A)
- Clinical trial application - notification (CTA-N)
- Pre-clinical trial application consultation meeting (Pre-CTA)
- Developmental safety update report (DSUR)

Division 3

- Basic research applications: positron-emitting radiopharmaceuticals (BRAP)

Other

- Blood establishment (BE)

Veterinary drugs Division 1 and Division 8 - including administrative regulatory activities

- New drug submission (NDS)
- Abbreviated new drug submission (ANDS)
- Supplement to a new drug submission (SNDS)
- Supplement to an abbreviated new drug submission (SANDS)
- Notifiable change (NC)
- Application for drug Identification number application - veterinary (DINV)
- Periodic safety update report post-market vigilance (PSUR-PV)
- Experimental studies certificate (ESC)
- Experimental studies certificate (ESC) amendments
- Investigational new drug (IND)

- Investigational new drug (IND) amendments
- Protocol review (PRORE)
- Level 3 - Notice of change
- Pre-submission meeting (MPNDS, MPSNDS, MPANDS, MPSANDS, MPDIN, MDNC, MPESC)
- Notification of foreign action (NFA-PV)

Master files (existing master files only)

- Type I - Active substance master file
- Type II - Container closure system master file
- Type III - Excipient master file
- Type IV - Dosage form master file
- Type V - Facilities and equipment master file

Biocides

- New market authorization (BNMA)
- Biocide pre-submission meeting (BPSM)
- Post-authorization change (BPAC)
- Issue related report (IRR-PV)
- Post-authorization commitments (PA-PV)
- Post-authorization act and regulations (REG-PV)
- Notification of significant safety issue (NSSI-PV)
- Risk communication (RC-PV)
- Pre-submission meeting post market (MP-PV)

The regulatory information listed below are out of scope for filing in non-eCTD format.

- Products regulated under the *Natural Health Products Regulations*
- Site master files (submitted to Regulatory Operations and Enforcement Branch)
- Site reference file (SRF)
- Lot release documentation (group 1a, 1b, 2, 3, 4 fax-backs)
- Adverse reaction reports
- A response to a request issued under the Access to Information Act (ATIA)
- The annual drug notification form (ADNF) completed by the stakeholder
- New certificate of supplementary protection (CSP) applications
- CSP related correspondence
- Court documents (such as statements of claim, notices of application and notices of motion)
- Pipeline meeting

1.5 Definitions

Biocide identification number: A computer-generated 8-digit number assigned by Health Canada to a biocide that has been issued a market authorization under the *Biocides Regulations*.

Control number (submission number): A 6 digit unique number assigned by Health Canada in the drug submission tracking system (DSTS) for each regulatory activity submitted by a stakeholder.

Dossier: A collection of all regulatory activities throughout the life cycle of a product or products for a stakeholder.

For clinical trials, it is a collection of all regulatory activities throughout the life cycle of a single clinical trial protocol.
For biocides, it is a collection of biocide product(s) under one biocide market authorization for a company.

Dossier Identifier (ID): A code assigned by Health Canada to uniquely identify the dossier. The dossier ID is also called the top-level folder name. It consists of a lowercase letter followed by a unique set of 6 or 7 digits depending on the regulatory activity type.

Drug identification number (DIN): A computer-generated 8-digit number assigned by Health Canada to a drug upon market authorization under subsection C.01.014.2 (1) of the *Food and Drug Regulations*.

Drug submission tracking system - Industry access (DSTS-IA):
A web-based portal allowing access to information such as submission numbers, dossier IDs and submission statuses for specific drug submissions for authorised companies. Users require accounts to access this information. An account can be requested by emailing the Client Information Unit at client.information@hc-sc.gc.ca.

Drug substance (drug substances or intermediates in the production of drug substances): A pharmacologically active ingredient.

Electronic submissions gateway (ESG): a gateway used for a secure transmission of electronic transactions sent from a sponsor to Health Canada.

Leading sheet: A document describing the information being provided (for example, a document stating "this sub-folder contains the following documents…").

Master file (MF): A reference that provides information about specific processes or components used to manufacture, process or package a drug.

Non-eCTD validation rules: Rules used to validate every transaction received to Health Canada via the electronic gateway, by email or on media. Rules are posted on Health Canada's website.

Protocol number: A protocol number is a variable length, alpha-numeric sequence used by stakeholders to assign a reference number to their protocol. The protocol number for clinical trials should remain the same for the duration of the trial.

Regulatory activity: A collection of all regulatory transactions throughout the process of a specific activity.

Regulatory enrolment process (REP): facilitates the filing and processing of regulatory information related to:

- company
- dossier and product
- regulatory activity
- regulatory transaction

REP consists of web-based templates that capture information in a structured format. The REP templates replace existing Health Canada application and fee forms.

This process enables a move towards a common submission intake across product lines and allows Health Canada to automate the receipt and import of regulatory transactions into its repositories.

Regulatory transaction: Any information package sent by the stakeholder as part of a regulatory activity such as initial data, unsolicited and solicited data (for example, response to a clarification request, response to notice of non-compliance (NON), response to notice of deficiency (NOD) or drug notification form (DNF)).

Solicited and unsolicited information: Solicited information is considered any information that is requested by Health Canada during the processing, screening or review of a submission and application. For more details about solicited and unsolicited information, see *Guidance Document: Management of Drug Submissions and Application*.

Stakeholder: Company, sponsors, DIN owner, manufacturer of pharmaceutical or biological drug for regulatory activities filed according to the *Food and Drug Act* and its regulation, and owner, agent, manufacturer for master file.
For biocides (market authorization holder), a person who hold the market authorization for a biocide issued under the regulations.

2. Structure and content

All regulatory activities and subsequent regulatory transactions that are filed for review to Health Canada must be provided using the appropriate folder structure and document placement. Failure to file a transaction using the correct folder structure may result in the transaction not being accepted by Health Canada.

- General requirements for folder structures based on product lines are provided in this guidance document.
- Zipped folder structures, for specific product lines, are available on the Filing submissions electronically information page. Stakeholders can use them to build a regulatory transaction for filing to Health Canada.
- Document placement: details on the correct module 1 sub folders to place the documents in the regulatory transaction for human drugs and disinfectants, can be found on the Organization and document placement for Canadian module 1 document available on the Filing submissions electronically information page.
- For figures of the sample folder structures refer to Appendix E. The folders and subfolders shown in the figures are not exhaustive. Additional folders or subfolders may need to be added or removed depending on the regulatory activity and transaction submitted to Health Canada.

2.1 Cover letter

The cover letter provides a brief description of what is in a regulatory transaction, which is used to support the processing of the transaction. Every regulatory transaction must be filed with a cover letter, except for:

- transactions that contain the PDF form: Post NOC changes - level III (for DINB only)
- transactions that contain the PDF form: Notifying Health Canada of foreign actions in respect of a serious risk of injury to human health

For all other transactions related to Level III and NFA-PV regulatory activities, such as responses to information requests, a cover letter that clearly indicates the name of the requester as well as the intent of the filing is still to be provided in order to facilitate the processing of the regulatory transaction.

The information entered on the REP regulatory transaction template, master file application form or the biocide application form must align with the information on the cover letter. Delays will occur if conflicting information is provided, as Health Canada will need to confirm the intent to accurately process the transaction.

General cover letter requirements:

- Regulatory transactions that are sent on media should include a paper cover letter in addition to the electronic copy.
- A cover letter must be less than 4 pages in length.
- A signature is not required on the cover letter.
- Supporting data should not be included.
- A cover letter should contain the details, as outlined below.

Required details for all cover letters:

- Clearly state what is being provided
- Reason for filing
- Stakeholder name, role, phone number and email address
- Brand name
- Dossier Identifier (ID) - if using REP and for all master files
- Regulatory activity type
- Control number (if known)
- Include reference to a correspondence or a request letter issued by Health Canada (including an advisement letter) (if applicable)
- Clearly state any cross-referenced regulatory activity (include the date the regulatory activity was approved)
- Indicate the email address where the validation report should be sent
- Responses to requests for clarification should clearly indicate the name of the requester

Cover letters for the following transactions require extra information, in addition to the details above:

- Other sale notifications:
    - Notification for interruption of sale (DIN dormant) should indicate:
        - DIN(s) affected
        - Date the product was last sold or the last day of the 12-month period without sale
    - Discontinuation of sale notification should indicate:
        - DIN(s) to be cancelled
        - Discontinuation date
        - If the product was previously marketed, the lot number and expiry date of the last lot distributed in Canada

For biocides: when providing sale notifications for biocides, consult the BAF user guide, sales-related information section.

- DSUR should also indicate which of the following applies:
  - Requested - requested by Health Canada
  - Voluntary - important new safety information

- Clinical trial regulatory transactions should include the relevant protocol number.

- Master files:
  - conversions and reactivations must indicate if a new letter of access is included that has not been previously registered
  - letters of access withdrawals should indicate the company name for which the access is being withdrawn
  - agent name changes or agent withdrawals should indicate the agent name

- DINA regulatory activities should indicate if there is a labelling reference product.

The cover letter must not contain the following:

- Scientific information
- Summary response in a question and answer format
- Response to request for additional information
- List of documents provided in the transaction

2.2 Folder structure and file naming convention

The content of the regulatory transaction must be organized in folders. Multiple documents must not be bundled into one file, but instead provided as separated documents. Each file or document must be placed in the right subfolders of the appropriate structure. The complete folder structure for certain product lines is available as zipped file on the Filing submissions electronically information page. These zipped files can be downloaded and used to prepare a regulatory transaction for filing:

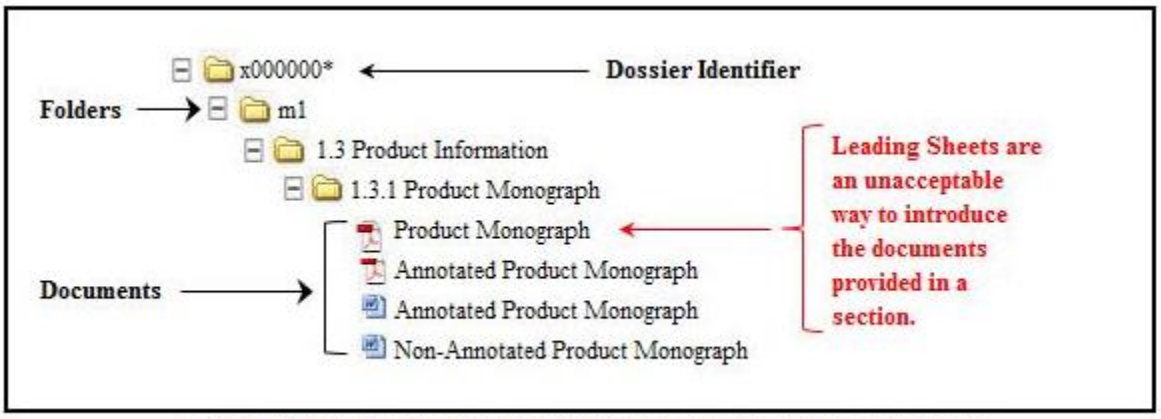
- Human drugs, disinfectants and clinical trial applications (division 1 and 5)
- Master files
- Veterinary drugs (Division 1 and 8)
- Biocides

The following are common folder structure errors to avoid:

- The top-level folder must be the dossier ID for regulatory transactions using:
  - REP regulatory transaction (RT XML file) or
  - master file application form (XML file) or
  - biocide application form (HTML and XML file); otherwise, the transaction will fail validation.
- The top-level folder must not contain any files. It should only contain the required sub-folders (m1 or part I).
- Multiple documents provided as a single PDF file is not acceptable.
- Information already provided in previous transactions must not be provided again unless it is affected by a change.
- Do not include empty folders in the structure. If you are using the zipped folder structures, ensure to delete all subfolders that do not contain a file before sending the transaction to Health Canada.

- Do not include leading sheets at the beginning of sub-folders (indicating a folder is not applicable or describing the content).

Figure 1: Leading sheet



* A letter followed by 6 or 7 digits depending on the regulatory activity type.

For a detailed list of what files and documents to include in each folder for human drugs, disinfectants and clinical trial applications, refer to the document Organisation and document placement for Canadian module 1. For information on modules 2 to 5 of the CTD structure, refer to the M4: The Common Technical Document (CTD) developed by the International Council for Harmonisation (ICH).

For a detailed list of what files and documents to include in each folder for veterinary drugs transactions refer to Appendix V: Master Index of the Guidance for Industry Preparation of Veterinary New Drug submissions.

For a detailed list of what files and documents to include in each folder for biocides transactions, refer to the section "Folder structure and document placement" of the guidance on Management of Biocide Applications.

2.2.1 Top level folder and dossier identifier

The top-level folder is the main folder of a regulatory transaction that is filed to Health Canada and must be included with every transaction. All the subfolders and content files are located within the top-level folder.

The top-level folder must be the dossier identifier (dossier ID), unless specified otherwise below. The dossier ID is a lower case letter:

- followed by 6 digits for pharmaceutical, biological, clinical trial, veterinary and biocide dossiers
- followed by 7 digits for master file dossiers

All regulatory activities and associated transactions for a dossier must be filed under the same dossier ID. For product line specific details, see sections below and Table 1: Dossier information.

Human drugs and disinfectants

A dossier ID must be requested using the dossier ID request form for pharmaceutical and biologic dossiers before filing.

For an existing dossier where the dossier ID is unknown, use the Drug submission tracking system - Industry access (DSTS-IA) to find the assigned dossier ID. Do this by searching for a recent regulatory activity submitted to Health Canada that has the same medicinal ingredient(s) and brand name as the one you intend to file. For information on creating a DSTS-IA account, contact client.information@hc-sc.gc.ca.

Note: For regulatory transactions being filed under the administrative pathway, a new dossier ID may be required. For details refer to the "Help Text 6" on the dossier ID request form.

Veterinary drugs

A dossier ID must be requested using the dossier ID request form for veterinary drugs before filing.

For an existing dossier where the dossier ID is unknown, use the Drug submission tracking system - Industry access (DSTS-IA) to find the assigned dossier ID. Do this by searching for a recent regulatory activity submitted to Health Canada that has the same medicinal ingredient(s) and brand name as the one you intend to file. For information on creating a DSTS-IA account, contact client.information@hc-sc.gc.ca.

Alternatively, you can contact veterinary drug directorate (VDD) at vdd.skmd.so-dgps.dmv.cp@hc-sc.gc.ca.

Note: For regulatory transactions being filed under the administrative pathway, a new dossier ID may be required. For details refer to the "Help Text 5" on the dossier ID request form.

The dossier ID request does not apply to experimental studies certificate (ESC), investigational new drug (IND) and their amendments.

Clinical trials and DSUR

For the first transaction associated with a new protocol, the top-level folder must be the product name or the protocol number. The dossier ID will be issued upon receipt of the pre-submission meeting or clinical trial application and must be used for all subsequent transactions associated with this protocol.

For the first transaction associated with a new DSUR, the top-level folder must be the product name. The dossier ID will be issued upon receipt of the DSUR and must be used for all subsequent DSURs or DSUR related transactions.

The dossier ID request does not apply to clinical trials.

Master files

If you do not know your master file number, contact the Master File Administration Unit at dmf.enquiries-fmm@hc-sc.gc.ca.

The dossier ID request form does not apply to master files.

Biocides

A dossier ID must be requested by completing the dossier ID request form for biocides.

Note: Previously issued "d" dossiers for disinfectants regulated under the *Food and Drug Regulations* cannot be used to file transactions under the *Biocides Regulations.* The "d" dossiers can only be used if you are continuing to file under the *Food and Drug Regulations* before transitioning to *Biocides Regulations*.
Transition of disinfectants to the *Biocide Regulations*: https://www.canada.ca/en/health-canada/services/drugs-health-products/biocides/guidance/transition-to-regulations.html

Where applicable, a request for a dossier ID should be sent a maximum of 8 weeks before filing a regulatory transaction. Dossier IDs that have not been used within 12 months of their issuance are automatically deleted from Health Canada's tracking system without any notification to the sponsor. If a sponsor intends to use a dossier ID that has been deleted, a new dossier ID request form will be required. However, the request should indicate the previously issued dossier ID.

Table 1: Dossier information

Dossier type	**Dossier ID format**	**Dossier ID request**
Pharmaceutical	dXXXXXX*	Dossier ID request form: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/filing-submissions-electronically/pharmaceutical-dossier-template.html
Biological	dXXXXXX*	Dossier ID request form: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/filing-submissions-electronically/pharmaceutical-dossier-template.html
Veterinary	vXXXXXX*	Dossier ID request form: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/filing-submissions-electronically/veterinary-dossier-template.html with exception to ESC, IND and their amendments
Clinical trial	cXXXXXX*	Dossier ID request does not apply
Master file	fXXXXXXX**	Dossier ID request does not apply
Biocide	qXXXXXX*	Dossier ID request form: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/filing-submissions-electronically/dossier-id-request-form-biocide.html

*followed by 6 digits for pharmaceutical, biological, clinical trial, veterinary and biocide dossiers
**followed by 7 digits for master file dossiers

2.2.2 Common technical document (CTD) folder structure

The ICH CTD structure must be used to organize the documents provided for human drug and disinfectant regulatory transactions, pursuant to division 1, division 5 and master files. This structure consists of 5 modules, each containing multiple subfolders to be used for specific documents.

Module 1 folders

The requirements for module 1 of the CTD structure is regional and therefore defined by Health Canada. Refer to the Organisation and document placement for Canadian module 1, for detailed list of documents required in each subfolder in this module.

Additional module 1 requirements for:
Clinical trials

- When filing clinical trial applications, stakeholders may also refer to "Table 1: Contents of Submission Package in accordance with CTD Format" of the Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications for further clarity.

Master files

- When providing MF Types I, II, III, IV and V the folders in module 1 will be considered as the Restricted Part (RP). See Appendix C of this document for illustrations.
- Refer to the Guidance on procedures and administrative requirements for master files as well as the folder structures provided in Appendix C of this document for more information on the structure of module 1 for each MF type.

Modules 2 to 5 folders

The structure and names of the modules 2 to 5 folders are defined in the M4: Common Technical Document found on the International Council for Harmonisation (ICH) website.

When providing information in the module 3: Regional information section, the following subfolders should be created for specific documents:

- 3.2.R.1 Production documentation
- 3.2.R.2 Medical devices
- 3.2.R.3 Lot release documentation
- 3.2.R.4 Yearly biologic product report
- 3.2.R.5 Assessment of similarity
- 3.2.R.6 On site evaluation
- 3.2.R.7 Other regional information
- 3.2.R.8 Product lifecycle management information

Additional module 2 to 5 requirements for:
Clinical trials

- For clinical trial applications, stakeholders may also refer to "Table 1: Contents of Submission Package in accordance with CTD Format" of the *Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications* for further clarity.

- Literature references for non-clinical or clinical studies, should be placed in module 4 (section 4.3 literature references, non-clinical related) or module 5 (section 5.4 literature references, clinical related). Study related information, such as study synopses, study summary, should be placed in appropriate sections and subsections of module 4 and module 5 respectively.

Master files

- MF types I and IV, two separate documents (both in PDF and Word format) should be included in the folder "2.3 Quality Overall Summary," a "QOS (RP)" and a "QOS (AP)" file.

- MF Type I - Drug substance (for illustration see figure C-1):
  - The folder "3.2.S Drug Substance" should be duplicated and each clearly identified as either the applicant's part or the restricted part using the abbreviations "AP" or "RP" respectively.
  - The folder "3.2.A Appendices" will be considered as the restricted part (RP).

- MF Type II - Container closure systems (for illustration see figure C-2), there are two possible options for structuring the folders in module 3:
  - A separate subfolder under "3.2.P.7 Container Closer System" can be used for each component provided, or
  - The folder "3.2.P Drug Products" (with all its subfolders) can be used for information that is common to all components and separate subfolders under "3.2.P.7 Container Closer System" can be used for information specific to each component.

- MF Type III - Excipients (for illustration see figure C-3):
  - The folder "3.2.P.4 Control of Excipients" in module 3 should be duplicated for each excipient provided.

- MF Type IV - Drug products (for illustration see figure C-4):
  - The folder "3.2.P Drug Products" should be duplicated and each clearly identified as either the applicant's part or the restricted part using the abbreviations "AP" or "RP" respectively.
  - The folders "3.2.A Appendices" and "3.2.R Regional Information" will be considered as the restricted part (RP).

- MF Type V - Facilities and equipment:
  - All facility and equipment information should be provided in the folder “3.2.A.1 Facilities and Equipment”.

A zipped folder structure is also available on the Filing submissions electronically page to assist stakeholders in preparing their regulatory activities.

2.2.3 Veterinary drugs folder structure

The structure and name of the folders for veterinary drug regulatory activities are defined in Appendix V: "Master Index" of the Guidance for Industry: Preparation of Veterinary New Drug Submissions.

Addition information on document placements:

Section 1.1 Cover letter can be used to place documents such as cover letter, pre-submission meeting request (.pdf) or notification of foreign action (NFA) form (.pdf).

Section 1.5 Drug submission application can be used to place the regulatory transaction REP RT XML file and the product information REP PI XML file.

Section 1.12 Submission and product summary can be used to place documents such as Health Canada issued correspondence (.pdf), summary response in a question and answer format (.pdf and .word), periodic safety update report (PSUR), meeting package, meeting slides, meeting minutes, drug notification form (DNF) and post-notice of compliance changes: level III form.

A zipped folder structure is also available on the Filing submissions electronically page to assist stakeholders in preparing their regulatory activities.

2.2.4 Biocides folder structure

The structure and name of the folders for biocides regulatory activities are defined in the "Folder Structure and Document Placement" section of the Guidance on Management of Biocide Applications.

A zipped folder structure is also available on the Filing submissions electronically page to assist stakeholders in preparing their regulatory activities.

2.3 File naming convention

Except for the file extension, the file naming convention within each folder is left to the stakeholder preparing the regulatory transaction. However, Health Canada suggests that the file names are kept as brief and meaningful as possible, while adhering to the following:

- File names should describe the content in a meaningful way and must be limited to a maximum of 50 characters, including the file extension.
- Commonly used and meaningful abbreviations, such as QOS for quality overall summary, may be used to shorten file names.
- Files provided electronically must not be password protected.
- .xml file names of application forms (RT, MF, BAF) are system generated and must not be modified.

3. Technical requirements for regulatory activities

3.1 File format

Electronic documents should be provided in PDF format (portable document format, saved as PDF versions 1.4, 1.5, 1.6, 1.7, PDF/A-1 and PDF/A-2) unless otherwise specified in table 2. PDF documents with attachments are not allowed.

The documents in the Table 2 must be provided in either PDF, Word 365 format(s) or both as specified.

PDF documents should be generated from electronic source documents and not from scanned materials, except where access to an electronic source document is unavailable or where a signature is required.

It is important that PDF files are properly bookmarked:

- Documents that are more then 10 pages should be bookmarked.
- Bookmarks are used by Health Canada as a document table of contents and should not include the regulatory activity level.

- Sections, subsections, tables, figures, and appendices should all be bookmarked.
- Do not create more than four levels of bookmarks:
    1 Heading
        1.1 Subheading
            1.1.1 Sub-subheading
                1.1.1.1 Sub-Sub-Subheading

Health Canada recognizes that bookmarks are generated automatically from document headings, but recommends they be kept concise.

It is important that PDF files be properly hyperlinked:

- Hyperlinks within the same PDF document are acceptable, but hyperlinks between different documents are not to be used.
- It is the responsibility of the stakeholder preparing the regulatory transaction to ensure that hyperlinks are functioning.
- Links must also include references to the specific section or page in the event the link is broken.
- The required hyperlinks to related information should be included only in the PDF version of files.

Table 2: Specific file format requirements

List of documents provided with human drugs		**File Format***	
		PDF	**Word**
Certified product information document (CPID)	Annotated	√	-
	Non-annotated	-	√
Comprehensive summary: bioequivalence		√	√
HC-SC3011 form (clinical trial applications only)		√	-
Label safety assessment update - sponsor attestation		√	√
Product monograph (PM)/prescribing information	Annotated	√	√
	Non-annotated	-	√
	Second language	√	-
Protocol safety and efficacy assessment template (PSEAT) - CTA		-	√
Quality overall Summary (QOS)	Clinical trial applications	-	√
	All other regulatory activities in scope of non-eCTD format	√	√
Response document for responses to clarification requests, SDN, NON, NOD		√	√
('**√**' = Required '-' = Not applicable)			
* When PDF **and** Word are selected, the document should be provided in both formats * HC-SC3011 can be provided in PDF **or** Word format. Both formats are not required.			

- Presentations for meetings with Health Canada (for example pre-submission meetings), can be provided in PowerPoint (.pptx) format.
- Division 1 - The "BE data sets" must be provided in ASCII format. For more information, see Health Canada's *Guidance for Industry: Preparation of Comparative Bioavailability Information for Drug Submissions in the CTD Format*, Appendix B: "Computer Format for the Submission of Data for Comparative Bioavailability Studies".
- Regulatory Enrolment Process (REP) files must be provided in XML format.
- Master file application form must be provided in XML format.

- Biocides application form (BAF) must be provided in .html format (including the .xml file as generated upon finalization).

To obtain a complete list of acceptable file formats, refer to the non-eCTD validation rules.

Contact us for other file formats that may be acceptable. See Appendix B for contact information.

3.2 Signatures

Documents that legally require signatures may be signed with an electronic signature (an image of the official's wet ink signature, digital signature), or the signature page can be printed, signed, scanned and saved as a PDF file.

If only one page of a multi-page PDF document contains a signature, the stakeholder should scan that page and then include the scanned page at the same location in the PDF file of the document. Each document should have only one PDF file.

Certain Health Canada documents, such as the electronic PDF fillable form available on the Health Canada website, may have alternate instructions for signatures.

The cover letter does not require a signature. However, contact information, including printed name, phone number and email address, should be provided.

3.3 Validation of transaction

All regulatory transactions should be validated before being transmitted to Health Canada. For non-eCTD validation rules refer to the posted validation rules on Health Canada's website.

3.4 Transmission of electronic data

The acceptable methods of transmission are ESG, media and email. All other methods of transmission, such as Dropbox and secure FTP sites, are not acceptable.

3.4.1 Electronic submission gateway (ESG)

The use of the ESG is mandatory to the following regulatory transactions:

- Transactions within scope of REP [drugs and disinfectants for human use (Division 1), veterinary drugs]
- Master file transactions
- Biocide transactions

Before using the gateway, stakeholder must create a gateway account. For more information, refer to the ESG information page.

3.4.2 Media

Regulatory transactions not accepted by ESG, should be provided on media. A paper copy of the cover letter and media should be mailed to the appropriate address as indicated in Appendix B of this document.

The accepted media formats for providing regulatory transactions are:

- Compact disc-recordable (CD-R) conforming to the Joliet specification
- Universal serial bus (USB) 2.0 or 3.0 drive
- Digital Versatile disc (DVD-RAM and DVD+R/-R) in universal disk format (UDF) standard

All media must be labelled with the following information:

- Stakeholder name
- Brand name

After burning the CD, DVD or transferring data to an USB, stakeholders should ensure that all files can be opened, files are not corrupted, and "Thumb.db" files are removed.

Clinical trial and DSUR

Clinical trial and DSUR transactions must be sent directly to the relevant directorate either Office of Clinical Trials at PDD for Pharmaceuticals or Office of Regulatory Affairs at BRDD for biologics and radiopharmaceuticals using the address provided in Appendix B of this document.

3.4.3 Email

The below specified regulatory transactions may be provided to Health Canada by email. However, the stakeholder assumes the risk of transmitting "Protected B" information through email.

Regulatory transactions provided by email must meet the following requirements:

- The maximum email size is 20 megabytes, anything larger should be sent on media.
- If the regulatory transaction is provided by email, a duplicate copy must not be provided by mail.
- The regulatory transaction must be organized in folders (see section 2.2 of this guidance document) and provided as a zipped file.
- The body of the email should only contain the zipped regulatory transaction No other documents or related information should be included.
- Zipped documents contained in the email should not be password protected.

Clinical trials

If the clinical trial related transaction is larger than 20 megabytes, the transaction may be split and sent as separate emails. For example, one email for module 1, and one email for modules 2 and 3. The subject lines of the emails should clearly indicate their sequence and connection. For example, “Email 1 of 2” followed by a relevant subject.

- Responses to a clarification request (IR) for clinical trials should be sent by email:
  - email should be addressed to the requestor(s) identified in the clarification request
  - the subject line of the email should include the statement:
    - Division 5 - IR - protocol number(s) - control number(s)
  - the zipped file should be named:
    - IR - protocol number(s) - control number(s)
- Responses to a no objection letter (NOL) for clinical trials should be sent by email to:
  - brdd.cta-dec.dmbr@hc-sc.gc.ca for biologic and radiopharmaceutical drugs
  - oct.smd-dgp.bec@hc-sc.gc.ca for pharmaceutical drugs
  - the subject line of the email should include the statement:

        - Division 5 - response to NOL - protocol number(s) - control number(s)
    - the zipped file should be named:
        - response to NOL - protocol number(s) - control number(s)
- Clinical trial application notifications (CTA-N) should be sent by email to:
    - brdd.ctan-ndec.dmbr@hc-sc.gc.ca for biologic and radiopharmaceutical drugs
    - oct.ctan-ndec.bec@hc-sc.gc.ca for pharmaceutical drugs
    - the subject line of the email should include the statement:
        - Division 5 - CTA-N - protocol number(s) - parent CTA control number(s)
    - the zipped file should be named:
        - CTA-N - protocol number(s) - parent CTA control number(s)
- DSURs should be sent by email to:
    - brdd.cta-dec.dmbr@hc-sc.gc.ca for biologic and radiopharmaceutical drugs
    - pdd-pv-dmp@hc-sc.gc.ca for pharmaceutical drugs
    - the subject line of the email should include the statement: DSUR - drug name
    - the zipped file should be named: DSUR - drug name
- Basic research application PERS (BRAP) regulatory transactions should be sent by email to brdd.bra-daerf.dmbr@hc-sc.gc.ca.

3.5 Technical evaluation of a regulatory transaction

Upon receiving a regulatory transaction, Health Canada conducts a technical evaluation to ensure that it conforms to the requirements outlined in this and other applicable documents available on the Filing submissions electronically information page.

At each stage of technical evaluation, Health Canada will issue written correspondence by email if any errors or deficiencies are identified in the transaction. Stakeholders may reply to the email to discuss these issues in greater detail.

When required, the stakeholder must correct the previously submitted regulatory transaction and re-file it to Health Canada in a timely manner. The re-filed transaction undergoes technical evaluation again. This process is iterative.

During the technical evaluation, the document content of the regulatory transaction is not reviewed.

3.5.1 ESG compliance

For transactions received through ESG, the first stage of technical evaluation includes, but is not limited to, extracting the transaction, verifying the regulatory transaction xml file, verifying the top-level folder, and checking the folder file path.

If any issues are identified at this stage, written communication, sometimes including the validation report, will be sent to the stakeholder by email.

3.5.2 Technical validation

The technical validation is conducted by a validation software using the latest published validation rules for transactions in non-eCTD format.

If any validation errors are identified at this stage, a validation report describing the errors will be emailed, as a PDF attachment, to the stakeholder.

3.5.3 Processing and manual verification

The third stage is carried out according to the processing section and associated timelines outlined in the applicable guidance documents: *Management of drug submissions and applications, Procedures and administrative requirements for master files, and Management of Biocide Applications*. This stage also includes verifying the dossier type, dossier ID and folder structure.

4. Important considerations

1. For transactions sent incorrectly through the ESG, the stakeholder must notify Health Canada by email before either modifying or resending the transaction through ESG. Health Canada will provide instructions on how to proceed. Do not resend without consultation and confirmation.
2. Issues identified during the technical evaluation such as extraction problems, missing XML file, validation errors, incorrect dossier type, or dossier ID discrepancies will result in Health Canada sending written correspondence (including the validation report, when applicable). To resolve these issues, stakeholders must correct the failed transaction and re-submit the entire transaction (submission). However, if Health Canada is requesting missing documents, new documents, or corrections to certain documents (identified during processing, screening, or review of the regulatory submission), then these types of responses require a subsequent transaction containing only the requested documents. In these cases, addressing the deficiency is sufficient, and in your subsequent transaction, do not re-submit the entire original submission. Instead, include a new cover letter explaining the reason for filing, copy of the issued correspondence, regulatory transaction XML file (MF XML for master files, BAF HTML for biocides) and the requested documents.
   The information on how to file a transaction that failed validation or has missing or incorrect documents is always outlined in the correspondence issued by Health Canada.
3. The content of the regulatory activity in non-eCTD format is the legal document. Therefore, convenience copies provided directly to Health Canada staff by email (with the exception of those indicated in section 3.4.3 of this document) have no legal value and will not be uploaded on the Health Canada internal systems.
4. When providing MF Types I, II, III, IV and V, the folders in module 1 will be considered as the Restricted Part (RP). See Appendix C of this document for illustrations.
5. Stakeholders who are unsure of which regulatory activity type to file should contact the applicable review bureau to confirm before filing. Refer to Appendix B for contact information.
6. For human drugs switching from non-eCTD to eCTD format is permitted with a new regulatory activity (sequence 0000 must be the first transaction for a new regulatory activity) or once a regulatory activity has been cleared (sequence 0000 can be post-clearance data). Switching format in the middle of screening and review is not permitted (sequence 0000 cannot be a response to clarification request).
   For master file conversions from non-eCTD to eCTD format, refer to the *Guidance on procedures and administrative requirements for master files*.

Appendices

Appendix A: Other resources

This resource should be read in conjunction with, but not limited to the following resources:

- Documents available on the Filing submissions electronically page

- Documents available on the REP information page
- *Guideline on Preparation of Drug Identification Number Submissions*
- *Guidance Document on Post-Drug Identification Number (DIN) Changes*
- *Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications*
- *Guidance on management of drug submissions and applications*
- *Guidance Document: Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs*
- *Guidance on procedures and administrative requirements for master files*
- *Guidance for Industry Preparation of Veterinary New Drug Submissions*
- *Guidance for Industry - Management of Regulatory Submissions (for Veterinary Drugs)*
- *Guidance for Industry - Preparation of Veterinary Abbreviated New Drug Submissions - Generic Drugs*
- *Draft Guidance for Industry: Preparation of Comparative Bioavailability Information for Drug Submissions in the CTD Format*
- *Guidance on Management of Biocide Applications*

Appendix B: Contacts

General enquiries electronic submissions: ereview@hc-sc.gc.ca

Master File Administration Unit: dmf.enquiries-fmm@hc-sc.gc.ca

Clinical trial applications - Pharmaceuticals
Office of Clinical Trials
Pharmaceutical Drugs Directorate
Health Canada
5th Floor, Holland Cross, Tower B
1600 Scott Street, Address Locator 3105A
Ottawa, ON, Canada
K1A 0K9

General enquiries email: oct.enquiries-requetes.bec@hc-sc.gc.ca
CTA-N email: oct.ctan-ndec.bec@hc-sc.gc.ca
DSUR email: pdd-pv-dmp@hc-sc.gc.ca

Clinical trial applications - Biologics and radiopharmaceuticals
Office of Regulatory Affairs
Biologics and Radiopharmaceutical Drugs Directorate
Ground Floor, Health Canada Building #6
100 Eglantine Driveway
Address Locator 0601C
Ottawa, ON, Canada
K1A 0K9

General enquiries email: brdd.ora@hc-sc.gc.ca
CTA-N email: brdd.ctan-ndec.dmbr@hc-sc.gc.ca

Veterinary Drugs Directorate (VDD)

General enquiries email: vdd.skmd.so-dgps.dmv.cp@hc-sc.gc.ca

Natural and Non-prescription Health Products Directorate (NNHPD)
General enquiries : nnhpd-dpsnso@hc-sc.gc.ca

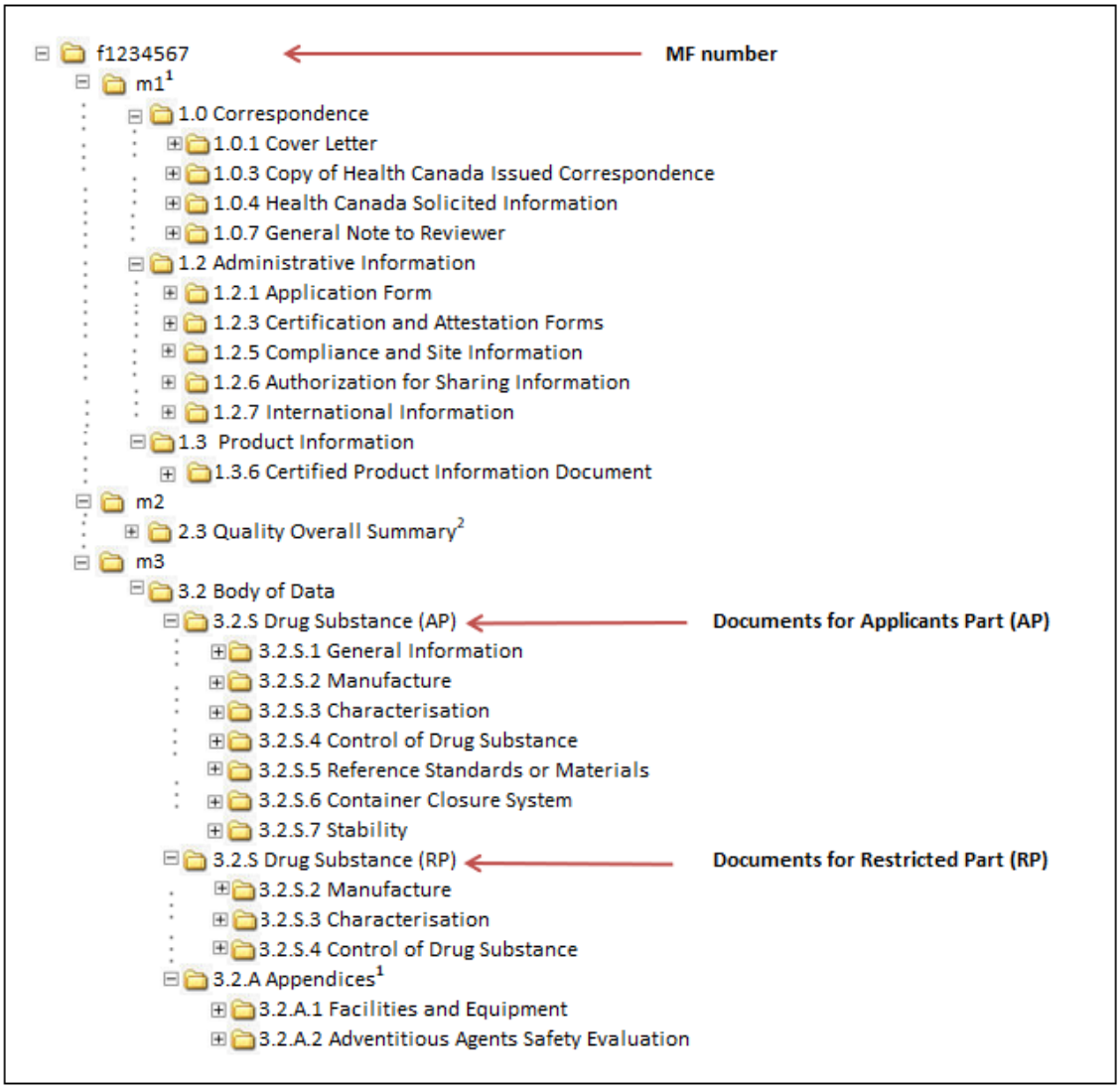
Marketed Health Products Directorate (MHPD)
General enquiries email:

- bbrs.rpm-gpr.bbra@hc-sc.gc.ca (biologics, radiopharmaceuticals, biocides and non-prescription products)
- mpb.rpm-gpr.bppc@hc-sc.gc.ca (pharmaceuticals)

Other
Contact information for specific review center, bureau or office responsibilities can be found in the *Guidance on management of drug submissions and applications*.

Appendix C: Sample folder structures for master files

Figure C-1: MF type I - active substance



1. All documents in this folder will be considered Restricted Part (RP) of the MF.
2. Two separate documents (both in pdf and word format) should be submitted in the folder "2.3 Quality Overall Summary," a "QOS (RP)" and a "QOS (AP)" file.
3. (AP) or (RP) should be used in the subfolder names to identify if the folder is Applicant Part or Restricted Part.

Figure C-2: MF type II - container closure system

Two options are recommended for providing multiple components in the M3 folder.

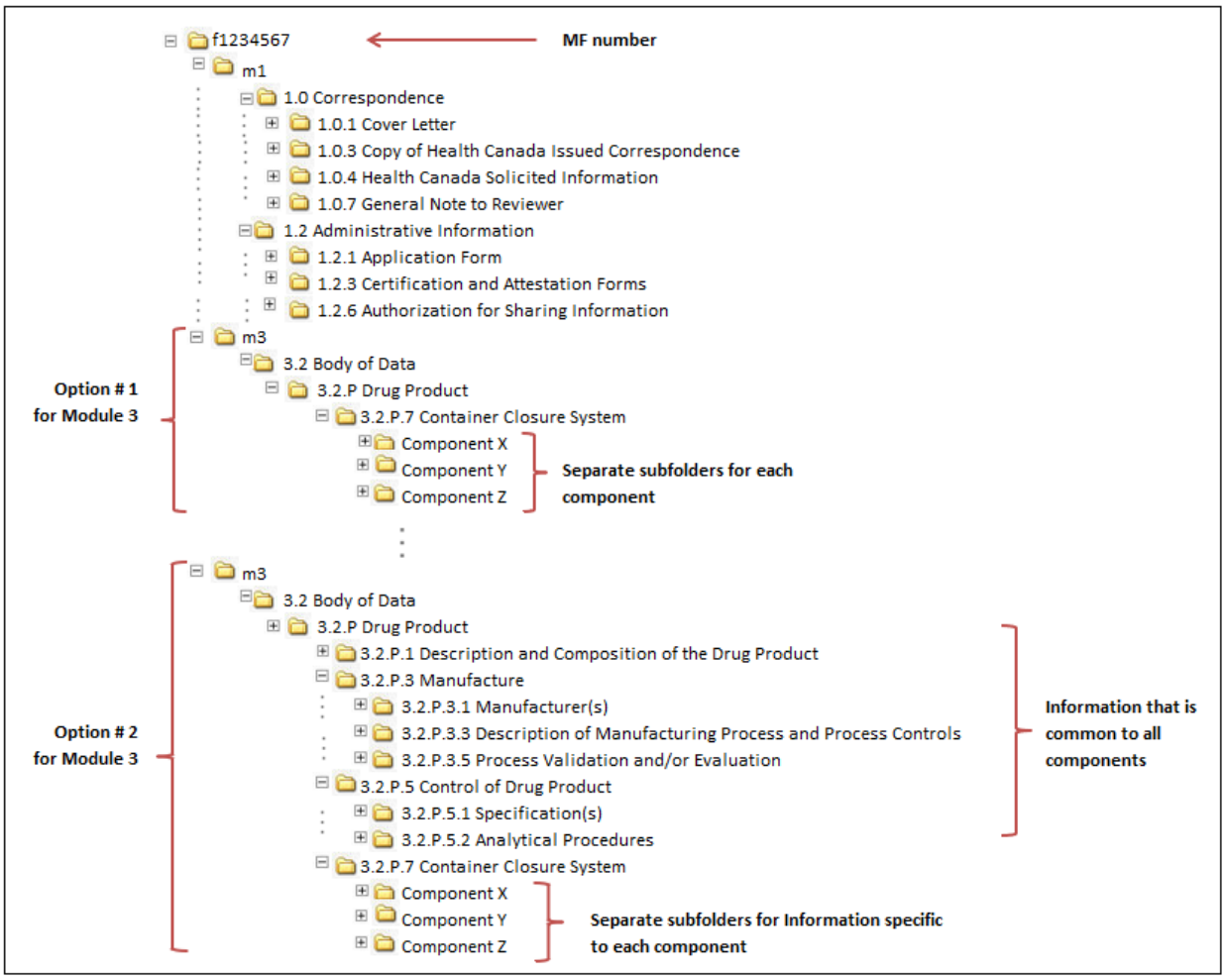


Figure C-3: MF type III - excipient

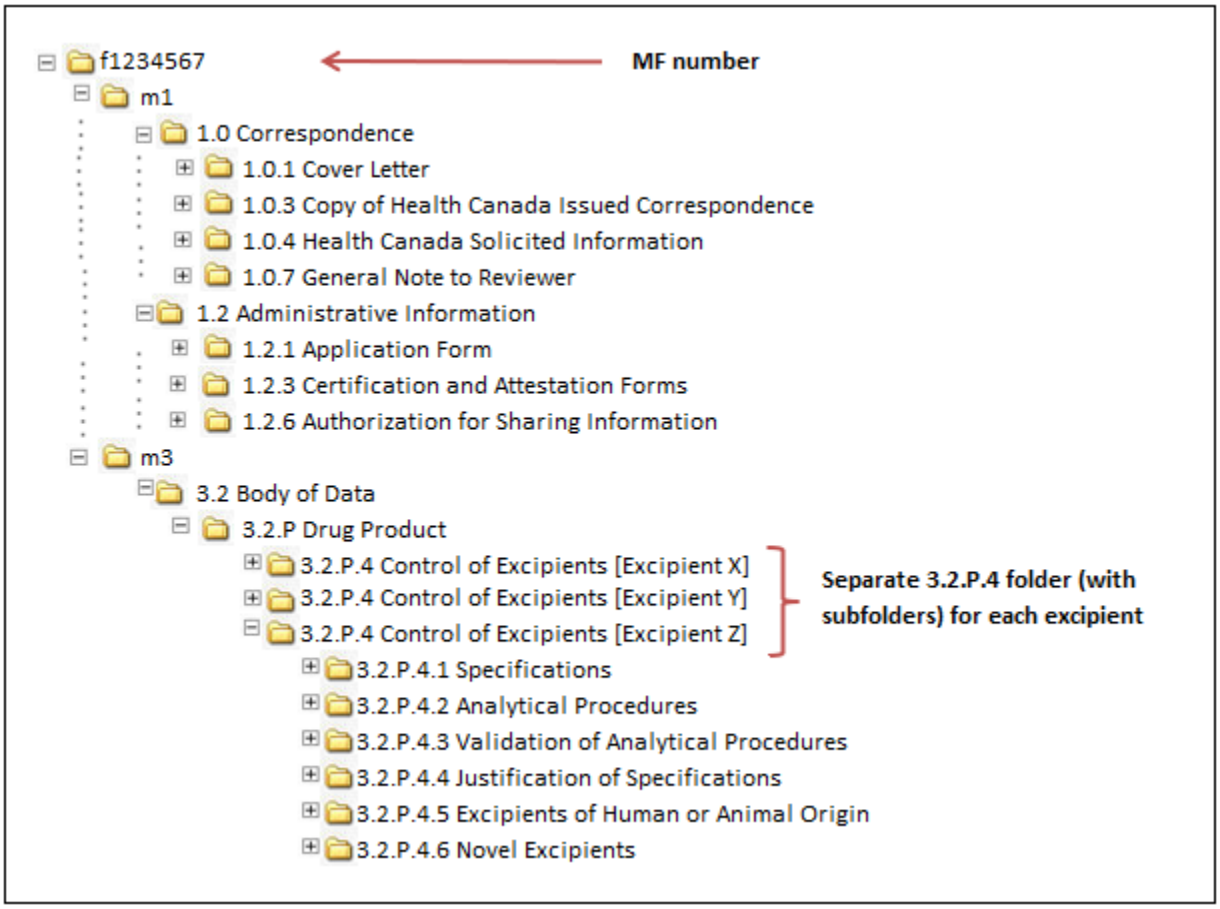
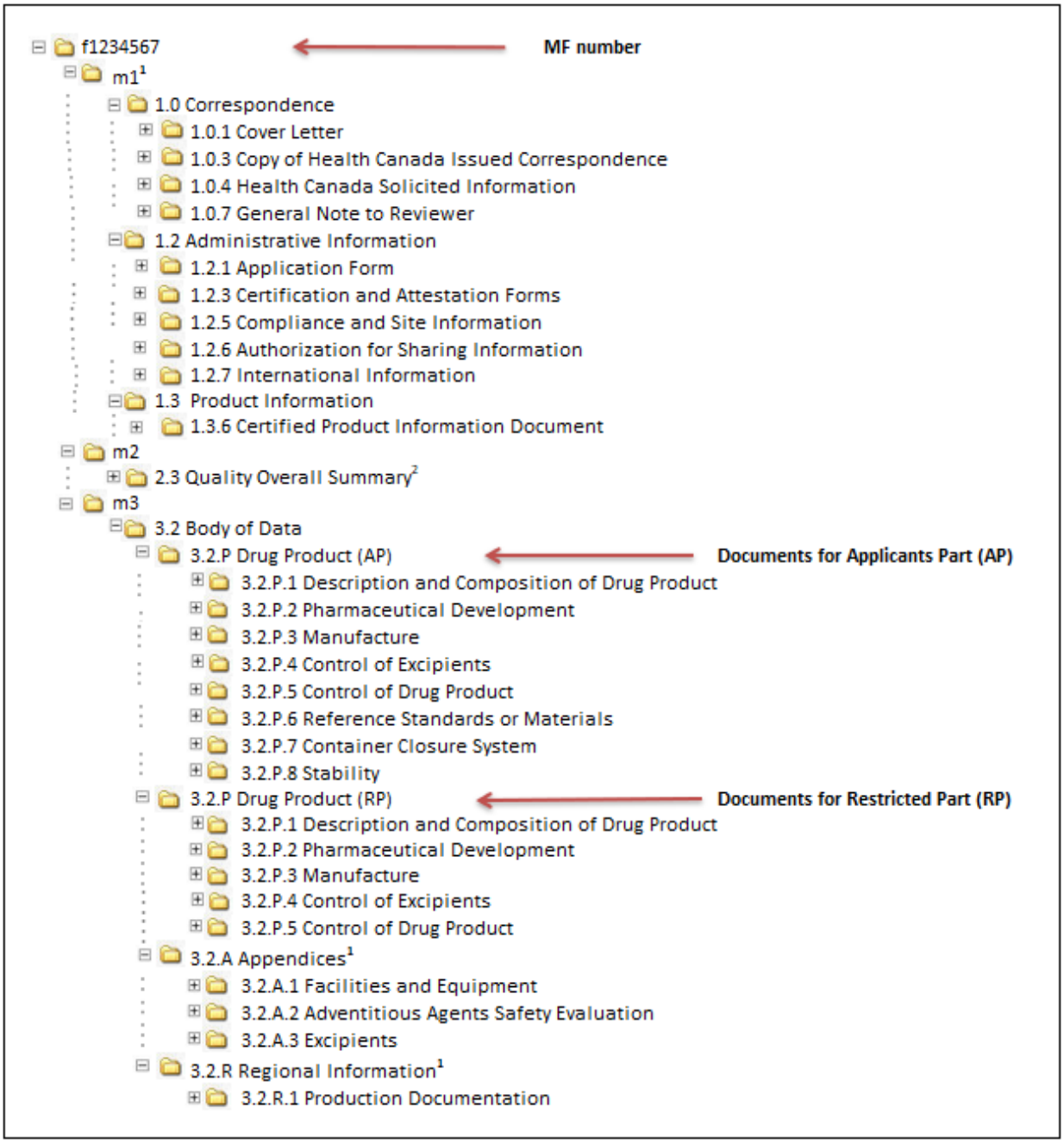


Figure C-4: MF type IV - dosage form



1. All documents in this folder will be considered Restricted Part (RP) of the MF.
2. Two separate documents (both in pdf and word format) should be submitted in the folder "2.3 Quality Overall Summary," a "QOS (RP)" and a "QOS (AP)" file.
3. (AP) or (RP) should be used in the subfolder names to identify if the folder is Applicant Part or Restricted Part.

Appendix D: Distribution of master file information between the applicant and restricted parts

Table D-1: MF type I - active substance

Module and Folder Names		Proposed 2015 applicant's part	Proposed 2015 restricted part
Module 1: Administrative and product information			
1.0	**Correspondence**		
1.0.1	Cover letter	-	√
1.0.3	Copy of Health Canada issued correspondence	-	√
1.0.4	Health Canada solicited information	-	√
1.0.7	General note to reviewer	-	√
1.2	**Administrative information**		
1.2.1	Application forms	-	√
1.2.3	Certification and attestation forms	-	√
1.2.5	Compliance and site information		
1.2.5.2	Establishment licensing	-	√
1.2.5.5	Good manufacturing practices	-	√
1.2.6	Authorization for sharing information	-	√
1.2.7	International information	-	√
1.3	**Product information**		
1.3.6	Certified product information document	-	√
Module 2: Common technical document summary			
2.3	**Quality overall summary (QOS)[1]**	√	√
Module 3: Quality			
3.2	**Body of data**		
3.2.S	**Drug substance**		
3.2.S.1	**General information**		
3.2.S.1.1	Nomenclature	√	-
3.2.S.1.2	Structure	√	-
3.2.S.1.3	General Properties	√	-
3.2.S.2	**Manufacture**		
3.2.S.2.1	Manufacturer(s)	√	-
3.2.S.2.2	Description of manufacturing process and process controls	√[2]	√[3]
3.2.S.2.3	Control of materials	-	√
3.2.S.2.4	Controls of critical steps and intermediates	√[4]	√[5]
3.2.S.2.5	Process validation and /or evaluation	-	√
3.2.S.2.6	Manufacturing process development	-	√
3.2.S.3	**Characterisation**		
3.2.S.3.1	Elucidation of structure and other characteristics	√	-

Module and Folder Names		Proposed 2015 applicant's part	Proposed 2015 restricted part
3.2.S.3.2	Impurities	√	√[6]
3.2.S.4	**Control of drug substance**		
3.2.S.4.1	Specification	√	-
3.2.S.4.2	Analytical procedures	√	-
3.2.S.4.3	Validation of analytical procedures	√	-
3.2.S.4.4	Batch analyses	√	-
3.2.S.4.5	Justification of specification	√	√[7]
3.2.S.5	**Reference standards or materials**	√	-
3.2.S.6	**Container closure system**	√	-
3.2.S.7	**Stability**		
3.2.S.7.1	Stability summary and conclusions	√	-
3.2.S.7.2	Post-approval stability protocol and stability commitment	√	-
3.2.S.7.3	Stability data	√	-
3.2.A	**Appendices**		
3.2.A.1	Facilities and equipment	-	√
3.2.A.2	Adventitious agents safety evaluation	-	√

('**√**' = Accepted / '-' = Not Applicable)

1. A separate QOS for each part (AP / RP) or a single QOS to cover both parts can be provided, deleting all sections of the QOS not relevant to the MF. In cases when a single QOS is provided, the confidential business information/trade secret sections should be clearly identified.
2. A flow chart (including molecular structures and all reagents/solvents) and a short description can be sufficient, if additional detailed information is presented in the restricted part. However, for sterile drug substances full validation data on the sterilisation process should be provided in the applicant's part (in cases where there is no further sterilisation of the final product).
3. Detailed information
4. Insofar as the information is also relevant for the applicant.
5. Insofar as this information is not relevant for the applicant.
6. Insofar as the information is related to the detailed description of the manufacturing process and the MF owner sufficiently justifies that there is no need to control these impurities in the final drug substance.
7. Insofar as the information is related to the detailed description of the manufacturing process, control of materials and process validation.

Table D-2: MF type IV - dosage form

Module and folder names		Proposed 2015 applicant's part	Proposed 2015 restricted part
Module 1: Administrative and product information			
1.0	**Correspondence**		
1.0.1	Cover letter	-	√
1.0.3	Copy of Health Canada issued correspondence	-	√
1.0.4	Health Canada solicited information	-	√
1.0.7	General note to reviewer	-	√
1.2	**Administrative Information**		
1.2.1	Application forms	-	√
1.2.3	Certification and attestation forms	-	√
1.2.5	Compliance and site information		
1.2.5.2	Establishment licensing	-	√
1.2.5.5	Good manufacturing practices	-	√
1.2.6	Authorization for sharing information	-	√
1.2.7	International information	-	√
1.3	**Product information**		
1.3.6	Certified product information document	-	√
Module 2: common technical document summary			
2.3	Quality overall summary (QOS)[1]	√	√
Module 3: Quality			
3.2	**Body of data**		
3.2.P	**Drug product**		
3.2.P.1	**Description and composition of the drug product**	√	√[3]
3.2.P.2	**Pharmaceutical development**	√[4]	√[3]
3.2.P.2.1	Components of the drug product*	√[5]	√
3.2.P.2.2	Drug product*	-	√
3.2.P.2.3	Manufacturing process development*	-	√
3.2.P.2.4	Container closure system*	-	√
3.2.P.2.5	Microbiological attributes*	-	√
3.2.P.2.6	Compatibility*	-	√
3.2.P.3	**Manufacture**		
3.2.P.3.1	Manufacturer(s)	√	√
3.2.P.3.2	Batch formula	√	√
3.2.P.3.3	Description of manufacturing process and process controls	√[2]	√[3]
3.2.P.3.4	Controls of critical steps and intermediates	√[4]	√[6]
3.2.P.3.5	Process validation and or evaluation	-	√
3.2.P.4	**Control of excipients**	√[4]	√[6]
3.2.P.4.1	Specifications	-	√

Module and folder names		Proposed 2015 applicant's part	Proposed 2015 restricted part
3.2.P.4.2	Analytical procedures	-	√
3.2.P.4.3	Validation of analytical procedures	-	√
3.2.P.4.4	Justification of specifications	-	√
3.2.P.4.5	Excipients of human or animal origin	-	√
3.2.P.4.6	Novel excipients	-	√
3.2.P.5	**Control of Drug Product**		
3.2.P.5.1	Specifications	√	-
3.2.P.5.2	Analytical procedures	√	-
3.2.P.5.3	Validation of analytical procedures	√	-
3.2.P.5.4	Batch analyses	√	-
3.2.P.5.5	Characterisation of impurities	√	√[7]
3.2.P.5.6	Justification of specifications	√	√[8]
3.2.P.6	**Reference standards or materials**	√	-
3.2.P.7	**Container closer system**	√	-
3.2.P.8	**Stability**		
3.2.P.8.1	Stability summary and conclusions	√	-
3.2.P.8.2	Post-approval stability protocol and stability commitment	√	-
3.2.P.8.3	Stability data	√	-
3.2.A	**Appendices**		
3.2.A.1	Facilities and equipment	-	√
3.2.A.2	Adventitious agents safety evaluation	-	√
3.2.A.3	Excipients	-	√
3.2.R	**Regional information**		
3.2.R.1	**Production documentation**		
3.2.R.1.1	Executed production documents	-	√
3.2.R.1.2	Master production documents	-	√

('**√**' = Accepted / '-' = Not applicable)

1. A separate QOS for each part (AP/RP) or a single QOS to cover both parts can be provided, deleting all sections of the QOS not relevant to the MF. In cases when a single QOS is provided, the confidential business information/trade secret sections should be clearly identified.
2. A flow chart (including all manufacturing steps, excipients and processing agents) and a short description can be sufficient, if additional detailed information is presented in the restricted part.
3. Detailed information.
4. Insofar as the information is also relevant for the applicant.
5. Complete qualitative composition is provided to the applicant.
6. Insofar as this information is not relevant for the applicant.

7. Insofar as the information is related to the detailed description of the manufacturing process and the MF owner sufficiently justifies that there is no need to control these impurities in the final drug product.
8. Insofar as the information is related to the detailed description of the manufacturing process, control of materials and process validation.

Appendix E: Sample folder structures for other product lines

This section provides sample folder structures for certain product lines that are filed in non-eCTD format.

The folders and subfolders shown in the figures are not exhaustive. Additional folders or subfolders may need to be added or removed depending on the regulatory activity and transaction submitted to Health Canada.

Zipped folder structures, for specific product lines, are available on the Filing submissions electronically information page.

Figure E-1: Sample folder structure for human biologic, pharmaceutical, radiopharmaceutical drugs and disinfectants

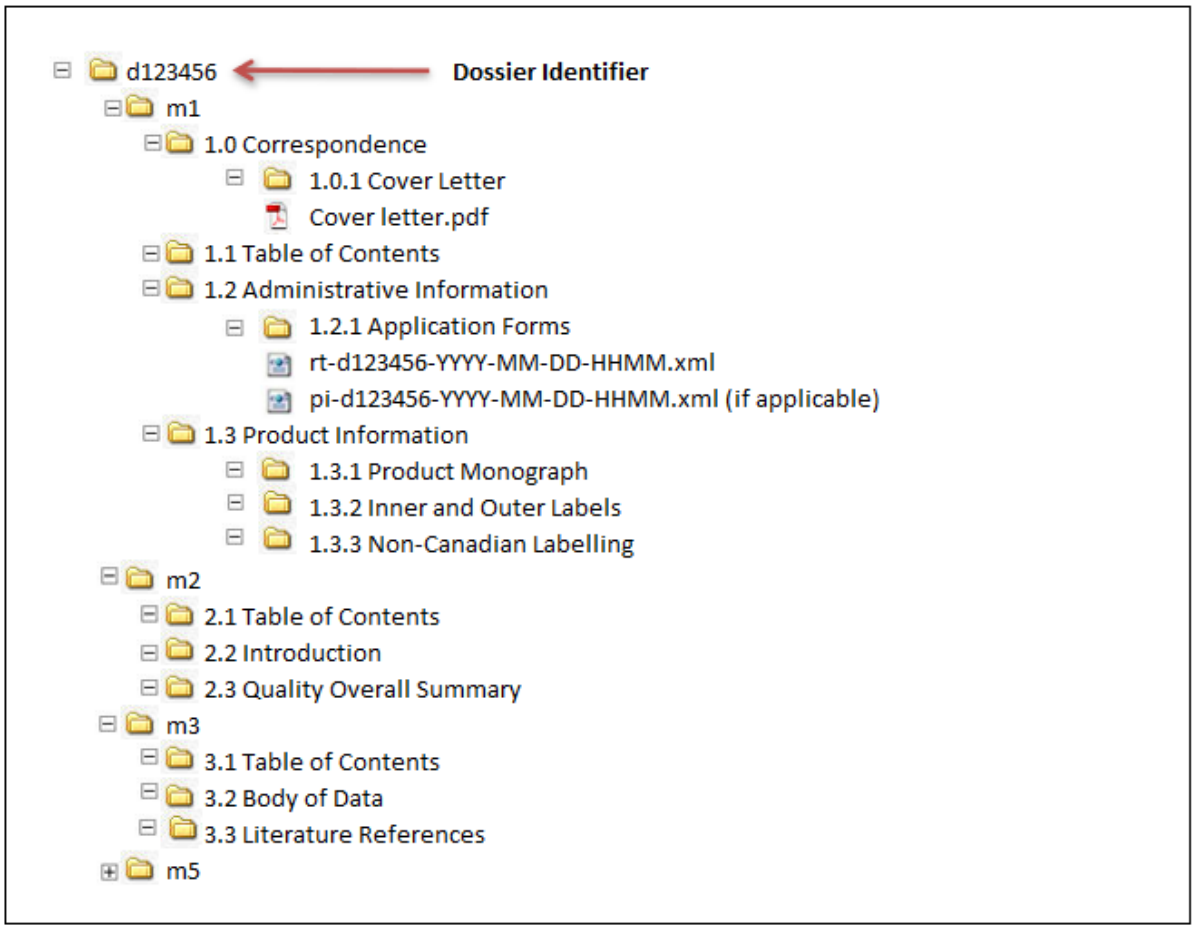
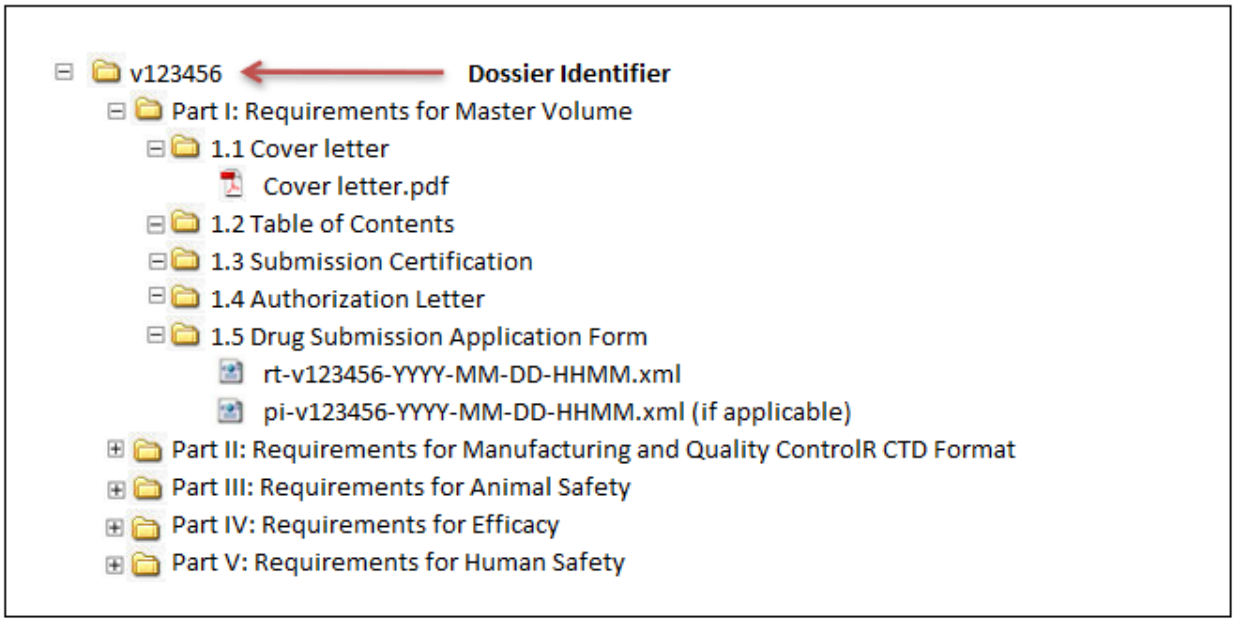
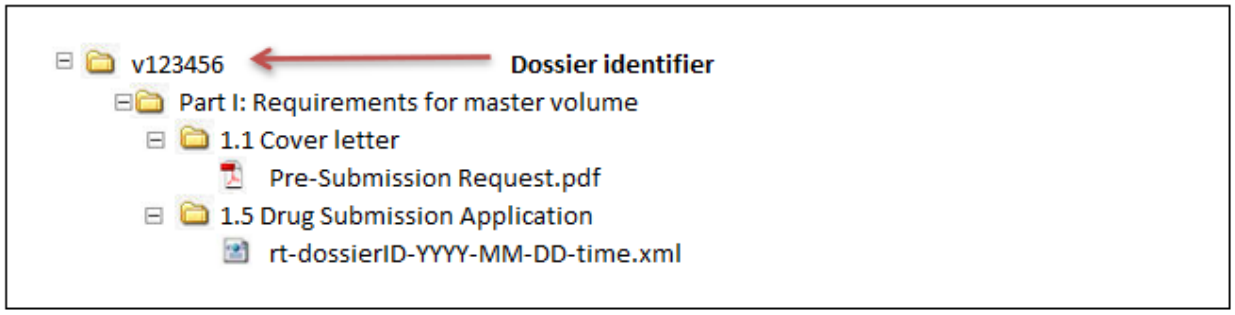


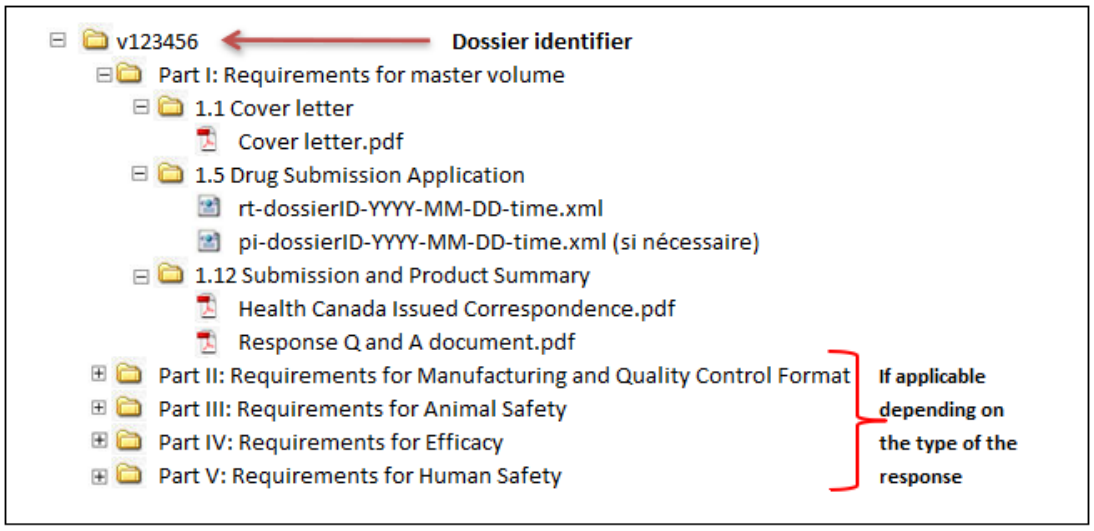
Figure E-2: Sample folder structure for veterinary drugs



Veterinary pre-submission meeting request transaction



Veterinary response to a clarification request transaction



Veternary PSUR transaction

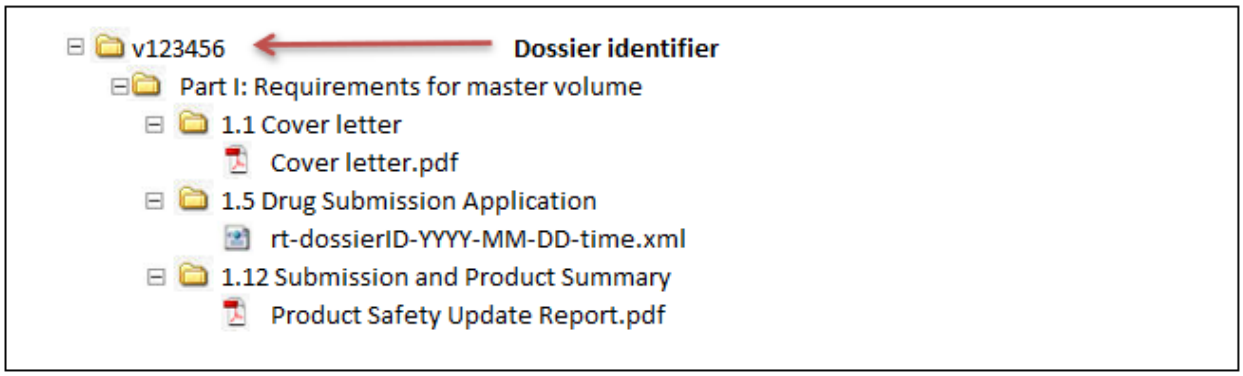


Figure E-3: Sample folder structure for clinical trial applications

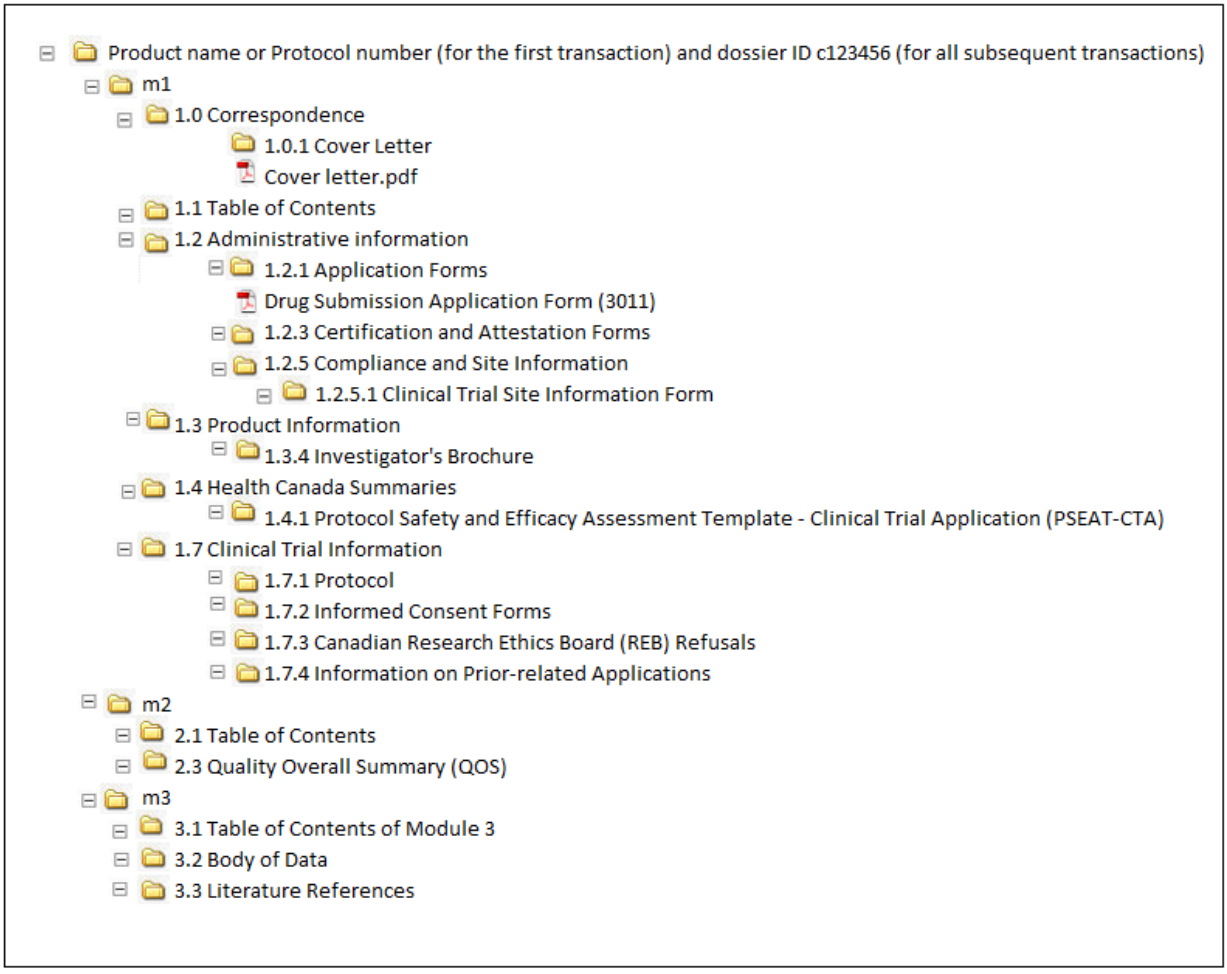


Figure E-4: Sample folder structure for biocides