Guidance on Drug Establishment Licences and Associated Fees

GUI-0002

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Canada

GUI-0002: Guidance on Drug Establishment Licences and Associated Fees

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Disclaimer

This document does not constitute part of the Food and Drugs Act (FDA) or its regulations and in the event of any inconsistency or conflict between the Act or regulations and this document, the Act or the regulations take precedence. This document is an administrative document that is intended to facilitate compliance by the regulated party with the Act, the regulations, and the applicable administrative policies.

Ce document est aussi disponible en français.

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About this document

A. Purpose

This guide is for companies in the drug manufacturing industry. It will help to facilitate understanding and compliance with Part C, Division 1A of the Food and Drug Regulations (FDR), and the Fees in Respect of Drugs and Medical Devices Regulations with regards to drug establishment licence (DEL) requirements and associated fees.

B. Scope

The scope of this document includes:

- Drug establishment licensing requirements outlined in Part C, Division 1A of the (FDR)
- Fees and payments associated with DELs as outlined in the Guidance document, Fees in Respect of Drugs and Medical Devices Regulations and the Establishment Licensing Fees (Veterinary Drugs) Regulations

The scope is therefore limited to the following drugs for human and veterinary use:

- Pharmaceutical drugs (including medical gases)
- Active ingredients
- Vaccines
- Biological drugs (Schedule D of the FDA)
- Radiopharmaceutical drugs (Schedule C of the FDA)
- Drugs controlled under the *Controlled Drugs and Substances Act* and narcotics as defined in the *Narcotic Control Regulations*
- Drugs containing cannabis as defined in subsection 2(1) of the Cannabis Act

While this document discusses the FDR drug establishment licensing requirements and associated fees and payments that apply to drugs, including controlled drugs and narcotics, this document does not discuss the licensing requirements, payments and fees outlined in the *Controlled Drugs and Substances Act* and its Regulations.

This document does not cover the licensing requirements or fees and payment information for:

- Medical devices
- Natural health products
- Whole blood for transfusion
- Tissue, cells and organs for transplantations

C. How Guidance Documents Work

Guidance documents like this one are meant to help industry and health care professionals understand how to comply with rules and regulations. They also provide guidance to Health Canada staff, so that the rules are enforced in a fair, consistent and effective way across Canada.

Guidance documents are administrative and do not have the force of law, and, because of this, they allow for flexibility in approach. This guide can be used to develop specific approaches that meet specific needs.

Health Canada endeavours to provide timely guidance. These guidelines are not the only way establishment licensing regulations can be interpreted, and are not intended to cover every possible case. In the case of a discrepancy between this guidance document and the regulations, the regulations always take precedence.

The following table shows the two types of icons used in this document, and the way they are intended to be used.

Important: Key or cautionary information for people to know.

Information: Supplementary information like quotes and legal references.

Application of DEL Requirements

1. Activities to which DEL Requirements Apply

The drug establishment licensing requirements apply to any person, with some exemptions listed in this section, who conducts any of the licensable activities listed below in Canada with respect to a drug:

- Fabricate
- Package / label
- Test
- Import
- Distribute
- Wholesale

The activities are defined as such:

Fabricate

Fabricate means to prepare and preserve a drug for the purpose of sale.

Package / label

Package/label means to put a drug in its immediate container or to affix the inner- or outer-label to the drug.

Test

Test means to perform the tests, including examinations, required under Part C, Division 2 of the FDR.

Import

Import means to import into Canada a drug for the purpose of sale.

Distribute

The activity of distribute refers to distribute as a distributor referred to in section C.01A.003 of the FDR and applies to the following distributors:

- a distributor of an active ingredient
- a distributor of a drug for which the distributor holds the Drug Identification Number (DIN)

A distributor is a person, including an association or partnership, who under their own name, or under a trade, design or word mark, trade name, or other name, word or mark controlled by them, sells a drug.

Wholesale

Wholesale means to sell, other than at retail, by a person who is not a distributor as described in section C.01A.003 of the FDR of one of the following drugs:

a) a drug in dosage form that is listed in Schedule C or D of the FDA
b) a drug that is a prescription drug or a controlled drug as defined in subsection G.01.001(1) of the FDR
c) an active ingredient
d) a narcotic as defined in Narcotic Control Regulations
e) a drug containing cannabis as defined in subsection 2(1) of the Cannabis Act

2. Exemptions

The drug establishment licensing requirements do not apply to the following:

Wholesaling Over-the-Counter Pharmaceutical Drugs or Non-Scheduled Drugs Including Non-Scheduled Ethical Drugs

A DEL is not required to wholesale finished dosage form drugs that are over-the-counter drugs (OTCs) or that are not listed on a Schedule of the FDA or its Regulations, and are not narcotics as defined in the *Narcotic Control Regulations*. Furthermore, a DEL is not required to wholesale unscheduled ethical drugs. However, a DEL is required to wholesale ethical drugs that are listed on a Schedule of the FDA or its Regulations (e.g. non-prescription biological or radiopharmaceutical drugs).

Distributing or Wholesaling Active Pharmaceutical Ingredients

A DEL is not required for distributing or wholesaling active pharmaceutical ingredients (APIs), including API for veterinary use set out on *List A: List of Certain Antimicrobial Active Pharmaceutical Ingredients*.

Wholesaling of a Drug Premix

A DEL is not required for wholesaling a drug premix.

Conducting Activities Related to a Drug that is Used for the Purpose of a Clinical Trial Authorized by Health Canada.

Clinical trial sponsors must submit a clinical trial application (CTA) to Health Canada for authorization to sell or import a drug for the purpose of a clinical trial. Activities that comply with an authorised clinical trial do not require a DEL, except for clinical trials involving a marketed product used according to its Health Canada market authorization, sometimes referred to as a Phase IV clinical trial.

For more information on Clinical Trial Applications, please refer to the Health Canada *Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications.*

Storing Drugs

Drug storage is not a licensable activity and a company that only stores drugs does not need to hold a DEL. However, the storing of the drug is an integral part of regulated activities and companies that fabricate, import, package / label, test, distribute or wholesale drugs must list all Canadian buildings where they store drugs on their DEL.

Transporting Drugs

Transporting drugs is not a licensable activity and a company that only transports drugs does not need to hold a DEL.

Importing or Compounding a Drug not Commercially Available for Sale in Canada

With the exception of importing API for veterinary use set out on *List A: List of Certain Antimicrobial Active Pharmaceutical Ingredients*, a DEL is not required to import or compound a drug that is not commercially available in Canada, pursuant to a prescription, if you are one of the following:

- a pharmacist
- a practitioner or
- a person who compounds a drug under the supervision of a practitioner

For more information on what activities are considered compounding versus manufacturing please refer to Health Canada's *Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051)*.

As of May 17, 2018, subject to regulatory transitional provisions, a DEL is required for the import of an API for veterinary use that is for the purpose of compounding, pursuant to a prescription, if that API is set out in *List A: List of Certain Antimicrobial Active Pharmaceutical Ingredients*, including when the API is imported by:

- a pharmacist
- a veterinary practitioner or
- a person who compounds a drug under the supervision of a veterinary practitioner

Assembling Kits and Promotional Material

Activities such as assembling multiple already packaged drugs in a secondary package (e.g. making a kit), or adding a leaflet of promotional information, does not require a DEL except in the cases below.

The following actions require a DEL for the activity of packaging/labelling:

- Opening the drug's primary package
- Removing the drug from its primary package
- Replacing or reprinting labelling information that is required by the FDR
- Putting the drug in a package that contains information required by the FDR
- Affixing a label containing information required by the FDR to the drug's package

Kits

While assembling multiple drugs together to make a kit may not require a DEL, it is important to note that other requirements in Part A and Part C Division 1 of the FDR also apply.

For additional information about drug labelling requirements you can consult the Guidance Document*: Labelling of Pharmaceutical Drugs for Human Use* and Guidance Document on Post-Drug Identification Number (DIN) Changes.

Conducting Activities Related to Antimicrobial Agents

Antimicrobial agents are exempt from the DEL requirements.

Activities Related to Biologicals for Veterinary Use

The DEL requirements apply to veterinary biologic drugs that require a DIN to be sold in Canada.

In Canada, not all veterinary biologic drugs require a DIN under the FDR. Those Veterinary biologicals that do not require a DIN are regulated by the Canadian Food Inspection Agency (CFIA), and include animal health products such as vaccines, antibody products, and in vitro diagnostic test kits that are used for the prevention, treatment, or diagnosis of infectious diseases in animals. These drugs are not subject to the DEL requirements.

For additional details, refer to the *Veterinary Biologics CFIA web page*.

3. Inclusions

For further clarity, the activities below are subject to the DEL requirements.

Third Party Performing Testing Required by Part C, Division 2 of the FDR

Third party companies that are testing or examining drugs as required by Part C, Division 2 of the FDR, including but not limited to, raw material testing (C.02.009), packaging material testing (C.02.016), finished product testing (C.02.018) and stability testing (C.02.027, C.02.028) must hold a DEL for the activity of test.

Sterilization of Raw Materials including Packaging Material

The sterilization of raw materials, including packaging materials, is considered a step in the fabrication of the finished drug and requires a DEL for the activity of fabricate, for the drug category associated with the finished drug (e.g. pharmaceuticals) for the dosage form “raw materials” or “packaging materials” as applicable.

Medical Gas Trans-Filling and Curbside Filling

Trans-filling of medical gas, whether performed onsite or curbside, is considered a packaging activity, pursuant to Section C.01A.001(1) of the FDR, which defines the term "package" as "to put a drug in its immediate container", and section C.01.001, which defines the term "immediate container" as "the receptacle that is in direct contact with a drug".

Curbside filling is authorised when performed in compliance with the FDR. The company must hold a DEL for packaging/labelling for the building where the vehicles used in curbside filling or the containers (e.g. cylinders) are replenished.

Fire departments, ambulance services, hospitals or health care facilities packaging medical gases for their own use or administration to a patient do not require a DEL.

Export

For the purpose of the FDR, exporting a drug product to another country is considered a sale in Canada. The requirements under Part C, Division 1A of the FDR are the same for domestic sale and for a sale for the purpose of export. As such, to export a drug, a DEL that authorizes the sale of the drug in Canada is required (e.g. distribute or wholesale).

Section 37 of the Food and Drugs Act

Section 37 of the FDA includes an exemption for the exportation of Drugs manufactured in Canada for export. For more information about section 37 you can consult Health Canada's *Import and Export Policy for Health Products under the Food and Drugs Act and its Regulations (POL-0060).*

4. Combination Products

The *Policy on Drug/Medical Device Combination Products* defines a combination product as:

> 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 into a singular product.

It is Health Canada's policy that a combination product will be subject to either the Medical Devices Regulations or the FDR according to the principal mechanism of action by which the claimed effect or purpose is achieved.

As such, combination products classified as drugs will be subject to the DEL requirements of Part C Division 1A of the FDR. Depending on the products, the medical device component can become a packaging material (e.g. when the medical device such as a syringe becomes the drug's immediate container).

For more information on combination products, consult the *Policy on Drug/Medical Device Combination Products*.

For more information on combination product classification decisions, consult the *Policy on Drug/Medical Device Combination Products - Decisions*.

Prohibition and Interpretation

5. Prohibition

No person shall, except in accordance with a DEL:

- Fabricate, package / label, import or test a drug in dosage form or an active ingredient
- Distribute a bulk process intermediate (BPI) or a drug in dosage form for which they hold the DIN
- Wholesale a drug in dosage form that is:
    - Listed in Schedule C (radiopharmaceutical drug) or D (biologic drug) of the FDA
    - A prescription drug
    - A controlled drug as defined in subsection G.01.001(1)
    - A narcotic as defined in the Narcotic Control Regulations
    - A drug containing cannabis as defined in subsection 2(1) of the Cannabis Act
- Wholesale an active ingredient that is listed in Schedule D (biologic drug) of the FDA

Exception - Test:

Licensed fabricators, packagers/labellers, distributors and importers do not require the activity of test on their DEL to perform tests, including examinations under Part C, Division 2 of the FDR for the drugs they fabricate, package/label, distribute, or import.

Similarly, foreign buildings listed on an importer's DEL as a fabricator or packager/labeller are not required to be listed on the importer's DEL as testers for the drugs the foreign buildings fabricates or packages/labels.

Exception – Package/Label for Fabricator:

When a licensed drug fabricator packages/labels a bulk drug or in-process drug they have fabricated, the packaging and labelling of the bulk containers are considered an integral part of the activity of fabrication and do not require a DEL for package/label when the drug is:

- Packaged in bulk, in a package not suitable or intended for retail sale; and,
- For sale to a drug fabricator or packager/labeler.

Exception – Label for Importers:

Labelling activities conducted by drug importers to satisfy the requirements of Part C Division 2 of the FDR are considered an integral part of the activity of importation and do not require a DEL for the activity of label when the drug is:

- Imported and sold in bulk, in a package not suitable or intended for retail sale; and,
- Sold in the same container it was imported in; and
- For sale to a drug fabricator or packager/labeler.

6. Drug Establishment Licensing Requirements

In Canada, licensable activities subject to DEL requirements can only be conducted in accordance with a valid DEL. Activities cannot be conducted with a suspended or cancelled DEL. For more information on suspension and cancellations please see section 20 and section 21 of this guide.

To fabricate, package / label, test, import, distribute or wholesale a drug in Canada, the company must hold a valid DEL that includes:

- The Canadian building where the activity is authorized
- The activity that is authorized to be conducted at the building
- The category of drugs for which the activity is authorized
- In the case of a sterile drug, the DEL must authorize sterile dosage form for the drug category

To import a drug into Canada, a company must comply with the above, including holding a DEL for the activity of import, and additionally have the following on their DEL:

- A foreign building annex including all the foreign buildings involved in the fabrication, packaging/labelling and/or testing of the finished dosage form drug, including finished dosage form intermediates, that is being imported. For each foreign building, the foreign building annex must include:
  - The activity that is authorized
  - The category of drugs for which the activity is authorized
  - In the case of a sterile drug, the DEL must authorize sterile dosage form for the drug category.

- An API foreign building annex including all the foreign buildings involved in the fabrication, packaging/labelling and/or testing of the APIs and/or List A APIs for veterinary use, including API intermediates, that are being imported, or that are used in the fabrication of the finished drugs that are being imported. For each foreign building, the API foreign building annex must include:
    - The authorized activity
    - The category of drugs for which the activity is authorized (API or List A API for veterinary use)

7. Category of Drugs

This section provides further clarifications with respect to drug categories to help understand what drug categories are required on a DEL.

The categories of drugs are:

- Active pharmaceutical ingredients
- Pharmaceuticals
- Vaccines
- Drugs that are listed in Schedule D of the FDA, other than vaccines
- Drugs listed in Schedule C of the FDA
- Drugs that are prescription drugs, controlled drugs as defined in subsection G.01.001(1), narcotics as defined in the Narcotic Control Regulations and drugs containing cannabis as defined in subsection 2(1) of the Cannabis Act - Sometimes called “Category 6 drugs”
- Active pharmaceutical ingredients set out in List A that are for veterinary use

Unless specified, the categories of drugs apply to both human and veterinary drugs.

Active Pharmaceutical Ingredients (API)

Companies conducting activities with respect to APIs require the drug category “active pharmaceutical ingredients” on their DEL for the domestic building conducting activities.

Importers of APIs and importers of pharmaceutical drugs are required to have the following foreign buildings listed on their DEL API foreign building annex under the drug category “API”:

- Foreign building(s) involved in fabrication, packaging/labeling and/or testing of the API and/or their intermediates they import
- Foreign building(s) involved in fabrication, packaging/labeling and/or testing of the API and their intermediates used in the fabrication of the finished dosage form pharmaceutical drugs they import

Atypical APIs

Importers of atypical APIs and finished dosage form importers of products formulated using listed atypical APIs are subject to the requirements above. For more information on atypical APIs you can consult the *Notice to Stakeholders - Implementation of Establishment Licensing Requirements for Atypical Active Pharmaceutical Ingredients*.

The drug category "Active Pharmaceutical Ingredients" includes:

- Active ingredients used in the manufacture of finished dosage form drugs that are pharmaceutical drugs and their intermediates
- Active ingredients used in the manufacture of finished dosage form drugs that are listed on Schedule C (radiopharmaceutical drugs) of the FDA that are not of biological origin and their intermediates

The drug category "Active Pharmaceutical Ingredients" does not include:

- Sterile active ingredients
- Active pharmaceutical ingredients set out in List A that are for veterinary use
- Active ingredients of biological origin used in the manufacture of finished dosage form drugs that are listed on Schedule C (radiopharmaceutical drugs) or Schedule D (biologic drugs) of the FDA

Important:

If a company fabricates an API and then uses the API in the fabrication of a finished pharmaceutical drug by either:

- Fabricating a drug into its finished dosage form
- Partially fabricating a finished drug (i.e. fabricating a finished dosage form intermediate)

- Sterilizing the API

The company is required to hold a DEL for the activity of fabricate APIs **and** fabricate pharmaceuticals.

Pharmaceuticals

Companies conducting activities with respect to pharmaceutical drugs in their finished dosage form and their intermediates require the drug category "Pharmaceuticals" on their DEL for the domestic building conducting activities.

Importers of pharmaceutical drugs in their finished dosage form or their intermediates are required to have the foreign buildings that are involved in the fabrication, packaging/labeling and/or testing of the finished dosage form drugs or finished dosage form intermediate listed on the foreign building annex of their DEL under the drug category "Pharmaceuticals".

The drug category "Pharmaceuticals" includes:

- Finished dosage form drugs and their intermediates other than drugs listed in Schedule C or D to the FDA
- Finished dosage form narcotic drugs and controlled drugs and their intermediates that are not listed in Schedule C or D of the FDA

Test

For the activity of test when the test performed is used to satisfy the GMP requirements associated with an activity related to finished dosage form pharmaceutical drugs, the tester, including third party tester, requires a DEL with the drug category "Pharmaceuticals".

As an example, the tests performed by a third party tester on an API prior to its use in the fabrication of a finished dosage form drug to satisfy C.02.009(1) require a DEL including Test Pharmaceuticals.

Sterile Active Pharmaceutical Ingredients

Activities performed on sterile active pharmaceutical ingredients require the drug category "Pharmaceuticals" to be listed on the DEL.

The sterilisation of active pharmaceutical ingredients is considered as a step in the fabrication of the finished drug and requires a licence for the fabrication of pharmaceuticals. Also, the importation of sterile APIs is

considered importation of a finished pharmaceutical drug. In both cases, the drug category “Pharmaceuticals” is required to be listed on the DEL.

Wholesale

Health Canada does not issue a DEL for wholesale within the drug category of pharmaceuticals. For more information on the drug category applicable for the wholesale of pharmaceutical drugs, see the information provided under the drug category Prescription Drug List, Schedule G, Drugs Containing Cannabis and/or Narcotics below.

Biologics

Companies conducting activities with respect to biologic drugs require the drug category “Biologics” on their DEL for the domestic building conducting activities.

Importers of biologic drugs are required to have the foreign buildings that are involved in the fabrication, packaging/labeling and/or testing of the biologic drugs listed on the foreign building annex of their DEL under the drug category “Biologics”.

The drug category “Biologics” includes:

- Drugs listed in Schedule D of the FDA
- Narcotics and controlled drugs that are listed in Schedule D of the FDA
- Active ingredients of biological origin that are used in the fabrication of a drug that is listed on Schedule C of the FDA
- Active ingredients that are used in the fabrication of a drug that is listed on Schedule D of the FDA

Vaccines

Companies conducting activities with respect to vaccines or vaccine active ingredients require the drug category “Vaccines” on their DEL for the domestic building conducting activities.

Importers of vaccines or vaccine active ingredients are required to have the foreign buildings that are involved in the fabrication, packaging/labeling and/or testing of the vaccine and/or vaccine active ingredients listed on the foreign building annex of their DEL under the drug category “Vaccines”.

Radiopharmaceuticals

Companies conducting activities with respect to finished dosage form radiopharmaceutical drugs and their intermediates require the drug category "Radiopharmaceutical" on their DEL for the domestic building conducting activities.

Importers of finished dosage form radiopharmaceutical drugs and their intermediates are required to have the foreign buildings that are involved in the fabrication, packaging/labeling and/or testing of the finished dosage form radiopharmaceutical drugs and their intermediates listed on the foreign building annex of their DEL under the drug category "Radiopharmaceuticals".

The drug category "Radiopharmaceuticals" includes:

- Finished dosage form drugs and their intermediates listed in Schedule C of the FDA
- Finished dosage form narcotics and controlled drugs and their intermediates that are listed in Schedule C of the FDA

The drug category "Radiopharmaceuticals" excludes:

- Active ingredients used in the manufacture of finished dosage form drugs that are listed on Schedule C (radiopharmaceutical drugs) of the FDA that are not of biological origin (see category of drug: active pharmaceutical ingredients)

Prescription Drug List, Schedule G, Drugs Containing Cannabis, and/or Narcotics

The activity of wholesale does not apply to all pharmaceutical drugs. It only applies to pharmaceutical drugs that:

- Are listed on the *Prescription Drug List*
- Are controlled drugs as defined in Schedule G of the FDR
- Are narcotics as defined in the Narcotic Control Regulations
- Are drugs containing cannabis as defined in subsection 2(1) of the Cannabis Act

As such, wholesalers of prescription drugs, controlled drugs, drugs containing cannabis or narcotics are required to have the drug category "Prescription Drug List, Schedule G, Cannabis, and/or Narcotics" on their DEL under the wholesale activity.

Health Canada does not issue DELs with the drug category "Prescription Drug List, Schedule G, Cannabis, and/or Narcotics" for any other activities. For activities other than wholesale, another

drug category listed in this section that applies to your drug is required. In most cases, this would be the drug category “Pharmaceuticals”.

The licensing requirements under the *Controlled Drugs and Substances Act* and its regulations – including Part G and J of the FDR are not discussed in this guide.

List A API for Veterinary Use

Companies conducting activities with respect to List A APIs for veterinary use require the drug category “List A API for veterinary use” on their DEL for the domestic building conducting activities.

Importers of List A API for veterinary use and importers of pharmaceutical drugs for veterinary use containing List A API are required to have the following foreign buildings listed on their API foreign building annex with the drug category “List A API for veterinary use”:

- Foreign buildings involved in fabrication, packaging/labeling and/or testing of the List A API for veterinary use and/or their intermediates they import
- Foreign buildings involved in fabrication, packaging/labeling and/or testing of the List A API and or their intermediates used in the fabrication of the finished dosage form pharmaceutical drugs for veterinary use they import

The drug category “List A API for veterinary use” includes:

- API set out in List A that are for veterinary use and their intermediates

8. Storing Drugs as a DEL Holder

Canadian fabricators, importers, packagers/labelers, distributors, wholesalers, or testers are required to hold a DEL for the activities they conduct. In addition, their DEL must include every building in Canada where they store drugs. Buildings where drugs are being stored and where no licensable activities are being conducted are listed on the DEL Warehouse Annex.

9. Alternate Sample Retention

Every distributor and importer of drugs is required to retain in Canada a sample of each lot or batch of the packaged/labelled drug for a period of at least one year after the expiration date of the label of the drug.

All buildings outside of Canada where an importer or distributor is authorized to store samples (as per section C.02.025 of the FDR) are listed on the Alternate sample retention Annex of the DEL.

For more information, please refer to *GUI-0014: Alternate Sample Retention Site Guidelines*.

DEL Application

10. Application Types

This section provides a high level description of the various application types.

New DEL Application (C.01A.005)

This type of application is to be submitted by companies that do not hold a DEL. This includes applications submitted by companies that are requesting the re-activation of a cancelled DEL.

Amendment Application (C.01A.006)

This type of application is to be submitted by companies that hold a DEL and wish to make a change to their DEL, including but not limited to the addition, modification or removal of:

- A building in Canada where regulated activities are conducted
- A foreign building from which a drug is imported
- An activity for a specific building
- A category of drugs for a specific activity
- The authorization of sterile dosage forms for a specific category of drugs
- A building in Canada where drugs are stored (Canadian warehouse)
- An alternate sample retention site (ASR)
- Terms and Conditions

Annual Licence Review (ALR) Application (C.01A.009)

This type of application is to be submitted each year before April 1st by companies that hold a valid DEL. This application is required for Health Canada to conduct the annual review of the DEL.

New Licence Holders

Every DEL holder is required to submit an ALR application by April 1st of every year. Companies that are issued a DEL close to April 1st (e.g. March), are still required to submit an ALR application by April 1st.

NERBY Application (C.01A.009/C.01A.006)

In lieu of submitting GMP evidence as part of the ALR application for all foreign buildings listed on a DEL holder's licence, DEL holders are provided as part of their ALR package the option of signing "Undertaking B" form, thereby committing to submit GMP evidence prior to the New Evidence Required By (NERBY) date indicated on their DEL. A NERBY application is an amendment application intended to meet the commitment that the DEL holder made as part of their ALR application and to request the amendment of the DEL to update the NERBY date.

The NERBY amendment application must include valid and current evidence to demonstrate that each of the foreign fabricator's, packager/labeller's and tester's buildings, equipment, practices and procedures meet the applicable GMP requirements of Part C, Division 2 of the FDR. For more information about NERBY, please consult: *How to demonstrate foreign building compliance with drug good manufacturing practices (GUI-0080).*

Reinstatement Application (C.01A.018)

When a company's DEL has been suspended in full or in part by Health Canada and the company wishes to request the reinstatement of the DEL, a reinstatement request may be submitted to Health Canada via *FRM-0033: Drug Establishment Licence Application: Forms and Instructions*.

The processing of the request is subject to an inspection and associated performance standard.

Important:

When a DEL has been suspended for a period of more than 12 months, regardless of whether a reinstatement request was submitted to Health Canada, the DEL cannot be reinstated as the DEL is cancelled pursuant to C.01A.018.1 of the FDR.

Health Canada's authority to reinstate a DEL is limited to suspended DELs. If a DEL is cancelled and the company wishes to resume activities, an application for a new DEL pursuant to C.01A.005 or an amended DEL pursuant to C.01A.006 of the FDR must be submitted as applicable.

To avoid situations where a DEL would be cancelled before a reinstatement decision can be made by Health Canada, Health Canada accepts applications under C.01A.005/C.01A.006 from the holder of suspended DELs who have taken adequate steps to correct the situation on which the suspension was based.

By submitting a new DEL application or an application to amend a DEL rather than an application for reinstatement, Health Canada can process the application irrespective of whether the DEL becomes cancelled pursuant to C.01A.008.1.

Cancellation Application

If a company wishes to cancel their DEL, the company must send a cover letter or e-mail stating the intention to cancel their DEL. The requestor must be a contact currently on file with Health Canada. Once the request has been processed, confirmation will be sent by Health Canada.

11. Submitting a DEL Application other than ALR

All application types listed below must be submitted by completing the most current version of the application form established by the Minister – FRM-0033 and Table A when applicable:

- Application for a new DEL (C.01A.005)
- Application to amend a DEL (C.01A.006)
- NERBY application (C.01A.006/C.01A.009)
- Application to request the reinstatement of a DEL after the situation on which the suspension was based has been rectified

It is recommended that applicants also include a cover page to provide further information with regards to the application or provide clarifications.

Complete applications must be submitted to Hc.el.applications-le.sc@canada.ca.

When completing an application for a new DEL or for a reinstatement, all the information below must be provided. For amendment applications and NERBY applications, only the information relevant to the change being made or the foreign building that is being renewed is required.

FRM-0033

FRM-0033 is the form prescribed by the Minister to submit DEL applications. A complete FRM-0033 must be submitted with every application and include the following information:

- Applicant information
- Canadian building information
- Foreign building information

Table A

A complete and comprehensive Table A must be submitted with every application pertaining to foreign buildings conducting activities with respect to APIs.

Table A

Table A is used to list all foreign buildings conducting licensable activities with regards to APIs imported into Canada and/or for all APIs used in the fabrication of finished dosage forms drugs for import into Canada. Interested stakeholders who wish to obtain this document may send a request to the Drug Establishment Licence Unit.

Evidence of Compliance with GMP – Domestic Buildings

- Evidence of compliance with GMP of Canadian buildings is not required to be submitted with an application. GMP evidence will be requested by Health Canada as part of the processing of the application. An onsite inspection by Health Canada Inspectors may also be performed.

Evidence of Compliance with GMP – Foreign Buildings

- Guidance related to the type of GMP evidence to be submitted as part of a DEL application for foreign buildings is available in *GUI-0080 – How to demonstrate foreign building compliance with drug good manufacturing practices*.

12. Authority to Request Additional Information, Inspect and Request Samples

Additional Information

When receiving an application, Health Canada may request additional information from the applicant to enable Health Canada to make a licensing decision. Failure to provide the information requested within the allotted timeframe may result in a refusal to issue, amend or reinstate the DEL.

Inspection

Health Canada has the authority to inspect any building in Canada subject to an application where the applicant proposes to conduct a licensable activity, store drugs or maintain records. The inspection may occur at any time and date as determined by Health Canada within normal business hours. While Health Canada will try to accommodate the company's schedule when possible, Health Canada reserves the right to select the inspection date unilaterally. Should an applicant refuse to be inspected at the date selected by Health Canada for any reason, including because they are not ready for an inspection, this may result in Health Canada not issuing,

amending or reinstating the DEL, thereby closing the applications associated with the inspection. Therefore, it is recommended that companies only submit a DEL application once they are ready for an inspection.

Health Canada considers the observations made during the inspection when making licensing decisions on the application.

The following are guidelines and policies that help an applicant prepare for a GMP inspection:

- *Drug Establishment Good Manufacturing Practices—Pre-Application Package (Importers, Distributors and Wholesalers)*
- *Good manufacturing practices guide for drug products (GUI-0001)*
- *Annex 1 to the Good manufacturing practices guide - Manufacture of sterile drugs*
- *Risk classification guide for drug good manufacturing practices observations (GUI-0023)*
- *Guidance on Good Manufacturing Practices for Active Pharmaceutical Ingredients (APIs) (GUI-0104)*
- *Good manufacturing practices for medical gases (GUI-0031)*
- *GMP Inspection Policy for Canadian Drug Establishments (POL-0011)*

Samples

Health Canada has the authority to require that an applicant applying for the activity of fabrication, packaging/labelling, testing, distribution, or importation supply samples of any material to be used in the fabrication, packaging/labelling or testing of a drug. Health Canada considers the information obtained from these samples when making licensing decisions on the application.

13. Refusal to Issue or Amend or Reinstate

Health Canada may refuse to issue or amend an establishment licence in respect of any or all matters subject to an application if:

- The applicant had an establishment licence suspended in respect of the matter.

Health Canada may refuse to issue, amend or reinstate an establishment licence in respect of any or all matters subject to an application if:

- The applicant made a false or misleading statement in relation to the application for the licence.

Health Canada will refuse to issue, amend or reinstate an establishment licence in respect of any or all matters subject to an application if:

- Health Canada has reasonable grounds to believe that issuing or amending an establishment licence would constitute a risk to the health of the consumer.

14. Issuance

Health Canada issues DELs pursuant to section C.01A.008 of the regulations. Unless Health Canada has grounds to refuse the application under C.01A.010, a licence will be issued when C.01A.008 is met.

In order to meet the requirements of C.01A.008, all application requirements set out in C.01A.005 to C.01A.007 must be satisfied, including demonstrating compliance with GMP, and compliance with any information request, inspection request and sample request made by Health Canada.

Issuance with Terms and Conditions

When making a licensing decision, Health Canada may issue an establishment licence that includes terms and conditions to help prevent injury or ensure drugs are not unsafe for use. DEL holders must comply with all terms and conditions listed on their DEL. DEL holders found to be in contravention of the terms and conditions of their licence will be subject to compliance and enforcement actions. Health Canada will take compliance and enforcement actions considering the particularities of each situation while adhering to the legislative framework and the principles of Policy-0001 – Compliance and Enforcement Policy for Health Products.

15. The DEL and its Annexes

When issuing a DEL for the first time, Health Canada issues a full DEL with all applicable sections and annexes. When issuing an amended DEL, only the section subject to the amendment will be issued and will replace the previously issued section or annex.

Domestic Buildings

A DEL lists each domestic building on its own section (usually one page). For each domestic building the following information is provided:

- The DEL number including the domestic building letter identifier (e.g. 3-001234-A for building A)
- The name of the licence holder
- The address of the Canadian building where licensable activities are authorized

- The licensable activities authorized to be conducted in each building
- The categories of drugs
- Whether sterile dosage forms are authorized for each activity and drug category
- Date of the last GMP inspection
- A list of all the annexes applicable for the domestic building
- The Minister's designate's signature
- The date of issuance or amendment

DEL Annexes

The annexes below are not part of every DEL. They will be present if applicable, based on the application or Health Canada's licensing decision. Each annex is associated with a specific Canadian building. Companies with multiple Canadian buildings on their DEL may have each type of annex for each domestic building.

Example of a DEL with Multiple Buildings

An importer with DEL 100000 including building A (100000-A) and building B (100000-B) where both buildings are licenced for import will have a Foreign Building Annex and an API Foreign Building Annex for 100000-A and another Foreign Building Annex and an API Foreign Building Annex for 100000-B. The 2 Foreign Building Annexes may have different foreign buildings listed if the drugs imported by building A are not the same as the drugs imported by building B. The same applies for the API Foreign Building Annex.

Terms and Conditions Annex: This annex is where Health Canada will list the terms and conditions associated with a particular Canadian building. This annex contains the DEL number and the building letter to which the terms and conditions apply (e.g. 3-001234-A for building A). This annex may also include terms and conditions regarding an API foreign building associated with this domestic building. When the terms and conditions apply to an API foreign building, the terms and conditions will specifically mention the foreign building.

Terms and conditions are also listed on the Foreign Building Annex.

DEL holders are required to comply with the terms and conditions listed in this annex.

Foreign Building Annex: This annex lists all of the foreign buildings which fabricate, package/label and test the drugs imported by the DEL holder to the associated Canadian building. The annex authorizes the DEL holder to import drugs from those foreign buildings.

Each foreign building will have its own section within the annex (usually one page). For each authorized foreign building, Health Canada will include the following information on the Foreign Building Annex:

- The DEL number including the domestic building letter identifier (e.g. 3-001234-A for building A)
- The name of the foreign company
- The address of the foreign building
- The new evidence required by (NERBY) date before which updated GMP evidence must be submitted
- The activities authorized to be conducted at the foreign building
- The categories of drugs
- Whether sterile dosage forms are authorized for each activity and drug category
- Applicable terms and conditions associated with the foreign building

DEL holders are required to comply with the terms and conditions listed on this annex.

Alternate Sample Retention Annex: This annex applies to distributors and importers of drugs and is where Health Canada will list all buildings outside of Canada where the importer/distributor is authorized to store samples. For full details, see *Alternate Sample Retention Site Guidelines (GUI-0014)*.

This annex includes the following information:

- The DEL number including the domestic building letter identifier (e.g. 3-001234-A for building A)
- The name and address of the foreign building where samples are authorized to be stored
- The name and the DIN of the drug for which samples are authorized to be stored at the foreign building

Warehouse Annex: This annex lists all the Canadian buildings where the DEL holder is authorized to store drugs.

This annex includes the following information:

- The DEL number including the domestic building letter identifier (e.g. 3-001234-A for building A)
- The name and address of the domestic building where the DEL holder is authorized to store drugs

Active Pharmaceutical Ingredient Foreign Building Annex: This annex lists all the foreign buildings authorised to fabricate, package/label and test:

- Non-sterile APIs imported by the DEL holder
- Non-sterile APIs used in the fabrication of the finished drugs imported by the DEL holder

API importers are authorized to import APIs from any foreign building listed on this annex.

This annex includes the following information:

- The DEL number including the domestic building letter identifier (e.g. 3-001234-A for building A)
- API name
- Activity
- Foreign building name
- Foreign building address
- The category of drug (API or List A API for veterinary use)

16. Submitting an ALR Application

ALR Package

ALR applications do not require the use of FRM-0033. Every year, Health Canada will send an ALR package to all companies holding a DEL that is not suspended. The package will include instructions on how to submit and what revisions are permitted in an ALR application and which ones are not. Companies must submit their ALR application to Health Canada before April 1.

Companies that do not receive their ALR application package by January 1 of each year must request one by contacting Health Canada at hc.del.alr-eal.lepp.sc@canada.ca.

Companies that have been issued a DEL for the first time after December of a given year will receive an ALR application package soon after they have received their DEL. The ALR application must be submitted to Health Canada before April 1.

ALR GMP Evidence Requirements

As part of their ALR application, companies are required to provide all applicable information and documents outlined under C.01A.005 including evidence of compliance with GMP. However, Health Canada aims to reduce this burden at ALR by the following:

Domestic GMP Requirements

When submitting an ALR application for a Canadian building inspected by Health Canada, GMP evidence is not required, unless specifically requested by Health Canada. Health Canada monitors the GMP compliance of domestic buildings via its GMP inspection program and additional evidence is not required to be submitted as part of an ALR application.

GMP Requirements for Foreign Buildings Located in an MRA Country

GMP evidence is not required as part of an ALR application for foreign buildings listed on a DEL that are located in a Mutual Recognition Agreement (MRA) country and where all the activities, category of drugs and dosage forms associated with the foreign building are recognized by the MRA regulatory authority as being in compliance with GMP.

Other Foreign Buildings that Require GMP Evidence Include:

- Foreign buildings located in a non-MRA country listed on a DEL, or
- Foreign buildings located in a MRA country, where not all the activities, categories, and dosage forms are covered by the Certificate of Compliance (CoC)

However, Health Canada has implemented the NERBY process to reduce the burden on importers and prevent requesting the same evidence multiple times from year to year. In lieu of the requirement to provide GMP evidence for the foreign building every year as part of ALR, importers can sign and submit Undertaking B as part of their ALR thus allowing for the submission of GMP evidence by the NERBY date associated with the buildings on the DEL. If Undertaking B is not signed GMP evidence for every foreign building listed on the DEL is required with the ALR application.

Importers that sign and submit Undertaking B as part of their ALR application will be notified via a letter that the foreign building has been cancelled from the DEL when they fail do to either of the following:

- Submit GMP evidence before the NERBY date
- Apply for an extension of the current NERBY date

For more information on NERBY, including the assignment of NERBY date and extension of NERBY date, consult *GUI-0080*.

17. ALR Review Outcomes

Where the review of an ALR application identifies the application as incomplete, Health Canada will follow up with the DEL holder to address the deficiencies. Where the deficiencies are not addressed within the allotted timeframe, the part of the DEL associated with the deficiency will be **cancelled**.

If Health Canada does not receive your ALR application before April 1, Health Canada will take steps to cancel your DEL.

When a DEL is cancelled in full or in part, the company is no longer authorized to conduct the cancelled activities.

To resume activities, the company must obtain a new DEL or an amended DEL that includes the activity the company intends to conduct. To request a new DEL or an amended DEL, an application must be submitted, along with the applicable fees and the application will be subject to the regular service standard.

18. Notification Requirements

MRA Permits

Importers must notify Health Canada **immediately** if a MRA foreign building listed on the importer's DEL no longer holds a valid permit, licence, or authorisation from the MRA regulatory authority.

Contravention to GMP that may affect quality, safety or efficacy of a drug

DEL holders must notify Health Canada in writing within 15 calendar days after an event occurs that results in their being in contravention of any of the applicable requirements of Divisions 2 to 4 of the FDR, where it may affect the quality, safety or efficacy of a drug fabricated, packaged/labelled, tested as required under Division 2 or stored by them.

Notifications, pursuant to C.01A.013 (b) of the Regulations are to be sent to Hc.el.applications-le.sc@canada.ca using the subject "C.01A.13 Notification". The notification should include a description of the contravention, a description of the impact the contravention may have on quality, safety and/or efficacy. If available at the time of notification, any action that has been taken or is planned to address the contravention and mitigate the health risk the drug may pose to the consumer should also be submitted to Health Canada.

Quality, safety or efficacy incidents resulting in a recall decision must be reported to the applicable Health Product Compliance Regional Office in line with the requirements and processes outlined in the Recall Policy (POL-0016).

It is recommended that bankruptcies be notified to Health Canada under C.01A.013 (b).

Notifiable Changes

DEL holders must notify Health Canada in writing within 15 calendar days of making the following changes:

- Change to the licence holder's name, address or contact information
- Changes to the emergency contact's name or contact information
- Change of address for a building in Canada where records will be maintained

Change of Address

When the city or municipality where a building is located changes the address of the building by renaming the street or making any other change to the building address, the change is a notification. However, when a company moves its operations into a different building, this is a change that requires an amendment to the DEL before conducting activities at the new location.

Health Canada recommends that notifications that pertain to a matter that appears on the DEL be submitted using FRM-0033 as an amendment. This does not change the requirement to submit the application within 15 calendar days of the changes but will allow Health Canada to make the change to the DEL (e.g. amend the address of a building) and will meet the notification requirements.

19. Amalgamations and Changes of Ownership

Whenever a business transaction is being planned, it is recommended that Health Canada be contacted at Hc.del.questions-leppp.sc@canada.ca for more information with respect to the regulatory requirements and associated processes. Business transactions include, but are not limited to:

- Mergers/amalgamations
- Acquisition of assets, particularly acquisitions of buildings where regulated activities are conducted

Compliance and Enforcement

20. Suspension Authority

Health Canada can suspend a DEL in full or in part when:

- Health Canada has reason to believe that the DEL holder has contravened the FDA or FDR, including when a GMP inspection results in a Non-Compliant rating
- It is found that the DEL holder made false or misleading statements when applying for the licence or an amendment to an existing DEL
- It is necessary to do so to prevent a risk to the health of consumers
- The licensee fails to comply with an order to assess, issued under section 21.31 of the FDA, to demonstrate that the licensee's buildings, equipment or practices meet GMP requirements
- The licensee complies with an order to assess, issued under section 21.31 of the FDA, but fails to demonstrate that the licensee's buildings, equipment or practices meet GMP requirements

When a DEL is suspended, the DEL holder must cease all suspended activities.

21. Cancellation

The minister must cancel a DEL when:

- The licence has been suspended for a period of more than 12 months
- The licence holder has failed to submit an application for the review of their licence in accordance with subsection C.01A.009(1)

22. Authority to Add or Amend Terms and Conditions

Health Canada can add or modify terms and conditions to a DEL at any time when Health Canada determines that restrictions are necessary to ensure that the drug is not unsafe for use, or to prevent injury to the health of consumers.

Paying fees

23. Understanding DEL Fees

A fee must be paid when applying for a new DEL, annual licence review of a DEL, certain amendments to a DEL, reinstatement of a suspended DEL, or re-activation of a cancelled or withdrawn DEL. These fees cover a portion of the cost of Health Canada's regulatory programs for drugs. Specifically, the fees reflect the costs related to:

- Application review: Assessing and evaluating activities, categories of drugs, dosage form classes and foreign buildings.
- GMP inspection: Inspecting an establishment to verify that drugs are fabricated, packaged, labelled, imported, distributed, wholesaled and/or tested in a way that complies with the Regulations.
- Drug/laboratory analysis: The average cost of conducting product analysis for different drug categories across all establishments dealing with that category of drug. Different product classes are charged based on the relative risk of these products and the resulting need for laboratory surveillance. The drug/laboratory analysis provides additional evidence on the effectiveness of an establishment's quality control processes.

DEL fees do not apply for:

- a publicly funded health care facility
- a branch or agency of the Government of Canada
- a branch or agency of a provincial government
- an establishment that conducts licensable activities solely for APIs [A]

[A] Please note that some active ingredients are not included in the drug category of API and are, therefore, subject to fees. For more details regarding drug categories, please refer to the Category of Drugs section.

24. How DEL Fees are calculated

The fee payable for the examination of a DEL in respect of a single building is calculated based on the most "upstream" activity that is to be conducted at that building. A licence for an upstream activity can include downstream activities without additional fees payable. However, where the applicant proposes to conduct an activity in respect to unique categories and unique dosage form classes, increasingly higher fees apply proportional to the number of unique dosage forms/categories in the building, based on the most upstream activity. The fee payable associated with each building is the sum of each of these fee components.

Licensable activities are listed below, in the order of most upstream to downstream:

- Fabricator
- Packager/labeller
- Importer; distributor[b]
- Wholesaler; distributor[b]
- Tester

[B] Distribution of a drug for which the distributor holds the DIN is a more upstream activity compared to the distribution of an active ingredient or of a radiopharmaceutical drug that is in dosage form

Licensable Activity Fees

In general, fees are charged for:

- Each building where the activity takes place
- The number of unique drug categories to be fabricated, packaged, imported or distributed at each building
- The number of unique dosage form classes to be fabricated, packaged, imported or distributed at each building
- Fabrication of a sterile dosage form
- Each foreign building used to fabricate drugs that are to be imported
- Each foreign building used to fabricate sterile packaging
- Each additional dosage form at each foreign building fabricating

For drugs in the "medical gas" dosage form class, there is one flat fee to package in the form of trans-filling at multiple buildings (as opposed to a fee for each building). However, additional fees

apply for each downstream activity (i.e. importation, distribution or testing of medical gas) at each building where the trans-filling takes place. See table 1 below for examples.

Table 1. Medical Gas dosage form class example

Building Name	Authorized Activity in the Building	Fee Charged for the Building
Building A	Packaging/Testing	Packaging
Building B	Packaging only	None
Building C	Fabricating/Packaging/ Importing/Testing	Fabricate + Foreign buildings
Building D	Packaging/Testing	Testing
Building E	Packaging/Importing	Importing + Foreign buildings
Building F	Fabricating/Packaging	Fabricating

Please note that DEL fees **increase by 2% every year**, rounded up to the nearest dollar. However, beginning on April 1, 2019, for establishments that conduct licensable activities involving only veterinary drugs, DEL fees are adjusted according to the Consumer Price Index for Canada for the previous fiscal year.

Drug Analysis Fees

In addition to the fees that apply for each licensable activity, a drug analysis fee may be required of the owner or designated importer of a marketed DIN for the following products:

- Vaccines
- Schedule D drugs that are not vaccines or whole blood and its components
- Prescription drugs for human use, controlled drugs, drugs containing cannabis as defined in subsection 2(1) of the cannabis act or narcotics
- Drugs with dins, for human use, not included in any other item (includes disinfectants labelled for use on medical devices)
- Drugs for veterinary use only

There are also some products where there is no drug analysis fee. These include:

- Radiopharmaceuticals
- Whole blood and its components
- Hemodialysis products

- Disinfectants that are not labelled for use on medical devices
- Class monographs with one of following titles:
    - Acne therapies
    - Antidandruff products
    - Antiperspirants
    - Antiseptic skin cleaners
    - Athlete's foot treatments
    - Contact lens disinfectants
    - Fluoride containing anti-caries products
    - Medicated skin care products
    - Sunburn protectants
    - Throat lozenges

For more information on the applicable fees for **human and human/veterinary** DELs, see sections 19 to 25 of the Fees in Respect of Drugs and Medical Devices Regulations.

For more information on applicable fees for DELs for **veterinary drugs only**, see sections 4 to 10 of the Establishment Licensing Fees (Veterinary Drug) Regulations.

25. Fees for Amendments

The following types of amendments are subject to fees:

- Adding a domestic building (including relocations)
- Adding an upstream activity
- Adding a category of drug
- Adding a sterile dosage form for the first time at a building (for fabricators only)

If an existing building that is currently conducting a licensable activity is removed, no fee is required. However, the amendment application must be completed. Any previous fees paid for that building will not be refunded.

If an activity is to be added that is upstream from the activity currently authorized at a building, the applicable fee for that level of activity is required. However, if an activity is to be added downstream from the one currently authorized at a building (e.g. a DEL holder is authorized for

fabrication and wants to add packaging or distribution to the DEL), there are no fees for the downstream activity. The fees for the downstream activity will have already been covered by the fees paid for the upstream activity.

26. Requesting a Reduced Fee

The fees covering Health Canada's review of a DEL application may be reduced to a percentage of the annual gross revenue generated from the activities conducted under the licence. This is known as a fee remission.

The **annual gross revenue** is the amount earned by an establishment during a calendar year from activities that require a DEL. This includes revenue for the export of drugs, except those listed under section 37 of the FDA.

If licensable activities for human drugs or human/veterinary drugs are conducted, a DEL holder is eligible for a fee remission if the DEL fee is more than **1%** of the annual gross revenue generated from the activities under the licence.

Example:

If the human/veterinary DEL fee is $16,075, a fee remission can be received if the gross revenue was less than $1,607,500 in the previous calendar year.

If licensable activities for veterinary drugs only are conducted, fee remission can be received if the DEL fee is more than **1.5%** of one's annual gross revenue.

Example:

If the Vet Only DEL fee is $3,000 a fee remission can be received if the gross revenue was less than $200,000 in the previous calendar year.

Applying for a Fee Remission

To be considered for a fee remission **a request must be submitted every year as part of the annual licence review application**. To request a fee remission, the application must include:

- A complete annual licence review application form
- A certified statement of revenue, signed by the signing financial authority, showing the actual gross revenue generated from activities conducted under the del in the previous calendar year

Health Canada provides a template for the certified statement of revenue (Appendices J and K) in the ALR package. This document must clearly demonstrate the actual gross revenue, from all activities for which a DEL was required, generated during the last calendar year. The statement must be signed by the official responsible for a company's financial affairs.

A Certified Statement of Revenue can also be a signed letter on company letterhead, a signed copy of your ledger, or a signed copy of the sales logs from your general ledger.

We also encourage the submission of a calculation chart with the application. This tool is used by Health Canada to help determine the total fee and the potential fee remission for a DEL. For a copy of the DEL calculation chart, please contact Health Canada at HC.CRIU_UFRC.SC@canada.ca. If a fee remission is approved, an electronic invoice will be issued from Health Canada to pay the reduced amount. If the application does not qualify, an invoice for the full fee will be issued.

If there is disagreement with the calculation of the fee, Health Canada may be asked to reconsider the fees by sending a request to the Cost Recovery Invoicing Unit at HC.CRIU_UFRC.SC@canada.ca.

Audited Sales Records

If Health Canada considers the information provided in a fee remission request not adequate in determining gross revenue, the DEL holder may be required to provide sales records that have been audited by a qualified independent auditor.

If audited sales records are not submitted **within 60 calendar days** after Health Canada requests them, the fee remission request will be automatically denied and the full DEL fee will be payable with interest. (The limit is 90 calendar days for DELs for veterinary drugs only.)

Any costs associated with the independent audit are not the responsibility of, nor will be reimbursed by, Health Canada.

27. Paying your DEL Fees

Fee Deadlines

Annual licence review or amendment applications submitted to Health Canada are not required to include payment. Invoices are issued following review of applications (to reduce the possibility of incorrect calculations).

If a fee remission is requested, a completed Certified Statement of Revenue must be included with the annual licence review application otherwise an invoice for full payment will be issued. DEL holders that have submitted their annual licence review application with a fee remission request will receive an invoice for the reduced fee.

If applying for a new DEL, the fee is deferred as follows:

- For **human and human/veterinary drugs**, the fee is deferred until the end of the first full calendar year of activities under the licence.
- For **veterinary drugs only**, the fee is due within 90 calendar days after the day on which that first calendar year ends.

Example:

If an applicant never held a DEL, and was issued a DEL for human drugs on any day in 2016, payment is deferred until the final business day of December 2017.

If the applicant's DEL is for veterinary drugs only, payment would be due before April 1, 2018.

Health Canada will contact new applicants to notify them of their fee requirements and obligations. New applicants will then have **30 calendar days** to submit the payment along with a fee remission request, if applicable.

How to Pay Fees

DEL fees can be paid using one of the following methods:

- Credit card
- Cheque
- Money order
- International bank draft
- Bank wire

For step-by-step instructions on how to pay DEL fees, please read How to Pay Your Establishment License Fees .

Health Canada strongly advises paying fees in Canadian funds. Paying in non-Canadian funds or by bank wire may cause delays in account crediting. There is also the risk of underpayment due to fluctuating exchange rates or interest rates. Health Canada does not accept credit card information by e-mail.

Overpayment of Fees

Overpayments will be automatically credited to an account and refunded unless otherwise advised.

Late Payments

The responsibility of submitting payments on time lies with the applicant. Interest will be charged for all late payments (i.e. payments received after 30 days of the invoice date). Interest will not be waived once it is accrued.

In the case of an overdue account, monthly statements will be received until the debt is cleared. If Health Canada is unable to recover the outstanding balance of the account, the account may be turned over to a collection agency.

If the account is in arrears, it is encouraged that Accounts Receivable be contacted at 1-800-815-0506 or hc.ar-cr.sc@canada.ca to work out a monthly payment arrangement. The account will not be sent to a collection agency as long as the debt is repaid according to the terms and conditions established by the agreement.

Contact Information

Generic email accounts have been set up to provide subject specific guidance. These generic email accounts are regularly monitored by trained and knowledgeable staff.

Please send questions to the following generic email accounts based on the subject.

- General enquiries: Hc.del.questions-leppp.sc@canada.ca
- Fee-related enquiries: HC.CRIU_UFRC.SC@canada.ca
- API-related enquiries: hc.api.questions-ipa.sc@canada.ca
- Foreign building GMP enquiries: hc.foreign.site-etranger.sc@canada.ca
- General GMP enquiries: hc.drug.gmp.questions-bpf.medicaments.sc@canada.ca

Appendix A - Glossary

Acronyms

ALR	Annual Licence Review
API	Active Pharmaceutical Ingredient
ASR	Alternate Sample Retention
BPI	Bulk Process Intermediate
CDSA	Controlled Drugs and Substances Act
CFIA	Canadian Food Inspection Agency
CoC	Certificate of Compliance
CTA	Clinical Trial Application
DEL	Drug Establishment Licence
DIN	Drug Identification Number
FDA	Food and Drugs Act
FDR	Food and Drug Regulations
GMP	Good Manufacturing Practices
MRA	Mutual Recognition Agreement
NC	Non-Compliant
NERBY	New Evidence Required By
OTC	Over-the-Counter drugs

Terms

These definitions explain how terms are used in this document. If there is a conflict with a definition in the FDA or any of the regulations cited in this document, the definition in the FDA or regulations prevails.

Active ingredient – A drug that, when used as a raw material in the fabrication of a drug in dosage form, provides its intended effect. (FDR C.01A.001)

Active pharmaceutical ingredient (API) – An active ingredient that is used in the fabrication of a pharmaceutical. (FDR C.01A.001)

Alternate sample retention (ASR) – An alternate site specified on a DEL for the storage of samples

pursuant to section C.02.025 (1) of the FDR.

Alternate sample retention (ASR) site annex – A listing of the ASR sites that have been assessed against good manufacturing practices. This annex is a part of the DEL.

Antimicrobial agent – Antimicrobial agent means a drug that is capable of destroying pathogenic micro-organisms and that is labelled as being for use in the disinfection of environmental surfaces or medical devices, as defined in the *Medical Devices Regulations*, that

(a) are not invasive devices as defined in those Regulations; and

(b) are intended to come into contact with intact skin only.

Antimicrobial agents include environmental hard surfaces disinfectants used to clean surfaces such as desks and benches.

Active pharmaceutical ingredient intermediate – A material (isolated or not) produced during steps of the processing of an API that undergoes further molecular change or purification before it becomes a final API.

Biological drug – Any drug that is listed in Schedule D of the FDA that is in dosage form. This also includes any drug that is a bulk process intermediate that can be used to prepare a drug listed in Schedule D of the FDA.

Bulk process intermediate – Any intermediate form of a Schedule C or D drug (e.g. final bulk intermediate, bulk material, bulk concentrate, drug substance) that must undergo further processing before it becomes a final product.

Certified statement of revenue – A statement signed by the individual responsible for the company's financial affairs, showing the annual gross revenue from the sales generated by activities conducted under an establishment licence. It can be a signed letter on company letterhead, a signed copy of your ledger, or a signed copy of the sales logs from your general ledger.

Clinical trial – An investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug. (FDR C.05.001)

Controlled drug – A substance included in Schedule I, II, III, IV or V of the *Controlled Drugs and Substances Act*.

Distributor – A person, including an association or partnership, who under their own name, or

under a trade, design or word mark, trade name or other name, word or mark controlled by them, sells a food or drug.

Divisions 1A and 2 to 4 of the FDR apply to the following distributors:

a) a distributor of an active ingredient
b) a distributor of a drug for which the distributor holds the DIN (FDR C.01A.003)

Drug – Any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, a disorder, an abnormal physical state or the symptoms thereof, in humans or animals; (b) restoring, correcting or modifying organic functions in humans or animals; or (c) "disinfection" in premises in which food is manufactured, prepared or kept. (Section 2 of the FDA)

In Division 1A and Division 2 of the FDR, "drug" does not include any of the following:

(a) a dilute drug premix;

(b) a medicated feed as defined in subsection 2(1) of the Feeds Regulations, 1983;

(c) an active ingredient that is for veterinary use and that is not an active pharmaceutical ingredient;

(d) an active pharmaceutical ingredient for veterinary use that is not required to be sold pursuant to a prescription and that is also a natural health product as defined in subsection 1(1) of the Natural Health Products Regulations;

(e) a drug that is used only for the purposes of an experimental study in accordance with a certificate issued under section C.08.015 of the FDR. (C.01A.001(2))

Drug establishment licence (DEL) – A licence that allows a person to conduct licensable activities in a building in Canada.

Drug identification number (DIN) – A drug identification number (DIN) is an eight (8)-digit numerical code assigned by Health Canada to each drug product marketed under the FDA and Regulations. A DIN uniquely identifies the following product characteristics: manufacturer, brand name, medicinal ingredient(s), strength of medicinal ingredients(s), pharmaceutical form, route of administration.

Drug premix – A drug for veterinary use to which a drug identification number has been assigned, where the directions on its label specify that it is to be mixed with feed as defined in section 2 of the *Feeds Act*. (FDR C.01A.001)

Ethical drug – a drug that, in accordance with Federal Legislation, does not require a prescription,

but that is generally prescribed by a medical practitioner (e.g. nitroglycerine).

Fabricate – To prepare and preserve a drug for the purposes of sale. (FDR C.01A.001). This definition applies to Division 1A, 2, 3 and 4 of the FDR.

Fee remission – A process to help support small and medium-sized businesses by reducing the fee to apply for an establishment licence. The fee can be reduced if the fee payable is greater than 1% of the actual gross revenue generated from activities conducted under a licence during the previous calendar year.

Finished dosage form (FDF) intermediate – Any physical mix, starting when any 2 ingredients (e.g., active ingredient, anti-oxidant, preservative, filler, binder, solvent, etc.) are first added to the drug lot being manufactured, and before it becomes a drug in dosage form. Partially processed drug product intermediate, in-process drugs or bulk drug are examples of drug in dosage form intermediates

Foreign building – A building outside of Canada where the following licensable activities are conducted for drugs that are sold in Canada: fabrication, packaging/labelling, and/or testing.

Import – To import into Canada a drug for the purpose of sale. (FDR C.01A.001(1))

Inspection – Assessment of compliance against any of the applicable requirements of the FDA and its associated regulations by a designated inspector.

Invasive devices – means a medical device that is intended to come into contact with the surface of the eye or penetrate the body, either through a body orifice or through the body surface.

Label – Any legend, word or mark attached to, included in, belonging to or accompanying any food, drug, cosmetic, device or package. (Section 2 of the FDA). The action of labelling refers to affixing the inner or outer label to the drug. (FDR C.01A.001)

Licensable activity – Activities that require a licence (DEL). The six activities are fabricating, packaging/labelling, importing, distributing, wholesaling and testing.

List A APIs - List A names certain antimicrobial APIs that are important in human medicine.

Medical gas – Any gas or mixture of gases manufactured, sold or represented for use as a drug. (FDR C.02.002).

Mutual recognition agreement (MRA) – An international agreement that provides for the mutual recognition of compliance certification for good manufacturing practices for drugs. (FDR C.01A.001)

Natural health product – A substance set out in Schedule 1 of the Natural Health Products Regulations or a combination of substances in which all the medicinal ingredients are substances set out in Schedule 1, a homeopathic medicine or a traditional medicine that is manufactured, sold or represented for use in:

a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans
b) restoring or correcting organic functions in humans
c) modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health

However, a natural health product does not include a substance set out in Schedule 2, any combination of substances that includes a substance set out in Schedule 2 or a homeopathic medicine or a traditional medicine that is or includes a substance set out in Schedule 2.

Also, in accordance with subsection 2(2) of the NHPR, a substance or combination of substances or a traditional medicine is not considered to be a natural health product if its sale, under the FDR, is required to be pursuant to a prescription when it is sold other than in accordance with section C.01.043 of the FDR.

Over-the-counter drug – drugs that do not appear on a schedule or the Prescription Drug List or are not recommended to appear on any schedule.

Package/label – To put a drug in its immediate container or to affix the inner or outer label to the drug. (FDR C.01A.001)

This definition also applies to the replacement of packaging or labelling of previously packaged and labelled products (i.e. re-packing/re-labelling).

Pharmaceutical – A drug other than a drug listed in Schedule C or D to the FDA. (FDR C.01A.001)

This definition applies to Division 1A, 2, 3 and 4 of the FDR.

Pharmacist – An individual who (a) is registered or otherwise authorized under the laws of a province to practise pharmacy; and (b) is practising pharmacy in that province. (FDR C.01.001)

Practitioner – A person who (a) is entitled under the laws of a province to treat patients with a prescription drug; and (b) is practising their profession in that province. (FDR C.01.001)

Radiopharmaceutical – A drug that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. (FDR C.03.201)

These drugs are listed in Schedule C to the FDA.

Retail sale – The sale of goods to the public for use or consumption rather than for resale.

Regulatory authority – A government agency or other entity in an MRA country that has a legal right to control the use or sale of drugs within that country and that may take enforcement action to ensure that drugs marketed within its jurisdiction comply with legal requirements. (FDR C.01A.001)

Sell – To offer for sale, expose for sale, have in possession for sale and distribute, whether or not the distribution is made for consideration. (Section 2 of the FDA)

Sterile – Free from viable microorganisms.

Test – To perform the tests, including examinations, required under Part C, Division 2 of the FDR.

Vaccine – A preparation of a weakened or killed pathogen (such as a bacterium or virus) that, upon administration, stimulates antibody production or cellular immunity against the pathogen. Vaccines are listed in Schedule D to the FDA.

Wholesaler – A person who is not a distributor described in section C.01A.003 of the FDR and who sells any of the following drugs other than at retail sale:

a) a drug in dosage form that is listed in Schedule C or D of the FDA, a drug that is a prescription drug or a controlled drug as defined in subsection G.01.001(1)
b) an active ingredient
c) a narcotic as defined in Narcotic Control Regulations
d) drugs containing cannabis as defined in subsection 2(1) of the Cannabis Act

Appendix B - References

Laws

Controlled Drugs and Substances Act
http://laws-lois.justice.gc.ca/eng/acts/C-38.8/

Establishment Licensing Fees (Veterinary Drugs) Regulations
laws-lois.justice.gc.ca/eng/regulations/sor-98-4/page-1.html

Feeds Act
http://laws-lois.justice.gc.ca/eng/acts/F-9/

Fees in Respect of Drugs and Medical Devices Regulations
laws-lois.justice.gc.ca/eng/regulations/SOR-2011-79/index.html

Food and Drugs Act
laws-lois.justice.gc.ca/eng/acts/f-27

Food and Drug Regulations
laws-lois.justice.gc.ca/eng/regulations/c.r.c.,_c._870/index.html

Narcotic Control Regulations
http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._1041/

Prescription Drug List
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/prescription-drug-list/list.html

Guidelines

GUI-0001: Good manufacturing practices guide for drug products
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/gmp-guidelines-0001.html

GUI-0014: Alternate Sample Retention Site Guidelines
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/establishment-licences/forms/alternate-sample-retention-site-guidelines-0014.html

GUI-0023: Risk classification guide for drug good manufacturing practices observations
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/risk-classification-drug-gmp-observations-0023.html

GUI-0031: Good Manufacturing Practices for Medical Gases
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/gmp-guidelines-0031/document.html

GUI-0080: How to demonstrate foreign building compliance with drug good manufacturing practices
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/guidance-evidence-demonstrate-drug-compliance-foreign-sites-0080.html

GUI-0104: Good Manufacturing Practices Guidelines for Active Pharmaceutical Ingredients
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/drugs/guidelines-active-pharmaceutical-ingredients-0104.html

GUI-0119: Annex 1 to the Good manufacturing practices guide - Manufacture of sterile drugs
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/gmp-guidelines-annex-1-manufacture-sterile-drugs-0119.html

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

Policies

POL-0001: Compliance and Enforcement Policy for Health Products
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/policies-standards/compliance-enforcement-policy-0001.html

POL-0004: Drug Good Manufacturing Practices and Establishment Licensing Enforcement Directive
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/establishment-licences/directives-guidance-documents-policies/drug-good-manufacturing-practices-establishment-licensing-enforcement-directive-0004.html

POL-0011: GMP Inspection Policy for Canadian Drug Establishment
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/policies-standards/inspection-policy-canadian-drug-establishments.html

POL-0016: Recall Policy
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/drugs/recall-policy-0016.html

POL-0051: Policy on Manufacturing and Compounding Drug Products in Canada
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/policy-manufacturing-compounding-drug-products.html

POL-0060: Import and Export Policy for Health Products under the Food and Drugs Act and its Regulations
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/importation-exportation/policy-health-products-under-food-drugs-act-regulations-0060.html

Policy on Drug/Medical Device Combination Products
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/policies/drug-medical-device-combination-products.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

Forms

FRM-0033: Drug Establishment Licence Application: Form and Instructions
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/establishment-licences/forms/drug-establishment-licence-application-instructions-0033.html

Other related documents and tools

Drug Establishment Good Manufacturing Practices – Pre-Application Package (Importers, Distributors and Wholesalers)
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/application-package-importers-distributors-wholesalers.html

Drug Establishment Licensing Fees
https://www.canada.ca/en/health-canada/services/drugs-health-products/funding-fees/fees-respect-human-drugs-medical-devices/drug-establishment-licence-funding-fees-drugs-health-products.html

How to Pay Fees to Health Products and Food Branch
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/cost-recovery/pay-fees.html

List A: List of Certain Antimicrobial Active Pharmaceutical Ingredients
https://www.canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/animals/veterinary-antimicrobial-sales-reporting/list-a.html

Mutual Recognition Agreement Regulatory Authorities
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/international/mutual-recognition-agreements/updates/regulatory-authorities.html

Notice to Stakeholders - Implementation of Establishment Licensing Requirements for Atypical Active Pharmaceutical Ingredients
https://www.canada.ca/en/health-canada/services/drugs-health-products/public-involvement-consultations/compliance-enforcement/notice-stakeholders-implementation-establishment-licensing-requirements-atypical-active-pharmaceutical-ingredients.html

Veterinary Biologics CFIA web page
http://www.inspection.gc.ca/animals/veterinary-biologics/eng/1299159403979/1320545281259