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Good manufacturing practices inspection policy for drug establishments



POL-0011

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Canada 

Good manufacturing practices inspection policy for drug establishments (POL-0011)

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Disclaimer

This document does not constitute part of the *Food and Drugs Act* (the Act) 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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The following are 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.

About this document

1. Purpose

Health Canada inspects buildings where drugs are fabricated, packaged/labelled, tested, imported, distributed, or wholesaled against requirements for good manufacturing practices (GMP). This helps verify that safety and quality standards are met by those selling drugs to Canadians.

This policy describes the inspection strategy for GMP inspections of:

- Canadian buildings that require a drug establishment licence (DEL)
- foreign buildings that must be authorized on a DEL

It also describes the inspection process we use to assess whether the activities performed in a building comply with the:

- [Food and Drugs Act](#) (the Act)
- [Food and Drug Regulations](#) (the Regulations)

Health Canada's authority to inspect buildings in Canada comes from section 23 of the Act. Health Canada inspectors are designated under subsection 22(1) of the Act.

The main objectives of Health Canada's inspection strategy are to:

1. minimize the health risks throughout the drug supply chain
2. assess through inspections the compliance of those that fabricate, package/label, test, import, distribute, or wholesale drugs with GMP requirements
3. take compliance and enforcement action when needed
4. maintain national consistency
5. foster transparency with industry, Canadians, international regulatory partners, and other global stakeholders

2. Scope

This policy applies to buildings where drugs are fabricated, packaged/labelled, tested, imported, distributed, or wholesaled as outlined in the following table.

Table 1.0: Licensable activities by type of establishment

Type of building	Fabricator	Packager Labeller	Importer	Distributor	Wholesaler	Tester
Domestic – Finished dosage forms	✓	✓	✓	✓	✓	✓
Domestic – Active pharmaceutical ingredients (APIs)	✓	✓	✓	N/A ²	N/A ²	✓
Foreign ¹	✓	✓	N/A ²	N/A ²	N/A ²	✓

¹ Foreign buildings are not issued a licence. They are listed on the license of a Canadian holder of a DEL.

² Not applicable

This policy does not apply to activities that are exempt from establishment licensing – see [Guidance on Drug Establishment Licences and Associated Fees \(GUI-0002\)](#) for more information on which activities are exempt.



The scope of this policy does not include inspections for:

- **Blood establishments** – see [Inspection Strategy for Blood and Source Plasma Establishments \(POL-0039\)](#)
- **Semen establishments** – see [Inspection Strategy For Semen Establishments \(POL-0023\)](#)
- **Clinical trials** – see [Inspection Strategy for Clinical Trials \(POL-0030\)](#)
- **Cells, Tissues and Organs** – see [Inspection Policy for Cells, Tissues and Organs Establishments \(POL-0057\)](#)
- **Biological drugs for veterinary use** that are regulated under the [Health of Animals Act and Regulations](#) administered by Agriculture and Agri-Food Canada and the Canadian Food Inspection Agency.

3. Introduction

Health Canada is committed to helping ensure that health products are safe for Canadians to use. We work with regulated parties to manage the health-related risks and benefits of health products by:

- minimizing health risk factors to Canadians
- maximizing the safety provided by the regulatory system
- providing clear information to help Canadians make informed decisions

To meet these commitments, Health Canada manages an inspection program to enforce the regulations and promote industry compliance.

Before drugs can be sold to Canadians, they must meet high safety and quality standards. Canadians rely on drugs produced from both domestic and foreign manufacturers through complex global supply chains involving both raw materials and finished dosage forms. A high percentage of health products are imported into Canada, with many products containing ingredients from other countries.

To facilitate uniform application of these requirements and help the industry to comply, Health Canada has developed a series of guides — see [Good manufacturing practices \(GMP\) guide for drug products \(GUI-0001\)](#) and [Good manufacturing practices for active pharmaceutical ingredients \(GUI-0104\)](#) for more information on GMP requirements.

Drugs can only be imported for sale in Canada if GMPs are followed where they are made. The GMP standards are harmonized with other countries through international cooperation bodies such as the [World Health Organization \(WHO\)](#), the [Pharmaceutical Inspection Cooperation/Scheme \(PIC/S\)](#), and the [International Council for Harmonisation \(ICH\)](#). We establish [mutual recognition agreements](#) (MRA) with regulatory authorities around the world that have equivalent GMP standards.

The objective of an MRA is to recognize the equivalency of the drug GMP program between regulatory authorities through a formal evaluation process. Once an MRA is in place, the import of drugs from MRA countries is made easier by exchanging certificates of GMP compliance. The frequency of GMP inspection in MRA countries has been a standard that Health Canada has consistently considered when scheduling domestic GMP inspections. This helps provide a fair and uniform level of domestic inspection oversight among regulatory authorities that operate under an MRA.

Foreign buildings must comply with GMP requirements to be listed on a Canadian DEL in order for their products to be sold in Canada. To do this, we may be informed by inspection results from trusted international regulatory partners and perform paper-based reviews of the information to make regulatory decisions in Canada. Health Canada also performs a number of on-site inspections of facilities outside Canada each year. You may find guidance on the type of information that should be submitted to Health Canada to assess the GMP compliance of foreign buildings in the guide on [*How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)*](#).

Results of on-site inspections and paper-based reviews are listed in the [Drug and Health Product Inspections Database](#).

With Canadian establishments importing a high number of drugs manufactured abroad, Health Canada is increasing its oversight of foreign drug manufacturers and the number of on-site foreign GMP inspections. Health Canada works with international regulatory partners and takes a risk-based approach to plan and conduct foreign on-site inspections, where possible. This risk-based approach will help promote an appropriate level of regulatory oversight, efficient and effective use of resources, and a collaborative global approach for compliance and enforcement actions.

This increased scrutiny of foreign buildings helps to protect the health of Canadians and improve our contribution to the harmonization of international inspection standards, procedures, and practices. This objective must also be balanced with expectations for Health Canada to maintain appropriate levels of oversight on Canadian industry. It will enable Health Canada to be adaptable to current and future realities by increasing its agility and being more present globally while balancing oversight of domestic and foreign establishments.



Canada has worked hard to harmonize its GMP inspection program with international regulators. Key milestones include:

- **1997** – Division 1A (Establishment Licences) of the Food and Drug Regulations came into force. These regulations brought forward a licensing scheme harmonizing Canadian requirements with other international approaches. They apply to drug fabricators, packagers/labellers, testers, distributors, importers and wholesalers.
- **1998** – MRAs are ratified with the European Community (EC) and Switzerland. Soon after, MRAs are signed with Australia and the European Economic Area – European Free Trade Association (EEA EFTA).
- **1999** – Canada is accepted as a member of the PIC/S.

- **2013** – Division 1A (Establishment Licences) and Division 2 (Good Manufacturing Practices) of the Food and Drug Regulations are amended to include active ingredients in drugs for human use. Additional amendments were made in **2017** to include active ingredients in drugs for veterinary use. These regulations aligned Canadian requirements for active ingredients with the requirements of international regulatory partners.

Inspection policy

4. Policy statement

Any establishment within the scope of this policy must comply with:

- the *Food and Drugs Act*
- the Food and Drug Regulations

Health Canada will assess GMP compliance by conducting inspections. The frequency and duration of these inspections will be based on the inherent risk posed by the nature of the activities performed. If compliance risks are identified or other risk mitigation strategies are needed, inspections will be scheduled more frequently.

5. Inspection process

Before an inspection

In most cases, Health Canada gives notice to an establishment before an inspection takes place. An inspector contacts the establishment to schedule the inspection. Health Canada may also request that the establishment provide certain information in advance of an inspection.

Health Canada is not required to provide advance notice of every inspection before it happens. Inspectors may not give advance notice if:

- there is an immediate risk to health and safety
- this approach will better assess compliance with the Act and its regulations

Once the date of the inspection has been set and the establishment is informed, the inspection generally takes place on the date scheduled. Requests for changes to dates of scheduled inspections will only be accepted at Health Canada's discretion, with proper justification from the establishment.

During an inspection

During an inspection, Health Canada inspectors observe and discuss the drug establishment's processes and review its records, documents and procedures. Our inspections are detailed, rigorous and follow international standards.

Inspectors look carefully at many different areas to assess the GMP requirements in Part C, Division 2 of the Regulations, including:

- pharmaceutical quality system
- facility design
- integrity of data and record keeping
- qualification and validation processes
- equipment qualification and maintenance
- staff training
- written procedures
- raw material controls
- storage facilities
- processing operations
- environmental and contamination controls
- sanitary conditions
- product testing and stability
- packaging
- distribution
- supplier qualification

Risk observations

Inspectors make “observations” when they note areas where the establishment is not adequately meeting its regulatory requirements. Each observation is classified by level of risk:

- **Critical observation (Risk 1)** – describes a situation that is likely to result in a product that may result in an immediate or latent health risk, or that involves fraud, misrepresentation or falsification of processes, products or data.
- **Major observation (Risk 2)** – describes a situation that may result in the production of a drug not consistently meeting its marketing authorization.
- **Other observation (Risk 3)** – describes a situation that is neither critical nor major, but is a departure from the GMPs.

At the end of an inspection

At the end of an inspection, Health Canada discusses the observations with the establishment during an “exit meeting,” then sends the establishment an inspection “exit notice.” This document outlines any observations (deficiencies) noted by the inspector. The establishment must take corrective actions to fully comply with the Act and its regulations. The establishment may also need to create and implement a corrective action and preventive action (CAPA) plan that includes target dates for completion. The timeline to respond to Health Canada and provide the plan is 20 working days.



Your written response to the exit notice should include a CAPA plan. This should be developed using quality risk management principles.

You should consider including the following in your written response that details the CAPA plan:

- details of formalised risk assessments
- outcomes of root cause analyses that clearly identify the underlying causes of the problems
- corrections, corrective actions, and preventive actions
- how and when you will verify the appropriateness of the measures you have taken to address the deficiencies

You can find additional information about quality risk management and CAPA in [*ICH Q9: Quality Risk Management*](#) and [*ICH Q10: Pharmaceutical Quality Systems*](#).

The exit notice also gives the establishment an overall inspection rating. This rating is based on the number and risk level of observations at the time of the inspection:

- **Compliant (C)** – the establishment has shown its activities comply with the applicable requirements of the Act and its regulations.
- **Non-compliant (NC)** – the establishment has not shown its activities comply with the applicable requirements of the Act and its regulations.

When an establishment is given a non-compliant rating, it must also immediately address high risk deficiencies.



Health Canada assigns inspection ratings based on the [Risk classification guide for drug good manufacturing practices observations \(GUI-0023\)](#).



Health Canada may also consider enforcement actions following an inspection. This can include suspending a DEL. Options are outlined in the [Compliance and Enforcement Policy \(POL-0001\)](#) and the [Drug Good Manufacturing Practices \(GMP\) and Establishment Licencing \(EL\) Enforcement Directive \(POL-0004\)](#).

Reporting

Health Canada posts on its website detailed report cards for drug inspections. Each inspection report card summarizes the inspection observations and ratings, and makes them available to the public. You can find them on the [Drug and Health Product Inspections Database](#).



GMP inspection results may be shared with international regulatory partners. Compliant GMP inspection results are used to issue DELs, as well as Certificates of GMP Compliance that are exchanged between regulators under the framework of MRAs.

6. Inspection frequency

Inspection of domestic establishments

Health Canada inspects Canadian drug establishments against GMP standards to verify that safety and quality standards are met before drugs are sold to Canadians.

Inspections for new licences

Health Canada inspects Canadian establishments before it issues them a DEL, according to the requirements described in Division 1A of the Food and Drug Regulations.

When Health Canada receives a new application for a DEL, its service standard is 250 days to consider the application, verify GMP compliance, and determine whether to issue or refuse a licence. We will perform an initial on-site inspection of the establishment during that period. We then typically conduct a regular inspection within 12 months of the initial inspection (but it may be performed at an earlier or later date based on the level of risk).



New establishments applying for a DEL must be ready for an inspection when submitting their application. Health Canada requires all information and systems to be in place at the time of inspection.

An application will be considered incomplete and no licence will be issued if an establishment is not prepared for an initial inspection when contacted. The establishment will be required to submit a new application with all supporting information. The service standard of 250 days will apply to the resubmitted information from the time the new application is received by Health Canada.

Inspections for licence amendments

When Health Canada receives an application for amendment to a DEL, we may conduct an inspection to verify GMP compliance in support of the application to amend a licence if required.



Establishments making an amendment must be ready for an inspection when submitting their application. Health Canada requires all necessary information and systems to be in place at the time of inspection.

Regular inspections

Health Canada's inspection of domestic establishments is based on defined frequencies, similar to those of regulators in other jurisdictions. The inspection frequency is based on the licenced activity's level of risk. The frequency also takes into account Health Canada's resources and priorities. Table 2.0 Domestic Establishment Inspection Frequency provides the length of time between inspections.

Table 2.0 Domestic Establishment Inspection Frequency

Activity ¹	Sterile	Non-Sterile	Inspection Frequency (target - years)
Sterile Fabrication (includes sterile packaging)	✓	N/A ³	2
Non-sterile Fabrication	N/A ³	✓	3
Primary Packaging/Labelling	N/A ³	✓	3
Testing	✓	✓	3
Medical Mixed Gases — All Licensable Activities	N/A ³	✓	3
Secondary Packaging/Labelling	✓	✓	4
Importation	✓	✓	4
Distribution ²	✓	✓	4
Wholesale ²	✓	✓	4
Medical Single Gases — All Licensable Activities	N/A ³	✓	4

¹ If an establishment is conducting multiple activities at the same time, the higher risk activity may dictate the inspection cycle.

² Distribution and wholesale are not licensable activities for APIs.

³ Not applicable

These inspection frequencies are guidelines that Health Canada may change as required. More frequent inspections may occur when risks have been identified based on:

- current state of compliance and compliance history
- size of the establishment
- type and risk of activities
- supply chain importance

Also, Health Canada may periodically perform unannounced random inspections to assess compliance.

Inspection of foreign buildings

Foreign establishments must comply with the GMP requirements in Division 2 to be listed on a Canadian DEL under Division 1A of the Regulations.

Health Canada has increased the number of foreign on-site inspections in order to enhance its regulatory oversight and global presence. Furthermore, Health Canada works collaboratively with international regulatory partners to schedule and conduct inspections, where possible.

Health Canada has adopted a comprehensive risk-based approach for selecting foreign buildings for an on-site inspection. This approach considers, among other things:

- type of GMP evidence available for the foreign building
- information indicating the GMP compliance history of the foreign building
- lack of recent GMP evidence
- medical necessity of the drug product manufactured at the foreign building
- the date that new GMP evidence is required to be submitted to HC.

Once foreign buildings are selected, Health Canada communicates its inspection intent to Importers that have the selected foreign building(s) listed on their DEL. Health Canada will also request contractual arrangements to be signed by the importers and foreign buildings.

As per C.01A.005 of the Food and Drug Regulations, Health Canada also conducts paper-based reviews of corporate/consultant audits or inspection reports from inspections conducted by qualified/regulatory authorities. More information on this process is in Health Canada's guidance [*How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)*](#).

Inspection duration

The average time required for an inspection will vary depending on the:

- size of the establishment
- type and risk of activities
- information indicating the current state of GMP compliance and compliance history

In general, inspectors will typically spend up to ten days on site when inspecting a fabricator. The duration on site for other activities is typically up to three days. More time will be added on site if needed to effectively evaluate activities and assess compliance.



The above averages are for time spent **on site** at a facility. The total time allocated to an inspection is longer, as activities include pre- and post-inspection meetings and analysis of information.

Appendices

Appendix A – Glossary

Acronyms

API: Active pharmaceutical ingredient

C: Compliant

CAPA: Corrective Action and Preventive Action

DEL: Drug establishment licence

EC: European Community

EEA-EFTA: European Economic Area – European Free Trade Association

GMP: Good manufacturing practices

ICH: International Council for Harmonisation

MRA: Mutual recognition agreement

NC: Non-compliant

PIC/S: Pharmaceutical Inspection Cooperation/Scheme

WHO: World Health Organization

Terms



These definitions explain how terms are used in this document. If there is a conflict with a definition in the [Food and Drugs Act](#) or [Food and Drug Regulations](#), the definition in the Act/Regulations prevails.

Corrective Action: Action to eliminate the cause of a detected non-conformity or other undesirable situation. NOTE: Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. (ICH Q9 and ISO 9000:2005)

Inspection: Assessment of compliance against any of the applicable requirements of the *Food and Drugs Act* and its associated regulations by a designated inspector. Inspections are conducted at predetermined intervals or on a risk basis.

Initial inspection: The first inspection conducted at an establishment, where not all applicable requirements of the Act and its associated regulations are assessed. This is not considered to be a regular inspection. For drug sites, this is done before issuing a new/first DEL.

Preventive Action: Action to eliminate the cause of a potential non-conformity or other undesirable potential situation. NOTE: Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence. (ICH Q9 and ISO 9000:2005)

Regular inspection: An inspection that is conducted against all applicable requirements of the Act and its associated regulations, and that focuses mainly on risk and the systems of control in place at an establishment.

Re-inspection: A follow-up inspection carried out in response to the assignment of a non-compliant (“NC”) inspection rating. The inspection is focused on, but not restricted to, those requirements of the Act and its associated regulations where contraventions were observed.

Re-assessment: A follow-up inspection carried out in situations where the establishment was assigned an overall compliant (“C”) inspection rating on the previous inspection, but the number or type of observations contained in the previous inspection exit notice require corrective action in a timely manner. The inspection is focused on, but not restricted to, those requirements of the Act and its associated regulations where contraventions were observed.

Appendix B – References

Laws and regulations

Food and Drugs Act

laws-lois.justice.gc.ca/eng/acts/f-27/

Food and Drug Regulations

http://laws-lois.justice.gc.ca/eng/regulations/c.r.c.,_c._870/index.html

Health of Animals Act

<http://laws-lois.justice.gc.ca/eng/acts/H-3.3/>

Related documents

Compliance and Enforcement Policy (POL-0001)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/policies-standards/compliance-enforcement-policy-0001.html>

Drug Good Manufacturing Practices (GMP) and Establishment Licencing (EL) Enforcement Directive (POL-0004)

<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>

Good manufacturing practices guide for drug products (GUI-0001)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/gmp-guidelines-0001.html>

Good manufacturing practices for active pharmaceutical ingredients (GUI-0104)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/drugs/guidelines-active-pharmaceutical-ingredients-0104.html>

Guidance on Drug Establishment Licences and Associated Fees (GUI-0002)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/establishment-licences/directives-guidance-documents-policies/guidance-drug-establishment-licences-drug-establishment-licensing-fees-0002.html>

ICH Q9: Quality Risk Management

<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/quality/adoption-international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use.html>

ICH Q10: Pharmaceutical Quality System

<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/quality/adoption-international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-guidance-pharmaceutical-quality-system.html>

Inspection Strategy for Blood and Source Plasma Establishments (POL-0039)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/blood-donor/inspection-strategy-blood-establishments-0039-summary.html>

Inspection Strategy for Clinical Trials (POL-0030)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/guidance-documents/inspection-strategy-clinical-trials.html>

Inspection Strategy for Semen Establishments (POL-0023)

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/donor-semen/inspection-strategy-semen-establishments-policy-0023.html>

Risk classification guide for drug good manufacturing practices observations (GUI-0023)

<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>

How to demonstrate foreign building compliance with drug good manufacturing practices (GUI-0080).

<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>

Other

[Drug and Health Product Inspections Database](https://www.canada.ca/en/health-canada/services/inspecting-monitoring-drug-health-products/drug-health-product-inspections.html)

<https://www.canada.ca/en/health-canada/services/inspecting-monitoring-drug-health-products/drug-health-product-inspections.html>