Health Canada Santé Canada

SITE LICENSING GUIDANCE DOCUMENT

NATURAL HEALTH PRODUCTS DIRECTORATE

August 2006
Version 2.0

Canada

“Our mission is to help the people of Canada maintain and improve their health, while respecting individual choices and circumstances.”

Health Canada

“Our role is to ensure that Canadians have ready access to natural health products that are safe, effective and of high quality while respecting freedom of choice and philosophical and cultural diversity.”

Natural Health Products Directorate

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ABOUT THIS GUIDANCE DOCUMENT

This guidance document is intended for manufacturers, packagers and labellers of natural health products (NHPs) within and outside of Canada, and for Canadian importers of NHPs for sale in Canada.

This guidance document was written to explain Part 2 of the *Natural Health Products Regulations* (the Regulations), which addresses site licensing. This document outlines what a site licence is, when it is required, who must hold one, how to apply for one and how to change and renew one. It also describes the process applications go through when they reach the Natural Health Products Directorate (NHPD), and includes samples of all the necessary forms. It can be used as an aid to complete an effective site licence application, to provide clarity on how to maintain a valid site licence and to gain a better overall understanding of the site licensing process and regulations. Currently, the NHPD's site licensing process consists of a document review to assess the compliance of the applicant's site to Part 3 – Good Manufacturing Practices of the Natural Health Products Regulations. The Quality Assurance Report (QAR) that applicants may submit to NHPD describing the site's good manufacturing practices (see **chapter 2.1** for more details on the QAR and its alternatives) is considered to be an attestation by the applicant that the site meets all the requirements of Part 3. However, when the NHPD needs more information to assess the application then, according to section 37 of the Regulations, it may request additional information from the applicant. The NHPD will be re-examining this site licensing process with the intent to determine if it is necessary to increase the requirements to the use of on-site inspection reports written by third party auditors or Health Canada inspectors.

To determine if the contents of this document will apply to your operations, refer to **chapter 1.3**.

Boxes with the text of the Regulations appear in relevant locations throughout the text. A complete version of the Regulations is available on the Internet at http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/acts-lois/prodnatur/regs_cg2_e.html.

The definitions of terms used in this guidance document are provided in the **Glossary**.

This guidance document was developed in consultation with knowledgeable individuals from the Natural Health Products industry. The information is based on the *Natural Health Products Regulations*, which were published in Canada Gazette, Part II, on June 18, 2003. The Regulations came into force on January 1, 2004.

TABLE OF CONTENTS

1.0 GENERAL OVERVIEW

1.1 Purpose of the Site Licence Regulations

Part 2 (sections 26 to 42) of the *Natural Health Products Regulations* (the Regulations) sets out the requirements and rights of the licensee and the Natural Health Product Directorate (NHPD) in regards to site licensing. The purposes of Part 2 are:

- to ensure that the NHPD is aware of and has identified all the sites at which businesses are manufacturing, packaging, labelling and importing NHPs in Canada;
- to set the requirement that businesses assure the NHPD that they are meeting the regulatory requirements related to manufacturing, packaging, labelling and importing NHPs; and
- to ensure that all natural health products (NHPs) on the market in Canada are safe, of good quality, and are manufactured, packaged, labelled and stored in sites that comply with the good manufacturing practices outlined in Part 3 of the Regulations.

1.2 What is a Site Licence?

A site licence issued by the NHPD gives the licensee authorization to manufacture, package, label and/or import NHPs. Section 27 of the Regulations states the conditions for which a site licence is required and the activities that are covered by the licence.

PART 2: SITE LICENCES
Prohibition
Section 27

(1) Subject to subsection (2), no person shall manufacture, package, label or import a NHP for sale unless

(a) the person holds a site licence issued in respect of the activity; and

(b) the person conducts the activity in accordance with the requirements set out in Part 3.

(2) No person who holds a site licence shall manufacture, package, label or import a NHP for sale

(a) during the period of any suspension of the licence under section 39 or 40; or

(b) after cancellation of the licence under paragraph 41(b).

These activities must be carried out according to the good manufacturing practices in Part 3 of the Regulations. For more information on the good manufacturing practices see the *Good Manufacturing Practices Guidance Document*. A licensee must stop performing all previously authorized activities during a period of any suspension or cancellation of the site licence (**chapter 5.4**). In order to maintain the status of the site licence, licensees must renew (**chapter 5.1**) and amend (**chapter 5.2**) their licence as required by the Regulations, and notify the NHPD of changes to the information submitted on their Site Licence Application Form (**chapter 5.3**), as required by the Regulations.

1.3 Who Requires a Site Licence?

A site licence is required by all businesses in Canada that wish to **manufacture, package, label and/or import** a NHP for sale and who meet the following criteria:

- the business includes a physical site in Canada at which the activities occur. The NHPD defines *site* as a place of or for an activity specified under the Regulations.
- the NHP that is manufactured, packaged, labelled and/or imported at the above site does not require further processing to be ready for consumption by the consumer.

Further notes on importing NHPs:

- Any business or individual that brings into Canada a NHP for the purpose of sale is considered to be an importer.
- Importers that ship a product directly to the retailer without first storing the product still require a site licence and, therefore, must be compliant with all the good manufacturing practice requirements for obtaining a site licence.
- Retailers selling products obtained from a business that does not take responsibility as the importer and, therefore, does not have a site licence, will themselves be considered the importer and will require a site licence.

Note: A business involved in manufacturing, packaging, labelling or importing a NHP may choose to apply for one site licence for all business operations (i.e. at multiple buildings or locations) or for individual site licences for each of the respective buildings or locations.

A site licence is **not** required by:

- A pharmacist, health care practitioner, aboriginal healer or traditional Chinese medicine practitioner who, at the request of a patient, compounds a NHP for the purpose of sale solely to that individual. For clarification on what activities performed by a practitioner will require a Site Licence, refer to the NHP Compounding Policy that will soon be made available on the NHPD Web site (see **Appendix 1**).
- Distributors that do not import NHPs from other countries into Canada are not required to have a site licence , however, they must follow good manufacturing practices (as stated in section 43 of the Regulations) .
- Businesses performing the activities of growing, harvesting, cleaning, sorting, packaging and/or importing raw material that do not produce a product that is ready for consumption by the consumer. For further clarification on how the NHPD defines a raw material, refer to the NHP Raw Material Policy that will soon be made available on the NHPD Web site (see **Appendix 1**).
- Businesses that manufacture, package, or label NHPs for the sole purpose of exporting outside of Canada.

Note: Section 26 of the Regulations states that when a NHP is being manufactured, packaged, labelled or imported solely for the purpose of a clinical trial, the site licensing requirements under Part 2 of the Regulations do not apply. However, the products and activities must conform

to the provisions outlined in Part 4 of the Regulations (Clinical Trials Involving Human Subjects). For more information on clinical trials, see the *Clinical Trials For Natural Health Products* guidance document.

Note: Individuals wishing to import a NHP solely for personal use may import a less than three month supply under the Importation of Human Use Drugs for Personal Use Enforcement Directive and do not require a site licence. Further information on this directive can be found on the following Web site:
http://www.hc-sc.gc.ca/dhp-mps/compli-conform/int/export-import/drugs-drogues_tc-tm_e.html

2.0 APPLYING FOR A SITE LICENCE

Section 28 of the Regulations outlines the basic requirements for a complete site licence application.

> PART 2: SITE LICENCES
> Licence Application
> Section 28
>
> An application for a site licence shall be submitted to the Minister and shall contain the following information and documents:
>
> (a) the name, address and telephone number, and if applicable, the facsimile number and electronic mail address of the applicant;
>
> (b) a statement specifying which one or more of the activities of manufacturing, packaging, labelling or importing the applicant is proposing to conduct;
>
> (c) if the applicant is proposing to manufacture, package or label a NHP, the address of each building in which each activity is proposed to be conducted;
>
> (d) if the applicant is proposing to import a NHP, the address of each building in which that NHP is proposed to be stored;
>
> (e) for each activity specified under paragraph (b), a statement indicating whether or not the applicant is proposing to conduct the activity in respect of a NHP in sterile dosage form; and
>
> (f) in respect of the buildings, equipment, practices and procedures used to conduct each activity specified under paragraph (b), a report from a quality assurance person demonstrating that they comply with the requirements set out in Part 3.

To apply for a site licence, applicants must provide to the NHPD for assessment a site licence application which includes the following forms and documents:

- **Site Licence Application Form.** This form captures all of the information outlined in Section 28 (a) to (e) of the Regulations. The links to the Web version of this form and the instructions on how to complete the form can be found in **Appendix 1**.
- **Quality Assurance Report Form.** A report prepared by either a quality assurance person or a third party auditor who has the training, experience and technical knowledge relating to the activity conducted and the requirements of Part 3 (Good Manufacturing Practices) of the Regulations. This report is based on the assessment against the good manufacturing practices requirements set out in the *Good Manufacturing Practices Guidance Document*. It is considered to be an assessment document and evidence of good manufacturing practices compliance. The Quality Assurance Report may also be considered to be an attestation by the applicant that the site meets all the requirements of Part 3. However, when the NHPD needs more information to assess the application then, according to section 37 of the Regulations, it may request additional information from the applicant. The Quality Assurance Report is valid for one year (minus one day) from the date it was completed by the quality assurance person or third party auditor.
  - **Alternatives to the Quality Assurance Report Form**.
    - Establishment licence holders may submit a copy of their current establishment licence with the site licence application in place of the Quality Assurance Report

form. The establishment licence lists the last date of inspection as well as all buildings where manufacturing, packaging, labelling, importing and distributing are authorized for drug products under the *Food and Drug Regulations*. When the activities and buildings match up exactly with those mentioned in the site licence application form for which a licence is requested, no further evidence of compliance relating to the good manufacturing practices is required. Establishment licence holders must submit a separate Quality Assurance Report form or equivalent for those additional activities and buildings that are not listed in the establishment licence dealing exclusively with NHPs.

- A valid drug Good Manufacturing Practices (GMP) inspection report by a Health Canada inspector can also be used in place of the Quality Assurance Report form. This type of inspection report remains valid for a period of three years (minus one day) from the date of inspection.
- A corporate audit report that includes the rationale to why this corporate audit report is submitted in place of a Quality Assurance Report. In addition, the report must meet the following conditions:
- The qualifications and experience of the individual(s) performing the inspection must be stated. As a minimum, the individual(s) must have sufficient technical knowledge, training and experience of the NHP GMP and must be qualified.
- The inspection is conducted against the Canadian drug GMP, NHP GMP, or equivalent guidelines (e.g. PIC/s GMP, US cGMP) and all applicable sections are assessed.
- Corrective measures taken to address the noted deficiencies are included in the report. The adequacy of these corrective measures are assessed by the corporate auditor or auditing team.
- The report is signed and dated.

- Other reports such as company Quality Manuals (ISO 9001:2000) may be used in place of the Quality Assurance Report so long as they demonstrate (with evidence) an adherence to all relevant NHP GMP requirements and a commitment to follow the Regulations. Any other types of reports may be acceptable as determined on a case-by-case basis.

Appendix 1 provides links to the Quality Assurance Report Form and the instructions on how to complete the form. See also the *Good Manufacturing Practices Guidance Document*.

- **Supplementary Quality Assurance Report Form (when applicable).** Manufacturers of NHPs used in homeopathy must complete and submit this form in addition to the standard Quality Assurance Report form. This form covers all the additional good manufacturing practices requirements for homeopathic medicines as outlined in chapter 2 of the *Good Manufacturing Practices Guidance Document.* **Appendix 1** provides links to the Supplementary Quality Assurance Report form and the instructions on how to complete the form.
- **Designated Party Authorization Form (when applicable)**. Applicants who have designated a third party person to file a submission with the NHPD on their behalf must submit a Designated Party Authorization Form. This form must be resubmitted should the designated party change at any time. **Appendix 1** provides links to the Designated Party Authorization Form.

2.1 Filing a Site Licence Submission

Completed submissions including site licence applications, amendments, notifications and renewals with their respective attachments should be submitted to the NHPD at the following address:

Health Canada
Health Products and Food Branch
Natural Health Products Directorate
Bureau of Product Review and Assessment
Submission Management Division
Basement, Qualicum Building, Tower A
2936 Baseline Rd.
AL 3300C
Ottawa, ON K1A 0K9 (Couriers: K2H 1B3)

See **Appendix 2** for a list of common application deficiencies. This list can be used as a guide to check for completeness when compiling a site licence application package for submission. Deficiencies are also addressed in **chapter 3.1.**

2.2 How to Submit a General Submission Inquiry

Please contact the relevant processor or site licence assessment officer for questions specific to a submission. Any inquiries relating to GMPs, the submission process, requirements and/or requests for site licence applications may be submitted by mail or fax to the address in **chapter 2.1**, or by e-mail or phone at the coordinates listed below.

E-mail: NHPD_DPSN@hc-sc.gc.ca
Phone: 1-888-774-5555

3.0 SUBMISSION MANAGEMENT

This chapter briefly outlines how the NHPD manages the information that site licence applicants/licensees submit.

The NHPD accepts applications for a new site licence, renewal of a site licence, and notifications/amendments to a site licence. For detailed information on the requirements for these different submissions, please refer to:

- **chapter 5.1** for site licence renewals.
- **chapter 5.2** for amendments to a site licence; and
- **chapter 5.3** for notifications to a site licence.

3.1 Deficiencies in the Application

The application will be assessed for deficiencies at each level. These deficiencies can range from minor and easily correctable (e.g. application missing company name or phone numbers) to major deficiencies (e.g. no procedures for finished product release, inadequate sanitation program) that may prevent the applicant from achieving GMP compliance and thus prevent the applicant from meeting the requirements set by the Regulations. Deficiencies may prevent any further assessment of the application without the provision of additional information from the applicant. Should the information be deemed inadequate by the NHPD, deficiencies may ultimately, prevent the granting of a site licence to the applicant. **Appendix 2** provides a list of deficiencies that may result in these actions.

3.2 Screening and Assessment of the Application

The NHPD verifies administrative information and assigns each application a file number (for new applications) and a submission number. The NHPD issues an acknowledgment notice to the applicant confirming receipt of the application. The notice lists the file number and submission number, and notes the date of receipt. Applicants/Licensees should use the file number assigned on all subsequent correspondence about the submission including renewal, amendment and notification submissions. If an applicant/licensee does not know the file number, he or she should mention his or her name or the company's name, the address and the activity being performed.

The NHPD checks the site licence application forms for completeness and that the appropriate supporting data is provided for that submission. This supporting data includes the Quality Assurance Report Form (with Standard Operating Procedures listed and their respective records/logs attached) or its equivalent as outlined in **chapter 2** of this document and, when applicable, the Supplementary Quality Assurance Report Form and the Designated Party Authorization Form.

The application form and supporting data are then assessed for compliance with the Regulations.

When the NHPD needs more information to assess the submission then, according to section 37 of the Regulations, it may request additional information from the applicant.

PART 2: SITE LICENCES
Additional Information
Section 37

If the information and documents submitted in respect of an application under section 28, an application for amendment under subsection 32(2) or a request for renewal under section 36 are insufficient to enable the Minister to determine whether the licence should be issued, amended or renewed, as the case may be, the Minister may request that the applicant provide the Minister with such additional information as is necessary to make the determination.

The additional information requested may include, but is not limited to, more details about specific standard operating procedures and clarification on operational records. When more information is required the NHPD sends the applicant an Information Request Notice. The applicant should respond within 30 calendar days from the date the notice is issued.

Based on the information submitted, the NHPD Assessment Officer makes a recommendation for or against issuing a site licence.

3.3 Decision

Sections 29 to 31 of the Regulations outline the reasons and procedures for the issuance or refusal to issue a site licence.

PART 2: SITE LICENCES
Issuance and Amendment
Section 29

(1) The Minister shall issue or amend a site licence if

(a) the applicant submits an application to the Minister that is in accordance with section 28 or subsection 32(2), as the case may be;

(b) the applicant provides the Minister with all additional information requested under section 37; and

(c) the applicant does not make a false or misleading statement in the application.

(2) If the Minister issues a site licence, the Minister shall assign that licence a site licence number.

PART 2: SITE LICENCES
Refusal to Issue or Amend
Sections 30 and 31.

(1) If the Minister refuses to issue or amend a site licence, the Minister shall send the applicant a notice that sets out the reason for the refusal.

(2) Within 30 days after the day on which the notice is sent, the applicant may make a request that the Minister reconsider the application.

(3) If the applicant makes a request in accordance with subsection (2), the Minister shall

(a) give the applicant an opportunity to be heard in respect of the application; and

(b) reconsider the application after giving the applicant that opportunity.

(4) After reconsidering the application, the Minister shall issue or amend the site licence if the requirements of subsection 29(1) are met.

(5) If the Minister again refuses to issue or amend the site licence, the Minister shall send the applicant a final notice that sets out the reason for the refusal.

The NHPD only issues or amends a site licence according to section 29 of the Regulations when the applicant has submitted a complete submission with all the required supporting data (as per sections 28 and 32(2) of the Regulations) and has also provided the NHPD with all the requested additional information (as per section 37 of the Regulations) needed to assess whether the applicant is fully compliant with the Regulations. The applicant must also ensure that there is no false or misleading information in the submission.

The NHPD may refuse to issue or amend a site licence when the site is not compliant with the good manufacturing practices requirements set out in Part 3 of the Regulations, when it finds the application to be deficient, when the applicant does not provide additional information on request, or when the information submitted is false or misleading.

When a site licence application is refused, the NHPD sends the applicant a notice stating the reasons for refusal. If the applicant would like the NHPD to reconsider this refusal, he or she may make such a request within 30 calendar days after the day on which the notice is sent. If such is the case, the NHPD will give the applicant an opportunity to be heard about the refusal, after which the NHPD will reconsider the initial refusal and decide whether to issue or amend a site licence. When the decision is made to uphold the refusal to issue or amend a site licence, the NHPD sends the applicant a final notice stating the reasons for refusal. Applicants have the right to appeal decisions relating to the issuance of a licence. For detailed information on the appeal process, contact the NHPD by one of the methods listed earlier in this document in **chapter 2.2**.

PART 2: SITE LICENCES
Licence Contents
Section 34

A site licence shall set out the following information:

(a) the name and address of the licensee;

(b) the site licence number;

(c) each activity that the licensee is authorized to conduct and a statement indicating whether the activity is authorized to be conducted in respect of a NHP in sterile dosage form;

(d) if the licensee is authorized to manufacture, package or label a NHP, the address of each building in which the licensee is authorized to conduct that activity; and

(e) if the licensee is authorized to import a NHP, the address of each building in which the licensee is authorized to store that NHP.

When the NHPD issues a site licence, it assigns a site licence number and sends a site licence certificate to the licensee. The licence contains the name and address of the licensee, authorized activities, activities authorized to be performed in sterile dosage forms (when applicable) and the address of each building in which the licensee is authorized to conduct that activity. For importers, the licence will also include the name(s) and address(es) of the foreign site(s) from which the importer is authorized to import NHPs.

4.0 PRODUCTS MANUFACTURED AT FOREIGN SITES

Canadian importers must be licensed and the onus is on them to provide evidence that imported products come from sites that meet Canadian good manufacturing practices (GMPs) under Part 3 of the Regulations or equivalent standards.

One of the following types of evidence is required from importers with respect to the foreign sites:

- A Quality Assurance Report signed and dated by a quality assurance person or third-party auditor responsible for assuring the quality of the NHP before it is made available for sale from that site and who has the training, experience and technical knowledge relating to the activity conducted and the requirements of Part 3 (Good Manufacturing Practices) of the Regulations.
- A Certificate of Compliance (CoC) issued by a Regulatory Authority from any of the countries listed in **Appendix 3** for a Site/Recognized Building for which the date of inspection indicated is no more than three years old.
- The most recent inspection report (including the corrective actions taken) that is no more than three years old issued by a Regulatory Authority from any of the countries listed in **Appendix 3** for a Site/Recognized Building as long as the inspection has been conducted based on its GMP standard or the Canadian GMP guidelines.
- The most recent inspection report (including the corrective actions taken) from a Qualified Authority (see **Appendix 3**) for a site located within or outside its jurisdiction.
- A corporate audit report where no recent (less than three years old) inspection report from a Regulatory Authority (MRA), a Qualified Authority or the Inspectorate is available. To be accepted for review by the NHPD, this corporate report must clearly indicate which products are to be imported from a foreign site and the rationale to why this corporate audit report is submitted. In addition, the report must meet the following conditions:
  - The qualifications and experience of the individual(s) performing the inspection must be stated. As a minimum, the individual(s) must have sufficient technical knowledge, training and experience of the NHP GMP and must be qualified.
  - The inspection is conducted against the Canadian drug GMP, NHP GMP, or equivalent guidelines (e.g. PIC/s GMP, US cGMP) and all applicable sections are assessed.
  - Corrective measures taken to address the noted deficiencies are included in the report. The adequacy of these corrective measures are assessed by the corporate auditor or auditing team.
  - The report is signed and dated.
  - If an outdated (more than three years old) inspection report from a Regulatory Authority, a Qualified Authority or any other Authority not listed as qualified is available, the said report should accompany the corporate report.
- Other reports such as company Quality Manuals (ISO 9001:2000) and WHO Inspection Reports may be used in place of the Quality Assurance Report as long as they demonstrate (with evidence) an adherence to all relevant NHP GMP requirements and a commitment to follow the Regulations. Any other types of reports may be acceptable as determined on a case-by-case basis.

Foreign sites listed as compliant on the foreign site annex of a current establishment licence held by the importer do not require further evidence of compliance. However, any sites not listed on this annex must submit evidence in one of the forms described above.

Importers must submit the Quality Assurance Report, or its equivalent as described above, for each foreign site with their site licence application or renewal. If the foreign site evidence that was submitted to the NHPD with the applicant's previous Site Licence or renewal application remains valid upon submitting a subsequent renewal application, then the applicant will not be required to resubmit the foreign site evidence with this subsequent application. The site licence must be renewed according to the cycle outlined in **chapter 5.1**. The Quality Assurance Report form for a foreign site is valid for one year (minus one day) from the date it was completed by the quality assurance person or third party auditor. The Quality Assurance Report may be submitted for review at any time during that calendar year with the site licence application or renewal.

It is the importer's responsibility that the reports submitted to the NHPD are complete and that all requirements of the NHPD GMPs are met. Additional information may be requested.

Adding or deleting a foreign site requires an amendment to the importer's site licence. Adding a foreign site requires the submission of the Quality Assurance Report or its equivalent for that foreign site. Foreign site information is listed on the importer's site licence.

5.0 OBLIGATIONS OF LICENSEES

This chapter explains the obligations licensees must meet to maintain their site licence. In particular, it explains when the licence expires and how it can be renewed before it expires (**chapter 5.1**), when it requires amendment (**chapter 5.2**) or notification (**chapter 5.3**), the different situations that will lead to a suspension or cancellation of a licence, and how licensees can prevent this from happening (**chapter 5.4**).

5.1 Licence Expiry and Renewal

PART 2: SITE LICENCES
Expiry
Section 35

(1) A site licence expires on the first anniversary of the day on which it was issued unless it is renewed in accordance with section 36.

(2) A site licence that is renewed in accordance with section 36 expires on the day on which the renewal period ends unless the licence is further renewed in accordance with section 36.

PART 2: SITE LICENCES
Renewal
Section 36

(1) The Minister shall renew a site licence if

the licensee submits a request to renew the licence to the Minister no later than 30 days before the day on which the licence expires;

(a) the licensee provides the Minister with all additional information requested under section 37; and

(b) the renewal of the licence is not likely to result in injury to the health of a purchaser or consumer.

(2) If the Minister renews a site licence, the Minister shall renew it for a period of

(a) one year, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of less than three years;

(b) two years, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of at least three years but less than nine years; or

(c) three years, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of nine years or more.

(3) A site licence renewal becomes effective on the day after the anniversary of the day on which the licence was issued.

The site licence must be renewed as follows:

- every year, when the licensee has held the licence less than three years from the date of issuance;

- every two years, when the licensee has held the licence for a period of at least three years from the date of issuance but less than nine years; and
- every three years, when the licensee has held the licence for nine years from the date of issuance or more.

When a company has been renewing a licence for three years or more and then adds a building or activity, it may continue renewing according to the renewal process (i.e. without starting again from the beginning of the renewal cycle).

Licensees may renew their licence by the method described below or they may submit a complete application form with all the required supporting data.

The NHPD sends the licensee an expiry notice 60 calendar days prior to the expiry. This notice includes the Renewal Summary Report and Record of Change form. The renewal summary report includes all the information in the most recent submission for which a licence was issued. The licensee must sign the Renewal Summary Report and the Record of Change form indicating that there have been no changes to the information since that time. When there are changes to the name, address, telephone number, e-mail address or facsimile number, or a substantial change to the building, equipment practice or procedure (i.e. changes that constitute a notification), the licensee must indicate these on the record of change form. In any case, licensees must submit a new Quality Assurance Report form or its equivalent (as outlined in **chapter 2** of this document and below) with the renewal summary report. Note that Quality Assurance Reports submitted with a previous submission may not be resubmitted for a renewal application.

According to section 36-1(a) of the Regulations, licensees must submit a request for renewal no later than 30 calendar days before the day on which their licences expire. For example, if a site licence is issued on January 1, 2004, and it is valid until January 1, 2005, the licensee must submit a request for renewal to the NHPD *before* December 1, 2004.

Establishment licence holders who also hold a site licence must renew their site licence according to section 36 of the Regulations. In place of the Quality Assurance Report Form, establishment licence holders may submit a copy of their establishment licence with the application for renewal. The establishment licence lists the last date of inspection as well as all buildings where manufacturing, packaging, labelling, importing and distributing are authorized for drug products under the *Food and Drug Regulations*. When the activities and buildings match up exactly with those mentioned in the site licence application form for which a licence is requested, no further evidence of compliance relating to the good manufacturing practices is required. Establishment licence holders must submit a separate Quality Assurance Report form for those additional activities and buildings that are not listed in the establishment licence dealing exclusively with NHPs.

Sections 36 and 37 of the NHP Regulations allow the NHPD to request additional information which may include, but is not limited to, details about specific standard operating procedures and clarification of operational records while assessing a request for renewal. This information is used to ensure that the site complies with good manufacturing practices and to ensure that the

licence renewal would not result in injury to the health of purchasers or consumers of products dealt with at that site.

5.1.1 Example of a Site Licence Renewal Schedule

A company applies for a site licence for the first time and the NHPD issues the licence on January 1, 2004. The issued licence bears the following information:

Site Licence No.: 000001 **Issued to: ABC Ltd** **To perform the following activities at authorized buildings:**		
✖ Packaging	✖ Sterile dosage	
Issued on: January 1, 2004	**Amended on:**	**Expires on:** January 1, 2005

The company would renew its licence as follows:

Date of issuance	**Date of renewal for the first three years**	**Date of renewal for years four to nine**	**Date of renewal after nine years**
January 1, 2004	January 1, 2005 January 1, 2006 January 1, 2007 (i.e. every year)	January 1, 2009 January 1, 2011 January 1, 2013 (i.e. every second year)	January 1, 2016 January 1, 2019, etc. (i.e. every three years)

If, after 2007, this company adds an activity to its licence (see **chapter 5.2**) then it would be allowed to continue renewing according to the renewal process (i.e. without starting again from the beginning of the renewal cycle). The updated licence would bear the following information:

Site Licence No.: 000001 **Issued to: ABC Ltd** **To perform the following activities at authorized buildings:**		
✖ Packaging ✖ Labelling	✖ Sterile dosage ✖ Sterile dosage	
Issued on: January 1, 2004	**Amended on:** May 1, 2007	**Expires on:** January 1, 2009

The company would then renew its licence as follows:

Date of issuance	**Date of renewal for years three to nine**	**Date of renewal after nine years**
January 1, 2004	January 1 2009 January 1, 2011 January 1, 2013 (i.e. every second year)	January 1, 2016 January 1, 2019, etc. (i.e. every three years)

5.2 Licence Amendment

Section 32 of the Regulations defines changes that require a site licence amendment. The licensee is forbidden from conducting any additional activities until authorized by NHPD.

PART 2: SITE LICENCES
Amendment
Section 32

(1) A licensee shall not conduct any of the following activities unless the site licence is amended accordingly:

(a) conduct any activity for a which a site licence is required that the licensee is not already authorized to conduct;

(b) if the licensee is authorized to manufacture, package or label a natural health product, conduct that activity in a building that is not one in which the conduct of that activity is authorized;

(c) if the licensee is authorized to import a natural health product, store a natural health product in a building that is not one in which the storage is authorized; or

(d) if the licensee is authorized to conduct an activity, but not already authorized to conduct it in respect of a natural health product in sterile dosage form, conduct the activity in respect of a natural health product in that form.

(2) An application to amend a site licence shall be submitted to the Minister and shall contain the following information and documents:

(a) the licence number;

(b) a statement that specifies each activity referred to in subsection (1) that the licensee is proposing to conduct; and

(c) a report from a quality assurance person demonstrating that the buildings, equipment, practices and procedures used in respect of each activity conducted by the licensee will remain in compliance with the requirements set out in Part 3.

A licence amendment is required for one or more of the following changes to a site licence:

- adding a new activity;
- adding a new building for operations or storage;
- changing from manufacturing, packaging, labelling or importing a non-sterile dosage form to sterile dosage form; and
- adding a new foreign site

Example

Existing site licence

Building No.: 1
Activity: Manufacturing
Performing non-sterile dosage form (with respect to the activity): Yes

The following changes would require the licence to be amended:

- adding any new activity in Building 1 apart from manufacturing;
- performing manufacturing in sterile dosage form; and
- adding a new building.

When the licensee seeks an amendment to a site licence, he or she must provide an amendment submission including the application form (**Appendix 1** provides a link to the amendment form) containing the following information:

- the licence number;
- the amendment being requested (i.e. each new building or new activity that the licensee is proposing to conduct); and
- a detailed Quality Assurance Report form indicating that the buildings, equipment, practices and procedures used in each new activity comply with the requirements set out in Part 3 of the Regulations.

Note: It is recommended that multiple amendments to the Site Licence be made within one amendment application; however, the applicant may submit applications for additional amendments prior to the final approval by the NHPD of their previous amendment applications.

PART 2: SITE LICENCES
Relinquishment of Authorization
Section 38

(1) A licensee may, by amendment of the site licence, relinquish any part of the authorization given to the licensee under this Part.

(2) An application to amend the site licence for the purposes of subsection (1) shall be submitted to the Minister and shall contain the following information and documents:

(a) a document, signed and dated by the licensee, that sets out the site licence number and that specifies each activity or, by address, each building, in respect of which the authorization is requested to be relinquished; and

(b) an attestation, signed and dated by a quality assurance person, stating that after the relinquishment, the buildings, equipment, practices and procedures used in respect of each activity conducted by the licensee will remain in compliance with the requirements set out in Part 3.

(3) The Minister shall amend the site licence as requested by the licensee in paragraph (2)(a) if the licensee provides the Minister with an application that is in accordance with subsection (2).

There may be times when a licensee no longer wants an activity or building to be authorized by the site licence. For example, a site licence holder may sell a building and wish to have it removed from the site licence, or a company may cease to perform one of its authorized functions (for example, continuing to manufacture natural health products, but contracting out the packaging and labelling) and may wish to remove this activity from the list of authorized activities on the site licence. Under section 38 of the Regulations, a licensee may request an amendment to delete or relinquish this part of the authorization.

To do this, the licensee must submit an amendment submission including the application form, which is signed and dated by the person who originally signed the application or the licensee's senior signing official, with the following information:

- the licence number and the specific building or activity that is being surrendered; and
- an attestation signed and dated by a quality assurance person stating that after surrendering the licensed building or activity, other activities and buildings still comply with the good manufacturing practices set out in Part 3 of the Regulations.

The NHPD manages submissions for amendment as described in **chapter 3**.

5.3 Licence Notification

PART 2: SITE LICENCES
Notification
Section 33

If the licensee makes any of the following changes, the licensee shall notify the Minister of the change within 60 days after the day on which the change is made:

(a) a change to the information submitted under paragraph 28(a); and

(b) a change that substantially alters any building, equipment, practice or procedure in respect of which a report from a quality assurance person was submitted under paragraph 28(f).

Section 33 of the Regulations specifies the situations under which licensees must notify the NHPD within 60 calendar days of a change in the information contained in their original submission. These changes are as follows:

- a change in the name, mailing address, telephone number, facsimile number or e-mail address; and
- any substantial change that alters any building, equipment, practice or procedure that was previously referred to in the Quality Assurance Report Form submitted to the NHPD.

Examples of such changes include the following:

- adding another wing or an extension to an authorized building;
- changing the production flow in a significant way;
- changing from conventional methods to advanced processes; and
- changing from general cleaning to other practices such as fumigation and dry heat cleaning.

When notifying the NHPD of changes related to business information (name, address, telephone number etc.), the licensee must provide a revised copy of the site licence application form indicating the changes.

When notifying the NHPD of changes related to the building, equipment, practice or procedure, the licensee must provide a completed Notification form (**Appendix 1** provides a link to the Notification form), along with the revised site licence application form indicating the changes.

The Notification form must be accompanied by an attestation from the quality assurance person stating that the activities and buildings authorized by the site licence will remain in compliance with the good manufacturing practices set out in Part 3 of the Regulations.

The NHPD manages submissions for notification as described in **chapter 3**. Licensees are issued an acknowledgment letter indicating that the NHPD received the notification and is reviewing it. When necessary, the NHPD will ask for information relating to the notified change which may include, but is not limited to, details about specific standard operating procedures, an updated floor plan or flow diagram, or an updated Quality Assurance Report Form. A full site assessment may also be conducted when the NHPD deems it necessary.

5.4 Licence Suspension and Cancellation

Sections 39 to 41 of the Regulations outline the reasons and procedures by which a site licence may be suspended or cancelled.

PART 2: SITE LICENCES
Suspension and Cancellation
Sections 39, 40, 41 and 42.

39. (1) Subject to subsection (2), the Minister may suspend a site licence if the Minister has reasonable grounds to believe that

(a) the licensee has contravened any provision of the Act or these Regulations; or

(b) the licensee has made a false or misleading statement in the application submitted under section 28 or the application for amendment under subsection 32(2).

(2) Subject to section 40, the Minister shall not suspend a site licence unless

(a) the Minister has sent the licensee a notice that sets out the reason for the intended suspension; and

(b) the licensee has not, within 90 days after the day on which the notice referred to in paragraph (a) is received, provided the Minister with information or documents demonstrating that the licence should not be suspended on the grounds that

(i) the situation giving rise to the intended suspension did not exist, or

(ii) the situation giving rise to the intended suspension has been corrected.

40. The Minister shall suspend a site licence before giving the licensee an opportunity to be heard if, as a result of any circumstance, the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a purchaser or consumer.

41. If the Minister suspends a site licence under section 39 or 40, the Minister shall send the licensee a notice that sets out the reason for suspension and the day on which the suspension is effective, and the Minister shall

(a) reinstate the licence if, within 90 days after the day on which the suspension is effective, the licensee provides the Minister with information or documents demonstrating that the situation giving rise to the suspension did not exist or that it has been corrected; or

(b) cancel the licence if, within 90 days after the day on which the suspension is effective, the licensee has not provided the Minister with the information or documents referred to in paragraph (a).

42. If the Minister cancels a licence under paragraph 41(b), the Minister shall send the licensee a notice that sets out the reason for the cancellation and the day on which the cancellation is effective.

The NHPD may suspend a site licence under the following circumstances:

- the licensee is found to have contravened the Regulations or any provision of the *Food and Drugs Act*;
- the licensee is found to have made a false or misleading statement in the site licence application or application to amend the site licence; or
- the NHPD has enough evidence to believe that it is necessary to suspend the licence to prevent injury to the health of purchasers or consumers.

In the last case, suspension may be immediate. Otherwise, the NHPD sends the licensee a notice of the intention to suspend indicating the reason for the suspension. The licensee has 90 calendar days to respond from the date of issuance of the notice and to do the following:

- submit evidence to the NHPD that the situation that led to the intended suspension has been rectified; or
- provide the NHPD with evidence demonstrating that the situation giving rise to the intended suspension does not exist.

When the licensee does not submit this information to the NHPD within 90 calendar days the licence is suspended. The NHPD will reinstate the licence if within 90 calendar days of the effective date of suspension, the licensee provides the NHPD with evidence demonstrating that the situation giving rise to suspension does not exist or has been corrected.

The licence is cancelled when, within 90 calendar days of the effective date of suspension, the licensee does not provide the NHPD with any information relating to the situation that led to the site licence suspension. If the NHPD cancels the site licence, a notice of cancellation, setting out the reasons and effective date of cancellation, is sent to the licensee.

No manufacturer, packager, labeller or importer may conduct any activity authorized by the site licence while the licence is suspended (as per section 39 or 40) and after it is cancelled (as per section 41(b)).

Licensees have the right to appeal decisions relating to the suspension or cancellation of a licence. For detailed information on the appeal process, contact the Submissions Management Division of the NHPD.

GLOSSARY

The definitions used here apply to this guidance document and may have different meanings in other contexts.

Acknowledgment letter. A letter issued to all applicants to confirm the receipt of their application. The acknowledgment letter includes the file number, transaction number and date or receipt of application and request for clarity to company information, if required.

Building. A place where some activity is being or has been conducted. It is one location at the same address.

Certificate of Compliance (CoC). A certificate issued by a Regulatory Authority attesting the Good Manufacturing Practices compliance of a site in that country. In Canada, the CoC is issued by the Inspectorate.

Dwelling house. Place of residence.

Diploma. A document issued by an educational institution, such as a university, college or technical institute, vouching that the recipient has earned a degree or successfully completed a particular course of study.

Distributor. A person who sells a NHP to another person for the purpose of further sale by that other person.

Education. The act or process of imparting or acquiring knowledge or skills, and the learning of information by instruction, training or study, which can be testified to by a degree, certificate or diploma.

Establishment licence. A licence issued by the Health Products and Food Branch that is required for all businesses in Canada engaged in any of the six activities related to the manufacturing and testing of all drugs in dosage form and bulk intermediates of Schedule C (radiopharmaceuticals) and D (biological) drugs. The six activities are: fabrication, packaging/labelling, importation, distribution, wholesale, and testing.

Experience. Active participation in events or activities leading to the acquirement of knowledge or skills; the knowledge or skills retained from personally observing, encountering or undergoing something.

Food and Drugs Act **(FDA).** A federal statute regulating the health and safety of food, drugs, NHPs, cosmetics, and medical devices. The Minister of Health is responsible for the administration of the Act.

File number. A number assigned by the NHPD (six digits) to the original submission which will be maintained to track all subsequent notifications and amendments to the initial submission.

Finished product. A product that has undergone all stages of production, including packaging in its final container and labelling.

Good manufacturing practices (GMP). Measures to ensure an overall effective approach to product quality control and risk management. They apply to places, people, processes and products with respect to which activities are being conducted. Please refer to Part 3 of the *Natural Health Products Regulations* and the *Good Manufacturing Practices Guidance Document*.

Health Canada inspection report. A written inspection report prepared by an inspector from Health Canada, using either the drug or NHP good manufacturing practices as the basis for the site assessment.

Homeopathic medicine. Medicines that are manufactured from or contain as medicinal ingredients only those substances or sources referenced in the *Homeopathic Pharmacopoeia of the United States*, the *Homöopathische Arzneimittel*, the *Pharmacopée française* or the *European Pharmacopoeia*, as amended from time to time, and that are prepared in accordance with these pharmacopoeias.

Import. To bring into Canada a NHP for the purpose of sale.

Importer. A person who imports a NHP (including bulk NHPs) into Canada for the purpose of sale.

Information Request Notice. A notice issued to request additional information related to the submission that is required as per sections 15, 37 or 73 of the NHP Regulations.

Label (n). Includes any legend, word or mark attached to, included in, belonging to or accompanying any food, drug, cosmetic, device or package. NHPs are included.

Label (v). To affix the inner or outer label of the NHP.

Manufacture. To fabricate or process a product for the purpose of sale.

Manufacturer. A person who fabricates or processes a NHP for the purpose of sale, but does not include a pharmacist or other health care practitioner who, at the request of a patient, compounds a NHP for the purpose of sale to that patient.

MRA Country. A country that is a participant in a mutual recognition agreement with Canada.

Mutual Recognition Agreement. An international agreement that provides for the mutual recognition of compliance certification for good manufacturing practices for drugs.

Natural health product (NHP). A substance set out in Schedule 1 of the Regulations or a combination of substances in which all the medicinal ingredients are substances set out in

Schedule 1, a homeopathic preparation or a traditional medicine that is manufactured, sold or represented for use in:

- diagnosing, treating, mitigating or preventing a disease, disorder or abnormal physical state or its symptoms in humans;
- restoring or correcting organic functions in humans; or
- modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health.

However, a NHP 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. (in French *produit de santé naturel*)

Notice of cancellation of licence. A notice issued when corrective action is not taken after suspension.

Notice of intent to suspend a licence. A notice issued when a licensee contravenes the Natural Health Products Regulations. The licensee should within 90 calendar days of receipt provide information that the situation did not exist or has been corrected. If the information is not received in 90 calendar days the licence is suspended.

Notice of suspension of licence. A notice that is issued to suspend a licence, when the licensee fails to take corrective action within 90 calendar days of receiving the notice of intent to suspend.

Notice of withdrawal. A notice issued to inform the applicant of the retraction of the submission from NHPD.

Package. Includes container in which any food, drug, cosmetic or device is wholly or partly contained, placed or packed.

Qualification. Requirement to be eligible for an office, position or task by having the proper or necessary skills, knowledge, credentials, accomplishments or qualities.

Qualified authority. An authority member of the PIC/S or the *United States Food and Drug Administration* (USFDA).

Quality Assurance Person. The person who is responsible for assuring the quality of the NHP before it is made available for sale. This person has the training, experience and technical knowledge relating to the specific activity conducted (i.e. manufacturing, packaging, labelling and importing) and the requirements of Part 3 of the *Natural Health Products Regulations*.

Regulatory authority. As defined in section C.01A.001(1) of the *Food and Drugs Regulations*, a government agency or other entity in a 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.

Sell (section 2 of the *Food and Drugs Act*). Sell includes offer for sale, expose for sale, have in possession for sale and distribute, regardless of whether the distribution is made for consideration.

Site. A place of or for an activity specified under the Regulations.

Site licence number. A number issued by Health Canada's Natural Health Products Directorate based on the requirements set out in the *Natural Health Products Regulations* as proof of authorization to conduct specified activities at the listed locations.

Site licence submission. A request for authorization to manufacture, package, label and/or import a NHP.

Standard Operating Procedure (SOP). A written procedure giving instructions for performing operations not necessarily specific to a given product or material but of a more general nature (e.g., equipment operation; maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documents.

Sterile dosage form. A dosage form that is free from microbial contamination.

Submission number. A number assigned by the NHPD (six digits) to distinguish between different submissions within the same file (i.e. an amendment to a site licence would have the same file number as the original submission but a new submission number).

Submission Receipt Acknowledgement Notice. A notice issued to confirm receipt of submission. The notice includes the application type, company code, file number and submission number, and the date of receipt. Applicants must reference the submission and file numbers assigned on all subsequent correspondence about the particular submission. This notice may also include a request for missing information if the application is incomplete, as per the NHPD Compliance Policy.

Training. To make proficient with specialized instruction and practice.

Third-party auditor. An auditor who is independent of the company he or she is auditing and who is qualified by education, training, and experience to conduct a NHP good manufacturing practices site audit.

APPENDIX 1: LINKS TO GUIDANCE DOCUMENTS AND FORMS RELEVANT TO SITE LICENCE APPLICATION

- All required forms for Site Licence Application and instructions on how to complete the forms:

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-site-exploit/form/index_e.html

- *Good Manufacturing Practices Guidance Document*

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/docs/gmp-bpf_e.html

- *Overview of Natural Health Products Regulations Guidance Document*

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/docs/regula-regle_over-apercu_e.html

- *Natural Health Product Regulations*

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/acts-lois/prodnatur/regs_cg2_e.html

- *Site Licensing – A Step by Step Guide*

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-site-exploit/guide/index_e.html

- Natural Health Product Directorate Home Page

http://www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hpfb-dgpsa/nhpd-dpsn/index_e.html

APPENDIX 2: LIST OF SITE LICENCE APPLICATION DEFICIENCIES

The following list contains examples of deficiencies but is not intended to be a complete list of all possible deficiencies. This list can be used as a guide to check for completeness when compiling a site licence application package for submission.

- Site Licence Application (SLA) form missing any of the following:
  - company information/Canadian address;
  - contact information;
  - submission type;
  - Canadian site information;
    - building type and name;
    - activity type;
    - contact person information;
    - Quality Assurance Person name;
  - foreign site information (for importers only);
    - building type and name;
    - activity type;
    - contact person information;
    - Quality Assurance Person name; or
  - signed attestation.

- Evidence of GMP compliance for Canadian and/or foreign sites not included with submission (see **chapters 2 and 4** of this document for types of acceptable evidence)

- A Supplementary Quality Assurance Report (SQAR) was not included in the submission package along with the QAR for applications that have Homeopathic Medicines checked off for activity type

- Establishment Licence (EL) holders:
  - a valid copy of current EL not attached; or
  - activity type(s) and/or site address(es) on the SLA form do not match those on the EL and a complete QAR has not been included for any activity or site not listed in the EL.

- Quality Assurance Report (QAR) information:
  - information provided in the General Information section of the QAR conflicts with information provided in Part A of the SLA form;
  - inspection date not filled in;
  - question(s) not answered (rationale must be provided for any questions considered non-applicable by the applicant);
  - all activity types listed in the SLA are not accounted for in the QAR form (ie. the forms do not match upon cross reference);
  - a completed answer (not including N/A) does not have a list of relevant Standard Operating Procedures (SOPs);
  - a SOP listed in the QAR does not have at least one corresponding sample record attached; or

- attachments (such as SOPs, records, resumes, certificates, floor plans, etc.) referenced in the QAR are not included with the submission.

- Good Manufacturing Practices (GMP) activities of the applicant (as outlined in the QAR) do not meet the requirements set out by Part 3 of the *Natural Health Products Regulations*. The following is a short list of examples in this regard and is not meant to be comprehensive:
  - lack of or inadequate pest control program;
  - building design does not prevent cross-contamination or mix-up of the NHP(s);
  - lack of or inadequate procedures for cleaning and maintaining equipment;
  - lack of or inadequate sanitation program;
  - lack of or inadequate procedures to assess finished NHPs against written specifications;
  - lack of or inadequate procedures for approval of product release for sale and resale;
  - lack of or inadequate procedures for complaint handling;
  - lack of or inadequate procedures for sample retention;
  - lack of or inadequate procedures to ensure the effective recall of a product;
  - required records are not maintained as per the Regulations; or
  - lack of or inadequate procedures to initially establish the expiry date of the product.

Note: In order to facilitate the assessment process we ask that you present all supporting documentation in the same order as the QAR questions and that you reference each attachment with the appropriate QAR question.

APPENDIX 3: ACCEPTABLE FOREIGN INSPECTION REPORTS

The Health Products and Food Branch Inspectorate presently have Mutual Recognition Agreement (MRA) related to GMP with the following countries.

- Switzerland

- The European Community (EC):
  - Austria;
  - Belgium;
  - Czech Republic;
  - Denmark;
  - Finland;
  - France;
  - Germany;
  - Greece;
  - Hungary;
  - Ireland;
  - Italy;
  - Netherlands;
  - Portugal;
  - Spain;
  - Sweden; and
  - United Kingdom.

- The European Free Trade Association (EFTA):
  - Iceland;
  - Liechtenstein; and
  - Norway

- Australia

Note: For up-to-date information please refer to the MRA - Mutual Recognition Agreements on Drugs/Medicinal Products Good Manufacturing Practices Compliance Programmes. It is available at the following address:

http://www.hc-sc.gc.ca/dhp-mps/compli-conform/int/index_e.html

MRA countries can submit alternate GMP evidence in one of two forms:

- A Certificate of Compliance (CoC) issued by a Regulatory Authority for a Site/Recognized Building for which the date of inspection indicated is no more than three years old. or
- The most recent inspection report (including corrective actions taken) that is no more than three years old issued by a Regulatory Authority for a site located outside its jurisdiction as long as the inspection has been conducted based on its GMP standard or the Canadian GMP guidelines.

Non-MRA countries can submit alternate GMP evidence in one of three forms:

- The most recent inspection report (including corrective actions taken) that is no more than three years old issued by a Regulatory Authority for a site located outside its jurisdiction as long as the inspection has been conducted based on its GMP standard or the Canadian GMP guidelines.
- The most recent inspection report (including the corrective actions taken) from a Qualified Authority for a site located within or outside its jurisdiction.
- A Good Manufacturing Practices Certificate issued by a Qualified Authority for a Site/Recognized Building located in its jurisdiction for which the date of inspection indicated is no more than three years old.

Qualified Authority: An authority member of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) or the United States Food and Drug Administration (USFDA).

The Pharmaceutical Inspection Cooperation Scheme (PIC/S) includes the following member countries:

Australia	France	Latvia	Romania
Austria	Germany	Leichtenstein	Singapore
Belgium	Greece	Malaysia	Slovak Republic
Canada	Hungary	Netherlands	Spain
Czech Republic	Iceland	Norway	Sweden
Denmark	Ireland	Poland	Switzerland
Finland	Italy	Portugal	United Kingdom

For a list of the Qualified Authorities for each country refer to the Web site:
http://www.hc-sc.gc.ca/dhp-mps/compli-conform/int/mra-arm/update-miseajour_tc-tm_e.html