Health Canada Santé Canada

# POST LICENSING GUIDANCE DOCUMENT

## NATURAL HEALTH PRODUCTS DIRECTORATE

December 2007
**Version 1.0**

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*

Également offert en français sous le titre :
*Procédure à suivre après la délivrance de la licence*

This publication is also available electronically at the following address: www.healthcanada.gc.ca/nhp



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# 1. INTRODUCTION

Once a Natural Health Product (NHP) has been granted a Natural Product Number (NPN, or DIN-HM for homeopathic medicines), it is not uncommon for licensees to make changes to the product; such changes are referred to as post-licensing changes. A post-licensing change is any change that is made to a licensed NHP pursuant to section 7 and 11 or 12 of the *Natural Health Products Regulations* (NHPR). Changes made to licensed products are categorized as amendments, notifications, or fundamental changes.

A stop sale provision and a suspension and cancellation provision have been included in the post licensing scheme. These provisions can be invoked when Health Canada has reasonable grounds to believe that the product may not be safe under the recommended conditions of use for the consumer. The suspension and cancellation provisions allow for immediate suspension of the licence, and also provide that the product cannot be sold, even at the retail level. The licensee is provided with a time period of 90 days to demonstrate to the Minister that the suspension is not warranted or alternatively that the licence should be reinstated.

## 1.1 Guidance Objectives

This guidance document provides an interpretation of sections 11-13 and 16-21 of the NHPR by:

- Providing the licensee with criteria to assist in the determination of the appropriate regulatory requirement(s) for the change the licensee has made or intends to make.
- Providing licensees with recommendations on how to submit the required documentation.
- Providing the licensee with information on the documentation that will be issued by the NHPD at the various stages of the post-licensing process.
- Providing licensees with information on the documentation that will be sent to licence holders and the regulatory actions required in the event that Health Canada has reasonable grounds to believe that an NHP may not be safe under the recommended conditions of use.

## 1.2 Safety, Efficacy, and Quality Concerns

Any change to an NHP may have an impact on the safety, efficacy, and/or quality of that product. As such, all post-licensing changes, which are categorized as either amendments or notifications, are subject to the requirements set out in Section 7 and 11 or 12 of the NHPR. An amendment to a product licence shall only be issued when all of the requirements set out in section 11 (2) are satisfied. Should the licensee not satisfy these requirements, the submission will be refused as per Section 9 of the NHPR.

Submissions identified as notifications should not pose any significant impact to the safety, efficacy, or quality of the product.

## 1.3 Scope & Application

Information regarding general submission requirements may be found in the following NHPD guidance documents: Product Licensing, Compendium of Monographs, Evidence for Homeopathic Medicines, Evidence for Quality of Finished Natural Health Products, Evidence for Safety and Efficacy of Finished Natural Health Products, and Labelling.

As of the effective date, the Post-Licensing Guidance Document will supersede the following guidance document:

*Product Licensing Guidance Document* (December 2006 – Version 2.0) – Section 3.1

## 2. REGULATORY REQUIREMENTS RESULTING FROM POST-LICENSING CHANGES

A description of the regulatory requirements and criteria for a post-licensing change is provided below. Please see Appendix 1 of this guidance document for a detailed list of changes to NHPs and the corresponding regulatory requirement(s).

If according to the NHPR, outlined below, the licensee has inappropriately identified the submission type, the licensee will be notified at the screening stage and the submission will be reclassified to the relevant submission type. Please refer to Appendix 1 for a listing of the regulatory requirements resulting from changes to products.

This guidance document does not provide an exhaustive description of all post-licensing changes. If further information or clarification is required, licensees are encouraged to contact the NHPD's Client Services Unit by phone or e-mail. However, any change not mentioned in this document that could potentially have a significant impact on the product should be submitted to the NHPD.

Client Services
Telephone: 1-888-774-5555
Fax: (613) 948-6810
Email: NHPD_DPSN@hc-sc.gc.ca

## 2.1 Notification

Part 1: PRODUCT LICENCES
*Notification*
Section 12

12. (1) If the licensee makes any of the changes described in subsection (2) in respect of the natural health product, the licensee shall, within 60 days after the day on which the change is made,

(a) notify the Minister of the change; and
(b) provide the Minister with the text of each label used in conjunction with the natural health product since the change, if the change is any of those described in paragraphs (2)(d) to (f).

(2) For the purposes of subsection (1), changes in respect of a natural health product are

(a) a change to any of the information submitted under paragraph 5(a) or (b);
(b) a change to any of the information provided under section 22;
(c) the addition or substitution of a non-medicinal ingredient, the addition or substitution of which does not affect its safety or efficacy;
(d) its sale under a brand name other than one submitted under paragraph 5(e);
(e) a change of the common or proper name of any of its medicinal ingredients; and
(f) the addition of risk information to any of its labels, including the addition of a caution, warning, contra-indication or known adverse reaction associated with its use.

Notifications are considered to be those changes to an NHP that do not have a significant impact on the safety, efficacy and/or quality of the product. Any changes made to the NHP identified in Section 12 shall be filed as a notification. The NHPD must be notified of the change within 60 days after the day on which the change is made. Please note that **changes are only considered notifications when there is no significant impact on the safety, efficacy and/or quality of the product**.

## 2.2 Amendment

Part 1: PRODUCT LICENCES
*Amendments*
Section 11

11. (1) If the licensee makes any of the following changes in respect of the natural health product, the licensee shall not sell any lot or batch of the natural health product affected by the change unless the product licence is amended accordingly:

(a) a change to its recommended dose;
(b) a change to its recommended duration of use;
(c) the deletion or modification of risk information shown on any of its labels, including the deletion or modification of a caution, warning, contra-indication or known adverse reaction associated with its use;
(d) a change of its recommended use or purpose;
(e) a change of the source material of any of its medicinal ingredients;
(f) changing any of its medicinal ingredients to or from being synthetically manufactured;
(g) a change to the potency of any of its medicinal ingredients;
(h) a change affecting its safety or efficacy that does not arise as a result of
    (i) a change to the quantity of a medicinal ingredient per dosage unit,
    (ii) the addition or substitution of a medicinal ingredient,
    (iii) a change to its dosage form, or
    (iv) a change to its recommended route of administration; or
*(i)* one or more of the following changes to its specifications, namely,
    (i) the removal of a test method set out in the specifications,
    (ii) the modification of a test method set out in the specifications in a manner that widens the purity tolerances of the natural health product or the quantity, identity or potency tolerances of any of its medicinal ingredients, or
    (iii) the modification of a test method set out in the specifications in a manner that renders it less precise, accurate, specific or sensitive.

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

(a) the product number of the natural health product;
(b) a statement identifying each change described in subsection (1) that has been made;
(c) information demonstrating that the natural health product is safe and efficacious after the change;
(d) the text of each label to be used in conjunction with the natural health product after the change, if the change is any of those described in paragraphs (1)(a) to (h); and
(e) a copy of the revised specifications, if the change is any of those described in paragraph (1)(g) or (i).

Amendments are considered to be those changes to an NHP that may have an impact on the safety, efficacy and/or quality of the product. Any changes made to an NHP identified in Section 11 shall be filed as an amendment. Submissions for amendments must demonstrate that the NHP remains safe and efficacious. **The change may not be implemented until approval is obtained and the product licence is amended accordingly.**

## 2.3 Fundamental Change

Part 1: PRODUCT LICENCES
*Fundamental Change*
Section 13

13. For greater certainty, if the licensee makes any of the following fundamental changes in respect of the natural health product, the licensee may not sell the natural health product affected by the change unless a product licence is issued in accordance with section 7 for the natural health product as changed:

(a) a change to the quantity of a medicinal ingredient per dosage unit;
(b) the addition or substitution of a medicinal ingredient;
(c) a change to its dosage form; or
(d) a change to its recommended route of administration.

Fundamental changes are considered to be those changes to an NHP that have a significant impact on the safety, efficacy and/or quality of the product. Any change made under Section 13 shall be filed as a new Product Licence Application (PLA) in accordance with section 7 of the NHPR. **The change may not be implemented until a new product licence is issued.**

# 3. SUBMISSION MANAGEMENT

The following section provides recommendations for licensees when preparing a notification and/or an amendment submission.

## 3.1 How to submit a notification and/or amendment

The PLA form may be downloaded from the Web at www.healthcanada.gc.ca/nhp.

Completed notification and/or amendment submissions should be sent to:

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

## 3.2 Acknowledgement of Notifications

Upon receipt of a notification, the Submission Management Division will review the documentation to ensure that the change does not pose any safety, efficacy and/or quality concerns. If the change is deemed acceptable, the Submission Management Division will issue a Notification Acknowledgement Notice. This notice will state the submission number, file number and company code assigned to the application. Additionally, the notice will inform the licensee that the NHPD's database and records have been updated accordingly. Please note that a notification retains its original file number but a new submission number is granted. The new submission number and original file number should be quoted on all further notices or inquiries regarding this notification submission, including responses sent to the NHPD.

Please note that due to the volume of changes submitted under paragraphs 5(a) and (b) pertaining to company information, the NHPD will issue one acknowledgement notice per company for changes submitted in bulk. The notice will include a listing of all of the implicated file numbers and NPNs/DIN-HMs.

## 3.3 Acknowledgement of Amendments

Upon receipt of an amendment, the Submission Management Division will issue an Amendment Acknowledgement Notice by fax or by mail. For amendments, this notice will state the submission number, file number and company code assigned to the application. Please note that an amendment retains its original file number but a new submission number is granted. The new submission number and original file number should be quoted on all further notices regarding this amendment submission, including responses sent to the NHPD.

Once an amendment submission has been assigned to a submission coordinator, all further correspondence regarding this amendment submission, including responses to notices sent by the NHPD, should be addressed to the relevant submission coordinator in the Submission Management Division at the address listed above or may be faxed to the Product Submission Coordination Unit (refer to fax number indicated in the correspondence from the respective units).

## 3.4 Acknowledgement of combined Amendments and Notifications

Upon receipt of a combined amendment and notification submission, the Submission Management Division will issue a Notification and Amendment Acknowledgement notice by fax or by mail. This notice will state the submission number, file number and company code assigned to the application. Please note that a combined submission retains its original file number but a new submission number is granted. The new submission number and original file number should be quoted on all further notices, including responses sent to the NHPD.

If the change indicated in the notification is considered acceptable, the acknowledgment notice will inform the licensee that the NHPD's database and records have been updated accordingly. The amendment portion of the submission will not be approved at this time. Its approval is contingent upon assessment.

## 3.5 Document Presentation Recommendations

The following recommendations will assist the NHPD in processing the application more efficiently and simplify document management during the screening and assessment stages. Please note that notifications and/or amendments should be typed (handwritten submissions are not accepted) and submitted by mail/courier.

**Cover Letter:**
A description of the change is required as per Section 11 of the NHPR for Amendments and is strongly recommended for Notifications; it provides the NHPD with a necessary overview of the change or proposed change. Any

information which may be considered important to note (e.g., addition of information, deletion of information, or substitution of information) or which may raise questions or concerns during the review or assessment, should be addressed in a cover letter. The letter should clearly indicate that the information being submitted is a post-licensing change. The letter should also cite the NPN/DIN-HM and file number for which the notification and/or amendment is being filed. If both an amendment and a notification are being filed then this should be indicated in the cover letter. Please refer to Appendices 2, 3, and 4 for sample cover letters.

**PLA form:**
Licensees are asked to submit only those pages of the PLA that are affected by the change. The page(s) should include all of the original information as well as the changes relevant to the notification and/or amendment (e.g., additions, substitutions, or deletions of information). The licensee shall ensure that no changes other than those outlined in the cover letter have been made. Un-identified changes may impede the notification and/or amendment process and result in significant delays. **Note:** Licensees are encouraged to submit page 1 of the PLA form to facilitate the acknowledgement process. If information submitted on page 1 varies from the company information currently on file at the NHPD, please be sure to outline these changes in the cover letter as they are considered a notification and should be identified as such.

**Safety & Efficacy Information and Finished Product Specifications:**
Licensees are asked to submit evidence and finished product specifications only when required. Licensees should not re-submit documents that the NHPD currently has on file. The re-submission of documents may impede the notification and/or amendment process and result in significant delays.

<u>Examples of post-licensing changes and the documentation required</u>

**Notification**
If the licensee adds magnesium stearate as an NMI to the product, the following must be submitted:

- Cover letter indicating that the submission is a notification and outlining the addition of the NMI
- Statement in the cover letter confirming that the acceptability of the NMI has been cross-verified with NHPD's NMI acceptable list
- Page 1 and 2 of the PLA form
- Page 5 of the PLA form with the entire listing of previously approved NMIs along with the addition of magnesium stearate at the end of the NMI list
- A revised copy of the product label which includes the addition of magnesium stearate under the heading *Non-Medicinal Ingredients*.
- Animal Tissue Form, if applicable

**Amendment**
If the licensee intends to delete one of the approved recommended uses or purposes (e.g., “For the maintenance of good health,”) the following must be submitted:

- Cover letter indicating that the submission is an amendment and outlining the deletion of the recommended use or purpose
- Page 1 and 2 of the PLA form
- Revised Page 6 of the PLA form which includes all of the previously approved information and no longer includes the recommended use or purpose “For the maintenance of good health.”
- A revised copy of the product label which no longer includes the recommended use or purpose “For the maintenance of good health.”

## 3.6 Monograph Revisions

As monographs play an important role in facilitating the assessment of submissions, the NHPD is committed to revising and updating existing monographs on an on-going basis to reflect new research and evidence.

In the event that a monograph is revised, licensees are required to submit either a notification and/or an amendment as per section 11 and 12 of the NHPR. The submission must include revised information that reflects the revised monograph. Licensees should note that amendments must be approved by the NHPD before proceeding with a new label run.

When completing the PLA form for the notification and/or amendment submission, licensees should refer to Part 2, Block B of the form and place a check mark in the box and provide the name of the NHPD Monograph. The licensee must also provide the NPN in Section 55 of the PLA form. The cover letter provided with the submission should clearly state that the revisions are being made to comply with the monograph and that no other revisions are being made.

When monograph revisions significantly impact the safety and/or efficacy of licensed products, the NHPD will issue a letter to all affected product licence holders informing them of the revision. Please refer to section 4.1 of this guidance document for further information on requests made by the NHPD as per section 16 of the NHPR.

In the rare instance that a change is made to the monograph that results in one or more changes to the medicinal ingredient(s), the quantity of the medicinal ingredient or route of administration, which are considered fundamental changes, licensees will be contacted by NHPD with instructions on how to proceed. For a more inclusive list of fundamental changes please see Appendix 1.

## 3.7 Issuance of Revised Licences

For amendments, as described in section 7 of the NHPR*,* a product licence will be amended upon approval of the submission. The amended product licence will be sent to the licensee. However, if the licensee's mailing address is outside of Canada, the product licence and any other regulatory mail will be sent to the designated Canadian representative. In addition to the revised product licence, the licensee or the Canadian representative will receive a *No Objection Letter* that indicates the change(s) for which they have obtained approval.

Please note that the product licence will not be re-issued for notifications. The Notification Acknowledgement Notice should be maintained by the licensee as the record that the notification has been received by the NHPD.

# 4. SAFETY INFORMATION AND REGULATORY ACTIONS

## 4.1 Safety Information

Part 1: PRODUCT LICENCES
*Safety Information*
Section 16

16. If the Minister has reasonable grounds to believe that a natural health product may no longer be safe when used under the recommended conditions of use, the Minister may request that the licensee provide the Minister, within 15 days after the day on which the request is received, with information and documents demonstrating that the natural health product is safe when used under the recommended conditions of use.

If at any time Health Canada has reasonable grounds to believe that an NHP may not be safe under the recommended conditions of use, the NHPD will request the licensee to submit, within 15 days of receipt of the notice, information and supporting data demonstrating that the NHP is in fact safe under the recommended conditions of use. If the licensee does not respond, or the response is inadequate, Health Canada may issue a direction to stop sale.

## 4.2 Direction to Stop Sale

Part 1: PRODUCT LICENCES
*Direction to Stop Sale*
Section 17

17. (1) The Minister may direct the licensee, manufacturer, importer and distributor to stop their sale of a natural health product if

(a) the licensee does not, within the required period, provide the Minister with the information and documents requested under section 16;
(b) the information and documents provided by the licensee in accordance with section 16 do not demonstrate that the natural health product is safe when used under the recommended conditions of use;
(c) in the case of a natural health product that is imported, the Minister has reasonable grounds to believe that the natural health product is not manufactured, packaged, labelled, imported, distributed or stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3;
(d) in the case of a natural health product that is not imported, the Minister has reasonable grounds to believe that the natural health product is not manufactured, packaged, labelled, distributed or stored in accordance with the requirements set out in Part 3; or
(e) the Minister has reasonable grounds to believe that the natural health product is not packaged or labelled in accordance with the requirements set out in Part 5.

(2) The Minister shall lift a direction to stop the sale of a natural health product if the licensee provides the Minister with information and documents demonstrating that

(a) in the case of a direction to stop sale arising under either paragraph (1) (a) or (b), the natural health product is safe when used under the recommended conditions of use;
(b) in the case of a direction to stop sale arising under paragraph (1)(c), the natural health product is manufactured, packaged, labelled, imported, distributed and stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3;
(c) in the case of a direction to stop sale arising under paragraph (1)(d), the natural health product is manufactured, packaged, labelled, distributed and stored in accordance with the requirements set out in Part 3;
(d) in the case of a direction to stop sale arising under paragraph (1) (e), the natural health product is packaged and labelled in accordance with the requirements of Part 5; or
(e) the situation giving rise to the direction to stop the sale of the natural health product did not exist.

A direction to stop sale is a request to stop shipping a product. Manufacturers, packagers, labellers, distributors, and importers must comply with this direction. Retailers can continue to sell the product until a final decision on the safety of the product is reached. A direction to stop sale is designed to allow the licensee time to provide Health Canada with additional information, when requested, or to require certain corrective changes (for example, the addition of risk information to a product label) without having to suspend or cancel a product licence.

Health Canada will lift the direction to stop sale when the licensee can show that the problem that led to the concerns has been adequately addressed or that it never existed.

## 4.3 Suspension and Cancellation

Part 1: PRODUCT LICENCES
*Suspension of Cancellation*
Section 18

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

(a) the licensee has contravened these Regulations or any provision of the Act relating to the natural health product; or
(b) the licensee has made a false or misleading statement in the application submitted under section 5 or the application for amendment under subsection 11(2).

(2) Subject to section 19, the Minister shall not suspend a product 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.

Part 1: PRODUCT LICENCES
*Suspension of Cancellation*
Section 19

19. The Minister shall suspend a product 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.

Part 1: PRODUCT LICENCES
*Suspension of Cancellation*
Section 20

20. If the Minister suspends a product licence under section 18 or 19, the Minister shall send the licensee a notice that sets out the reason for the 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).

Part 1: PRODUCT LICENCES
*Suspension of Cancellation*
Section 21

21. If the Minister cancels a licence under paragraph 20(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.

A suspension of a product licence halts all sales of the NHP, including at the retail level. Health Canada may suspend a product licence in the following circumstances:

1. The licensee is found to be in contravention of the NHPR or any provision of the *Food and Drugs Act* relating to the NHPR;
2. The licensee is found to have made a false or misleading statement in the PLA or application to amend the product licence; or
3. Health Canada 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 third case, suspension is immediate. Otherwise, the NHPD sends the licensee a notice of the intention to suspend, indicating the reason for suspension. The licensee has 90 days to respond from the date the notice is issued.

Once a product licence is suspended, Health Canada sends the licensee a notice outlining the reasons for the suspension and the effective date of the suspension. If the licensee can demonstrate within 90 days of the effective date of the suspension that the reasons giving rise to the suspension either did not exist or have been corrected, the licence will be re-instated. If the licensee has not clarified or corrected the problems within 90 days of the effective date of suspension, the licence will be cancelled.

Cancellation of a product licence means that the product licence no longer exists, and thus the product that is the subject of the licence cannot be sold in Canada. If an individual or company wishes to sell this product again, a new PLA must be submitted. When a licence is cancelled, Health Canada sends the licensee a notice that sets out the reasons for the cancellation, as well as the date on which the cancellation is effective.

Any holders of NPNs and DIN-HMs that do not comply with the Regulations will be addressed according to the provisions in the Regulations and the HPFBI's Compliance and Enforcement Policy (POL-0001).

# APPENDIX 1 - REGULATORY REQUIREMENTS RESULTING FROM CHANGES TO PRODUCTS

**√ - Required**
**▲ - May be required depending on the proposed change**

| Type of Change | Regulatory Requirement | Safety & Efficacy Evidence | Finished Product Specifications |
|---|---|---|---|
| **Recommended dose** | | | |
| Change to amount of dosage unit | Amendment | √ | |
| Change to frequency | Amendment | √ | |
| Change to sub-population group | Amendment | √ | |
| Change to directions of use appearing on the label | Notification | ▲ | |
| **Recommended duration of use** | | | |
| Lengthening the recommended duration of use | Amendment | √ | |
| Shortening the recommended duration of use | Amendment | ▲ | |
| **Risk information shown on any label** | | | |
| Deletion of risk information | Amendment | √ | |
| Addition of risk information | Notification | ▲ | |
| Modification of risk information | Amendment | ▲ | |
| **Recommended use or purpose** | | | |
| Modification to the recommended use or purpose | Amendment | ▲ | |
| Deletion of part of the recommended use or purpose | Amendment | | |
| Addition to the recommended use or purpose | Amendment | √ | |

| Type of Change | Regulatory Requirement | Safety & Efficacy Evidence | Finished Product Specifications |
|---|---|---|---|
| **Source material of any medicinal ingredients** | | | |
| Change to the part or tissue used | Amendment | ▲ | |
| Change to the source material from a monograph source to a source not listed on a monograph | Amendment | √ | |
| Change of source within a monograph | Amendment | | |
| Change from a source not listed on a monograph to a source listed on a monograph | Amendment | | |
| Change of source material to an animal-derived source | Amendment | | |
| Change to information submitted on the Animal Tissue Form | Amendment | | |
| Change to the salt or derivative used | Amendment | ▲ | |
| Change to the strain used | Amendment | √ | |
| **Changing any of medicinal ingredients to or from being synthetically manufactured** | | | |
| Change from being synthetically manufactured to a natural ingredient | Amendment | | |
| Change from a natural source to a synthetically source | Amendment | | |
| **Potency of any medicinal ingredients** | | | |
| Addition of a potency | Amendment | ▲ | √ |
| Deletion of a potency | Amendment | ▲ | √ |
| Change in the potency | Amendment | ▲ | √ |
| **Change affecting safety and efficacy (other than those listed in paragraph 11(h))** | | | |
| Change in manufacturing information | Amendment | | ▲ |
| **Change to the quantity of a medicinal ingredient per dosage form** | | | |
| Decrease in quantity | Fundamental Change | ▲ | √ |
| Increase in quantity | Fundamental Change | ▲ | √ |

| Type of Change | Regulatory Requirement | Safety & Efficacy Evidence | Finished Product Specifications |
|---|---|---|---|
| **Addition or substitution of a medicinal ingredient** | | | |
| Adding a medicinal ingredient | Fundamental Change | √ | √ |
| Removing a medicinal ingredient | Fundamental Change | ▲ | √ |
| Substituting a medicinal ingredient for one not already found in the product | Fundamental Change | √ | √ |
| **Dosage form** | | | |
| Change in the dosage form | Fundamental Change | √ | √ |
| **Recommended route of administration** | | | |
| Any change in route of administration | Fundamental Change | √ | |
| **Removal of a test method set out in the specifications** | | | |
| Any removal of test methods in the specification | Amendment | | √ |
| **Modification of a test method set out in the specifications** | | | |
| Any modification to test methods in the specification | Amendment | | √ |
| **Change to information submitted under paragraphs 5(a) and (b)** | | | |
| Change in the name of the product licence holder or applicant | Notification | | |
| Change in ownership of the product licence | Notification | | |
| Mergers between companies | Notification | | |
| Change of senior official | Notification | | |
| Change of title, phone number, fax number, e-mail address or mailing address of senior official | Notification | | |
| Change of contact person for the application | Notification | | |
| Change of title, phone number, fax number, e-mail address or mailing address of the contact person for application | Notification | | |
| Change of company name for Regulatory Affairs Information in Canada | Notification | | |
| Change to contact information for Regulatory Affairs Information in Canada | Notification | | |

| Type of Change | Regulatory Requirement | Safety & Efficacy Evidence | Finished Product Specifications |
|---|---|---|---|
| **Information provided under section 22** | | | |
| Addition of a manufacturer, packager, labeller, importer or distributor | Notification | | |
| Removal of a manufacturer, packager, labeller, importer or distributor | No need to communicate with the NHPD | | |
| **Addition or substitution of a non-medicinal ingredient** | | | |
| Changing from an ingredient on the "acceptable" list to one not on that list | Amendment | √ | |
| Changing to a different ingredient on the "acceptable" list | Notification | | |
| **Sale under a brand name other than one submitted under paragraph 5(e)** | | | |
| The addition or modification of a brand name | Notification | | |

# APPENDIX 2 – SAMPLE NOTIFICATION COVER LETTER

**SUBMISSION OF NOTIFICATION**

| | | |
|---|---|---|
| TO:<br>Submission Management Division | | FROM:<br>Senior Official, Application Contact |
| DATE:<br>May 23, 2010 | | COMPANY:<br>Company A |
| FAX NUMBER: | | PAGE(S):<br>X |
| PHONE NUMBER: | | SENDER'S TELEPHONE NUMBER:<br>(XXX) XXX-XXXX/FAX: (XXX) XXX-XXXX |
| SUBJECT:<br>**Notification** | | COMPANY CODE:<br>XXXXX |
| FILE NO.:<br>XXXXXX | NPN/DIN-HM NO.:<br>8XXXXXXX | SUBMISSION NO.:<br>XXXXXX |

Dear Submission Management Division:

Please note that we have added the following **non-medicinal ingredient** to our product and have verified its acceptability:

**- Magnesium Stearate**

We have also added the following **brand name** to the product:

**- Fabulous Vitamins**

We have attached the following documents:

- Page 1 of the PLA form
- New page 2 of the PLA form
- Revised page 4 of the PLA form to include the additional brand name
- Revised page 5 of the PLA form to include the new NMI
- Revised label which reflects the additional brand name and the additional NMI.

No other changes have been made to these documents apart from those mentioned above.

Should you have any questions regarding this notification, please discuss with the application contact, Mr. /Mrs. Contact.

Sincerely,

Senior Official
Company A

# APPENDIX 3 – SAMPLE AMENDMENT COVER LETTER

**SUBMISSION OF AMENDMENT**

| | | |
|---|---|---|
| TO:<br>Submission Management Division | | FROM:<br>Senior Official, Application Contact |
| DATE:<br>May 23, 2010 | | COMPANY:<br>Company A |
| FAX NUMBER: | | PAGE(S):<br>X |
| PHONE NUMBER: | | SENDER'S TELEPHONE NUMBER:<br>(XXX) XXX-XXXX/FAX: (XXX) XXX-XXXX |
| SUBJECT:<br>**Amendment** | | COMPANY CODE:<br>XXXXX |
| FILE NO.:<br>XXXXXX | NPN/DIN-HM NO.:<br>8XXXXXXX | SUBMISSION NO.:<br>XXXXXX |

Dear Submission Management Division:

Please note that we have modified the recommended use or purpose to the following:

**For the maintenance of good health**

We have also removed the following risk information:

**Do not take if pregnant or breastfeeding.**

We have attached the following documents:

- Page 1 of the PLA form
- New page 2 of the PLA form
- Revised page 6 to include the modified recommended use or purpose and the removal of risk information
- Revised label which reflects the modified recommended use or purpose and removal of risk information
- Safety & Efficacy evidence to support the modified claim and removal of risk

No other changes have been made to these documents apart from those mentioned above.

Should you have any questions regarding this notification, please discuss with the application contact, Mr. /Mrs. Contact.

Sincerely,

Senior Official
Company A

# APPENDIX 4 – SAMPLE NOTIFICATION & AMENDMENT COVER LETTER

**SUBMISSION OF NOTIFICATION & AMENDMENT**

| | | |
|---|---|---|
| TO:<br>Submission Management Division | | FROM:<br>Senior Official, Application Contact |
| DATE:<br>May 23, 2010 | | COMPANY:<br>Company A |
| FAX NUMBER: | | PAGE(S):<br>X |
| PHONE NUMBER: | | SENDER'S TELEPHONE NUMBER:<br>(XXX) XXX-XXXX/FAX: (XXX) XXX-XXXX |
| SUBJECT:<br>**Notification & Amendment** | | COMPANY CODE:<br>XXXXX |
| FILE NO.:<br>XXXXXX | NPN/DIN-HM NO.:<br>8XXXXXXX | SUBMISSION NO.:<br>XXXXXX |

Dear Submission Management Division:

Notification
We have added the following risk information to the product:

**Consult a health care practitioner if symptoms persist.**

Amendment
We have also modified a test method set out in the finished product specifications.

We have attached the following documents:

- Page 1 of the PLA form
- New page 2 of the PLA form
- Revised 6 of the PLA form to include the additional risk information
- Revised label which includes the additional risk information
- Revised copy of the finished product specifications which include the revised test method

No other changes have been made to these documents apart from those mentioned above.

Should you have any questions regarding this notification, please discuss with the application contact, Mr. /Mrs. Contact.

Sincerely,

Senior Official
Company A