Management of Product License Applications (PLA) for natural health products

1. Purpose

The purpose of this policy is to outline the way the Natural Health Products Directorate (NHPD) will manage Product Licence Applications for natural health products submitted in accordance with the *Natural Health Products Regulations*. The policy also outlines the responsibilities and expectations for natural health product applicants before and throughout the application review process.

2. Scope

This policy applies to all natural health product application types including- Compendial, Non-traditional, Traditional, Homeopathic, Homeopathic Medicine Labelling Standards, TPD Category IV Monographs/ Labelling Standards (containing NHP ingredients), and Post Licensing Changes. This policy also highlights a new three-class review system and associated timelines.

All applications will be examined for completeness and suitability for review. In addition, subsequent solicited or unsolicited information will be subjected to a screening process. All information and data submitted in support of a Product License Application (PLA) will be retained by Health Canada.

3. Before filing product license applications

3.1 Ingredients

The applicant must ensure that the medicinal ingredients contained in the product are natural health product ingredients in accordance with Schedules 1 and 2 of the *Natural Health Products Regulations*. All medicinal and non-medicinal ingredients found in the product must be found within the Natural Health Products Ingredients Database (NHPID) and listed with their appropriate role. Please note that some ingredients within the NHPID have associated limits or restrictions and these must also be adhered to when filing. In addition, the NHPID also lists some ingredients which are not natural health product ingredients and those are clearly indicated as not acceptable. An entry in the database does not imply that the ingredient has been reviewed for safety and additional information may be requested during review.

If these ingredients are not listed in the NHPID, applicants are responsible for submitting a request to NHPD to add these ingredients to the database before the application is filed. The application can only be filed once the ingredients are deemed acceptable and added to the database.

Applicants must also ensure that the dosage form, route of administration and non-medicinal ingredient purposes for the product are recognized by NHPD and therefore

found within the NHPID. Applicants are reminded to consult any associated monograph(s) available in the NHPID in order to support their ingredients in their PLAs. The list of monographs is also available within the NHPID.

For more information on how to request the addition of ingredients or other information to the NHPID, please see the NHPID issue form.

3.2 Trading partner agreement

If applicants wish to correspond and submit application packages with NHPD electronically they must do so via NHPD's chosen secure communication service – epost Connect™. Applicants must first enrol as a Trading Partner (TP) with NHPD. Please see: Guidance document on how to interact with the Natural Health Products Directorate electronically

4. Filing of product license applications

4.1 Submitting a Product License Application (PLA) form

Please note that it is the intent of NHPD that the electronic PLA (ePLA) will be the only form accepted in the future. NHPD cannot commit to the service standards outlined in this document for applications received in any other format. Applicants using other application formats should expect a substantial increase in processing time; however, all applications will be assessed within 180 calendar days. The ePLA provides several benefits to both applicants and NHPD which include:

- Reduces possibility of the application being rejected / refused thanks to embedded rules and checks for specific regulatory requirements
- Eliminates duplication of manual entry of product information
- Reduces mail / courier costs
- Reduces paper use
- Ensures adherence to standard terminology for easier processing
- Ensures adherence to timelines outlined in this document

4.1.1 Filing of electronic product licence applications (ePLA) by secure email

NHPD strongly encourages applicants to file PLAs, Post Licensing Changes, Clarification Request Responses and Information Request Notices (IRN) Responses electronically via NHPD's secure email service - epost Connect™. In order to use epost Connect™, applicants must be enrolled as a Trading Partner. For more information on how to enrol as a Trading Partner, please see section 3.2 above.

4.1.2 Filing of electronic Product Licence Applications (ePLA) on CD or DVD

Although applicants are strongly encouraged to enrol as Trading Partners and submit applications via NHPD's secure email service - epost Connect™ - as mentioned in

section 4.1.1 above, it is also possible to submit the ePLA and supporting documents by mail or courier. If submitting by mail or courier, applicants are encouraged to submit a CD or DVD containing the ePLA and all supporting documents.

Applications submitted by mail or courier may be sent to:

Health Canada
Health Products and Food Branch
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

4.1.3 Filing of electronic Product Licence Applications (ePLA) in paper format

If applicants cannot submit through NHPD's secure email service - epost Connect™ - and cannot submit applications and supporting documents on CD or DVD, the ePLA and supporting documents can be printed and submitted by mail or courier. When completed, the ePLA will generate a bar-code which can be scanned by NHPD to extract the data electronically. The capture of this data requires an extra step by NHPD staff and therefore delays the processing of the application. Therefore, applicants are encouraged to submit applications as described in sections 4.1.1 and 4.1.2 above.

Applications submitted by mail or courier can be sent to the address indicated in section 4.1.2 above.

4.2 Additional information to submit along with a Product License Application (PLA) form

4.2.1 Attestation to NHPD monographs

Applications containing one or more ingredient(s) complying with all parameters of NHPD monograph(s) are required to submit a **Monograph Attestation.** The attestation reminds applicants of their obligation to meet all monograph parameters. The attestation can be found on the ePLA or as a standalone form available on the NHPD website, Class specific instructions are outlined in sections 5.1 and 5.2.

5. Processing and assessment of product license applications

5.1 Class I

Class Iis comprised of products that comply with all parameters of an **individual NHPD monograph.** Please note that applicants can note reference more than one NHPD monograph at a time under Class I. Applicants submitting products complying with all parameters of an individual NHPD monograph, must select **"Compendial" or "Homeopathic Medicine Labelling Standard"** as the application type. For Compendial applications, applicants must complete the **Monograph Attestation** embedded in the ePLA. For "Homeopathic Medicine Labelling Standard" applications, applicants must complete the standalone **Monograph Attestation Form** and select the box which indicates that the Product solely contains information that is supported by NHPD monographs.

Class I applications will be examined for completeness. Complete applications submitted using the ePLA and complying with all Class I requirements, will receive a **Product License (PL)** within ten (10) business days.

Applications that are deficient with respect to administrative content will result in the issuance of a **Rejection Notice- Administrative Deficiency**. Additionally, NHPD reserves the right to issue an **Application Refusal Letter** for applications that do not comply with all Class I requirements. If the applicant wishes to re-submit the application at a future time, it will be processed as a new application.

5.2 Class II and class III

Applications requiring Class II or III assessment include "**Traditional**", "**Non-traditional**", "**Homeopathic**" and **"TPD Category IV/ Labelling Standards"**. Applicants should select the appropriate application type on the ePLA.

Applicants should refer to the "Pathway for Licencing NHPs Making Modern Health Claims", "Pathway for Licencing NHPs Making Traditional Health Claims" and "Evidence for Homeopathic Medicines" Guidance Documents for information on how to support the safety and efficacy of their products.

"**Non-Traditional"** and "**Traditional"** applications supported ***entirely*** by a **combination of NHPD monographs** as well as **"Homeopathic with Non-Specific Claim"** and **"TPD Category IV/ Labelling Standards"** will be classified as Class II[1] products. Please note that applicants cannot select "Compendial" as the application type for a combination of NHPD monographs. Applicants must complete the standalone **Monograph Attestation Form** and select the box which indicates that the PLA solely contains information that is supported by NHPD monographs.

"**Non-Traditional", "Traditional" and "Homeopathic with a Specific Claim"** applications requiring full assessment will be classified as a Class III product. Class III may include, not limited, to the following products:

1 NHPD reserves the right to request further safety information and shift lower certainty combination products to Class III review

- Innovative products with partially or completely novel safety and efficacy profiles
- Applications partially referencing monograph information but still requiring some assessment
- Applications containing a mixture of monograph ingredients and additional supporting evidence, for example a dosage form or route of administration not indicated on the monograph(s) that requires further assessment

Class III applications containing one or more ingredient(s) that comply with all monograph parameters must complete the standalone **Monograph Attestation Form** and indicate which ingredients and recommended uses (if any) are supported by NHPD monographs.

5.2.1 **Screening**

All Class II and III applications will be examined for administrative completeness. Applications meeting all administrative requirements will be sent an **Application Acknowledgement letter**. Applications that are deficient with respect to administrative content will result in the issuance of a **Rejection Notice- Administrative Deficiency**.

Applications meeting all administrative requirements will be further screened against minimum application requirements as outlined in the NHPD`s **Product Licensing guidance document**. In addition, these applications will be subject to screening for safety and efficacy evidence.

If deficiencies are identified during Screening, NHPD will issue the applicant a **Clarification Request**.

Complete Class II applications submitted using the ePLA and complying with all monograph specifications, will receive a **Product License (PL)** within thirty (30) calendar days of receipt. Alternatively, all successfully screened Class III applications will be sent for full assessment after the thirty (30) calendar day screening period is complete.

If major deficiencies are identified during the screening of these applications, an **Application Refusal Letter** will be issued to the applicant. If the applicant wishes to re-submit the application at a future time, it will be processed as a new application.

5.2.2 **Full Assessment**

Upon successful completion of the screening process, applications will enter the assessment queue and be classified as Class III. Applications classified as a Class III application will be reviewed for the safety and efficacy requirements outlined in the *Natural Health Product Regulations* and in the aforementioned guidance documents. Once all requirements are met a **Product License** will be issued within one hundred and eighty (180) calendar days.

Significant deficiencies or information omissions that preclude the on-going review may be transmitted to the applicant in an **Application Refusal Letter**.

However, in most instances, NHPD will provide the opportunity for the applicant to address deficiencies or information omissions through an **Information Request Notice (IRN)** or **clarification request.** For the purpose of implementing and maintaining an efficient assessment process, the directorate will target to issue one comprehensive IRN. In certain situations though, a second IRN or clarification request may be issued. Once a response is deemed complete, the review process will resume. NHPD reserves the right to request clarification on the information submitted.

If the IRN response is deemed deficient or if the applicant does not satisfy all Class III requirements, an **Application Refusal Letter** may be issued. If the applicant wishes to re-submit the application at a future time, it will be processed as a new application.

5.3 Communication

Applicants wishing to contact NHPD to receive advice regarding regulatory notices or decisions issued by NHPD, policies, guidance, procedures, tools, and initiatives are encouraged to send an e-mail at any point during the review process.

5.3.1 Requests for information

NHPD may communicate with applicants by telephone, e-mail (including epost Connect ™) or fax at any point upon application receipt. The directorate may issue correspondences with a maximum specified response time. Applicants will be given two (2) business days to respond to a clarification request and fifteen (15) or thirty (30) Calendar days to respond to an IRN, depending on the complexity of the information requested. The NHPD reserves the right to request clarification of the information submitted and/or issue an **Application Refusal Letter** if the applicant does not provide a complete response in the allocated timeframe

5.3.2 Really Simple Syndication (RSS) Feed

NHPD has added a Really Simple Syndication (RSS) feed to our website to inform stakeholders on the latest web related activities and postings; including updates regarding workshops, new documents (i.e. pre-cleared information), new initiatives or other information deemed relevant for NHP applicants. Once stakeholders have signed up for NHPD's RSS feed, they will be alerted via RSS reader or via email of new postings on NHPD's pages

5.4 Unsolicited information

At any time during the assessment process, applicants are encouraged to submit information to supplement or correct information on the regulatory status of the product

in other countries, problem reports impacting the safety or efficacy of the product submitted to other Regulatory Agencies, and safety information enhancing the safe use of the natural health product, including updated safety-related labelling. The submission of such information does not constitute significant changes to the PLA under assessment.

Changes to non-medicinal ingredients and brand name(s) are acceptable at any stage provided the changes do not affect the safety, efficacy and / or quality of the product. For example, any non-medicinal ingredients being added must be present in the NHPID and adhere to any limits or restrictions.

Applicants are requested to clearly identify the relevant application by referencing the Submission Number in a cover letter so that the new information can be forwarded efficiently to the appropriate review team. Applicants may send this information by email.

5.4.1 **Unacceptable application or formulation changes during review**

Notwithstanding section 5.4.2 below, changes to the application which would result in a re-review by NHPD are not permitted; these changes include product reformulation, the addition of medicinal ingredients, addition of claims, changes to dosing, changes to route of administration and / or changes to dosage form.

5.4.2 **Exceptions**

At any time, applicants may remove proposed claims. Additionally, applicants are always encouraged to align their product with NHPD monographs. Applicants can therefore revise proposed claims, ingredient quantities, dosing information or risk information to align with NHPD monographs and submit the standalone attestation form as per section 4.2.1.

Other revisions related to monographed information may be acceptable, but the applicant is advised to confirm with NHPD before proceeding, in order to ensure acceptability. Applicants may send this information by email.

5.5 Decision issuance

A **product license** will be issued to applications satisfying all Class I, II or III requirements and thus meeting all requirements outlined in the *Natural Health Product Regulations* and in the aforementioned guidance documents.

A **rejection notice- administrative deficiency** will be issued to all applications deficient with respect to administrative content.

A **refusal letter** will be issued in the following circumstances:

- failure to meet the requirements of the *Natural Health Product Regulations* or any provisions of the Act, after a comprehensive assessment; or
- failure to submit the requested information in response to an **clarification request or IRN** within the timelines specified above, or submission of an incomplete or deficient response to **clarification request or IRN.**

The **refusal letter** will contain the specific reasons or deficiencies that resulted in the decision to refuse issuance or amendment of a Product Licence. All decisions to refuse an application are without prejudice to re-filing. If an applicant wishes to resubmit an application at a future time, the application will be processed as a new application. Information and data submitted to support the original application will not be returned to the applicant. Such data may be cross-referenced only if re-filing of the new application occurs within six (6) months of the date of the Refusal Letter.

An applicant may request a reconsideration of the Directorate's decision to refuse their application in accordance with the NHPD Reconsideration Process. For more information on NHPD's Reconsideration Process, please see section 6.3.

5.6 Withdrawal

At any time during the review of their application, an applicant may withdraw their application by submitting their intent via email. All withdrawal letters will be acknowledged in writing. The status of the application will be recorded as "withdrawn by applicant".

Withdrawal of an application is without prejudice to re-filing. If an applicant wishes to resubmit an application at a future time, the application will be processed as a new application. Information and data submitted to support the original application will not be returned to the applicant. Such data may be cross-referenced only if re-filing of the new application occurs within six (6) months of the date of withdrawal.

6. Post decision issuance activities

6.1 Post licensing change

Applicants submitting Post Licensing Changes should select the "Post Licensing change" option on the ePLA and consult the requirements for each Class, outlined in section 5 above. Applicants submitting post licensing changes complying with all parameters of one or more NHPD monographs are required to submit the standalone attestation form along with their revised PLA. Applicants submitting post licensing changes which are not supported by NHPD monographs, are required to submit additional evidence to support the desired changes, as described in section 5.2 above.

6.2 Reviewers report

Following receipt of a Product Licence or **Refusal Letter as a result of Full Assessment**, an applicant or licensee may request reviewers' reports by writing to the Submission Management Division Manager and referencing the submission number. NHPD will target to provide a copy of the requested reports to the applicant within fifteen (15) working days from receipt of the request.

6.3 Request for reconsideration

The purpose of a request for reconsideration is to allow the NHPD and a PLA applicant to discuss issues related to a Directorate decision on an application. The parties may clarify and justify their positions using information available to the NHPD when the decision was made. The request for reconsideration must be based on the same information and material as the original decision. Information and material not submitted at the time of the initial decision will not be accepted.

The Reconsideration Process does not apply to the challenge of existing policies, guidelines or standards. The Directorate maintains other mechanisms to review and revise these documents which involve input from and consultation with a broad range of stakeholders. The Reconsideration Process also does not apply to issues related to changes in requirements resulting from the evolution of regulatory policy that have resulted in other products reaching the market under less stringent or more favourable conditions. Where requests for reconsideration involve these types of issues, the request will be denied.

6.4 Re-filing an application

Applicants may re-file previously withdrawn applications or applications for which a **Refusal Letter** was issued. In all cases, a re-filed application is considered to be a new application and will be managed according to this policy. In addition, a re-filed application is subject to any new policies, procedures and / or guidance documents in effect at the time of re-filing.

6.4.1 **Re-filing within six (6) months**

If an application is re-filed within six (6) months of a **Refusal Letter** or **Withdrawal Letter**, the applicant may submit only the material requested in the outstanding **IRN** or listed in the **Refusal Letter** provided there is appropriate cross-referencing to the original material submitted. If the applicant chooses to cross-reference original material previously filed, certification that the original material pertaining to the natural health product remains unchanged must be included with the re-filed application. Applicants must also clearly identify new and previously submitted information in the cover letter or table of contents accompanying the re-filed application.

6.4.2 **Re-filing after six (6) months**

If an application is re-filed after six (6) months of a **Refusal Letter** or Withdrawal Letter, the applicant must submit a completely new application, i.e. no cross-referencing to previously submitted material is allowed.

6.4.3 **Re-filing of a rejected application**

If an application has been rejected as described in section 5.1 and 5.2, the applicant must submit a completely new application, i.e., no cross-referencing to previously submitted material is allowed.

Health Canada Santé Canada

Proposed service standards for the management of product licence applications for natural health products

APPLICATION TYPE		ADMINISTRATIVE PROCESSING FOR APPLICATION COMPLETENESS	TYPE OF NOTICE ISSUED	SCREENNG	FULL ASSESSMENT	REGULATORY DECISION ISSUED
CLASS I	Compendial	10 Business Days	N/A	N/A	N/A	Product Licence, Rejection or Refusal Letter
	Homeopathic Medicine Labelling Standard					
	Post Licensing change attesting to a single monograph					
CLASS II	Non-Traditional	10 Calendar days	Application Acknowledgment Letter or Rejection Letter	20 Calendar Days	N/A	Product Licence or Refusal Letter
	Traditional					
	TPD Category IV/ Labelling Standard					
	Homeopathic Medicines with Non-Specific Claim					
	Post Licensing change attesting to multiple monographs					
CLASS III	Non-Traditional	10 Calendar days	Application Acknowledgment Letter or Rejection Letter	20 Calendar Days	180 Calendar Days	Product Licence or Refusal Letter
	Traditional					
	Homeopathic Medicines with Specific Claim					
	Post Licensing change requiring assessment of Safety and/or Efficacy					

*From successful completion of the screening process.

Canada

Appendix I

Pre-submission meeting

Applicants may wish to deliver a brief presentation to the NHPD prior to submitting a Product Licence Application (PLA). The purpose of pre-submission meetings is to discuss the presentation of evidence in support of the application. In addition, such meetings:

- familiarize assessment staff with the forthcoming application prior to its arrival, and provide a forum to discuss the evidence in the application to facilitate its assessment;
- have the potential to uncover any major unresolved problems or issues and manage disputes early in the application process;
- establish which studies the applicant is relying on to support the efficacy of the natural health product and discuss the adequacy and appropriateness of controls;
- provide an opportunity for the applicant to discuss details of the application with the NHPD and obtain feedback regarding any areas of concern based on current experience and regulatory requirements; and,
- provide NHPD the opportunity to re-align resources, if necessary, to accommodate the arrival of the application.

Best practices will be followed to ensure meetings are well-organized, efficient, productive, and properly documented.

Meeting requests

Meeting requests are to be submitted to the same address as identified above in section 4.1.2 or by email. Requests are to be made no less than 1 month prior to the proposed meeting date and should include the following information:

- the purpose of the meeting
- a brief description of the product to be discussed at the meeting
- three proposed dates for the meeting

In order to ensure efficient use of NHPD resources, requests should include adequate information to determine the utility of the meeting and to identify appropriate staff necessary to discuss proposed issues.

Pre-submission packages

Applicants will be requested to submit a pre-submission meeting information package at least 2 weeks in advance of the meeting. Packages should contain the following information:

- a cover letter
- an agenda for the meeting
- a list of specific issues the applicant would like to discuss or have addressed
- a brief summary of the natural health product for which the meeting is being called
- proposed strengths and dosages
- an overview of the market history of the product including the foreign regulatory status of the product
- identification of the indication(s) for which authorization is sought
- brief summaries of the safety and efficacy data relating to the product