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Pathway for Licensing Natural Health Products used as Traditional Medicines

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Pathway for Licensing Natural Health Products Used as Traditional Medicines, v1.0

Foreword

Guidance documents are meant to provide assistance to industry and health care practitioners on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments and therefore allow for flexibility. Alternate approaches to the principles and practices described in this document may be acceptable; licence applicants are invited to discuss these with the Natural Health Products Directorate prior to submitting an application.

As a corollary to the above, it is equally important to note that Health Canada may request information or material, or define conditions not specifically described in this document, in order to enable the Department to adequately assess the safety, efficacy or quality of a health product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the *Natural Health Products Regulations* and relevant sections of other applicable guidance documents.

Document Change Log			
Document	Pathway for Licensing Natural Health Products Used as Traditional Medicines, Version 1.0	Replaces	Evidence for Safety and Efficacy of Finished Natural Health Products, Version 2.0 Note: this document is also replaced by the following document: Pathway for Licensing Natural Health Products Making Modern Health Claims, Version 1.0
Date	December 2012	Date	December 2006

Change	Location (section, paragraph)	Nature of and/or Reason for Change
Extensive revisions	There were extensive revisions to the content including the addition of revised appendices and an extensive reorganization of the document.	The December 2006 document, Evidence for Safety and Efficacy of Finished Natural Health Products, Version 2.0, was revised in order to reflect some of the recommendations of the Natural Health Product Program Advisory Committee which were posted on the Health Canada website under the name Report of the Natural Health Products Program Advisory Committee to the Natural Health Products Program, January 26, 2010. It was also split into two guidance documents.

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1.0 Introduction

This guidance document provides information to help product licence applicants determine the evidence (type and amount of data) to be provided to support the safety (risk) and efficacy (benefit) of traditional medicines.

The intent of this document is to ensure that the levels of evidence are rigorous enough to protect public health and maintain consumer confidence, while providing industry with a clearly defined pathway to bring to market natural health products (NHPs) which are formulated based on traditional principles.

While not specifically included in this guidance document, other options for supporting safety and efficacy may be considered depending on the circumstances of a particular NHP.

The *Natural Health Products Regulations* (NHPR) set out the requirements governing the sale, manufacture, packaging, labelling, importation, distribution and storage of NHPs. The objective of the NHPR is to provide reasonable assurance that products offered for sale in Canada are safe, efficacious and of high quality. Evidence submitted as part of a product licence application must support the requirements set out in section 5, paragraphs (a) to (j) of the NHPR.

Did you know that you can submit evidence to Health Canada that is not outlined in this document? If you have an alternative way of supporting the safety and efficacy of your product, we'll look at that information.

1.1 Policy Objective

To provide reasonable assurance that NHPs offered for sale in Canada are safe and effective when used under their recommended conditions of use.

1.2 Policy Statement

The level of evidence (type and amount) that can be provided to support the safety and efficacy of an NHP varies depending on the proposed health claim(s) of the product and the overall risk profile of the product or its ingredients.

1.3 Scope and Application

This guidance document applies to product licence applications for traditional medicines. It does not apply to product licence applications for:

- NHPs that do not meet the definition of a traditional medicine;
- Homeopathic medicines;
- NHPs attesting to Natural Health Products Directorate (NHPD) Labelling Standards; and
- NHPs under the 60-day disposition clause (i.e., those citing a monograph from the NHPD's Compendium of Monographs as the sole source of information supporting the safety and efficacy of the product).

In addition, the requirements and restrictions outlined in this document do not apply to health care practitioners (including, but not limited to, practitioners of Traditional Chinese Medicine (TCM) or Ayurvedic Medicine) who compound products for their patients in the context of a practitioner-patient relationship. For more information, see the Natural Health Product Compounding Policy.

For NHPs with modern health claims, refer to the *Pathway for Licensing Natural Health Products Making Modern Health Claims*.

For NHPs with traditional use claims which do not meet the definition of a traditional medicine (e.g., products containing ingredients that are not supported for use within the same paradigm), refer to the *Pathway for Licensing Natural Health Products Making Modern Health Claims*.

For medicinal ingredients prepared in accordance with homeopathic pharmacy, refer to the *Evidence for Homeopathic Medicines Guidance Document*.

For more information on the 60-day disposition clause, refer to the *Compendium of Monographs Guidance Document*.

Looking for other [guidance documents relevant to NHPs?](#)

1.4 Background

The *Evidence for Safety and Efficacy of Finished Natural Health Products Guidance Document* (December 2006) is replaced by two new guidance documents: *Pathway for Licensing Natural Health Products Making Modern Health Claims* and *Pathway for Licensing Natural Health Products Used as Traditional Medicines*.

The current guidance document describes the levels of evidence for safety and efficacy of NHPs meeting NHPD's definition of traditional medicine.

1.5 Definitions

Natural Health Product

An NHP is a substance or a combination of substances described in Schedule 1 of the NHPR, a homeopathic medicine, or a traditional medicine, that is intended to provide a pharmacological activity or other direct effect in:

- diagnosing, treating, mitigating, or preventing a disease, disorder, or abnormal physiological 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.

Schedule 2 of the NHPR sets out substances which do not fall within the meaning of an NHP.

Medicinal Ingredient

A medicinal ingredient is a substance which is set out in Schedule 1 of the NHPR, is biologically active and is included in an NHP for the purposes of:

- 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.

A medicinal ingredient is characterized by its physical form, its chemical attributes, its source, its preparation, as well as its dose and pharmacological action.

Non-medicinal Ingredient

A non-medicinal ingredient is defined as any safe substance that is added to a product to confer suitable consistency or form to the medicinal ingredients (suitable as per dosage form and route of administration). Non-medicinal ingredients:

- should not exhibit pharmacological effects;
- should not have any effect contradictory to the product's recommended purpose;
- should not exceed the minimum concentration required for the formulation;
- should not adversely affect the bioavailability, pharmacological activity, or safety of the medicinal ingredients; and
- should be safe.

Recommended Conditions of Use

The recommended conditions of use are defined as:

- recommended use or purpose;
- dosage form;
- recommended route of administration;
- recommended dose (including sub-population, amount, dosage unit, frequency, and directions of use);
- recommended duration of use, if any; and
- risk information, including cautions, warnings, contraindications, or known adverse reactions associated with the use of the product or its medicinal ingredients.

Traditional Medicine

Traditional medicine is defined as medicine based on the sum total of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness. This definition is one modified from the World Health Organization Traditional Medicine Program, recognizing traditional medicines at their core as ancient medical practice that existed in human societies before the application of modern science to health and that have evolved to reflect different philosophical backgrounds and cultural origins.

Did you know that you can meet with staff of the Natural Health Products Directorate before submitting your application if you have questions? For more information, see the [Management of Product Licence Applications for NHPs](#).

2.0 Guidance for implementation

2.1 Roles and Responsibilities

Product licence applicant:

It is the responsibility of the applicant to provide a complete product licence application, including evidence demonstrating that safety (risk) has been established and any risks sufficiently mitigated; that efficacy (benefit) has been demonstrated; and that quality is supported.

Natural Health Products Directorate:

It is the responsibility of the NHPD to review the information provided as part of the product licence application in order to assess the safety, efficacy and quality of an NHP, to ensure benefits outweigh risks, and to clearly document the product licensing decision.

For further information on roles see the *Management of Product Licence Applications for Natural Health Products* policy. It explains how applicants can meet with the NHPD prior to submitting a product licence application and communicate with their submission coordinator throughout the application review process.

2.2 Health Canada Authorization Process

For other ways to make traditional use claims, refer to Annex I of the *Pathway to Licensing Natural Health Products Making Modern Health Claims*.

In order to obtain authorization to sell an NHP in Canada, a product licence application must be submitted to Health Canada. As part of this product licence application, evidence supporting the safety and efficacy of the NHP according to its recommended conditions of use must be included.

The purpose of the assessment is to determine whether the evidence supports the safety and efficacy of the product, including whether there is reasonable assurance that benefits of the product outweigh any risk inherent

You may be able to get a product licence quickly by using our pre-cleared information: check out our monographs and labelling standards via [the Natural Health Products Ingredients Database](#)

in the product's ingredients or associated use of the product. The assessment of safety (risk) for a product depends on a variety of factors, including the conditions of use and the physical form and pharmacology of each ingredient in the product as well as the product as a whole. The benefit-to-risk profile of a product is always considered prior to a product licensing decision being made (i.e., licence issuance or application rejection).

Refer to the [Management of Product Licence Applications for NHPs](#) for more information on the product application and assessment process.

2.3 Health Claims

A health claim is a statement that indicates the intended beneficial effect of a product when used in accordance with its recommended conditions of use. The term "recommended use or purpose" is often used interchangeably with "health claim" or "indications for use."

Given the definition of a traditional medicine, traditional use claims should reflect the sum total of knowledge, skills, and practices based on theories, beliefs, and experiences indigenous to a specific culture, used in the maintenance of health, as well as prevention, diagnosis, improvement, or treatment of physical and mental illness. For a claim to be categorized as "traditional use," it should be founded upon the theories, experiences and beliefs embodying the respective ancient practice of medicine.

2.3.1 General Health Claims

Products with general health claims include those that have low therapeutic impact and are therefore subject to the appropriate evidence requirements.

Annex I of the *Pathway for Licensing Natural Health Products Making Modern Health Claims* outlines a regulatory pathway for NHPs with general health claims. These claims can be used provided that the health and safety of Canadians would not be at risk; this is consistent with a risk-based product approach where health claims are indexed against the level of evidence provided to support the safe use of the products. For information on general health claim principles, see Annex I.

2.4 Demonstrating a Long History of Use

There are multiple ways to support a long history of use. Examples of ways to demonstrate a long history of use of an NHP (or medicinal ingredient) includes:

- Demonstrating a timespan representing two generations of safe traditional use. The most suitable and most adequate references describe:
 - The use in the context of a particular cultural belief system or system of traditional medicine that has been in existence for at least two generations;
 - A period that was at least two generations ago with the implication that the ingredient was used from that period onwards; or
 - A time-specific event even though neither a concrete date nor time frame was given (e.g., “used in the time of King Edward II to alleviate coughs”).
- Demonstrating that the product meets the European Directive on traditional herbal medicines - [Directive 2004/24/EC, Article 16](#).
- References supporting traditional use as per the Australian Therapeutic Goods Administration, i.e., used over three or more generations of recorded use for a specific health-related or medicinal purpose ([Guidelines for levels and kinds of evidence to support indications and claims](#))

2.5 Traditional Medicines

Products with multiple medicinal ingredients with “traditional use” claims are permitted for assessment as traditional medicines when certain conditions are met:

- Evidence should demonstrate “traditional use” of the medicinal ingredients within a **single** recognized system of traditional medicine (e.g., TCM, Ethnomedicines of the First Nations, Ayurvedic Medicine, Traditional Herbal Medicine) as a whole formulation; modifications of a classic recipe that would still be accepted within the system of traditional medicine; or as individual medicinal ingredients;
- Efficacy should be based on the belief systems, theories, and/or experiences specific to the relevant traditional healing paradigm, not on modern evidence;
- All ingredients should be documented medicinal ingredients within the same system of traditional medicine and have been prepared based on a suitable traditional method of preparation utilized for that medicinal ingredient; and
- A clear and logical rationale should be provided to support the presence of each medicinal ingredient. Not all ingredients in the formulation need to contribute to the recommended purpose; however, each ingredient should contribute in a logical manner to the overall safety and efficacy of the product within the given traditional system of medicine.

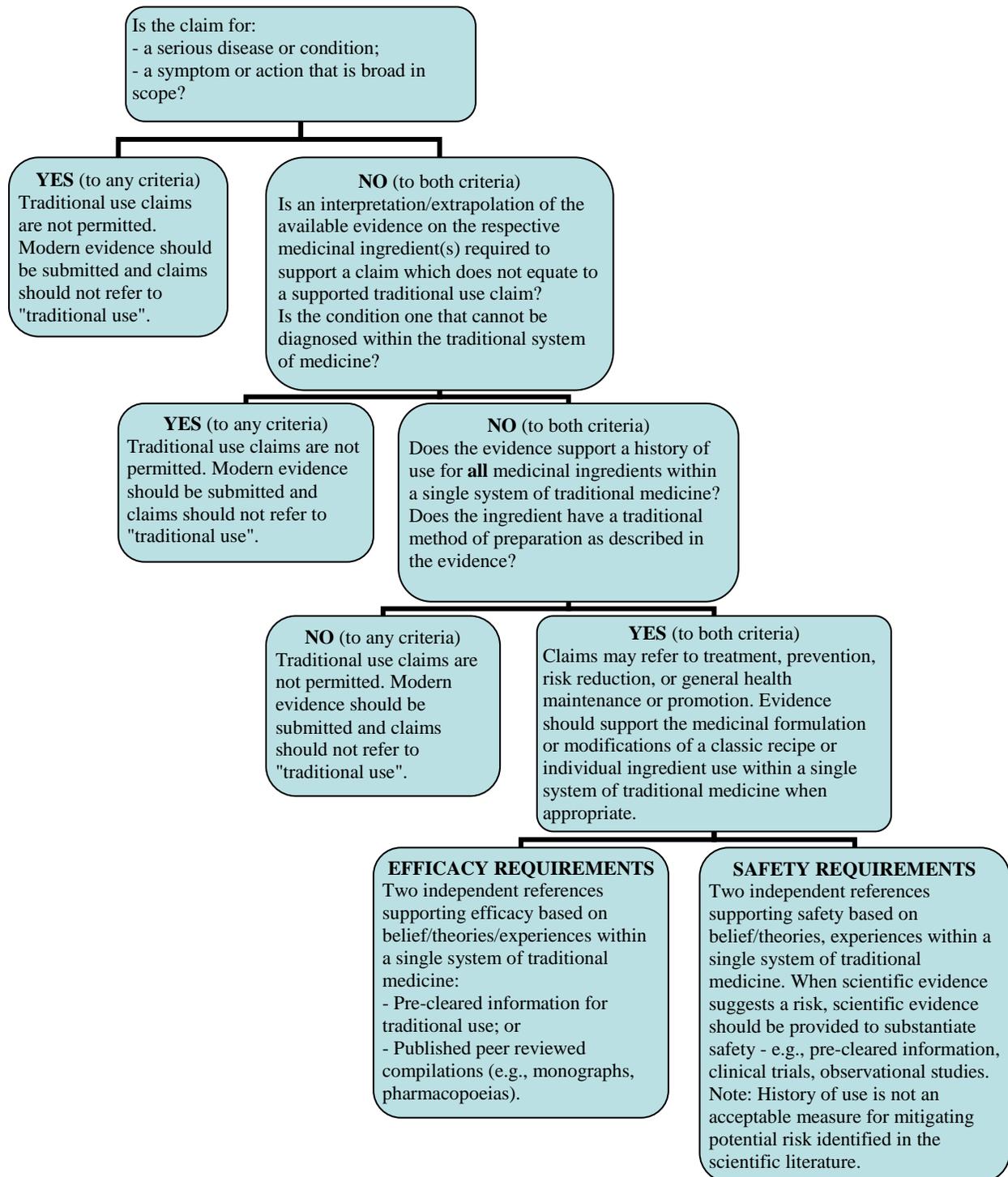
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The intent is to capture modifications to classic traditional formulations that are supported by the knowledge and experience of the traditional system of medicine. For example, modifications of the classical formula of a TCM that are still based on TCM principles would fall into this category, but the modifications of ingredients based on other evidence would not. The intent is also to capture formulations in Traditional Herbal Medicine or Traditional Ayurvedic Medicine that are logical within those systems of medicine, but not additions of unrelated herbs, vitamins, minerals or other ingredients.

If the recommended conditions of use (i.e., the recommended use or purpose, dose including the method of preparation, dosage form, or route of administration) for the product are not comparable to the recommended conditions of use contained within the references on the traditional use of the product, the product will not be assessed as a traditional medicine, a traditional use claim may not be permitted, and additional evidence requirements may apply.

Figure 1: Risk-Based Approach for determining when Traditional Use Claims are Appropriate for Traditional Medicines



2.6 Demonstrating Traditional Use

As per section 2.4, there are many ways to demonstrate a long history of use. Ideally, the references help to establish the paradigm in question, in addition to providing information on the conditions of use (indications, dose, cautions and contra-indications, etc.) of specific ingredients within that paradigm.

Does your product use a method of preparation not listed in this document? It may be considered traditional if you can support it with at least one reference describing the method's use within the practice of traditional medicine.

References should also refer to a health condition that can be diagnosed in the relevant system of traditional medicine independent of whether the reference indicates "traditionally used" or not. For example, hyperlipidemia is a health condition that cannot be diagnosed within a traditional system of medicine.

References should also refer to use, dosage form, route of administration, dose, and duration of use, when applicable, that is consistent with traditional use and comparable to that of the recommended product. This includes traditional methods of preparation such as:

- the use of a whole organism or specific parts (leaf, root, fruiting body, etc.), whether fresh, dried or freeze-dried, or preserved with alcohol, honey, or sugar;
- extracts produced by the application of pressure to the source material;
- aqueous extracts such as infusions, decoctions, and syrups;
- ethanol-based extracts such as tinctures, fluid extracts, and succi;
- glycerine-based extracts;
- vinegar-based extracts;
- oil, grease, or fat-based infusions; or
- beeswax salves and ointments.

Other methods of preparation may be considered traditional if supported by at least one reference describing the method's use within the practice of traditional medicine and assessed as acceptable by NHPD.

2.7 Safety Evidence for Traditional Medicines

Safety is supported in several ways. History of use is an important consideration. References demonstrating that the ingredient has an extensive history of use should be submitted (see section 2.4). Although the indication need not be the same, other conditions of use (dose, duration of use, source material, method of preparation, etc.) should be comparable to the conditions of use being proposed.

Cautions, warnings and contra-indications found in the accompanying references are a primary source of safety information. In many cases, safety concerns can be mitigated by limiting dose and/or duration of use, by adding risk statements or by limiting sub-populations, e.g., pregnant and breastfeeding women.

Finally, a search should be made of the totality of evidence to ensure that no new, unknown safety concerns have been identified by the findings outside of evidence for traditional use. In many cases other data will not exist to confirm safety, in which case existing safety data as described above will be considered sufficient. Should the available evidence suggest that a medicinal ingredient is unsafe when used according to the product's recommended conditions of use, it will be necessary to submit further evidence of equal or higher validity, causality, and

credibility to demonstrate that the balance of evidence supports a favorable benefit to risk ratio for the product. Theoretical concerns will not be considered in the absence of clinical data.

2.7.1 Safety Evidence Recommendations for Non-medicinal Ingredients

It is important to note that non-medicinal ingredients listed in the Natural Health Products Ingredient Database (NHPID) have not necessarily been reviewed for safety or suitability in NHPs. Additional information may be requested to support the safety or nature of any non-medicinal ingredient. Information to support the recommended conditions of use for all non-medicinal ingredients should be available upon request, such as quantity, purpose in formulation, alternative formulations and specifications, identity information, safety information or other manufacturing information.

Did you know that you can provide evidence to support non-medicinal ingredients that are not present in the Natural Health Products Ingredient Database with a [Issue Form](#).

When evidence to support safety is requested, it should reflect the daily dose and purpose of the non-medicinal ingredient, should be appropriate to the route of administration, and should consider exposure. Non-medicinal ingredients should not be indiscriminately included within a product's formulation. The safety requirements for non-medicinal ingredients generally mirror those of medicinal ingredients. However, when risk or uncertainty is identified, additional evidence may be requested to help characterize the risk.

Manufacturers may add substances to their medicinal ingredients to aid stability or manufacturing processes. If these remain in significant quantities in the finished NHP (e.g., including any quantity that still provides a technical effect), they must be declared as non-medicinal ingredients on the product licence application form and label. It may be necessary to communicate with the manufacturer directly in order to identify these types of ingredients.

The individual components of mixtures should be listed separately except when the mixture has a common name in the NHPID (exceptions may be made when the NHPID does not adequately describe the components of the mixture) or the mixture is a proprietary blend of flavours that may be qualitatively described (e.g., artificial strawberry kiwi flavour blend).

If you provide pharmacopoeial evidence to support your product's efficacy, you only need one piece of evidence.

2.8 Efficacy Evidence for Traditional Medicines

Traditional use claims for traditional medicines are divided into two sub-categories according to the evidence provided:

- pharmacopoeial evidence alone; or
- other types and/or combinations of references supporting traditional use.

To help ensure that product licence applications for traditional medicines are processed in a timely manner, applicants are asked to provide a cover letter with their applications that clearly indicates which of the two evidence categories their product is intended for.

2.8.1 Pharmacopoeial Evidence for Traditional Medicines

Products providing only pharmacopoeial evidence and answering “yes” to all elements of the Checklist for the Traditional Pharmacopoeial Evidence Category (Appendix A) only require one supporting reference. Answering “no” to any of the questions posed on this checklist excludes the product from being assessed within the pharmacopoeial stream.

Applications suitable for assessment within the pharmacopoeial evidence category should provide one of the following as evidence in supporting the claim:

- A copy of the relevant pages of a monograph from a recognized pharmacopoeia (e.g., *The Ayurvedic Pharmacopoeia of India*, *The Pharmacopoeia of the People's Republic of China* (PPRC)); or
- A copy of a monograph published by a reputable agency with a definition of traditional medicines comparable to that of the NHPD (e.g., translated version of the *Drug Standard of People's Republic of China* [also called the *State Drug Standard* (SDS)]);

Note: An English or French translation of the relevant monograph pages should be provided (in addition to a copy of the original) if the language of publication is neither English nor French. The accuracy and completeness of any and all translated documents should be verified as lack thereof may result in refusal of the submission.

The information on Part 4 of the Product Licence Application form (e.g., medicinal ingredients, route of administration, dose, duration of use, method of preparation, etc.) should be comparable to that stipulated in the supporting monograph or reference. As an exception, when a monograph specifies an indication related to a serious disease, condition, or abnormal physical state (e.g., cancer, depression, alcoholism), revisions are permitted to make the claim more appropriate for a non-prescription product. Serious diseases/conditions are those for which treatment requires supervision by a doctor, or are debilitating or potentially life threatening without effective treatment.

A multiple ingredient rationale is *not* required and the Checklist for the Traditional Pharmacopoeial Assessment Evidence Category does not need to be included with the application when pharmacopoeial evidence is provided.

2.8.2 Other Types of Efficacy Evidence for Traditional Medicines

Products providing more than pharmacopoeial evidence as the evidence supporting efficacy or answering “no” to any of the elements of the Checklist for the Traditional Pharmacopoeial Evidence Category should provide at least two independent references that support the recommended conditions of use. Independent references are those that do not cite the same source, or each other, as the main source of information regarding the traditional use of the ingredient. The references should be authoritative and from a reputable source as determined by NHPD. Appendix B provides a partial list of selected references that are recommended.

In the case where only one written reference exists or where multiple references refer back to a single original source, an expert opinion based on practitioner experience and knowledge may be considered as a possible substitute for a second reference. Refer to Appendix G for more information on expert opinions.

2.9 Qualifying Claims

When a product meets the NHPD definition of traditional medicine and relies on traditional evidence to support safety or efficacy, claims should be prefaced with qualifiers indicating the specific traditional system of medicine, such as “traditionally used in Ayurvedic medicine,” to identify for consumers that efficacy is based on a specific system of traditional medicine. If the claim uses terminology specific to a particular culture or system of medicine, that specific terminology along with the culture or system of medicine should be specified in the claim (e.g., “TCM used to replenish *Qi* (vital energy)...” or “traditionally used in Ayurvedic medicine to improve *agni* [digestive fire]).

If both traditional use evidence and modern evidence are available to support a proposed claim, the use of the wording “traditionally used” is optional; however, a product making a traditional use claim based primarily on traditional use evidence is to be assessed as a traditional medicine. If a health claim is solely supported by modern evidence, it should not include the words “traditionally used.”

The NHPD recognizes that some systems of traditional medicine may communicate risk information in language that is specific to that healing paradigm or culture. In cases where it is not evident to the consumer that the risk information is based on use within a traditional system of medicine, a traditional qualifier can be included in the risk information as an option (e.g., “do not use in cases of external pathogenic heat [TCM]”).

2.10 Linking Evidence to Conditions of Use, Ingredient Form and Use of Extracts

Refer to **Appendix C** for recommendations on how to link safety and efficacy evidence to a product’s conditions of use.

Refer to **Appendix D** for recommendations on how to link safety and efficacy evidence to an ingredient’s chemical and physical form.

Refer to **Appendix E** for information on linking safety and efficacy evidence to the use of an extract (i.e., comparability of an extract to the evidence).

For more information on qualifying claims, refer to Annex I of the *Pathway to Licensing Natural Health Products Making Modern Health Claims*.

2.11 Final Check before Submitting the Product Licence Application

Refer to Appendix F for the evidence criteria for traditional use claims, which can be used as a final check before submitting a product licence application to ensure that the application is not missing any evidence and meets a minimum level of validity.

Appendices

Appendix A: Checklist for the Traditional Pharmacopoeial Evidence Category

Appendix B: Partial List of Recommended References for Supporting Traditional Use Claims

Appendix C: Linking Evidence to Conditions of Use

Appendix D: Linking Evidence to Ingredient Form

Appendix E: Linking Evidence to Use of Extracts

Appendix F: Evidence Criteria for Traditional Medicines

Appendix G: Expert Opinion

Appendix A: Checklist for the Traditional Pharmacopoeial Evidence Category

This checklist is for use by applicants but does not need to be submitted with the product licence application. However, responding "no" to any of the questions posed on this checklist excludes the product from being assessed within the pharmacopoeial stream. Products that can answer "yes" to all criteria require only one approved reference.

Information Captures	Pharmacopoeial evidence identical/comparable to the <i>Pharmacopoeia of the People's Republic of China</i> (PPRC) or the <i>Drug Standard of People's Republic of China</i> (also called the <i>State Drug Standard</i> (SDS)) or <i>The Ayurvedic Pharmacopoeia of India</i>
<i>All medicinal ingredients</i>	
<i>Quantity of the medicinal ingredients as per crude material equivalent, when applicable</i>	
<i>All recommended uses or purposes</i>	
<i>Recommended dose</i>	
<i>Recommended route of administration</i>	
<i>Recommended duration of use (if any)</i>	
<i>Dosage form</i>	
<i>Directions of use</i>	
<i>Risk information (cautions, warnings, contraindications, known adverse reactions)</i>	
<i>Methods of preparation (traditional)</i>	
<i>Copy of the relevant pages from the Pharmacopoeia (in English or French)</i>	
<i>Product claim does not refer to or imply diseases listed on Schedule A to the Food and Drugs Act</i>	

Appendix B: Partial List of Recommended References for Supporting Traditional Use Claims

This appendix lists recommended references for supporting i) Traditional Chinese Medicines, ii) Traditional Ayurvedic Medicines and iii) Traditional Herbal (Eclectic) Medicines.

i) Traditional Chinese Medicines

- Dan Bensky, Andrew Gamble, Ted Kaptchuck. Chinese Herbal Medicine: Materia Medica (revised edition). Eastland Press, Seattle, Washington, 1993
- Dan Bensky, Steven Clavey, Erich Stoger. Chinese Herbal Medicine: Materia Medica (third edition). Eastland Press, Seattle, Washington, 2004
- Dan Bensky, Randall Barolet. Chinese Herbal Medicine: Formulas & Strategies. Eastland Press, Seattle, Washington, 1990
- Volker Scheid, Dan Bensky, Andrew Ellis, et al. Chinese Herbal Medicine: Formulas & Strategies (second edition). Eastland Press, Seattle, Washington, 2009
- Chongyun Liu, Angela Tseng, Sue Yang. Chinese Herbal Medicine, Modern Applications of Traditional Formulas. CRC Press, 2005:712
- Him-Che, Yeung. Handbook of Chinese Herbs. Institute of Chinese Medicine, Rosemead, CA, 1996
- Him-Che Yeung. Handbook of Chinese Herbal Formulas, second edition. Institute of Chinese Medicine, Rosemead, CA, 1998
- Hsu, Hong-yen, Chen Yuh-pan, She Shuenn-jyi, et al. Oriental Materia Medica, A concise Guide. Keats Publishing, Inc. New Canaan, Connecticut. 1986
- John K. Chen, Tina T. Chen. Chinese Herbal Formulas and Applications. Art of Medicine Press, City of Industry, CA, 2009
- John K, Chen , Tina T. Chen. Chinese Medical Herbology and Pharmacology. Art of Medicine Press, City of Industry, CA, 2004
- The State Pharmacopoeia Commission of the People's Republic of China. Pharmacopoeia of the People's Republic of China (English Edition). Chemical Industry Press, 2000
- The State Pharmacopoeia Commission of the People's Republic of China. Pharmacopoeia of the People's Republic of China (English Edition). People's Medical Publishing House, 2005
- The State Pharmacopoeia Commission of the People's Republic of China. Pharmacopoeia of the People's Republic of China (Chinese Edition). Chemical Industry Press, 2005
- Ou Ming. Chinese-English manual of common-used in traditional Chinese Medicine. Hong Kong: Joint Publishing, 1989
- National Standard Chinese Collegiate Textbooks in Traditional Chinese Medicine for Institutions of Traditional Chinese Medicine of Higher Education. The Chinese Materia Medica.
- National Standard Chinese Collegiate Textbooks in Traditional Chinese Medicine for Institutions of Traditional Chinese Medicine of Higher Education. The Chinese Formulas and Strategies.
- The State Pharmacopoeia Commission of the People's Republic of China (Chinese Edition). *State Drug Standard*.
- Jingshi Wu. National Non-Prescription Drugs Manual, (second edition) (Chinese Edition). People's Medical Publishing House, 2004.
- Editorial Committee of Comprehensive Chinese Materia Medica of State Administration of Traditional Chinese Medicine of People's Republic of China. Chinese Herbal Medicines

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(Zhonghua Bencao) (Chinese Edition). Shanghai Science and Technology Publishing House, 1996.

Xu Guojun, etc. Chinese Materia Medica (Chinese Edition). China Medical Science and Technology Press: 1996

ii) Traditional Ayurvedic Medicines

Ayurvedic Pharmacopoeia of India: Part 1 (Vol. 1 to 5)

Kapoor LD. Handbook of Ayurvedic Medicinal Plants

Gogte V.V.M. Ayurvedic Pharmacology and Therapeutic uses of Medicinal Plants (Dravyagunavuignyan)

Sudarshan S.R. Encyclopaedia of Indian Medicine. Volume 1-4.

Orient Longman. Indian Medicinal Plants. A Compendium of 500 Species.

Srikantha Murthy KR. Bhavprakasa of Bhavmisra Volumes 1 and 2

Khory RN. Materia Medica of India and Their Therapeutics.

iii) Traditional Herbal (Eclectic) Medicines

Note: Where more recent editions/versions of the following texts are submitted, the information should be presented in the reference in a way which appropriately reflects the *total knowledge, skills and practices of the paradigm*.

British Herbal Medicine Association. British Herbal Pharmacopoeia. Cowling (UK): British Herbal Medical Association, 1983.

Cook, Wm H. The Physiomedical Dispensatory. 1869.
(<http://www.henriettesherbal.com/eclectic/cook/index.html>)

Ellingwood, 1919: The American Materia Medica, Therapeutics and Pharmacognosy. Eclectic Medical, 1983 (Reprint 1919)(<http://www.henriettesherbal.com/eclectic/ellingwood/index.html>)

Felter and Lloyd. King's American Dispensatory. Eclectic Medical Publications, 1997 (Reprint 1898). (<http://www.henriettesherbal.com/eclectic/kings/index.html>)

Felter, Harvey W. The Eclectic Materia Medica, Pharmacology and Therapeutics. 1922.
(<http://www.henriettesherbal.com/eclectic/felter/index.html>)

Grieve, M. A Modern Herbal, Volume 1-2. New York (NY): Dover Publications, 1971 [Reprint of 1931 Harcourt, Brace & Company publication].
(<http://botanical.com/botanical/mgmh/comindx.html>)

NHPD monographs and other sources of Pre-Cleared Information bearing the qualifier "Traditional Herbal Medicine" or comparable wording. Note: Used in Herbal Medicine without the qualifier "traditional" is not acceptable.

Petersen, Julius. Materia Medica and Clinical Therapeutics. F.J. Peterson, 1905 (Reprint).
(<http://www.henriettesherbal.com/eclectic/petersen/index.html>)

Remington et al. The Dispensatory of the United States of America. J.B. Lippincott Company, 1918. (<http://www.henriettesherbal.com/eclectic/usdisp/index.html>)

Sayre, Lucius. A Manual of Organic Materia Medica and Pharmacognosy. P. Blakiston's Son & Company, 1917. (<http://www.henriettesherbal.com/eclectic/sayre/index.html>)

Health Canada

Pathway for Licensing Natural Health Products Used as Traditional Medicines, v1.0

Wren RC. Potter's Cyclopedia of Botanical Drugs and Preparations. London (GB): Potter and Clark, 1907.

Appendix C: Linking Evidence to Conditions of Use

Evidence is required to support the claim and all of the recommended conditions of use. **Table 1** provides a summary of important recommendations.

Table 1: Linking Evidence to the Conditions of Use

Part of the Application	Criteria
Recommended use or purpose (claim)	The references indicate the same claim as indicated in the product licence application form (but may use different words to describe it). For example: Reference 1: Increases urinary flow Reference 2: Diuretic (this has the same intent as Reference 1)
Proper name	The references include the proper name of the medicinal ingredient, since common names are not always used consistently. If a particular reference supports all of the conditions of use but indicates only a common name instead of a proper name, then the reference may be used along with another acceptable reference that links the proper name with that common name.
Source	The references support the source indicated in the product licence application form for each medicinal ingredient. For example: for a given herb, if the references support only the use of its roots as a source of the medicinal ingredient, then the flowers will not be acceptable as the source.
Dosage form	The dosage form is consistent with the route of administration. For example: the dosage form is a "capsule" and the route of administration supported by the references is "oral."
Route of administration	The references support the same route of administration that is indicated in the product licence application form.
Dose	The references support the same dose (or dosage range) that is indicated in the product licence application form. Indicate the crude material equivalent, when applicable. For example: The recommended dose is 3-4 g crude material equivalent. Reference 1: 2-4 g crude material equivalent Reference 2: 3-5 g crude material equivalent
Tinctures and extracts	The references provide sufficient information about tinctures or extracts to calculate the crude material equivalent, when applicable. Any variations in the solvent used, solvent concentration and extract ratio or potency from the cited references should be justified.
Risk information	Relevant safety information from all available sources, including references to traditional use and modern references, is used to determine the risk information associated with the NHP.

The evidence should adequately match both the ingredient form (physical and chemical form and sometimes source material) as well as the conditions under which it will be used (recommended use, dosage form, route of administration, dose, duration of use, target population).

For example:

- If the recommended dose is 1500 mg/day, provide evidence that specifically supports the efficacy of a dose of at least 1500 mg/day. It is acceptable to provide multiple references that demonstrate a dose range within which the recommended dose falls.
- If the ingredient is an extract, make sure sufficient manufacturing information is provided to allow comparison between the proposed daily dose and that in the references. This is especially important when the reference refers to a crude herb or an isolate. Conversely, when the supporting evidence refers only to an extracted amount or provides doses calculated on the basis of a particular constituent, information that allows for the determination of an associated quantity crude equivalent will be necessary, as dose calculations with traditional systems of medicine are not determined from standardized preparations.
- If the sub-population is "children," ensure that the evidence provided adequately supports safety and efficacy in children.
- If the dosage form is a "tablet" and the route of administration is "oral," ensure that the evidence provided supports oral use, not routes and forms that are not relevant, such as intravenous or topical.

If there is an established safety concern with long-term use, restrict the duration of use to what is implied by the evidence.

Appendix D: Linking Evidence to Ingredient Form

This table provides recommendations for ensuring that evidence will support the ingredient's chemical and physical form.

Table 2: Linking Evidence to Ingredient Form

Ingredient Characteristic	Recommendations for Safety and Efficacy Evidence
Identity	<p>Evidence should support:</p> <ul style="list-style-type: none"> - The unambiguous Latin binomial name or chemical name; - The part or derivative used; - The specificity of the ingredient's action. <p>For example, for botanicals, the evidence should be specific to the part of the plant used; if the evidence indicates "leaf" then "aerial parts" would not likely be supported unless evidence was provided to show that stem and other relevant parts have the same chemical/constituent profile at the same concentration.</p>
Source Material	<p>Evidence should:</p> <ul style="list-style-type: none"> - For a non-extracted or extracted MI - Describe the source material(s) that are utilized in sufficient detail to clearly identify the medicinal ingredient as comparable to that represented on the Product Licence Application form. As an example, the medicinal ingredient may be referred to as <i>Fructus Toosendan</i> in the evidence and further described as the dried ripe fruit of <i>Melia toosendan</i>. Consequently, this information would not support the use of <i>Melia azedarach</i> fruit or <i>Melia toosendan</i> aerial parts. Similarly reference to an ingredient such as mint should be sufficiently detailed to describe the type of mint (e.g., <i>Mentha viridis</i>, <i>Mentha x piperita</i>, etc.) and associated material (e.g., leaf or leaf oil, etc.). - For an isolated MI - Describe the source material and preparation of the isolate (when available) in sufficient detail to allow for a comparison to the medicinal ingredient represented on the product licence application form. As an example, the medicinal ingredient Camphor should be described in sufficient detail to distinguish between reference to <i>Cinnamomum camphora</i> - the plant, and Camphor (white crystalline compound) - obtained from the gum resin of <i>Cinnamomum camphora</i>, <i>Dryobalanops aromatica</i> or synthesized.
Blends of Ingredients	<p>Efficacy evidence should:</p> <ul style="list-style-type: none"> - Describe a blend of medicinal ingredients (X, Y, Z) only when X, Y, Z are all present in the recommended product at a similar dose.
Chemical Form	<p>Evidence should :</p> <ul style="list-style-type: none"> - Support the ingredient form as much as possible when the ingredient has undergone chemical processes that could affect its safety or efficacy (e.g., oxidation, reduction, purification, emulsification, etc.).

Ingredient Characteristic	Recommendations for Safety and Efficacy Evidence
Physical Form	Evidence should: <ul style="list-style-type: none"> - Support the ingredient form as much as possible when the ingredient has undergone physical processes that could affect its safety or efficacy (e.g., micronization, extraction, binding, stabilization, microencapsulation, etc.).
Dosage Form	Evidence should: <ul style="list-style-type: none"> - Support the ingredient form as much as possible when the dosage form has been altered in a way that could affect safety or efficacy (e.g., addition of coatings, etc.)

Types of evidence that may be useful to describe the form of the ingredient in the evidence or in the recommended product include: technical information sheets, raw material specifications, bioequivalence studies, other details obtained directly from the author of a clinical trial, information describing the method of preparation, phytochemical composition studies.

Appendix E: Linking Evidence to Use of Extracts

To support the comparability of an extract to the evidence, whether it is of plant, animal or microbial origin, information about the extract standardization or extract solvent system and the extract ratios should be provided. Considerable discrepancy in the methods of preparations could mean that the extracts are not comparable. Also, in order to compare modern studies on whole materials, or to relate the applicability of a study material to a commercial product, the study materials have to be adequately characterized.

In general, if the extract is standardized and modern evidence is provided to support safety, the extract should be of the same standardization. In this case, the Quantity Crude Equivalent (QCE) and solvent system is not required to support safety but may be provided as additional information. The QCE, extract ratio and solvent system can be used to support the safety and efficacy of a standardized extract when the quantity of the extracts match and the extract ratio and extraction solvents used are comparable to that in the evidence for traditional use.

If the extract is not standardized and is prepared from a known QCE or extract ratio, starting material, solvent and method of preparation (e.g., decoction), the evidence provided to support the safety and efficacy of the extract should match.

An evidence-based justification may be required to support comparability of extracts to one another. This rationale may include the methods of manufacture (e.g., comparisons of the solvents used), the characterization of the extracts (e.g., comparisons of phytochemical profiles), and different studies that compare different extract types.

Appendix F: Evidence Criteria for Traditional Medicines

Prior to submitting a product that has traditional use claims and meets NHPD's definition of traditional medicine, cross check supporting evidence against the Evidence Criteria below to ensure that it meets a minimum level of suitability and there is no missing evidence.

1. Evidence is provided to support the traditional use of the medicinal ingredient(s) [XXX and YYY].

Examples of missing evidence:

- The product licence application indicates that the product is composed of medicinal ingredients X, Y and Z. However, the evidence provided refers to the traditional use of medicinal ingredients X and Y, but no evidence has been provided to support the traditional use of medicinal ingredient Z.
- Use of texts such as Natural Medicines Comprehensive Database (NMCD) monographs, Physicians' Desk Reference (PDR), articles from Alternative Medicine Review, general textbooks, research focused journal articles etc. as primary references to support the *traditional use* of the medicinal ingredient (as opposed to supporting the *safety* of the medicinal ingredient) is unacceptable.

2. Evidence supports the use of the medicinal ingredient(s) [XXX and YYY] within the same identified traditional system of medicine [ZZZ].

Examples of missing evidence:

- The recommended use or purpose identifies the product as a traditional herbal medicine and the product licence application indicates that the product is composed of medicinal ingredients X, Y and Z. However, the evidence provided supports the traditional use of medicinal ingredients X and Y within one system of medicine (e.g., traditional herbal medicine), but the evidence provided to support the traditional use of medicinal ingredient Z is from a different system of medicine (e.g., traditional Ayurvedic medicine).
- The use of a reference that alludes to the use of an ingredient in a particular traditional system of medicine, but is not an authoritative reference on traditional uses within that system (e.g., attempting to support an Ayurvedic claim with the World Health Organization (WHO) monographs on selected medicinal plants is not acceptable).

3. The product and/or the medicinal ingredient(s) [XXX and YYY] on the product licence application form must be comparable to the product and/or medicinal ingredient(s) discussed in the evidence.

Examples of ingredients that are not comparable:

- The botanical species are different (e.g., *Panax ginseng* vs. *Panax notoginseng*).
- Source materials are different (e.g., *Echinacea angustifolia* leaf vs. *Echinacea angustifolia* root).
- Standardized extract vs. non-standardized plant material (e.g., *Zingiber officinale* rhizome extract standardized to 2% gingerols vs. non-standardized *Zingiber officinale* rhizome where a comparison of the respective quantity crude equivalent dose (QCE) is not possible).
- The medicinal ingredients are categorically different (e.g., Camphor (C₁₀H₁₆O), the isolate vs. camphor, *Cinnamomum camphora*, the plant).
- Methods of preparation are not similar (e.g., decoction vs. non-decocted, supercritical carbon dioxide vs. ethanolic extraction);
- The method of preparation in the product licence application is unclear (e.g., select, wash, extract and concentrate) as to the type of extraction and solvent used; The

evidence provided is for a combination of medicinal ingredients X, Y, Z, but the medicinal ingredients listed on the product licence application are W, S, Z.

NOTE: Authoritative references on Traditional Chinese Medicine (TCM), unless otherwise specified, provide dosage information for individual medicinal ingredients as a decoction and are not comparable to ethanol-based preparations or non-extracted powders.

4. Evidence provided is to support the safety of the product and/or the medicinal ingredient(s) [XXX and YYY] [within the target population [ZZZ]].

The safety of a product with a traditional use claim should be established based on both references about its traditional use and the modern literature. When the available evidence suggests that the medicinal ingredient is unsafe when used according to the product's recommended conditions of use, a higher level of evidence should be provided and the totality of evidence should favor benefit over risk for the product.

Examples of missing evidence:

- The product is intended for a target population that is broader and/or more vulnerable (e.g., children, pregnant or breastfeeding women, etc.) than supported by the submitted evidence.
- Evidence raises questions about the inherent toxicity of the medicinal ingredient (e.g., Cinnabaris, Realgar, *Symphytum officinale*, *Asarum* spp., *Acorus* spp., *Aristolochia* spp., *Piper methysticum*, *Senecio aureus*, *Aconitum* spp., etc.) that cannot be mitigated adequately by additional quality testing or through labelling, thus requiring additional studies to demonstrate a benefit to risk profile that is appropriate for self-care.

NOTE: For medicinal ingredients that are not comparable because the evidence is missing information to characterize the ingredient (as in criterion 3), it will be assumed that evidence in support of safety may also be lacking.

5. The phrase(s)/term(s) ["XXX" and "YYY"] as part of the recommended use or purpose/The recommended use or purpose "XXX" must be acceptable as it/they relate(s) to:

A serious disease, condition, abnormal physical state or Schedule A disease.

Examples of terms/phases that would be deemed inappropriate as a traditional use claim include references to:

- Menstrual irregularities, disorder of the menstrual flow, dysmenorrhea...
- Circulatory troubles, asthma, coronary heart disease...
- Diabetes, cleansing the blood, urinary system disorders...
- Healing broken bones, torn muscles and cartilage...

A condition that cannot be diagnosed within the identified traditional system of medicine.

Examples of recommended uses or purposes falling into this category would include the following:

- ...used as an adjuvant for hyperlipidemia and glucose intolerance.
- ...helps to reduce cholesterol levels.
- ...maintains a healthy blood pressure level.
- ...supports healthy blood glucose levels.
- ...as an antioxidant.

A specific pharmacological effect which should be substantiated based on modern evidence.

Examples of recommended uses or purposes or terms that would have a meaning so specific to require modern evidence and thus would be inappropriate as a traditional use claim would include:

- ...used to stimulate the immune system.
- ...the synergistic action of these herbs assists...
- ...immune-modulator.
- ...supports the endocrine system.

Broad/vague symptoms and/or actions which do not specify any meaningful or beneficial effect of the product.

Examples of these types of claims would include:

- ...useful for all chronic states of inflammation.
- ...unique formula of herbs that have specific affinity for the respiratory tract.
- ...useful for various cardiovascular and peripheral circulatory conditions.
- ...used as a healing aid for urinary disorders.

An interpretation/extrapolation of available evidence on the respective medicinal ingredient(s) to support a claim which is not in fact a traditional use.

This deficiency often results from inaccurate interpretation and/or extrapolation of traditional use evidence or misrepresentation of information based on modern evidence as traditional use experience.

Examples include weight loss claims and source of vitamin, essential fatty acids and/or minerals as well as claims related to nicotine addiction or other addictions etc.

6. Information on the dose of the medicinal ingredient(s) [XXX and YYY] [used topically/when applied externally] must be provided within the evidence submitted.

Examples of missing evidence:

- The evidence does not specify a dose for the medicinal ingredient.
- The quantity crude equivalent (QCE) of the medicinal ingredients cannot be calculated from the dosage information provided for an extracted medicinal ingredient.

7. Evidence submitted for the medicinal ingredient(s) [XXX and YYY] must pertain to the same route of administration as that indicated in the recommended conditions of use section of the product licence application (Insert reference(s)).

Example of missing evidence:

- The evidence provided for the medicinal ingredient(s) is based on oral use, but the product is used topically.

8. The daily doses indicated on the product licence application form for each of the medicinal ingredients listed must be within the dosage range indicated in the submitted evidence and there must be a basis to conclude [all or a subset] of the medicinal ingredients have an additive effect.

Examples of missing evidence:

- All of the medicinal ingredients of the product are at sub-therapeutic doses and the combination is not supported by the evidence or no rationale has been provided.

- Listing medicinal ingredients with different properties, entering different channels and/or having distinct properties (e.g., Ma Huang (Ephedra Stem) and Bai Shao (White Peony Root)) for a TCM formulation.
- Submitted information is inappropriate (e.g., based on non-comparable dosage preparations, dosages from text not considered as primary sources on traditional uses).
- Dosage information is not present in the evidence and cannot be verified.
- The submitted evidence does not support the interaction among the medicinal ingredients listed as being additive.

9. A multiple ingredient rationale must be provided for this product or alternatively, for a Traditional Chinese Medicine, a product monograph in support of the base formula must be provided. The submitted ingredient rationale must be sufficient/acceptable based on the submitted evidence.

For all products consisting of two or more medicinal ingredients, where the product formulation with respect to its traditional use cannot be supported on the basis of a single product monograph (e.g., *Pharmacopoeia of the People's Republic of China*, the *State Drug Standard* or the *Ayurvedic Pharmacopoeia of India*), the product formulation is to be based on combining medicinal ingredients that are logical and permissible (based on their respective uses within the same identified system of traditional medicine). The ingredient rationale should clearly indicate which medicinal ingredients are additive and which are not. The mechanism of action should be discussed when known. Example:

- A multiple ingredient rationale is not provided for the product and, based on the submitted evidence, it is not apparent what the respective role of each medicinal ingredient is.
- The multiple ingredient rationale does not address the differences (e.g., with respect to medicinal ingredients, relative proportions of medicinal ingredients, etc.) between the established formula/base formula and the TCM product represented on the PLA.

NOTE: For a product with a claim drawn from the TCM paradigm, unless the formulation is captured in a suitable stand-alone reference and the corresponding reference has been provided, the ingredient rationale should explain the respective role (e.g., king, minister, assistant and messenger) of each medicinal ingredient in the formulation, and the contribution to the overall efficacy of the product. The traditional formula used as the basis for the formulation should be provided. Furthermore, the ingredient rationale should speak to any deviations from the base formula and how any noted deviations impact or do not impact the efficacy/claim and safety of the formulation.

APPENDIX G: Expert Opinion

An expert opinion may be used to supplement information that is not available in the literature, (e.g., duration of use for an ingredient) or as supplementary information to support a new use for a previously approved ingredient. When using expert opinions, factors such as experience, education, the number of experts, and conflicts of interest should be considered. These factors along with any other relevant information provided, will contribute to the weighting of the expert opinion.

An expert should have:

- training in the field or healing paradigm related to the proposed NHP or medicinal ingredient(s);
- scientific qualifications, including experience in research methods and/or training in evidence-based health care; and
- no conflicts of interest or must disclose all conflicts of interest