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- Notice to Product Licence Applicants -

TRADITIONAL CLAIM SUBMISSIONS
Evidence Criteria and Evidence Assessment Template

August 2010

To further assist applicants in preparing complete and high quality Product Licence Applications (PLAs) for traditional claim submissions, the Natural Health Products Directorate (NHPD) has developed an Evidence Criteria and Evidence Assessment Template for this application type (i.e. traditional claim).

Both the Criteria and the Template are to be used by applicants to ensure that the evidence portions of their PLAs for traditional claim submissions are not critically deficient and meet a minimum level of quality.

The Evidence Criteria were developed based on a number of critical evidence deficiencies the NHPD has frequently encountered since it began assessing PLAs in January 2004. PLAs for traditional claim submissions without any of the evidence deficiencies will remain in queue for a comprehensive assessment of the product's safety, efficacy and quality. For submissions with critical deficiencies, applicants will be issued an Evidence Information Request Notice (E-IRN) outlining the deficiencies.

Upon receipt of the E-IRN, applicants will have thirty days to respond to the deficiencies or to withdraw their application. Applicants that do not provide a satisfactory response addressing all deficiencies within thirty days will be issued a notice of refusal for the submission.

Prior to submitting their PLAs for traditional claim submissions or responses to E-IRNs, applicants are strongly encouraged to cross check their supporting evidence against the Evidence Criteria and to use the Evidence Assessment Template (both provided in this notice) to ensure that the evidence they intend to submit is relevant and complete.

Applicants should note that PLAs for traditional claim submissions are not being subjected to new evidence requirements. The NHPD is simply modernizing its assessment process to ensure that PLAs with critically deficient evidence are identified at the outset and are addressed quickly rather than allowing them to sit in the assessment queue for lengthy periods of time without progress. The NHPD will continue to thoroughly assess all PLAs to ensure that the evidence provided is appropriate for the product.

Streamlining the IRN process will enable the NHPD to focus its assessment resources and expertise on higher quality submissions and ensure a more timely and efficient review of submissions. Furthermore, with the Evidence Assessment Template in hand, applicants now have an easy-to-use tool to ensure that their PLAs for traditional claim submissions meet the most fundamental evidence requirements.

TIPS AND RECOMMENDATIONS FOR APPLICANTS

Be aware of the evidence requirements

The *Evidence for Safety and Efficacy of Finished Natural Health Products* guidance document provides detailed information on the NHPD's evidence requirements. Applicants are encouraged to read, understand and follow this document as it provides essential guidance on the safety and efficacy requirements for traditional claim applications. This document is available at www.healthcanada.gc.ca/nhp under "guidance documents."

Perform a quality check of PLAs prior to submission

The NHPD has observed that in the vast majority of cases, the severely deficient PLAs received for traditional claim submissions are the result of applicants not properly crosschecking their PLA information against the NHPD's evidence requirements prior to submitting. Applicants should attain a working knowledge of the *Evidence for Safety and Efficacy of Finished Natural Health Products* guidance document and use the developed Criteria and Assessment Template to ensure that the evidence portions of their PLAs for traditional claim submissions are not critically deficient.

Copies of the Criteria and Template are available at the end of this notice. The Evidence Criteria and the Evidence Assessment Template will also be able to be accessed online at www.healthcanada.gc.ca/nhp in the near future.

The NHPD anticipates that this modernized approach will significantly strengthen the efficiency and timeliness of the review process, enabling applicants who have submitted complete and high quality PLAs for traditional claim submissions to have their application assessed within a reasonable and acceptable timeline.

Should you have any questions or concerns, please do not hesitate to contact your Submission Coordinator.

The Natural Health Products Directorate
Health Canada

www.healthcanada.gc.ca/nhp

Attachment(s)

- Evidence Criteria
- Appendix 1. Considerations for Multi-Medicinal Ingredient Products
- Evidence Assessment Template

Evidence Criteria

The Evidence Criteria were developed based on a number of critical evidence deficiencies the Natural Health Products Directorate (NHPD) has frequently encountered since it began assessing Product Licence Applications (PLAs) for traditional claim submissions in January 2004. Upon entry into the assessment level, the NHPD is now immediately screening submissions against the Criteria to ensure that the evidence provided is not critically deficient and meets a minimum level of quality.

Prior to submitting their PLAs for traditional claim submissions, applicants are strongly encouraged to cross check their supporting evidence against the Evidence Criteria below.

1) **Evidence has not been provided / The Evidence provided is not considered sufficient / to support the traditional use of the medicinal ingredient(s) [XXX and YYY].**

   Examples:

   - The PLA indicates that the product is composed of medicinal ingredients X, Y and Z. However, the evidence provided refers 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 has not been provided / The Evidence provided is not considered sufficient / to support the use of the medicinal ingredient(s) [XXX and YYY] within the same identified traditional healing paradigm [ZZZ].**

   Examples:

   - The recommended use or purpose identifies the product as a Traditional Herbal Medicine and the PLA 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 paradigm (e.g. Traditional Herbal Medicine), but the evidence provided to support the traditional use of medicinal ingredient Z is from a different paradigm (e.g. Traditional Ayurvedic Medicine).

   - The use of a reference that alludes to the use of an ingredient in a particular paradigm, but is not an authoritative reference on traditional uses within that

paradigm (e.g. attempting to support an Ayurvedic claim with the WHO monographs on selected medicinal plants).

3) The product and/or the medicinal ingredient(s) [XXX and YYY] on the PLA form is/are not comparable to the product and/or medicinal ingredient(s) discussed in the evidence (Insert reference(s)).

Examples:

- 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 equivalents (QCEs) is not possible).
- The medicinal ingredients are categorically different (e.g. Camphor ($C_{10}H_{16}O$), the isolate vs. camphor, *Cinnamomum camphora*, the plant).
- Methods of preparation are not similar (e.g. decoction vs. non-decocted, supercritical CO_2 versus ethanolic extraction);
- The Method of Preparation in the PLA 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 PLA 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 not considered adequate to support the safety of the product and/or the medicinal ingredient(s) [XXX and YYY] [within the subpopulation [ZZZ]].

The safety of a product with a traditional claim must be established based on both references about its traditional use and the scientific literature. Should the available scientific evidence suggest that the medicinal ingredient is unsafe when used according to the product's recommended conditions of use, a higher level of scientific evidence must be provided and the totality of evidence must demonstrate the contrary.

Examples:

- The product is intended for a subpopulation 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*, *Lobelia inflata*, *Asarum* spp., *Acorus* spp., *Aristolochia* spp., *Piper methysticum*, *Senecio*

aureus, *Aconitum* spp., etc.) that cannot be mitigated adequately through labelling and requires a corresponding or higher level of evidence (scientific studies) to demonstrate safety.

NOTE: For medicinal ingredients that are not comparable (as in criterion 3), it would be generally understood, due to the gaps in the evidence, that evidence in support of their 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" is/are not 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 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 healing paradigm.
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 must be substantiated based on scientific evidence.
Examples of recommended uses or purposes or terms that would have a meaning so specific to require scientific 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...
- …used as an adaptogen.
- …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.

Sexual desire, fertility, libido, impotence, etc.

The standards of evidence used to support traditional use claims are not suited for these types of claims. Hence, products intending to make claims of this nature must adhere to the requirements in place for non-traditional applications.

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 evidence or representation of information based on scientific investigations of a medicinal ingredient as traditional.

Examples include addiction cessation claims, weight loss claims and source of vitamin, essential fatty acids and/or minerals, etc claims.

6) **Information on the dose of the medicinal ingredient(s) [XXX and YYY] [used topically/when applied externally] is missing or incomplete within the evidence submitted (Insert reference(s)).**

Examples:

- 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] pertains to a different route of administration than that indicated in the recommended conditions of use section of the PLA (Insert reference(s)).**

Example:

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 PLA form for each of the medicinal ingredients listed are below the dosage range indicated in the submitted evidence and there is no basis to conclude [all or a subset] of the medicinal ingredients are additive.**

Examples:

- All of the medicinal ingredients of the product are at sub-therapeutic doses and the submitted Additive Combinations Evaluation (ACE) form is not supported by the evidence or no ACE form 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)) on the same ACE form for a TCM formulation.

- Information indicated on the ACE form is inappropriate (e.g. based on non-comparable dosage preparations, dosages from text not considered as primary sources on traditional uses).
- The ACE form includes dosage information that is not present in the evidence and cannot be verified.
- The submitted evidence does not support the interaction among the medicinal ingredients listed on the ACE form as being additive.

NOTE: When the daily dose of each medicinal ingredient is below that supported by the literature, it would not be possible for the recommended dose of the product to be supported unless two or more of the medicinal ingredients in the product are considered additive (based on the submitted evidence) and accompanied by an Additive Combinations Evaluation (ACE) form which adheres to the 80-120% rule. Appendix 1 should be consulted for more detailed information on considerations for multi-medicinal ingredient products including how to complete and support the information within an ACE form.

9) A combination rationale has not been provided for this product [including a product monograph in support of the base formula – (applicable to TCM formulas)] / The submitted combination rationale is insufficient / unacceptable 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 healing paradigm). The combination rationale should clearly indicate which medicinal ingredients are complementary, additive or antagonistic.

Example:

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

NOTES:
Only solicited changes are permitted during the assessment phase. Applicants must ensure that any revisions made to the PLA form and label are in accordance with the requirements outlined in the *Evidence for Safety and Efficacy of Finished Natural Health Products* guidance document for a Traditional Medicine and supported by the submitted evidence.

Applicants may request a reclassification of the application type, but must ensure that their application conforms fully to the requirements of the new application stream.

- Appendix 1 -

Considerations for Multi-Medicinal Ingredient Products

What is the purpose of the combination rationale?
A combination rationale is required for all multi-medicinal ingredient products (i.e. two or more medicinal ingredients in a single product), unless all of the medicinal ingredients of the product are captured in a single product monograph. At a minimum, the single product monograph must identify the respective dose for each medicinal ingredient and the recommended use or purpose for the product.

Thus, in the absence of a single product monograph that captures the product in its entirety, the combination rationale speaks to the following:

- The respective uses of each medicinal ingredient within the same identified traditional healing paradigm (e.g. Ayurveda, TCM, Traditional Herbal Medicine, etc);
- Why the combination of medicinal ingredients is not only permissible, but is logical based on the uses of the respective medicinal ingredients within the identified system of traditional medicine;
- Differences between the established formula/base formula and the product represented on the PLA with respect to the medicinal ingredients (e.g. substitution, additions, omissions), the relative proportions of medicinal ingredients (e.g. the product monograph identifies medicinal ingredients X, Y and Z in the proportions 3:5:2, but the proportions of medicinal ingredients X, Y and Z are 3:3:4 on the PLA), the recommended use or purpose and the recommended conditions of use.

What does a combination rationale look like?
The combination rationale plays a pivotal part in positioning the role of each medicinal ingredient within the context of the product claim and associated conditions of use and should be in agreement with the submitted evidence. There is no particular format as to what a combination rationale should look like, however it is intended to present an objective answer as to why each medicinal ingredient is present and the contribution of each medicinal ingredient to the overall efficacy and safety of the product. Consequently, such an answer must be founded on the submitted evidence.

Suppose a product consists of medicinal ingredients X, Y and Z, where their respective uses based on the submitted evidence are as follows:

- X is used in Traditional Herbal Medicine (THM) as a sleep aid (in cases of restlessness or insomnia due to mental stress);
- Y is used in THM to help relieve nervousness (calmative/sedative) and as a sleep aid (in cases of restlessness or insomnia due to stress);

- Z is traditionally used Herbal Medicine as a sedative for the relief of nervousness.

Based on the submitted evidence, it would be acceptable to indicate that the medicinal ingredients X, Y, Z are all used within traditional herbal medicine for their sedative properties and the combination of the medicinal ingredients is amenable to the product's recommended use or purpose of "Traditionally used in Herbal Medicine for the relief of restlessness".

Note: Traditional Chinese Medicine formulations are based on a hierarchical system of function which establishes the respective role (e.g. king, minister, assistant and messenger) of each medicinal ingredient in the formulation. Therefore the combination rationale for a TCM product must explain the role of each medicinal ingredient based on this hierarchical system.

Consider *Er chen tang*, a formula used for removing dampness and phlegm, typically consists of *Citrus reticulata*, *Pinellia ternata*, *Poria cocos*, *Glycyrrhiza uralensis* and in some cases *Zingiber officinale*.

- The function of *Pinellia ternata* can be described as to remove dampness and eliminate phlegm, lowers the adverse rising *qi* to relieve nausea and vomiting, disperse stagnation to relieve stiffness in the chest and epigastrium.
- Within *Er chen tang*, *Pinellia ternata* is considered to be a king medicinal ingredient as it addresses the main pattern of disharmony (i.e. dampness-phlegm).
- In contrast, *Glycyrrhiza uralensis* serves to tonify the spleen (regarded as the source of phlegm) and is regarded as an assistant within the formulation, whereas *Zingiber officinale* may be added as an envoy to reinforce the action of the king ingredient and integrate the actions of the other medicinal ingredients.

Suppose *Er chen tang* is provided as the base formula, but the product represented on the PLA has *Scutellaria baicalensis* in place of *Pinellia ternata*. At a minimum, the combination rationale must to explain why this substitution would be acceptable based on the theory of Traditional Chinese Medicine. Part of the rationale would be to demonstrate the interchangeability of *Scutellaria baicalensis* and *Pinellia ternata* by considering their properties (e.g. warm, cold, etc), channels entered (e.g. lung, spleen, liver, etc) and action (e.g. relief of Qi stagnation, clears heat, removes dampness, etc) as described in the submitted evidence. In order, for medicinal ingredients to be considered interchangeable, their properties, channels entered and actions must be alike.

What is an Additive Combinations Evaluation (ACE) form?

An Additive Combinations Evaluation (ACE) form is a table that lists the medicinal ingredient of a product that are regarded as additive (i.e. can be used for the same recommended use or purpose). To use the earlier example of a product consisting of medicinal ingredients X, Y and Z, where each medicinal ingredient is used within traditional herbal medicine for its sedative properties, it would be possible to support a claim of "Traditionally used in Herbal Medicine for the relief of restlessness" for a single medicinal ingredient product consisting of either X, Y or Z. This is an important factor in distinguishing whether the medicinal ingredients listed on an ACE

form are indeed additive, because the concept of additive medicinal ingredients is predicated on the idea that any of the medicinal ingredients considered to be additive, is capable of meeting the claim (for which it is additive) independently, provided that the respective dose for that ingredient is adjusted accordingly.

To introduce a new example, suppose a product consists of medicinal ingredients A, B, C, D and E where the product dose of each medicinal ingredient is 400 mg/day and the submitted evidence supports each of the medicinal ingredients as having been used singly at 1000 mg/day in Traditional Herbal Medicine (THM) for the following:

- A for sore throat;
- B and D for cold symptoms specifically cough and fever
- C as a nervine and expectorant
- E as mild diaphoretic in slight colds

There are a number of medicinal ingredients that could be considered additive, the most obvious being B and D. Now, if the recommended use or purpose for the product is "Used in Traditional Herbal Medicine to aid in the relief of feverish colds and cough", medicinal ingredients B, D and E could be considered as additive for "the relief of feverish colds" component of the claim. Medicinal ingredients B, C and D could be regarded as additive for the "cough" component of the claim.

Consequently, if the product claim is as described above, it would be most appropriate to submit two ACE forms, one for medicinal ingredients B, D and E and the other for medicinal ingredients B, C and D as a means of demonstrating that the sub-therapeutic doses (i.e. 400 mg/day) of the respective medicinal ingredients amounts to a full therapeutic dose based on a subset of the medicinal ingredients of the product being considered additive.

NOTE: Medicinal ingredients are considered additive if the submitted evidence establishes each of the respective medicinal ingredients as alleviating the same symptom (e.g. fever associated with a cold). If the submitted evidence established the respective medicinal ingredients as alleviating different symptoms (e.g. sore throat vs. expectorant) of the same health condition (e.g. cold), the medicinal ingredients would be complementary.

What does a completed ACE form look like?

An ACE form comprises of several important fields, each of which are explained.

- *Additive Indication* – identifies the action(s), effect(s) or symptom(s) for which a subset of or all of the medicinal ingredients of the product are regarded as additive towards.
- *Recommended Dose* – refers to the product's daily dosing regimen (e.g. 2 tablets, twice daily).
- *Medicinal Ingredient, Source, Single Ingredient Daily Reference Dose Range* – each medicinal ingredient should be listed by its proper name, source and the daily reference dose (from at least 2 of the submitted independent references in support of its traditional use). Note: If one reference supports a daily dose of 1-6 g and the other 2-8g, an overlap dose of 2-6 g should be indicated on the ACE form as this dose range would be supported by both references.

- *Minimum Daily Reference Dose (mg/day)* – minimum daily dose supported by the submitted evidence for the respective medicinal ingredient.
- *Maximum Daily Reference Dose (mg/day)* – maximum daily dose supported by the submitted evidence for the respective medicinal ingredient.
- *Weight per Dosage Unit (mg)* - the amount of the respective medicinal ingredient in each discrete dosage unit (e.g. tablet, capsule, pill, tea bag, etc).
- *Recommend Product Daily Dose (mg/day)* - the daily quantity of the respective medicinal ingredient.
- *% Min Daily Ref.* – calculated as the [(Recommended Product Daily Dose) / (Minimum Daily Reference Dose)] x 100 for the respective medicinal ingredient.
- *% Max Daily Ref.* – calculated as the [(Recommended Product Daily Dose) / (Maximum Daily Reference Dose)] x 100 for the respective medicinal ingredient.

A completed ACE form should include only the medicinal ingredients that can be considered as addressing the same symptom of a particular health condition. If the recommended use or purpose of the product identifies multiple symptoms and/or health conditions, then multiple ACE forms should be submitted. Doses reported on the ACE form must be expressed in terms of the quantity crude equivalent (QCE) for extracted medicinal ingredients.

Provided is an example of an appropriately completed ACE form, based on three medicinal ingredients (*Matricaria recutita* flowers, *Humulus lupulus* strobiles, *Passiflora incarnata* flowers) that can be regarded as additive based on the submitted evidence.

Product Name:	Rest-fully					
Additive Indication:	Traditionally used in herbal medicine as a sedative for restlessness.					
Recommended Dose:	2 tablets at bedtime					
Medicinal Ingredient, Source, Single Ingredient Daily Reference Dose Range	Min. Daily Ref. Dose (mg/day)	Max. Daily Ref.Dose (mg/day)	Weight Per Dosage Unit (mg)	Recommend. Product Daily Dose (mg/day)	% Min Daily Ref. Dose	% Max Daily Ref. Dose
Passiflora incarnata Dried flowers 250-1000 mg 3x/day[1, 2]	750	3000	300	2 x 300 = 600	600 / 750 = 80%	600 / 3000 = 20%
Humulus lupulus Dried strobiles 500-1000 mg/day[3, 4]	500	1000	150	2 x 150 = 300	300 / 500 = 60%	300 / 1000 = 30%
Matricaria recutita Dried flowers 2000-8000 mg 3x/day[5, 6]	6000	24000	500	2 x 500 = 1000	1000 / 6000 = 17%	1000 / 24000 = 4%
Sum of Percentages:					157%	54%

[1-6] Literature references providing conditions of use including single and daily doses, etc.

NOTE: At the product's recommended dose, the *Percent Minimum Daily Reference Dose* must be equal to or greater than 80% and represents efficacy, whereas the *Percent Maximum Daily Reference Dose* must be equal to or less than 120% and represents safety. Thus, the all completed ACE forms must conform to the 80% to 120% rule.

Evidence Assessment Template

The Evidence Assessment Template is a tool developed to help applicants in the review of the evidence and to ensure that the evidence they intend to submit as part of the Product Licence Application (PLA) for traditional claim submissions is complete and adequately supports the safety and efficacy of the natural health product for which a licence is being sought.

Applicants should use this template in conjunction with the Evidence Criteria.

Instructions on how to use the Evidence Assessment Template:

1. The Evidence Assessment Template consists of a series of questions with respect to EACH medicinal ingredient of the product and a question that relates specifically to the recommended use(s) or purpose(s) of the product.

2. Prior to answering any of the questions in the Evidence Assessment Template, it is imperative that the *Evidence for Safety and Efficacy of Finished Natural Health Products* guidance document has been read and understood.

3. For each question, except for point number 5, the applicant is to answer either “yes” or “no” based on their critical evaluation of the evidence being submitted for the respective medicinal ingredients of the product.

4. In the case of point number 5, the applicant is to answer either “yes” or “no” based solely on the wording of recommended use(s) or purpose(s) of the product.

5. For each question where the response is “yes”, a checkmark (✓) denoting this should be placed within the corresponding field. Similarly, a different mark (×) should be used when the response to a question is “no”.

6. Answering “no” to any of the questions of the Evidence Assessment Template means that the Product Licence Application is critically deficient and does not meet the most basic and fundamental evidence requirements.

Evidence Assessment Template

Criteria	Medicinal Ingredient						
	1	2	3	4	5	6	7
1. Sufficient evidence has been provided to support the traditional use of EACH medicinal ingredient of the product.							
2. Sufficient evidence has been provided to support the traditional use of EACH medicinal ingredient of the product within the same identified traditional healing paradigm.							
3. EACH medicinal ingredient of the product (as identified on the PLA form) is comparable to medicinal ingredient captured in the evidence.							
4. Evidence provided is adequate to support safety of EACH medicinal ingredient of the product within all of the indicated subpopulations.							
5. The recommended use or purpose **does not** include reference to: (i) a serious disease/condition or Schedule A disease (ii) a condition that is not diagnosable within the traditional healing paradigm (iii) a pharmacological effect requiring scientific evidence (iv) broad/vague symptoms and/or actions with an unclear beneficial effect (v) sexual desire, fertility, libido, impotence (vi) an interpretation/extrapolation of the available evidence to support a claim which is in fact not a traditional use	(i)						
	(ii)						
	(iii)						
	(iv)						
	(v)						
	(vi)						
6. Evidence includes complete information on the dose traditionally used for EACH medicinal ingredient of the product.							
7. Evidence submitted for EACH medicinal ingredient of the product pertains to the same route of administration indicated on the PLA form.							
8. The daily doses indicated on the PLA form for one or more of the medicinal ingredient(s) is within the dosage range captured in the evidence or an Additive Combinations Evaluation (ACE) form is provided.							
9. A combination rationale is provided and explains the role of EACH medicinal ingredient of the product within the same identified traditional healing paradigm.							