National Homeopathic Product Certification Board Standards

Pathway #2: Standards for Combination Formulations with All Active Ingredients Currently Listed in the Homeopathic Pharmacopoeia of the United States

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Introduction

This document provides preliminary standards for the National Homeopathic Product Certification Board (NHPCB), referred to in this document as Certification Board, **Pathway #2** (combination homeopathic formulations with two or more ingredients that are currently listed in the Homeopathic Pharmacopeia of the United States or single ingredients with multiple potencies listed in the Homeopathic Pharmacopeia of the United States) (HPUS).

A combination (multiple-ingredient) homeopathic drug formulation is defined as a homeopathic drug formulation manufactured from two or more medicinal ingredients. Combination homeopathic drug formulations may make specific claims if supported by homeopathic references.

Standards Principles

The Standards are based on 12 globally accepted principles for standard development (https://www.standardsportal.org/usa_en/standards_system/standards_strategy.aspx):

- Transparency
- Openness
- Impartiality
- Effectiveness and Relevance
- Performance Based
- Coherence
- Due Process
- Technical Assistance
- Flexibility
- Timeliness
- Balance

Compliance Principles on Which Standards are Based

The Standards are based on conformity principles consistent with the American National Standards Institute (https://www.standardsportal.org/usa_en/conformity_assessment/conformity_assessment.aspx). This includes the following:

- Open and Transparent Providing Equal Treatment
- Competently Conducted
- Procedures Based on National and International Standards
- Safety Focus Application Processes Publically Available
- Prompt and Timely Assessment Process

- Protection of Confidentiality and Proprietary Information
- Equal Treatment with Fees
- User Friendly Conformity Assessment Process
- Appropriate Transition Periods in Making Changes
- Effective Procedures for Reviewing Complaints
- Market Surveillance to Ensure Appropriate Usage of Seal

Scope

Product Specific

The Certified Homeopathic Seal is product specific, that is, it is affixed to a specific branded homeopathic product made by a specific manufacturer.

Potency

The Seal only applies to ingredients in potency. This includes Class C tinctures (labeled as a 1X potency). The Seal is not potency specific and can be used to apply for multiple potencies for a given product. Potencies are limited to the First Permissable Attenuation (FPA) as described in HPUS and above. For example if an individual application was made for *Arnica montana* and approved, where the FPA is 3X, the approval would be for all potencies from 3X and above.

This pathway (pathway #2) can also be used to apply for a single ingredient with multiple potencies in the same product (homochord or homeochord).

Route of Administration Specific

The Seal is vehicle of administration specific. For example, separate applications would need to be submitted for topical and oral forms of the homeopathic product. Vehicle of administration is currently limited to PO and Topical, although standards are in development for other vehicles of administration. Acceptable oral formulations include powders, granules, tablets, pellets, globules, pillules, liquids and oral sprays. Acceptable topical formulations include gels, ointments, creams and lotions.

Homeopathic Kits

The Seal is also available for homeopathic kits, if all of the products in the kit have been separately applied for and granted the Seal. Also, if there is additional marketing information or indications related to inserts for the kit, these need to be justified as per Criterion #7.

Three Step Application Process

There are three independent steps to the application process:

- Annual Certification Application for Brand Owner
- Annual Certification Application for Manufacturer
- Product Specific Application

Completion and acceptance of all three steps are necessary for granting the Certified Homeopathic Seal.

The Brand Owner is only required to submit product applications for a portion of their eligible homeopathic products. The Brand Owner submits a list of their eligible products and the NHPCB determines which of these products require a product specific application, based on a risk based approach. The number of product submissions is determined as follows:

- 1-249 Products: 10%
- 250 or More Products: 5%

National Adverse Event Database

Part of the submission process for the brand owner will be submission of adverse event data on their homeopathic products to be included in a National Homeopathic Product Adverse Event Database. This database will be used to examine and demonstrate to both regulatory authorities and to the scientific community, the relative safety of homeopathic products.

Other Pathways

Separate standards are being created for the following:

- Pathway #1: Single Ingredients Listed in HPUS
- Pathway #3: Single Ingredients Not Listed in HPUS
- Pathway #4: Complex Formulations with Ingredients Not Listed in HPUS

Current and Future Standards

Standards in black type represent current standards. Standards in red type indicate standards that are in development or under consideration.

Acknowledgement

These standards are currently based on FDA, GMP, HPUS and Canadian homeopathic standards. We acknowledge and are grateful for all the standards work that has gone on to support the homeopathic industry. These standards may expand to the usage of other international homeopathic standards in the future.

Definitions and Glossary

The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant. A glossary of terms is available in Appendix B.

For purposes of this document, HPUS is understood to include both the Homeopathic Pharmacopeia of the United States and its supporting documents.

Accompanying Documentation

As part of the application process, the Certification Board application is accompanied by documentation that demonstrates that the applicant meets the standards. Please see the document *Grid of AIH Seal Application Supporting Documentation* for further details.

Procedures for Review and Revision of AIH Label Standards

The NHPCB Standards Committee engages in a systematic and comprehensive review of its standards in order to ensure that its Standards continue to be appropriate for evaluating the quality of applications and continues to be relevant to and supportive of the homeopathic community. If the NHPCB Standards Committee determines, at any point during its systematic program of review that changes to the Standards are needed, action will be initiated within 3 months to make the changes. Action for revising the standards will be completed within six months. All relevant communities of interest, including manufacturers, homeopathic organizations, and members of the public, are notified of any proposed changes and will be given an opportunity to submit comments. The NHPCB Standards Committee will consider all comments received before finalizing the changes and considering them for adoption.

Additionally, new laws and regulations that apply to the manufacture of homeopathic drug formulations, such as the FDA, FTC or the HPUS, may necessitate corresponding revisions to the NHPCB Standards and policies. The NHPCB Standards Committee is responsible for overseeing and conducting the review of Standards and modifying it in accordance with new regulations.

The following are the procedures for conducting the Standards review. Note that the NHPCB Standards Committee may, at its discretion, adopt non-substantive changes (i.e., changes that do not alter meaning) in the Standards for the purpose of clarification, or adopt changes or additions to the Certification Board policies and procedures without implementing this review procedure.

a. Suggestions for change are reviewed by the Standards Committee and, if appropriate, incorporated into a draft proposal for change.
b. Draft proposals are presented to the Steering Committee for review.

c. If the draft proposal is approved by the Steering Committee, the NHPCB then provides opportunities for public comment which may include the solicitation of written comments, online standards surveys and public hearings.
d. The Standards Committee reviews all public comments (including all feedback from the homeopathic community) and decides whether or not to adopt the proposal either as written or with further revisions. For any Standards changes that are adopted, the NHPCB also specifies the implementation date. If major modifications of the draft proposal are deemed necessary, a second period of public review will be initiated.

Criterion #1: Identity and Nomenclature

1.1 Identity and Nomenclature for Active Ingredients

A. To be considered a homeopathic formulation for this pathway, the product must meet two criteria. It must:
    a. Have all active homeopathic ingredients listed in the HPUS, for which a monograph has been reviewed by the Convention and which has been approved for publication in the current Pharmacopœia by the Board of Directors;
    b. Prepared in accordance with the methods outlined in HPUS;
B. The Latin name, common name and source material of each of the homeopathic ingredients in the formulation are consistent with the HPUS monograph;
C. Other than the homeopathic ingredients, no other active ingredients are present;
D. The homeopathic potency nomenclature is consistent with HPUS guidelines for all ingredients;
E. The homeopathic potencies are consistent with the HPUS potency recommendations for the homeopathic drug. Note that the Certified Homeopathic Seal is only applicable for potencies at or above the First Permissible Attenuation (FPA) for OTC products as specified in the HPUS and First Permissable Attenuation for RX products as specified in the HPUS . Note that Hahnemannian and Korsakovian dilutions are considered interchangeable for purposes of these standards;

1.2 Identity and Nomenclature for Inactive Ingredients

A. Inactive (non-medicinal) ingredients are any ingredients that are added to the starting material (e.g. plant, chemical, mineral) to confer suitable form and consistency and that are contained in the final product. Non-medicinal ingredients may include, but are not limited to, capsule components, diluents, binders, lubricants, disintegrators, coloring agents and flavors;
B. Manufacturers may add substances to their medicinal ingredients to aid stability or manufacturing processes. If these remain in significant quantities in the finished product (e.g., including any quantity that still provides a technical effect), they must be declared as inactive ingredients on the label;
C. All Inactive Ingredients have been approved for usage by the FDA (https://www.fda.gov/drugs/drug-approvals-and-databases/inactive-ingredients-database-download);
D. Inactive ingredients are consistent with FDA standards of nomenclature;
E. Inactive 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;

1.3 Route of Administration

The vehicle of administration is consistent with the HPUS monograph. Note that the only acceptable routes of administration at this time are PO, Sublingual and Topical. Note that standards for other routes of administration are in development.

1.4 Dosage Form

A. Acceptable dosage forms for homeopathic drug formulations are those outlined in the HPUS. Dosage forms include, but are not limited to:

- powder;
- granule;
- pellet/globule/pillule;
- tablet;
- solution;
- ointment/cream/lotion/gel; or
- syrup.

This does not include foods or food-like dosage forms such as bars, chewing gums or beverages. We are considering adding these and other dosage forms in the future. All dosage forms must meet FDA and HPUS manufacturing standards, such as those related to quality and good manufacturing practices.

Criterion #2-Legal and Regulatory Compliance

2.1 **Legal/Registration**

A. Both the brand owner and the manufacturer must register as a drug establishment in conformance with Section 510 of the Act and 21 CFR 207, unless exempt under 21 CFR 207-17 (b) (private label distributors). (Private Label Distributor (fda.gov));

B. If the brand owner or the manufacturer of the homeopathic drug is located in the United States, they must meet the state's registration requirements;

C. If the manufacturer or brand owner is located outside the United States, the facility shall be legally licensed to operate within the jurisdiction (state, province or country) in which it operates;

D. The homeopathic manufacturer will have registered as a drug establishment for a period of at least one years;

E. The homeopathic brand owner (distributor) will have registered as a drug establishment for a period of at least one year;

F. Note that distributors who distribute products from a manufacturer, packager, labeler and/or importer must have FDA registration to conduct the activity, unless exempt under 21 CFR 207-17 (b) (private label distributors). (Private Label Distributor (fda.gov)). They must meet the state's registration requirements and are required to follow Good Manufacturing Practices themselves.

2.2 **Regulatory/Certification**

A. The manufacturing facility shall be in good standing (NAI or VAI) with FDA inspections for a period of three years (https://datadashboard.fda.gov/ora/index.htm). However, If standing with the FDA is OAI, the manufacturing facility shall share with the Certification Board any concerns, including warning letters generated by the FDA and how the manufacturer is addressing these concerns in a timely manner with appropriate documentation.

B. The brand owner facility shall be in good standing (NAI or VAI) with FDA inspections for a period of three years. (https://datadashboard.fda.gov/ora/index.htm). However, If standing with the FDA is OAI, the brand owner facility shall share with the Certification Board any concerns, including warning letters generated by the FDA and how the brand owner is addressing these concerns in a timely manner with appropriate documentation.

C. Failure to appropriately address the OAI concerns of the FDA will result in withdrawal of the Seal.

2.3 **Product Recalls**

Explain any product recalls in the last three years for this product including the problem that led to the recall and the remediation that was taken.

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2.4. **FTC Concerns**

Share any concerns from the FTC that have been shared with the brand owner or manufacturer in the last three years and the response of the company.

2.5 **Quality Agreement**

Brand Owners who are not manufacturers will be required to provide evidence of a quality agreement with their contract manufacturer ensuring compliance with GMP.

2.6. **Ethical Standards**

Provide evidence of social compliance policy demonstrating that both the manufacturer and brand owner meet ethical standards. Failure to comply with ethical standards will result in removal of the Seal. This policy should minimally contain the following:

- Honesty: Open and transparent communication
- Fairness: Fair and unbiased treatment of employees
- Responsibility: Taking responsibility for problem solving
- Respect in employee relationships: Colleagues and workers should always be respectful.
- Integrity: Do the right thing even if no one is watching
- Environmental consciousness: Employ non-polluting business practices and recycling at work.
- Respect for privacy and individuality in personal, professional and health matters.
- Commitment to constructive problem solving of workplace problems.
- Conducting one's business in accordance with legal and ethical principles.
- Commitment to providing quality products for one's customers and customer satisfaction.

Criterion #3-Labeling and Marketing Information

All label, carton and marketing information must be consistent with the HPUS Expanded Labeling Guidelines and FDA applicable labeling regulations including Sections 502 and 503 of the Federal Food, Drug, and Cosmetic Act, Part 201 Title 21 of the Code of Federal Regulations.

Criterion #4-Identity and Purity

4.1 General Requirements

A. Finished homeopathic drug formulations must meet the identity and purity requirements outlined in the HPUS and FDA, as they are amended from time to time;

4.2 Identity (physical and chemical) Requirements

Identity testing of medicinal ingredients must be conducted as outlined in HPUS. Identity testing is required for all types of medicinal ingredients (mineral, chemical, zoological, botanical and nosodes). Testing of the medicinal ingredients must be done at the starting material stage. Further information on identity testing can be found in the HPUS, USP and EP.

4.3. Testing for Below Analytically Detectable Presence (BADP)

A. All OTC drugs listed on the NHPCB Seal Ingredients of Concern list (Appendix C) require individual ingredient testing at the minimum potency verifying that no potentially toxic ingredient is detectible in the product. Individual drug testing of other ingredients is encouraged but not required. This testing should be done for each lot number, if a potentially toxic ingredient from among those listed in Appendix C. If an ingredient is added to the list after a product has received the Seal, the manufacturer will be required to begin this testing by the time of the next NHPCB Seal renewal. Homeopathic ingredients Generally Recognized as Safe (GRAS) are not required for this testing. Additional ingredients are being considered for inclusion on this list on the next version of these standards using a risk based approach.

   For all ingredients with QC Data listed in HPUS, BADP testing that is required above should follow the methods outlined in the QC Data. If an ingredient does not have QC Data listed in HPUS, the applicant should use another method (such as QBI using a validated process) that will be evaluated on a case-by case-basis and provide a detailed description of the testing method used.

A. All drugs that by their nature are primarily used by a homeopathic practitioner which are listed on the NHPCB Seal Ingredients of Concern list (Appendix C), require individual ingredient testing at the minimum potency verifying that the minimum potency is at or above the First Permissable Attenuation found in HPUS. Individual ingredient testing of other drugs is encouraged. This testing should be done regularly (for each lot number). If an ingredient is added to the list, after a product has received the Seal, the manufacturer will be required to begin this testing by the time of the next NHPCB Seal renewal. Additional

ingredients are being considered for inclusion on this list on the next version of these standards using a risk based approach.

For all ingredients with QC Data listed in HPUS, undetectability testing that is required above should follow the methods outlined in the QC Data. If an ingredient does not have QC Data listed in HPUS, the applicant should use another method that will be evaluated on a case-by case-basis and provide a detailed description of the testing method used.

4.4 Purity Requirements-Microbial

All homeopathic drug products, including topical products, must be tested for microbiological contaminants at the finished product stage as outlined in HPUS and in the FDA (USP 71). Because nosodes and sarcodes are, by nature, prone to microbial contamination, the AIH Label requires assurance of their sterility at the raw material stage. The sterilization technique used in the preparation of the homeopathic drug must comply with the sterility requirements in the HPUS and in the FDA (USP 1111).

Microbial Testing of Solid and Liquid Dosage Forms
Microbial testing is required for both solid and liquid dosage forms of homeopathic drugs for each manufactured lot.

4.5 Purity Requirements-Chemical Contaminant Testing

All homeopathic active ingredients and inactive ingredients used in the product, including topical products, must also be tested using validated methodologies for the chemical contaminants at the raw material stage, as outlined in HPUS and the FDA.

Criterion #5-Manufacture of Homeopathic Drug Products

5.1 Compliance with HPUS Guidelines

The homeopathic drug must be prepared according to the specifications of the relevant sections of the Homeopathic Pharmacopoeia of the United States. These guidelines must be consistently and accurately applied in the manufacturing process. We are considering adding other official international homeopathic pharmacopeias for the future.

A. Any deviations from the HPUS manufacturing specifications must be described in detail with a rationale provided for the deviation;

5.2 Compliance with CFR 211, Subpart E

The requirements of CFR 211, Subpart E must be complied with for all incoming components.

5.3 GMP Compliance

Homeopathic drug products must be manufactured in conformance with current good manufacturing practice, Section 501(a)(2)(B) of the Act and 21 CFR 211. However, due to the unique nature of these homeopathic products, some requirements of 21 CFR 211 are not applicable, as follows:

A. Section 211.137 (Expiration dating) specifically exempts homeopathic drug products from expiration dating requirements.

5.4 GMP Scope

Good manufacturing practices (GMPs) must be followed during the manufacturing, packaging, labeling, importing, distributing and storing of homeopathic drugs.

5.5 Letter of Attestation

A letter of attestation and supporting evidence documenting GMP and HPUS compliance is required. In the future we are considering adding third party certification requirements.

Criterion 6-Product Safety

6.1 Potency

The medicinal ingredients in some homeopathic drug products are potentially toxic at material doses. The serial dilutions involved in the manufacture of a homeopathic drug are a factor which mitigates the risk of toxicity from these medicinal ingredients. Minimum homeopathic potencies have been established by HPUS to ensure that such medicinal ingredients do not exceed a safe dose. Potency selection must follow Criteria for Minimum Safe Dilution as established by the HPUS;

6.2 Inactive ingredients

A. All inactive ingredients have at minimum been approved for use by the FDA. Ingredients not considered consistent with homeopathic principles may not be eligible for the Seal. Inactive ingredients that are included in Table E are excluded from usage as part of the NHPCB Seal.

B. All inactive ingredients should not adversely affect the safety of the medicinal ingredients.

C. Additional information may be requested about the rationale for inclusion of inactive ingredients including quantity, purpose in formulation, identity information, safety information or other manufacturing information.

6.3 Dosing and Directions for Use

A. Dosing instructions must meet the standards for Table A. Applicants may recommend a dose amount and frequency not outlined provided the recommendation is accompanied by an adequate rationale.

B. Applicants are not permitted to include the term “or as needed” (e.g. four times per day or as needed”) as part of the dose frequency (this limitation is not applicable to topical products). A statement to the effect of “four times per day, or as directed by a homeopathic practitioner” would be acceptable.

6.4 Duration of Use

A. Duration of use is required for all drug products with a specific clinical indication(s) or purpose. This refers to a time frame during which it is safe to consume the product without causing health concerns. For products which do not have a specific clinical indication(s), a duration of use statement indicating a specific time frame is optional;

B. Applicants are required to establish a duration of use that is appropriate to the condition and/or symptoms stated as the recommended use or purpose. The duration of use should take into consideration the following:

- For some conditions, it is expected that symptoms improve more slowly than for other conditions (homeopathic drugs may be taken for prolonged periods).
- The persistence and/or worsening of symptoms associated with some conditions will warrant consultation with a homeopathic practitioner*.
- The development of new symptoms may warrant consultation with a homeopathic practitioner*.

Therefore, statements such as “Consult a homeopathic practitioner if symptoms persist or worsen” or “Consult a homeopathic practitioner if symptoms do not improve within 7 days” would be acceptable for the Duration of Use, provided it reflects the principles stated above.

We are considering changing “homeopathic practitioner” to “qualified homeopathic practitioner” in a future version of the standards.

6.5 Risk Information/Cautions/Warnings/Contraindications

A. Risk information regarding cautions, warnings and contraindications is mandatory where safety concerns have been noted. It is the responsibility of the applicant to declare any known risk information associated with the use of their product on the product label.

B. The risk information, cautions, warnings, and contraindications are appropriate for the health condition(s) for which the product is being used;

C. Homeopathic drug products with a non-specific recommended use or purpose must include a risk statement to the effect of: “Consult a homeopathic practitioner if symptoms persist or worsen,” The wording “Or to be used as directed by a homeopathic practitioner” as a direction for use is not adequate to meet the above requirement and, in this case, applicants will be required to also add the statement “Consult a homeopathic practitioner if symptoms persist or worsen.”

D. Homeopathic drug products with a specific recommended use or purpose must either provide risk information appropriate to the proposed claim or a statement to the effect of “Consult a homeopathic practitioner if symptoms persist or worsen.”

Examples of additional risk information would be:

- “Do not use during pregnancy or breast feeding.”
- “Keep this and all medications out of the reach of children.”

E. If alcohol is present in the final drug, the maximum allowable amount of alcohol is 5%, if the drug is being used by children. For children younger than two years of age, it is recommended that the product be diluted in water.

6.6 Adverse Events and Serious Adverse Events

A. The homeopathic drug product has demonstrated a safety profile as exhibited by an analysis of the reported adverse events and serious adverse events related to the product;

B. The manufacturer has responded appropriately to customer complaints, including reporting of adverse events and serious adverse events.

6.7 Sub Population Groups

A. If there is a sub-population to which the homeopathic drug formulation is targeted, the sub-population should be identified. Most often, this will be “adults”, but may also be “children”, “infants”, “seniors”, “men” or “women.” If the homeopathic drug formulation is targeted to children or infants, the age group(s) must be indicated as well. The following age categories are recommended in most cases: infants less than one year of age; children 1-5 years; children 6-11 years; adults and children 12 and over;

B. If the homeopathic drug product is being used by special populations (eg. infancy, children, pregnancy etc.) describe any dosage modifications and warnings that are used to protect these populations.

6.8. Adverse Event Reporting or Overdosage

The label should contain the contact information to reach the brand owner in case of questions, adverse events or overdosage.

6.9 Child Resistant Caps

We are considering adding the requirement for child resistant caps for all OTC products in a future version of the standards.

Criterion #7-Clinical Indications

7.1 OTC Homeopathic Drugs

A. All OTC homeopathic drug products must have at least one clinical indication (recommended use or purpose);

B. Clinical indications (labeled and marketing) for all OTC homeopathic drug products are limited to self-care or self-limiting disease conditions. The term "self-care" refers to the activities individuals undertake for the prevention, treatment, and symptomatic relief of diseases, injuries or chronic conditions that individuals can recognize and manage on their own behalf, either independently or with participation from a homeopathic practitioner. The clinical indication may also be followed by wording to the effect of, "...or to be used as directed by a homeopathic practitioner";

C. All clinical indications follow current FDA applicable regulations.

7.2 Use Under Qualified Practitioner Supervision

Homeopathic drugs that are limited to use under qualified practitioner supervision, are not required to specify clinical indications.

7.3 Allowable Clinical Indications

A. The name of the product must be consistent with the homeopathic indications (if any) listed.

B. Indications listed are limited to symptoms only. They should not be used to make diagnostic claims, treatment claims, cure claims, prevention claims or risk reduction claims (see below):

- **Diagnostic claims** relate to the diagnosis of a disease, disorder, or abnormal physical state or its symptoms in humans (e.g., indicated for the detection of glucose intolerance in the diagnosis of diabetes mellitus);
- **Treatment claims** relate to the treatment or partial treatment and mitigation of a disease, disorder, or abnormal physical state or its symptoms (e.g., symptomatic relief claims) in humans;
- **Cure claims** describe a therapeutic effect that results in the elimination of a disease, disorder, or abnormal physical state in humans, either permanently or for a significant length of time;

- **Risk reduction claims** are based on significantly altering a major risk factor(s) for a disease or health-related condition. Diseases have multiple risk factors and altering one of these risk factors may or may not have a beneficial effect in preventing the health condition. The presentation of risk reduction claims should ensure that consumers do not interpret them as prevention claims. This can be accomplished, for example, by use of appropriate language and reference to other risk factors;
- **Prevention claims** relate to interventions which are proven to significantly reduce the incidence of the disease;
- **General health maintenance, support and promotion claims** describe the effect of a medicinal ingredient on restoration, correction, or modification of a structure or physiological function in the human body in a manner that maintains, supports or promotes health. Health function claims can vary from health maintenance (e.g., maintains healthy gums) to treatment of the symptoms or risk factors of a disease or condition (e.g., reduces plaque build-up along the gum line). Products with general health claims include those that have low therapeutic impact and are therefore subject to the appropriate evidence requirements.

C. If clinical indications are included, there should also be a statement to the effect that “Claims based on traditional homeopathic practice, not accepted medical evidence. Not FDA evaluated”.

7.4 Repertory Justifications

A. All clinical indications (labeled and marketing) should be justified using published homeopathic repertories;

B. If a repertory or materia medica justification does not exist, please provide an analysis outlining the rationale for inclusion. This may include any of the following:

- Well-designed systematic reviews and meta-analyses of randomized controlled trials or other clinical trials;
- At least one well-designed randomized controlled trial (preferably multi-centered)
- Well-designed clinical trials without randomization and/or control groups
- Well-designed descriptive and observational studies, such as correlational studies, cohort studies and case-control studies;

C. Repertorial evidence must include electronically imaged references for each indication. These photocopies must include:

- The text that makes reference to the recommended use or purpose. It is the responsibility of the applicant to underline (not highlight) the exact information being referenced in order to ensure clarity after photocopying; Applications containing evidence that is not underlined may take longer to assess than those where relevant sections have been clearly marked;
- The authorship;
- The edition;
- The name of the repertory.

D. Every homeopathic ingredient must be justified for at least one clinical indication using repertory.

7.5 Materia Medica Justifications

A. All clinical indications (labeled and marketing) can be justified using published homeopathic Materia Medica .

B. If a repertory and materia medica justification does not exist, please provide an analysis outlining the rationale for inclusion. This may include any of the following:

- Well-designed systematic reviews and meta-analyses of randomized controlled trials or other clinical trials;
- At least one well-designed randomized controlled trial (preferably multi-centered)
- Well-designed clinical trials without randomization and/or control groups
- Well-designed descriptive and observational studies, such as correlational studies, cohort studies and case-control studies;
- Direct quotes from published provings with references for said provings and relevant sections underlined.

C. Evidence must include photocopies or PDF’s of the references for each indication. These photocopies must include:

- The text that makes reference to the recommended use or purpose. It is the responsibility of the applicant to underline (not highlight) the exact information being referenced in order to ensure clarity after photocopying; Applications containing evidence that is not underlined may take longer to assess than those where relevant sections have been clearly marked;
- The title of the materia medica;
- The authorship;

- The edition;
- The year and the place of publication.

D. Every homeopathic ingredient must be justified for at least one clinical indication using materia medica.

Appendix A Dosage Standards

Dosage Form	Sub Population	Amount Range	Dosing Range Frequency
Granules (small pellets, pilules) (Oral)	Adults and Children >11 years	Up to 1 whole unit dose (tube or container)	Up to 4 times daily
Granules (small pellets, pilules) (Oral)	Children 1-11 years*	Up to 1 whole unit dose (tube or container)	Up to 4 times daily
Granules (small pellets, pilules) (Oral)	Infants 0-11 months*	Up to 1 whole unit dose (tube or container)	Up to 4 times daily
Granules (regular and large pellets)	Adults and Children >11 years	1-5 globules	Up to 4 times daily
Granules (regular and large pellets)	Children 1-11 years*	1-5 globules	Up to 4 times daily
Granules (regular and large pellets)	Infants 0-11 months*	1-5 globules	Up to 4 times daily
Tablets	Adults and Children >11 years	1-4 tablets	Up to 4 times daily
Tablets	Children 1-11 years*	1-4 tablets	Up to 4 times daily
Tablet (Rapid Dissolving)	Infants 0-12 months	1-2 tablets	Up to 4 times daily
Oral Drops	Adults and Children >11 years	1-20 drops	1-4 times per day
Oral Drops	Children 1-11 years	1-20 drops	1-4 times per day
Oral Drops	Infants 0-12 months	1-20 drops	1-4 times per day
Liquid (oral drinkable vials)	Adults and Children >11 years	Up to 1 ampoule	1-4 times per day
Liquid (oral drinkable vials)	Children 1-11 years	Up to 1 ampoule	1-4 times per day

Dosage Form	Sub Population	Amount Range	Dosing Range Frequency
Liquid (oral drinkable vials)	Infants 0-12 months	Up to 1 ampoule	1-4 times per day
Oral Solution (unit dose)	Adults and Children >11 years	Up to Unit Oral Dose	1-4 times per day
Oral Solution (unit dose)	Children 1-11 years	Up to Unit Oral Dose	1-4 times per day
Oral Solution (unit dose)	Infants 0-12 months	Up to Unit Oral Dose	1-4 times per day
Oral Syrup	Adults and Children >11 years	Up to 1-2 tsp	1-4 times per day
Oral Syrup	Children 1-11 years	Up to 1-2 tsp	1-4 times per day
Oral Syrup	Infants 0-12 months	Not Recommended	Not Recommended
Cream/Ointment	Adults and children	Cover affected area	1-4 times per day

* If not rapid dissolving, dissolve dose in a small amount of water before administration to children 0-2 years old

Appendix B: Glossary of Terms

Allersode: Homeopathic preparations of antigens, (substances which, under suitable conditions, can induce the formation of antibodies). Antigens include toxins, ferments, precipitinogens, agglutinogens, opsonogens, lysogens, venins, agglutinins, complements, opsonins, amboceptors, precipitins and most native proteins.

Antidote: Any substance, energetic stimulus, or procedure that clearly stops the curative action of a homeopathic remedy

Attenuation: See Homeopathic Potency

BADP: Below Analytically Detectable Presence

Batch or Lot: A batch is a definite quantity of a raw material or finished product produced under the same series of consistent conditions. A lot may be comprised of one or more batches and is received or released for further use.

Burgi Group: A series of ingredients in a complex formulation that are present at the same potency

C: Centesimal Hahnemannian dilution

CH: Centesimal Hahnemannian dilution

CK: Centesimal Korsakovian dilution

CFU: Colony forming units (Absent refers to < 10 CFU per g or per mL)

Chemical name: Any unambiguous chemical name provided by an authoritative reference such as the *Merck Index*, the *United States Pharmacopeia Dictionary*, etc., or a name determined using the *International Union of Pure and Applied Chemistry* (IUPAC) nomenclature system.

Combination (multiple-ingredient) homeopathic drug: A homeopathic drug manufactured from two or more medicinal ingredients.

D: Decimal Hahnemannian dilution

Dilution level: See Homeopathic Potency.

Efficacy: The extent to which a specific intervention, procedure, regimen or service produces a beneficial result under ideal conditions. In other words, it is the ability for a

homeopathic product to produce the desired health outcome, when it is used according to the Recommended Conditions of Use, under ideal conditions.

End Product (Finished Product): A product that has undergone all stages of production, including packaging in its final container and labelling

Expiry date: The earlier of:

- the date, expressed at minimum as a year and month, up to and including which a homeopathic product maintains its purity and physical characteristics and its medicinal ingredients maintain their quantity per dosage unit and their potency; and
- the date, expressed at minimum as a year and month, after which the manufacturer recommends that the homeopathic product should not be used.

Extemporaneous Product: An extemporaneous preparation is a homeopathic drug specially prepared because an appropriate drug is not readily available. Generally these are prepared for homeopathic practitioners.

External Use: Applied only to external parts of the body and not to the lips or any body surface covered by mucous membrane.

FPA: First Permissable Attenuation

Homeopathic Drug: Drugs that are manufactured only from those substances or sources referenced as monographs in the *Homeopathic Pharmacopeia of the United States* (HPUS), the *Homöopathisches ArzneiBuch* (HAB), the *Pharmacopée française* (PhF), the *European Pharmacopoeia* (Ph.Eur.) or the *Encyclopedia of Homeopathic Pharmacopoeia* (EHP), as they are amended from time to time, and that are prepared in accordance with these pharmacopoeias.

Hahnemannian Proving: Is a form of homeopathic research that was developed by Samuel Hahnemann, the founder of homeopathic medicine, circa 1800. Proving research explores the medicinal qualities of homeopathic substances by administering them to healthy subjects and recording the symptoms that these proving subjects develop over time. From this proving research a drug picture is obtained of the homeopathic medicine. The same medicine can then be administered to subjects that are ill with the same symptoms or drug picture. This homeopathic medicine if correctly prescribed would then act in a curative manner. This process is based on one of the fundamental homeopathic laws: the Law of Similars. The Law of Similars states that a substance when administered to healthy people which causes a certain set of symptoms, will then lessen that same set of symptoms when given to a patient who is sick with those symptoms. This is the fundamental principle on which the practice of

homeopathic medicine is based. During the process of proving, homeopaths use healthy volunteers who are given remedies, and the resulting symptoms are compiled by observers into a "Drug Picture". A Hahnemannian Proving is generally deemed sufficient to create this drug profile.

Homeopathy: A system of medicine founded by Dr. Samuel Hahnemann, based on:

- The law of similars wherein a medicine that produces symptoms in a healthy human being is capable of curing any illness that displays similar effects
- Potentization and minimum dose; homeopathic medicines are prepared by a process of dilution and succussion which creates an infinitesimal dose in a dynamized "potentized" form.

Homeopathic Drug: A homeopathic drug is a drug or ingredient(s) that is/are prepared homeopathically through serial dilution and succussion using standard methods described by Samuel Hahnemann and in the Homeopathic Pharmacopeia of the United States.

Homeopathic Potency: The strength or quantity of a homeopathic drug. Also called homeopathic attenuation, the potency refers to the number of times the original substance has been diluted and succussed according to a method described in one of the accepted homeopathic pharmacopoeia. Homeopathic potency is written as a number associated with one of the following letters or combinations of letters: X, D, C, CH, K, CK, M, MK, LM or Q. Examples: *Arnica montana* 6X, *Chamomilla* 30 CH.

C homeopathic remedies prepared by diluting the substance in a serial dilution of 1 to 100 (centesimal=C=100) followed by succussion

X homeopathic remedies prepared by diluting the substance in a serial dilution of 1 to 10 (decimal=x=10=D) followed by succussion

M 1000C

LM the last potency scale developed by Hahnemann; homeopathic remedies prepared by an initial 1 to 50,000 dilution followed by succussion; Hahnemann believed that this potency would permit more gentle treatment with less aggravations

Homochord (Homeochord): An ingredient in a complex formulation that is present at multiple potencies

HPLC: High-performance liquid chromatography

Indication for use: A specific symptom or set of symptoms that the drug is intended to treat. This term is replaced by the expression “recommended use or purpose”, as stated in the Regulations and other guidance documents.

K: Korsakovian dilution

Label: A display of written, printed, or graphic matter upon the immediate container of any article. The term 'immediate container' does not include package liners. Any word, statement, or other information appearing on the immediate container must also appear 'on the outside container or wrapper, if any there be, or the retail package of such article, or is easily legible through the outside container of wrapper.

LM: Fifty millesimal dilution

Lot: A quantity of any homeopathic product in dosage form, a raw material or a packaging material, homogeneous within specified limits, constituting all or part of a single batch and identified by a distinctive lot number which appears on the label of the finished product.

Lot number: Any combination of letters, figures, or both, by which a homeopathic product can be traced in manufacture and identified in distribution.

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

Materia Medica: Book(s) containing the compilation of reported symptoms from homeopathic drug proving and cured symptoms reported from clinical practice arranged by organ system

Monograph (Homeopathic): A monograph is a written description in a pharmacopoeia of an individual homeopathic medicinal ingredient. The description includes, but is not limited to, information about the ingredient name, name synonym, description of the substance, preparation and homeopathic potency for various purposes.

MSD: Minimum Safe Dilution (see First Permissable Attenuation)

NAI: No Action Indicated

NHPCB: National Homeopathic Product Certification Board

Nosode: Homeopathic preparations of: pathological organs or tissues; causative agents such as bacteria, fungi, ova, parasites, virus particles and yeast; disease products; excretions or secretions.

OAI: Official Action Indicated

OTC (Direct to Consumer): Over-the-counter medicine is also known as OTC or nonprescription medicine. All these terms refer to medicine that you can buy without a prescription.

Potency: See Homeopathic Potency

Prescription: Prescription drug means any human drug required by Federal law or regulation to be dispensed only by a prescription, including finished dosage forms and active ingredients subject to section 503(b) of the Federal Food, Drug, and Cosmetic Act.

Proving: Homeopathic drug testing on healthy volunteers where symptoms that develop are recorded, compiled, and organized into a materia medica and repertory.

Qualified Practitioner: A qualified practitioner is either a licensed health care practitioner (MD, DO, ND, DC, LAc, NP, DN) or an unlicensed health care practitioner who is nationally certified through the Council for Homeopathic Certification.

Quantity: Refers to the amount of medicinal ingredient(s) per dosage unit. A statement of quantity is required for all products as it represents the amount of medicinal ingredient in the product.

Raw material: See Starting Material. Any substance, other than in process product or packaging material, intended to be used in the manufacture of products, including those that appear in master formula but that do not appear in the finished product such as solvents and processing aids.

Recommended conditions of use: Refers to information about a homeopathic product that enables consumers to make an informed choice regarding its use. It includes the following elements:

- recommended use or purpose;
- dosage form;
- recommended route of administration;
- recommended dose;
- recommended duration of use, if any; and
- risk information, including any cautions, warnings, contraindications or known adverse reactions associated with its use.

Repertory: A book of symptoms associated with listings of remedies categorized into different systems of the body

Rubric: An individual entry in a repertory that describes a symptom

Rx: The potency at or above which a drug may only be offered for sale for internal use with a prescription; the Rx restriction would be valid up to the OTC potency noted for the drug in the table (see the explanation for "OTC" above). Conversely, the potency below which a drug may not be offered for sale to the public. For example, OTC=6X, Rx=2X, indicates that potencies 6X and above may be sold without a prescription, and the potencies 2X through 5X or 1C through 2C are restricted to sales with a prescription. Potencies below 2X, e.g., 1X, would be prohibited from being sold for consumption by the public.

Safety: The ability of a homeopathic product to produce a beneficial health outcome, outweighing the risk associated with using it, in humans, according to the recommended conditions of use.

Sarcode: Homeopathic preparations of wholesome organs, tissues, or metabolic factors obtained from healthy specimens.

Self-care: Activities individuals undertake for the prevention, treatment and symptomatic relief of diseases, injuries or chronic conditions that individuals can recognize and manage on their own behalf, either independently or with participation from a health care practitioner.

Series Therapy: Sequential potencies over time administered to enhance and deepen the homeopathic drug's effect

Single-ingredient homeopathic drug: A homeopathic drug with only one medicinal ingredient.

Source material: For homeopathic drugs, source material is the starting substance of medicinal value used to manufacture a homeopathic drug.

Starting material: The substance directly used to produce the homeopathic potency. A raw material might be necessary to product the starting material

Symptom: Any expression of the basic function of the human being that occupies the attention of the person; any sensation that reminds the person of his bodily parts. Symptoms may be either positive (eg. cured symptom) or negative.

TTC: Threshold of Toxicological Concern WHO**:** World Health Organization

TINC: A designation for tincture. It is used when the drug is used in tincture form from Class C or other appropriate classes.

Trituration: A process where substances that are insoluble in alcohol are brought to the 3C potency by grinding the substance with milk sugar in a mortar and pestle for a total of three hours

VAI: Voluntary Action Indicated

X: Decimal Hahnemannian dilution

Appendix C: List of Required Non-Detectability Testing Ingredients

Ingredient Latin Name	Common Name
Aconitum napellus	Monkshood
Aconitum, radix	Root of Monkshood
Agaricus muscarius	Fly Agaric
Antimonium arsenicosum	Antimony Arsenate
Antimonium crudum	Antimony Trisulfide
Antimonium iodatum	Antimony Iodide
Antimonium muriaticum	Antimony Chloride
Antimonium oxydatum	Antimony Oxide
Antimonium sulphuratum arueum	Golden Antimony Sulfide
Antimonium tartaricum	Antomony Potassium Tartrate
Arsenicum album	White Arsenic
Arsenicum bromatum	Arsenic Bromide
Arsenicum iodatum	Arsenic Iodide

Arsenicum metallicum	Arsenic
Arsenicum sulphuratum flavum	Orpiment
Arsenicum sulphuratum rubrum	Red Arsenic Sulfide
Atropinum	Atropine
Atropinum sulphuricum	Atropine Sulphate
Belladonna	Deadly Nightshade
Belladonna, Radix	Root of Deadly Nightshade
Cocculus indicus	Indian Nettle
Conium maculatum	Poison Hemlock
Eupatorium perfoliatum	Boneset
Gelsemium sempervirens	Yellow Jasmine
Glonoinum	Nitroglycerin
Hyoscyamus niger	Henbane
Ignatia amara	St. Ignatius Bean
Lachesis mutus	Bushmaster Snake

Mercurius hahnemanii solubilis	Mercury
Mercurius vivus	Mercury
Nux vomica	Poison Nut
Rhus toxicodendron	Poison Ivy
Stramonium	Thorn Apple
Strychninum arsenicosum	Strychnine Arsenate
Strychninum nitricum	Strychnine Nitrate
Strychninum phosphoricum	Strychnine Phosphate
Strychninum purum	Strychnine
Strychninum sulphuricum	Strychnine Sulphate
Veratrum album	White Hellebore
Viiscum album	Mistletoe

Appendix D: Listing of Substances Excluded As Inactive Ingredients Bearing the AIH Seal

All inactive ingredients in homeopathic formulations bearing the Seal must be on the FDA list of approved inactive ingredients. In addition, the following substances are also not permitted to be used as inactive ingredients because of insufficient evidence for their safety as excipients.

Albumin
Alcohol (above 5% in children's fomulas)
DMDM Hydantoin
FD&C Red #40
FD&C Yellow #5
Imidazolindinyl Urea
Maltodextrin Derived from GMO Corn and Wheat
Methylparaben
Polyethylene Glycol
Polyhexamethyenebiguanide
Polysorbate 80
Propylene Glycol
Propylparaben
Saccharin
Sodium Benzoate
Sodium Lauryl Sulfate
Talc