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Response to Docket No. FDA-2015-N-0540: Homeopathic Product Regulation - Evaluating the Food and Drug Administration's Regulatory on 04/20/15 Framework

Hahnemann Laboratories, Inc. (HL) respectfully submits our response regarding Labeling of Homeopathic Product for the public hearing in April 2015. Our lab manufactures homeopathic preparations exclusively and has been inspected many times by your agency. As per our last inspection, our records show 100% compliance with cGMP.

Our founder Michael Quinn's objective in expansion from a homeopathic compounding pharmacy established in 1985 to pharmaceutical manufacturing laboratory in 1996 had been to raise the level of quality of our homeopathic drug products to the standards of the US FDA cGMP of pharmaceutical manufacturing. Our goal is to supply safe and effective homeopathic products to the general public while measuring up to all FDA pharmaceutical manufacturing regulations.

Hahnemann Laboratories welcomes the opportunity to respond to the issues that are of specific interest to the Agency by providing hard facts, research data, and sources.

1. What are consumer and health care provider attitudes towards human drug and biological products labeled as homeopathic?

The trust consumers and professional healthcare providers show towards homeopathy is reflected by the size and categories of our client base as accumulated in our 30 years of customer service:

- 87,370 Total Customers most with repeat orders, among them:
- 7,177 Practitioners including the following:
- 5,902 Plastic Surgery and Dermatology Clinics
- 365 Physicians (MD)
- 113 Veterinarians (DVM)
- 110 Dentists (DDS)

Given the high level of education and experience, over 7,000 professionals would not be influenced into simply "believing" in homeopathy, but have proven by their steady support and repetitive orders that homeopathy works for their practice. Homeopathy is successfully used as complimentary, or even primary, medicine in multiple fields of healthcare.

Aside from our own records and experiences, homeopathy is a multi-million dollar industry in the U.S. (for inexpensive products costing roughly \$8-\$20) with robust growth every year, according to difference sources that monitor industry revenue and growth. Clearly, thousands if not millions of people are using homeopathy in the U.S., and therefore are expressing their positive attitude towards it with their money.

2. *What data sources can be identified or shared with FDA so that the Agency can better assess the risks and benefits of drug and biological products labeled as homeopathic?*

The extensive use of homeopathy for over 200 years supports a positive safety assessment. Exhaustive research indicates that we have found no deaths due to properly used homeopathic medicines in the United States recorded in the major medical online databases. Because homeopathic medicines are so safe, the FDA regulates almost all of them as Over-The-Counter (OTC) pharmaceuticals. A quarter century of FDA experience proves this initial safety assessment to be correct.

To our knowledge the FDA has not received a single Adverse Event Report on a homeopathic classical single remedy oral use above the safe dilution level of 6C potency (meaning a dilution factor of six times 1:100 = 0.000000000001). Some homeopathic products below the 6C level of potency were recalled by the FDA in the past.

In comparison Adverse Event Reporting System (FAERS) database relating to overall pharmaceutical use shows 711,232 serious events including 117,752 deaths just in 2013. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070461.htm>

According to the 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS), Table 22B "Demographic Profile of Single Substance Pharmaceutical Exposure Cases":

Acetaminophen alone caused 51 deaths (pg.1235) compared to Dietary Supplements/Herbal/Homeopathic Agents totaling 9,833 cases (pg. 1248), with just 1(one) "major event" and not a single death.

However, grouping Homeopathy with Dietary Supplements/Herbals may lead to skewed results as the two later categories contain significantly higher concentrations of the original source material and the potential for toxicity. Given that these three products are grouped together, we really have no accurate data regarding Poison Control's statistics for adverse effects as related specifically to homeopathy for adverse effects.

We request in order to provide clearer monitoring capabilities that the NPDS provide a further breakdown of statistical information which separates these three categories: Dietary Supplements, Herbal, and Homeopathic agents just as it does with the other major generic categories.

Table 17F. Substance Categories Most Frequently Identified in Drug Identification Calls (Top 25), pg 1058 Substance (major generic category)

Analgesics 185,035 cases meaning 40.15%

Dietary supplements/herbals/homeopathic 353 cases meaning 0.08%

https://aapcc.s3.amazonaws.com/pdfs/annual_reports/2013_NPDS_Annual_Report.pdf

According to the American Medical College of Homeopathy (AMCH) "Nearly three hundred studies have been conducted, studying a variety of conditions, with positive results for homeopathy demonstrated in about 85% of the studies. Several meta-analysis

studies of this research have been done demonstrating that the probability that the success of homeopathy is due to placebo alone is less than 1/50,000 (Lancet 1994).”

<http://amcofh.org/research/conventional>

Some sources of research results on risks and benefits of homeopathic preparations are:

- Clinical Trial Database of National Center of Homeopathy (NCH)

<http://www.homeopathycenter.org/research-article-bibliography-alphabetical-author>

- Evidence-Based Complementary and Alternative Medicine (eCAM) is an international peer-reviewed, open access journal.

<http://www.hindawi.com/search/all/homeopathy/>

Some examples of studies listed there are:

Are the Effects of Homeopathy Attributable to a Statistical Artifact?

Complementary and Alternative Medicines Use during Pregnancy
Testing Homeopathy in Mouse Emotional Response Models

Identification of Medicinally Active Ingredient in Ultradiluted *Digitalis purpurea*: Fluorescence Spectroscopic and Cyclic-Voltametric Study

A Review of Use of Enantiomers in Homeopathy (as toxicology blocker)

Modulation of Signal Proteins: A Plausible Mechanism to Explain How a Potentized Drug Secale Cor 30C Diluted beyond Avogadro's Limit Combats Skin Papilloma in Mice

Homeopathic Individualized Q-Potencies versus Fluoxetine for Moderate to Severe Depression: Double-Blind, Randomized Non-Inferiority Trial

Homeopathic Preparations of Quartz, Sulfur and Copper Sulfate Assessed by UV-Spectroscopy

Reporting Experiments in Homeopathic Basic Research

Homeopathic Doses of *Gelsemium sempervirens* Improve the Behavior of Mice in Response to Novel Environments

A Grounded Theory Study of Homeopathic Practitioners' Perceptions and Experiences of the Homeopathic Consultation

Use of Homeopathy in Pediatric Oncology in Germany

A Review of Three Simple Plant Models and Corresponding Statistical Tools for Basic Research in Homeopathy

Can Homeopathy Bring Additional Benefits to Thalassaemic Patients on Hydroxyurea Therapy?

Brief Homeopathic Pathogenetic Experimentation

Knowledge and Attitudes about HIV/AIDS among Homeopathic Practitioners and Educators in India

Scientific Research in Homeopathic Medicine: Validation, Methodology and Perspectives

Immunology and Homeopathy. 5. The Rationale of the 'Simile'

Immunology and Homeopathy. 2. Cells of the Immune System and Inflammation

Journeys in the Country of the Blind: Entanglement Theory and the Effects of Blinding on Trials of Homeopathy and Homeopathic Provings

CAM and Cell Fate Targeting: Molecular and Energetic Insights into Cell Growth and Differentiation

Thuja occidentalis (Arbor vitae): A Review of its Pharmaceutical, Pharmacological and Clinical Properties

- Dana Ullman's eBook: "Evidence Based Homeopathic Family Medicine" is providing research evaluating homeopathic treatment systematically organized
http://www.homeopathic.com/shoppingcart/Homeopathic_Family_Medicine_eBook.html

- Dr. Iris Bell, University of Arizona, Nanoparticle Research on Homeopathic Dilutions

Nanoparticles visible through extremely sophisticated scientific instruments and their electromagnetic charges play a part in the efficacy of homeopathic remedies. "AlterMed Research Foundation performs a one-year study on "Evidence-Based Research on the Nanoparticle Nature of Homeopathic Medicines." with Iris Bell, MD PhD, Head of the AMCH Department of Research, as the Principal Investigator for this project. (www.AlterMedResearch.org) Hahnemann Labs provides homeopathic dilutions for this study.

- World Health Organization (WHO) "Safety Issues on Preparation of Homeopathic Remedies" 2009 delineates remedy quality may be compromised when GMP is not followed, or by other factors.
<http://www.who.int/medicines/areas/traditional/prephomeopathic/en/>

- A German study evaluates effectiveness and safety of one drug in a clinical trial
http://www.researchgate.net/publication/235680454_Effectiveness_and_safety_of_a_homeopathic_drug_combination_in_the_treatment_of_chronic_low_back_pain._A_double-blind_randomized_placebo-controlled_clinical_trial

- ClinicalTrials.gov lists 82 studies in homeopathy as of April 2015
<https://clinicaltrials.gov/ct2/show/NCT01049373?term=homeopathy&rank=72>

- Individualized Homeopathic Treatment and Fluoxetine for Moderate to Severe Depression in Peri- and Postmenopausal Women (HOMDEP-MENOP Study): A Randomized, Double-Dummy, Double-Blind, Placebo-Controlled Trial
Published: March 13, 2015

- NIH Governments website; U.S. Library of Medicine
[http://collections.nlm.nih.gov/?f\[drep2.subjectAggregateDisplay\]\[\]=Homeopathy](http://collections.nlm.nih.gov/?f[drep2.subjectAggregateDisplay][]=Homeopathy)

- Large-scale application of highly-diluted bacteria for Leptospirosis epidemic control
<http://www.ncbi.nlm.nih.gov/pubmed/20674839>

- “Effects of Homeopathic Arnica montana on Bruising in Face-lifts, Results of a Randomized, Double-blind, Placebo-Controlled Clinical Trial,” Dr. Seeley, Dr. Denton, Dr. Ahn, Dr. Maas, Archives of Facial Plastic Surgery, Vol. 8, January/February 2006, p. 54-59.
- “A Randomized, Controlled Comparison between Arnica and Steroids in the Management of Post-rhinoplasty Ecchymosis and Edema,” Dr. Totonchi, Dr. Guyuron, Plastic and Reconstructive Surgery, Vol. 120, No. 1, July 2007, p. 271-274.
- “Arnica Montana and Homeopathic Medicine: Fact or Fiction,” Dr. Kulick, Research and Innovative Technology Scientific Session of the American Society for Aesthetic Plastic Surgery (ASAPS) meeting in Las Vegas, Nevada April 29, 2002
- Positive Research compiled by Robert Medhurst on hpathy.com
<http://hpathy.com/scientific-research/database-of-positive-homeopathy-research-studies/>

3. Are the current enforcement policies under the CPG appropriate to protect and promote public health in light of the tremendous growth in the homeopathic drug market?

Yes, as long as CPG, HPUS and cGMP are followed, the homeopathic product should be safe and effective, although there may be differences in quality, such as duration and depth of efficacy. The general homeopathic industry recommends consultation with a health practitioner trained in homeopathic principles.

For the safety of the public, we request vigorous FDA enforcement of the HPUS standards for specific remedy monograph designations of what is OTC and what is prescription only.

It is a Public Health concern that the general pharmaceutical and nutritional industry is now manufacturing homeopathic products in combination with multiple materials such as vitamins and juices. There is no guarantee that a mixed product will work as efficiently as single remedies tailored to exact symptoms as laid out in the Homeopathic Materia Medica. We voice our concerns regarding remedy integrity. The Public Health question is whether these vendors exploit homeopathy’s publicity without clearly proven claims.

The concern is when a nutritional product is manufactured and marketed as containing a pharmaceutical product yet lacks the necessary FDA oversight for drug manufacturing as a result. Aspirin has no place in nutritional products and neither should a homeopathic pharmaceutical.

FDA clearly states in CPG 400.400 Conditions Under Which Homeopathic Drugs May be Marketed, under Definitions, 2. “Drug product(s) containing homeopathic ingredients in combination with non-homeopathic active ingredients are not homeopathic drug products.” Mixing other active ingredients with homeopathic drug product(s) would lead to an adulterated and therefore illegal drug product.()We are requesting diligent enforcement of this regulation for the sake of protecting the consumer.

4. Are there alternatives to the current enforcement policies of the CPG that would inform FDA's regulatory oversight of drugs labeled as homeopathic? If so, please explain.

As long as a homeopathic product is contained within a consumable product, this should come under the authority of FDA pharmaceutical regulations, because homeopathic products are categorized as such.

HL recognizes restrictions on indications of use implemented by FDA to self-limiting conditions for OTC remedies. Our company consults prestigious classical literature by Hahnemann, Kent, Clarke and Boericke to select the conditions indicated on our labels. Potential indications may encompass several pages in volume. During a diligent case taking, a homeopathic practitioner considers the totality of symptoms of the client, instead of just a single one.

For the General Public we would prefer that the regulation of listing of indications for use on labels to be voluntary.

5. Are there areas of the current CPG that could benefit from additional clarity? If so, please explain.

Please see the previous point 4.

Homeopathy is a holistic medicine and does not treat individual symptoms. Instead of the current requirement to print at least one symptom on the label, the need to take the totality of symptoms into account maybe more accurately expressed by stating, for example: "Homeopathic remedies may be indicated for a variety of symptoms; consult a trained homeopathic practitioner."

6. Is there information regarding the regulation of homeopathic products in other countries that could inform FDA's thinking in this area?

There is a thorough compilation of different labeling standards collected by the World Health Organization (WHO) "Safety Issues on Preparation of Homeopathic Remedies" 2009, Pages 43 – 46, Annex 4: "Examples of national labelling requirements for homeopathic medicines in selected countries" (Australia, European Union, Canada, India, Switzerland) with references to original documents.

7. A large majority of human drug products labeled as homeopathic are marketed as OTC drugs. These products are available for a wide variety of indications, and many of these indications have never been considered for OTC use under a formal regulatory process. What would be an appropriate regulatory process for evaluating such indications for OTC use?

Indications for use are clearly and minutely delineated by classical literature specific to that one particular remedy referring to symptoms on different levels of human health, such as physical, mental and emotional. HL hopes that FDA considers to keep

homeopathic treatment available to all symptoms traditionally documented in the literature, as well as in more recently published homeopathic provings.

Currently HL are using information from the provings to provide the indication on the remedy label; indication choice is not arbitrary, but based on scientific documentation, namely the homeopathic drug trials themselves.

Because each and every homeopathic remedy has a broad scope of use as documented in the homeopathic Materia Medica, an appropriate labeling for homeopathic remedies would be to state that the remedy “may be indicated for a variety of symptoms,” rather than stating that it is used for a particular symptom.

The wide array of indications one homeopathic product may be used for would not lend itself to research symptom per symptom, because the complete holistic health picture of the patient would have to be considered. Therefore Hahnemann Labs refers to a qualified practitioner for the correct choice of the most efficient treatment. Sarcodes and nosodes are available only as prescribed by a licensed practitioner.

8. Given the wide range of indications on drug products labeled as homeopathic and available OTC, what processes do companies currently use to evaluate whether such products, including their indications for use, are appropriate for marketing as an OTC drug?

Remedy “Provings” are trials that have been the traditional method for establishing indications for homeopathic use. During provings healthy individuals take a homeopathic potency of a raw material and document their emerging symptoms over a defined period of time.

A trial substantiating the validity of homeopathic provings can be found under this link: “Homeopathic Pathogenetic Trials Produce Specific Symptoms Different from Placebo”

Möllinger H.^a · Schneider R.^b · Walach H.^c , Switzerland 2009

<http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowAbstract&ArtikelNr=209386&Ausgabe=247634&ProduktNr=224242>

Proving guidelines for clinical case studies are exemplified by Dr. Samuel Hahnemann’s Organon, the HPUS and recently also by The American Medical College of Homeopathy (AMCH) <http://amcofh.org/research/proving-trials>.

9. Do consumers and health care providers have adequate information to make informed decisions about drug products labeled as homeopathic? If not, what information, including, for example, information in labeling, would allow consumers and health care providers to be better informed about products labeled as homeopathic?

Because there is an abundance of information on the web and in stores, it may be difficult for people to find accurate information – which is a similar concern with respect to suspect products being made available to people. One way to support the public in their choice of a homeopathic pharmaceutical product is to consult with a trained homeopath.

Our company has experienced one big problem affecting listing of products labeled as homeopathic, which is categorizing homeopathic product as “not approved” or “unapproved” in FDA literature, or on the FDA website. On many occasions we received customer or distributor calls expressing their confusion about this classification, and as a result felt unsure about the inherent quality of our homeopathic product. At last year’s FDIC conference in San Francisco we obtained an answer from an FDA’s Director of Regulatory Affairs explaining that the terms mean that homeopathic remedies do not need FDA approval due to their low safety risk.

May we politely request to change this classification to “no need for FDA approval”?

To conclude our comments based on our 30 years of extensive experience with homeopathic pharmaceuticals, Hahnemann Labs, Inc. considers the existing FDA regulations sufficient for the sake of safety and efficacy to the General Public Health with just a few minor changes as suggested. We are asking to enforce existing statutes to keep homeopathic drug product effective and safe from adulteration.

With best regards,

April Eya, President and CEO

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