CHPA CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

May 19, 2020

Division of Dockets Management (HFA-305)
Food and Drug Administration
Via electronic submission
Docket FDA-2017-D-6580

Re: Drug Products Labeled as Homeopathic

In the Federal Register of December 20, 2017,[1] the Food and Drug Administration (FDA or the Agency) published a draft guidance document proposing how they would exercise enforcement discretion with respect to homeopathic drugs marketed without approved New Drug Applications. At the same time, the Agency noted that, upon issuance of a final guidance, Compliance Policy Guide (CPG) 400.400,[2] a policy which has effectively regulated homeopathic drugs since 1988, would be withdrawn. On October 25, 2019,[3] FDA released a revised draft guidance and, at the same time, revoked CPG 400.400.[4]

On behalf of the Consumer Healthcare Products Association (CHPA)[5], enclosed herein are comments on the 2019 revised draft guidance document as well as FDA's decision to revoke CPG 400.400. CHPA has had manufacturers of homeopathic products as members since its founding. Our member companies have an interest in this document and appreciate the opportunity to comment.

General Comments

CHPA welcomes updates contained in the October 2019 revised draft guidance document, including the addition of a definition for a "homeopathic drug product", FDA's stated intent to utilize a risk-based enforcement policy similar to that employed with other regulated categories and the addition of a list of prioritized categories which FDA will focus their enforcement and regulatory efforts on. However, we continue to believe that the withdrawal of the CPG will create ambiguity and inconsistency in how FDA regulates the homeopathic industry.

[1] 82 Fed. Reg. 60403-5; Drug Products Labeled as Homeopathic; Draft Guidance for Food and Drug Administration Staff and Industry; Availability

[2] FDA Compliance Policy Guide 400.400 "Conditions Under Which Homeopathic Drugs May Be Marketed", issued May 31, 1988

[3] 84 Fed. Reg. 57441-2; Drug Products Labeled as Homeopathic; Draft Guidance for Food and Drug Administration Staff and Industry

[4] 84 Fed. Reg. 57439-41; Compliance Policy Guide Sec. 400.400 Conditions Under Which Homeopathic Drugs May Be Marketed; Withdrawal of Guidance

[5] Founded in 1881, the Consumer Healthcare Products Association (CHPA) is the national trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines, dietary supplements, and consumer medical devices. Every dollar spent by consumers on OTC medicines saves the U.S. healthcare system more than $7, contributing a total of $146 billion in savings each year. CHPA is committed to empowering consumer self-care by preserving and expanding choice and availability of consumer healthcare products. chpa.org

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In our previous comments,[6] CHPA expressed concern regarding FDA's intent to replace the existing CPG with a guidance document, noting that this would lead to less regulatory direction for homeopathic product manufacturers and fail to adequately fulfill FDA's responsibility to consumers or the regulated industry. CHPA members remain strongly supportive of the CPG which, in conjunction with the Homeopathic Pharmacopeia of the United States (HPUS), has provided the guardrails necessary for FDA to carry out enforcement activities and for industry to clearly formulate, label and manufacture products since 1988.

Homeopathic Drug Product Labeling/Claims

The revised draft guidance fails to provide less experienced manufacturers and marketers of homeopathic drug products sufficient guidance on labeling issues. CHPA suggests that FDA add to the final guidance document references to applicable provisions in Title 21 of the Code of Federal Regulations (as were contained in CPG 400.400).

Established homeopathic materia medica,[7] used as a reference for supporting appropriate claims for a homeopathic ingredient, are missing from the draft guidance. As such, a monographed active ingredient could, presumably, be offered for any OTC indication regardless of whether or not evidence exists for its use in that indication as long as the seller avoided FDA's enforcement priority areas. We request that reference to these documents be provided in the final guidance.

In addition, revocation of CPG 400.400 raises the question of whether the OTC Drug Facts labeling requirements apply to homeopathic drugs. In a proposed Drug Facts format rule in 1997,[8] FDA noted that:

> "The proposed rule would not apply to any drug labeled as being homeopathic and which is also listed in the Homeopathic Pharmacopeia of the United States (H.P.U.S.). The labeling of such products is addressed in FDA's Compliance Policy Guide 7132.15, "Conditions Under Which Homeopathic Drugs May be Marketed.""

In the 1999 final rule,[9] FDA rejected an industry request for an express exemption from the Drug Facts format, explaining that:

> "…an express exemption would not be appropriate. However, . . . the agency's stated policy is that such products ordinarily will not be recommended for regulatory action if the product is a homeopathic drug as described in Compliance Policy Guide 7132.15 entitled "Conditions Under Which Homeopathic Drugs May Be Marketed"[10] … and the product follows the labeling and all other recommendations outlined in that guidance document. By its terms, the policy of generally not recommending homeopathic drugs for regulatory action will extend to the rule."[11]

[6] CHPA comments to Docket FDA-2017-D-6580; May 14, 2018 (enclosed herein)
[7] A Dictionary of Practical Materia Medica, John Henry Clarke, MD (3 volumes; Health Science Press); A Clinical Repertory to the Dictionary of Materia Medica, John Henry Clarke, MD (Health Science Press). The CPG also notes "These references must be reviewed in conjunction with other available literature on these drug substances."
[8] 62 Fed. Reg. 9024-62; Over-The-Counter Human Drugs; Proposed Labeling Requirements
[9] 64 Fed. Reg. 13254-13303; Over-The-Counter Human Drugs; Labeling Requirements; March 17, 1999
[10] later recodified as CPG 400.400
[11] 64 Fed. Reg. at 13258

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Revoking CPG 400.400 renders FDA's position on the applicability of Drug Facts labeling to homeopathic drugs unclear. CHPA believes that FDA should continue to exercise its enforcement discretion concerning Drug Facts labeling to single ingredient homeopathic drugs sold in small containers. While the Drug Facts labeling format has many advantages, most purchasers of homeopathic drug products containing a single active ingredient are accustomed to the older format and would gain no particular benefit if confronted by a new label format for an existing product.

Enforcement and Regulatory Priorities

The proposed criteria for enforcement action prioritization contained in the revised draft guidance are vague and, if finalized, likely to result in difficulties with both enforcement and compliance. FDA investigators, lacking the specific guidance contained in CPG 400.400, may be unclear as to the standards for inspecting/auditing homeopathic drug products, likely resulting in questions being directed to FDA headquarters. Experience has revealed that responding to internal questions about homeopathic drug products is a relatively low priority for the Agency, creating the potential for considerable delay and expense for importers of homeopathic products, which must be cleared before being released. Issues such as this led to the creation of CPG 400.400 more than 30 years ago.

- **Products with reports of injury that, after evaluation, raise potential safety concerns**

As noted above, CHPA is supportive of the Agency's intention to utilize a risk-based enforcement approach for homeopathic drug products as well as the addition to the draft guidance of several categories of homeopathic drug products for which FDA "*generally intends to prioritize enforcement and regulatory actions*". To enhance clarity for manufacturers, FDA should provide additional detail in this section stating how they will determine if there is a safety concern. This could include information or examples on what constitutes a "potential association between the product and an adverse event"; the process(es) utilized by the Agency to determine potential associations; and how potential associations/safety signals are validated.

- **Products that contain or purport to contain ingredients associated with potentially significant safety concerns**

FDA provides several examples in this category including "[m]*ultiple ingredients that, when used in combination, could result in possible interactions, synergistic effects, or additive effects of the various ingredients*…" As approximately 95% of marketed homeopathic products are combinations, it is unclear how this classification provides any sort of distinguishing characteristic for prioritization of risk-based enforcement.

CHPA suggests that FDA reference the need for compliance with HPUS in this section, since it provides recognized homeopathic ingredients and standards for these materials (including a defined process for calculating the first safe dilution of an ingredient) and is consistent with the FDCA.

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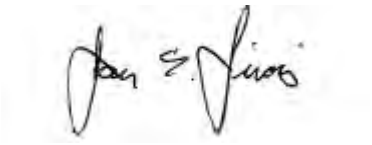
Conclusion

CHPA and our member companies are supportive of several updates made to the October 2019 draft guidance, including the provision of a definition for a "homeopathic drug product", FDA's risk-based enforcement policy and the list of prioritized categories which comprise FDA's focus for enforcement and regulatory efforts.

However, to better inform members of the homeopathic drug industry and aid the Agency in their enforcement efforts, it is critical that the unique aspects of homeopathic drug product regulation (including labeling, formulation, claims support and clarifying the role of the HPUS) be documented and preserved. We feel this can be best accomplished either by preserving CPG 400.400 or by amending the Draft Guidance with the suggestions we provide above.

We appreciate the opportunity to comment on the draft guidance and withdrawal of the CPG and look forward to working together with the industry to assure the continued availability of safe, properly manufactured homeopathic drug products.

Respectfully submitted,



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Re: Drug Products Labeled as Homeopathic

On behalf of the Consumer Healthcare Products Association (CHPA)[1], enclosed herein are comments on "Drug Products Labeled as Homeopathic; Guidance for FDA Staff and Industry", published as Draft Guidance[2]. CHPA has had manufacturers of homeopathic products as members since its founding. Our member companies have an interest in this document and appreciate the opportunity to comment.

General Comments

Homeopathic products, Rx and OTC, are regulated as drugs under the Federal Food, Drug & Cosmetic Act (FDCA), which also recognizes the U.S. Homeopathic Pharmacopoeia (HPUS) as a standard setting body. FDA has responsibility for protecting the public health regarding homeopathic products. Consumers, healthcare professionals and manufacturers must have a regulatory framework that provides for quality products that are labeled appropriately. Manufacturers, regulators and retailers must have clear guardrails so that compliant products may be distinguished from adulterated products. We are concerned, however, that FDA's intended issuance of a guidance document for homeopathic products to take the place of the existing compliance policy guide does not adequately fulfill FDA's responsibility to consumers or the regulated industry and could lead to less regulatory direction for homeopathic products.

Since 1988, FDA Compliance Policy Guide 400.400 (CPG), in conjunction with the HPUS, has provided the guardrails necessary for FDA to carry out enforcement activities and for industry to clearly formulate, label and manufacture products. Lack of adherence to the CPG and to broader OTC drug regulations has served as the basis of many warning and untitled letters to manufacturers of adulterated or misbranded products, including as recently as 2017 and 2018.[3] CHPA members remain strongly supportive of the CPG. This position was stated numerous times by many speakers at the FDA's Part 15 hearing in April 2015.

As announced in December 2017, FDA intends to withdraw the CPG and replace it with a Guidance Document representing a comprehensive enforcement approach. While outlining enforcement priorities, the Draft Guidance omits critical elements of a compliance approach that are in the CPG that

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[1] The Consumer Healthcare Products Association (CHPA) is the 137-year-old national trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines and dietary supplements. CHPA is committed to empowering consumer self-care by preserving and expanding choice and availability of consumer healthcare products.

[2] **Federal Register**, Vol 82, No. 243, December 20, 2017, pp 60403-5.

[3] *See, e.g.,* Warning Letter to Dae Young Food Company, Ltd. (Nov. 20, 2017); Warning Letter to HomeoCare Laboratories, Inc. (Sept. 7, 2017); Warning Letter to Nova Homeopathic Therapeutics, Inc. (Sept. 1, 2017); Warning Letter to Raritan Pharmaceuticals, Inc. (June 20, 2017); Warning Letter to King Bio, Inc (Jan. 11, 2018).

are important in guiding manufacturers with regard to FDA's requirements for homeopathic products. The industry is concerned that taking this action will have unintended consequences in the marketplace for retailers, consumers and healthcare professionals. For example, there is no definition of a homeopathic drug in the Draft Guidance. Other important elements from the CPG missing in the Draft Guidance, include labeling requirements, use of established texts and literature as the basis of indications and reference to the HPUS for ingredients and formulation. Absence of these elements does not create a necessary, comprehensive approach. Instead, it sets the stage for the potential for "rogue" homeopathic products to enter the market and for enforcement actions against such products to be unpredictable or nonexistent. Investigators will not know against what standards to inspect or audit. Ingredients not in the HPUS and for indications or at levels outside the HPUS may start appearing on the market. Without the guardrails of the CPG, enforcement activity may be seen as arbitrary. Unique aspects of the regulation of homeopathic products must be documented somewhere, and this can be done either by preserving the CPG or by amending the Draft Guidance. Industry needs reasonable clarity regarding all necessary elements to qualify for enforcement discretion.

Comments on Use of a Guidance Document vs. Compliance Policy Guide

The Draft Guidance as proposed is an incomplete replacement for the currently existing CPG Sec. 400.400, not only because the Draft Guidance currently lacks the critical elements described above. Rather, this is because CPGs have long served a different purpose than "Guidance for Industry" documents. First established as "Administrative Guidelines" in 1968, and then compiled into the Compliance Policy Guides manual in 1980, CPGs have historically provided direction to FDA's investigatory and compliance staff to help them to understand the practical import of FDA's legal authorities and alert them to the type of conduct FDA is seeking to target with its enforcement efforts. CPGs continue to be periodically issued and revised by the Agency[4] and the CPG Manual still includes language explaining that the CPGs are intended to "advise FDA's field inspection and compliance staffs, as well as the industry, as to the Agency's strategy and policies to be applied when determining industry compliance."[5] Although admittedly imperfect, CPG Sec. 400.400 has long served the traditional purpose of a CPG in that it "provides guidance" to "Agency compliance personnel" by identifying detailed information concerning when "homeopathic drugs which are not in compliance with the conditions described [in the CPG] will be considered for regulatory follow-up."

By contrast, FDA also continues to issue "Guidance for Industry" documents in parallel to CPGs, and these documents typically serve a different purpose. They, per the boilerplate language in the Draft Guidance, provide the regulated industry with "the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited." Per FDA's *Fact Sheet: FDA Good Guidance Practices*, these guidance documents "show stakeholders one way to reach their regulatory goal. However, stakeholders are free to use other approaches that satisfy the relevant law and regulations."[6]

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[4] *See* CPG Sec. 400.210, Radiofrequency Identification Feasibility Studies and Pilot Programs for Drugs (revised June 2013).

[5] FDA, *Foreword: Compliance Policy Guides (CPGs)*, available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm116271.htm (last visited Feb. 14, 2018).

[6] *Fact Sheet: FDA Good Guidance Practices* (Dec. 2017), available at https://www.fda.gov/AboutFDA/Transparency/TransparencyInitiative/ucm285282.htm (last visited Feb. 14, 2018).

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This is not to say that a Guidance for Industry document can never serve the purpose of a CPG. Indeed, a handful of guidance documents FDA has issued in recent years have both provided direction to FDA's investigatory and compliance staff concerning enforcement priorities, as well as advised industry about the steps they must take to avoid their products becoming the subject of an FDA enforcement action. One such recent example is FDA's draft *Guidance for Industry: Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy*, issued in June 2017. It explains the Agency's current thinking, permits for alternative approaches, and sets forth the information that FDA staff and industry should consider in determining whether a product is eligible for the enforcement discretion FDA announced in the guidance. Another example is the *Guidance for FDA Staff and Industry: Marketed Unapproved Drugs – Compliance Policy Guide Sec. 440.100 Marketed New Drugs Without Approved NDAs or ANDAs* (Sept. 2011). Issued as both a Guidance for Industry and a CPG, it not only specifies the Agency's enforcement priorities but also identifies five specific criteria that FDA will weigh when deciding whether to exercise enforcement discretion for the continued marketing of unapproved drug products introduced prior to September 19, 2011.

Proposed Risk-Based Priorities

CHPA is supportive of the concept of a risk-based system for prioritizing enforcement activities. This is commonly done across the agency where resources are limited. Our specific comments on FDA's proposed system are listed below by line number from the Draft Guidance.

139. The Draft Guidance identifies products with reported safety concerns as enforcement and regulatory priorities. FDA should state how it will determine if there is a safety concern. At what point does a potential signal exist and require follow-up? What process will be used? This would be an appropriate place to further explain what pharmacovigilance should look like for homeopathic drugs, how to validate safety signals and determine the quality of safety data.

143. The Draft Guidance states that products containing or purporting to contain ingredients associated with potentially significant safety concerns will be enforcement and regulatory priorities. As part of this category, FDA highlights products containing (or purporting to contain) multiple ingredients that raise safety concerns when used in combination and ingredients that pose potential toxic effects. The HPUS should be referenced in this section, since it provides recognized homeopathic ingredients and standards for these materials and is consistent with the FDCA.

149. Multiple ingredients/combinations – Additional explanation is needed here, since about 95% of marketed homeopathic products are combinations. This does not appear to be a distinguishing factor for priority setting and it is not clear why this is an area of concern.

152. The HPUS governs dilutions and has a defined process for calculating the first safe dilution of an ingredient. It would seem to be a higher priority to focus enforcement efforts on dilutions outside of those supported in the HPUS.

156. The Draft Guidance identifies products for routes of administration other than oral and topical as enforcement and regulatory priorities. FDA highlights "unapproved injectable drug products" and "unapproved ophthalmic drug products" as examples. It is confusing to label any specific products "unapproved", since FDA is saying that all homeopathic products are unapproved. The issue outlined here seems to be one of sterile products in general being potentially at higher risk. CHPA objects to naming certain sterile product categories, like ophthalmic products and stating, without reference, that they pose an unqualified greater risk of harm vs. other products.

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168. The Draft Guidance states that products for vulnerable populations (e.g., immunocompromised individuals, infants and children, the elderly, and pregnant women) will be enforcement and regulatory priorities. Homeopathic products have been safely and widely used in the populations listed. FDA should reference the need for compliance with HPUS standards and cGMPs vs. removal of access. These are important controls for all drugs used in these populations.

177. The Draft Guidance identifies products deemed adulterated under section 501 of the FDCA as enforcement and regulatory priorities, which CHPA agrees should be an enforcement priority.

Conclusion

FDA's stated intention is "to issue a new Draft Guidance that proposes a comprehensive, risk-based enforcement approach to drug products labeled as homeopathic and marketed without FDA approval"[7]. The Draft Guidance issued for comment in December 2017 is far from comprehensive. Key elements missing from a comprehensive document have been cited in these comments. It is our hope that FDA will revise the Draft Guidance to serve all stakeholders before withdrawing the longstanding CPG, by clarifying the role of the HPUS and providing more specificity regarding labeling, formulation and claims support. In this way, the Guidance can best serve the public health and the regulated industry.

We are available for further discussion of these comments. We believe future dialogue would be most productive if FDA would designate a clear point of contact for homeopathy matters. We look forward to FDA's response.

Respectfully submitted,

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[7] FDA News Release, *FDA Proposes New, Risk-Based Enforcement Priorities to Protect Consumers From Potentially Harmful, Unproven Homeopathic Drugs (Dec. 18, 2017).*

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