AMERICAN ASSOCIATION OF HOMEOPATHIC PHARMACISTS
Promoting Integrity · Quality · Trust Since 1923

4332 S.E. Logus Road,
Milwaukie, OR 97222
Ans.Serv. 1-513-402-8847
info@aahp.info
www.aahp.info

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Division of Dockets Management (HFA-305)
Food and Drug Administration
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Re: Docket FDA-2017-D-6580; Drug Products Labeled as Homeopathic

I. Introduction and Summary of Comments

A. Introduction

In the FEDERAL REGISTER of Dec. 20, 2017, 84 FED. REG. 60603, the Food and Drug Administration (FDA or the Agency) published a draft guidance document proposing how the Agency would exercise its enforcement discretion with respect to homeopathic drugs marketed without approved New Drug Applications. At the same time, the Agency proposed to withdraw Compliance Policy Guide (CPG) 400.400, *Conditions under Which Homeopathic Drugs May Be Marketed,* a policy which has successfully regulated homeopathic drugs since 1988. FDA asked for comments on the new draft guidance by March 20, 2018; the comment period was later extended to May 21, 2018.

These comments are being submitted by the American Association of Homeopathic Pharmacists (AAHP), a trade association representing manufacturers and marketers of homeopathic drugs in the United States. AAHP was founded in 1923 and many of its 35 member firms date to its founding. AAHP estimates that its members produce more than 90 percent of the homeopathic products sold in the United States (based on sales volume). As the principal organization of homeopathic product manufacturers, AAHP has a vital interest in the regulation of homeopathic drugs and substantial knowledge and experience about how the proposed new guidance would impact manufacturers, homeopathic professionals, consumers, and, indeed, FDA as well.

B. Summary of Comments

AAHP will demonstrate in these comments that the withdrawal of CPG 400.400 would create a void in how FDA regulates the homeopathic industry. Indeed, the lack of practical guidance would likely lead to an increase in FDA's workload because issues that currently can be readily resolved in the field, under the new guidance, would likely require decisions made at headquarters. And, paradoxically, the vagueness of the proposed guidance could easily result in fraudulent homeopathic products entering the market.

In 2015, FDA held a two-day hearing on the regulation of homeopathic drugs and received thousands of comments thereafter. The Agency posed specific questions for which it sought comments or data. Other than to acknowledge that it held that hearing, the proposed new guidance and its preamble ignored the questions FDA asked and the answers the public provided. Now, with no explanation or rationale, FDA simply proposes to revoke CPG 400.400 and replace it with an enforcement policy that provides little meaningful guidance. In proposing to revoke CPG 400.400, FDA has identified no specific issue which needs correction or improvement. Instead, the Agency simply proposes to toss out a CPG that has worked extremely well for 30 years and replace it with a vague statement of enforcement policy that provides no guidance to industry or Agency personnel.

C. Recommendations

AAHP agrees that FDA should use its limited enforcement resources in a manner which maximizes the public health. Accordingly, AAHP supports the use of a risk-based enforcement policy. However, by revoking CPG 400.400, FDA is eliminating the guidance needed to help industry and FDA personnel recognize compliant products. The proposed criteria for enforcement action priority are sufficiently vague that both enforcement and compliance will be compromised and become an area of uncertainty.

AAHP believes that FDA's risk-based approach should include some of the important criteria in CPG 400.400 not found elsewhere in Agency guidance or regulations. This approach would both focus FDA's enforcement resources where they are needed and provide industry, FDA personnel, and the public with the guideposts needed to market safe and properly labeled and manufactured products. Since FDA itself said that the proposed guidance would not impact the majority of homeopathic drugs on the market, the Agency has an obligation to assure that products sold as homeopathic are indeed homeopathic.

II. History of FDA Regulation of Homeopathy

1. Statutory Recognition of Homeopathic Drugs

Homeopathic drugs are the only form of alternative or complementary medicine which is explicitly recognized by the Federal Food, Drug, and Cosmetic Act (FDCA). Section 301(g)(1) of the Act, 21 USC. 321(g)(1), defines a drug as, *inter alia*, an article "recognized in the official United States Pharmacopeia [or] official Homoeopathic Pharmacopoeia of the United States." Section 501(b) of the FDCA, 21 USCA 351(b), provides that a drug shall be deemed to be adulterated, "if it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium." Similarly, Section 502(e)(3), 21 USCA 352(e)(3), provides that a drug labeled as homeopathic is misbranded unless it bears the "established name" of that drug in the Homeopathic Pharmacopoeia of the United States.

2. Pre-1988 Policy

Prior to the issuance of CPG 400.400 in 1988, FDA followed a different compliance policy guide, one which asserted that ALL homeopathic drugs were prescription only because of the supposed individuality of homeopathic diagnosis. That extreme position was substantially tempered by the fact that FDA didn't actually enforce it very often and virtually never against

domestic manufacturers. It did, however, episodically and inconsistently, enforce the Rx-only rule against imported products. An industry coalition met with the agency and noted that not only was the Rx-only rule incorrect, but that the Agency's enforcement against importers only probably constituted a non-tariff trade barrier in violation of U.S. trade treaty obligations. That meeting lead to a series of discussions which resulted in FDA's issuance of CPG 400.400.

3. OTC Review Exclusion

When FDA proposed to examine the safety and efficacy of OTC drugs in the aftermath of the 1962 Drug Amendments, it decided to take a different approach than the one taken for prescription drugs. Rather than review drugs individually, as it had done in the NAS-NRC Review, it decided to review them by active ingredient category. In announcing the OTC Review in 1972, FDA said that it was taking this approach for several reasons:

1. The Agency's limited resources would be overwhelmed by trying to review each OTC drug individually.

2. Litigation to remove violative drugs would have to be on a case-by-case basis, another enormously resource-intensive approach.

3. Litigation concerning the scope of the 1938 and 1962 grandfather clauses "would more than exhaust all present resources of the agency."

FDA said in 1972 that "because of the uniqueness of homeopathic drugs," it would "review them as a separate category at a later date after the present OTC drug review is complete." The OTC Review is far from over and there is no reason to expect that an OTC review of homeopathic drugs is in the near future. However, FDA's failure to fully implement the Drug Amendments of 1962 does not make homeopathic drugs illegal. There has been no judicial nor regulatory finding that homeopathic drugs are being marketed illegally. In short, FDA inaction does not determine the legal status of these products.

4. The Advent of CPG 400.400

As noted, the origins of FDA's CPG 400.400 go back to a series of meetings between industry and Agency enforcement personnel in the 1980s. The resulting CPG was unusual in that many of the provisions were simply a restatement of existing statutory or regulatory requirements, but their inclusion may have been due to FDA's recognition that much of the industry had little understanding of FDA regulatory requirements. At the same time, the CPG provided some education about homeopathy for FDA personnel as well. CPG 400.400 contained key definitions, including a definition of "homeopathic," an explanation of where traditional uses of homeopathic drugs could be located (*A Dictionary of Practical Materia Medica* by John Henry Clarke, M.D., (3 volumes; Health Science Press) and *A Clinical Repertory to the Dictionary of Materia Medica* by John Henry Clarke, M.D. (Health Science Press), how to handle instances in which the active ingredient was not in the HPUS, and recognition of the different way in which the strength of homeopathic active ingredients are declared (*e.g.*, 10X, 20X, 10C). The CPG, as noted, also contained a recitation of statutory and regulatory labeling requirements.

CPG 400.400 led to major changes in the homeopathic industry. Prior to 1988, the only indication on the label of most homeopathic drugs was, "Use accordingly to standard homeopathic indications." That indication fit well with the symptom-based approach that is at the core of homeopathy. FDA was unwilling to permit that approach to continue, insisting that the statute required a specific indication, and the CPG restates that position. The addition of familiar indications to homeopathic labels aided many consumers as they sought to avoid the possible side effects of allopathic OTC drugs, thus increasing demand for homeopathic drugs. As a result, mass marketers and chain drug stores began to carry homeopathic drugs and thus expand their availability. Today, depending on who one asks, the retail market for homeopathic drugs is between one and three billion dollars annually. To put this into perspective, the sale of all non-homeopathic OTC drugs in 2016 totaled $33,569,000,000.

5. FDA Enforcement Statistics

That CPG 400.400 has been an effective enforcement tool for FDA is evidenced by the fact that the Agency has issued numerous Warning Letters involving homeopathic drugs since 1990, when the 1988 guidance went into full effect. These Warning Letters have covered issues such as inappropriate labels and cGMP issues. FDA has also successfully prompted the recall of homeopathic drugs it considered to be non-compliant.

6. 2015 FDA Hearing

In the FEDERAL REGISTER of March 27, 2015, 80 FED. REG. 16,327, FDA announced that it would hold a public hearing "to obtain information and comments from stakeholders about the current use of human drug and biological products labeled as homeopathic, as well as the Agency's regulatory framework for such products." That hearing took place on April 20-21, 2015 at FDA headquarters. In addition to permitting oral testimony, FDA also announced that it would receive written comments. The comment period was subsequently reopened until Nov. 9, 2015. 80 FED. REG. 54,256 (Sept. 9, 2015).

In the March FEDERAL REGISTER notice, FDA explained that it

> is evaluating its current enforcement policies for drug products labeled as homeopathic from scientific, risk, and process perspectives. The Agency is now soliciting opinions about whether and how to adjust the current enforcement policies to reflect changes in the homeopathic product marketplace over the last approximately 25 years.

Eight published questions formed the basis of FDA's 2015 hearing. We restate those questions below, not because AAHP believes it is necessary to once again respond to them, but rather to note the specificity with which the Agency began this inquiry as compared to the consummate vagueness of the end product. AAHP's detailed responses to FDA's questions can be found in its written comments, filed on Nov. 9, 2015 (available at regulations.gov under tracking number 1jz-8mbr-afn6). These are the questions FDA asked in 2015:

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

Question 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?

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

Question 4. Are there areas of the current CPG that could benefit from additional clarity? If so, please explain.

Question 5. Is there information regarding the regulation of homeopathic products in other countries that could inform FDA's thinking in this area?

Question 6. 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?

Question 7. 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?

Question 8. 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?

It does not appear that FDA used any of the information submitted by a wide variety of commenters in drafting the proposed new guidance, despite the comments of CDER Director Janet Woodcock, M.D., at the 2015 hearing: "By providing specific feedback to our questions and our preliminary concepts, through your oral testimony and written comments to FDA's dockets, you will help us develop the appropriate path forward." The over 9,000 comments filed do not seem to have informed the Agency's path forward.

III. Claimed Safety Issues

AAHP is aware of no case in which FDA was unable to resolve any real or perceived safety issue involving a homeopathic drug on the basis of existing legal authority and the provisions of CPG 400.400.

IV. The Proposed Guidance

FDA's proposal to replace CPG 400.400 raises a number of important issues.

First, FDA's tone gives the impression that homeopathic products are being marketed illegally. (That was the clear message received and disseminated by the media.) In point of fact, as noted above, no regulatory or judicial process has reviewed homeopathic drugs and no

regulatory or judicial decision has adjudged them to be illegal. In fact, as noted above, FDA was told by Congress in 1962 to review the efficacy of drugs then on the market and FDA chose, for OTC drugs, to conduct the still ongoing OTC Drug Review, from which homeopathic drugs were exempted. FDA's failure to finish the OTC Review and to create a similar review for homeopathic drugs does not make homeopathic illegal. Using a proposed policy to give the impression that they are illegal is an abuse of Agency discretion.

Second, the proposed guidance simply states which categories of products labeled as homeopathic will attract FDA's regulatory attention. As noted above, AAHP supports a risk-based approach, but believes that the proposed guidance omits too much to be of any practical use to any party. For example, the proposed guidance lacks a definition of homeopathic. AAHP recognizes that the policy is aimed at products "labeled as homeopathic," which is arguably a broader term. However, since FDA said that the new policy would not affect most homeopathic products, the lack of a definition means that a marketer could label a product as homeopathic and so long as that product did not pose the kind of claimed safety risks which FDA said would attract its attention, it is unlikely that the product would be an FDA enforcement priority.

Third, because the risk-based approach provides no practical guidance, it is likely that FDA enforcement personnel, lacking the specific guidance in CPG 400.400, will simply forward to FDA headquarters homeopathic products about which they have questions. Long experience with the Center for Drug Evaluation and Research shows that responding to internal questions about homeopathic products is a relatively low priority. While this may not create problems for a domestic homeopathic manufacturer, it creates the potential for considerable delay and expense for importers of homeopathic products, which must be cleared by FDA before they are released by U.S. Customs and Border Protection. This, of course, is one of the issues that lead to the creation of CPG 400.400 30 years ago.

V. Problems with Proposed Guidance

AAHP believes that the proposed guidance suffers a number of significant problems. Happily, however, those problems can be readily resolved.

The principal defect in the proposed guidance is that it provides no real guidance to any party. It is akin to describing the earth from 30,000 feet when what is required is a view from ground level. A description of when the Agency will consider taking enforcement action produces a bunch of "maybes," but very little guidance. Below is a side-by-side comparison of the two guidance documents which highlights the gaps in the proposed new guidance.

Labeling Requirements			
Current Guidance CPG 400.400	**Draft Guidance: Drug Products Labeled as Homeopathic**	**Implications**	**Comments**
• **Directions for Use:** Each drug product offered for retail sale must bear adequate directions for use in conformance with Section 502(f) of the Act and 21 CFR 201.5. An exemption from adequate directions for use under Section 503 is applicable only to prescription drugs.	• Not addressed	• Lack of direction risks inadequately labeled products entering the market.	• FDA found it necessary to affirmatively require that homeopathic drug products bear adequate directions for use.
• **Indications for Use:** The labeling for those products offered for OTC retail sale must bear at least one major OTC indication for use, stated in terms likely to be understood by lay persons.	• Not addressed	• Absent direction risks inadequately labeled products entering the market.	• Homeopathic drug products historically did not bear label information for consumers. In the 1988 guidance FDA found it necessary to affirmatively require that homeopathic drug product labels bear indications for use. Affirmative restatement within the guidance reinforces direction to FDA field staff and industry.
• **Statement of Ingredients:** Ingredient information shall appear in accord with Section 502(e) of the Act and 21 CFR 201.10. Labeling must bear a statement of the quantity and amount of ingredient(s) in the product in conformance with Section 502(b) of the Act, as well as 21 CFR 201.10, expressed in homeopathic terms, e.g., lx, 2x.	• Not addressed	• Lack of clarity on this risks a misleading statement of ingredients.	• Homeopathic active ingredients are defined by their manufacturing process and have historically been expressed in homeopathic terms, e.g., lx, 2x. Active ingredients expressed in milligram amounts is inappropriate for homeopathic drug products and likely misleading.
• **Established Name:** The product must be in conformance with Section 502(e)(1) of the Act and must bear an established name in accord with Section 502(e)(3) of the Act and 21 CFR 201.10. Many homeopathic products bear Latin names which correspond to listings in the HPUS.	• Not addressed	• Absent clarity on this matter risks confusion among consumers.	• Use of common names is imprecise and risks consumer confusion in labeling. The Latin binomial traditionally used for homeopathic ingredients is precise and referenceable to the homeopathic medical literature.

Homeopathic Status			
Current Guidance CPG 400.400	**Draft Guidance: Drug Products Labeled as Homeopathic**	**Implications**	**Comments**
• A homeopathic drug is any drug labeled as homeopathic which is listed in the Homeopathic Pharmacopoeia of the United States.	• Not addressed	• Lack of guidance risks products entering the market labeled as homeopathic with ingredients of unknown providence.	• FDA has taken enforcement action against drug ingredients not referenced within the Homeopathic Pharmacopoeia of the United States as lacking evidence of their homeopathic nature.
• A guide to the use of homeopathic drugs (including potencies, dosing, and other parameters) may be found by referring to the following texts: *A Dictionary of Practical Materia Medica* by John Henry Clarke, M.D., and *A Clinical Repertory to the Dictionary of Materia Medica* by John Henry Clarke, M.D. These references must be reviewed in conjunction with other available literature on these drug substances.	• Not addressed	• Absent reference to the homeopathic literature risks products entering the market for which homeopathic use has not been established.	• Homeopathic drug products have been offered for uses consistent with the tenets of homeopathy for more than 150 years. The homeopathic literature forms the basis for uses indicated in labeling. FDA has looked to the homeopathic literature when evaluating claims made in homeopathic literature.
• Homeopathic drugs containing homeopathic ingredients in combination with non-homeopathic active ingredients are not homeopathic drugs.	• Not addressed	• Lack of guidance enables a wide variety of combinations of homeopathic and non-homeopathic ingredients to enter the market with unknown safety profiles.	• Subsequent to the publication of the current compliance policy guide FDA has taken action against products combining homeopathic and non-homeopathic ingredients.

Enforcement		
Current Guidance CPG 400.400	**Draft Guidance: Drug Products Labeled as Homeopathic**	**Comments**
• Those firms marketing homeopathic drugs which are not in compliance with the conditions described above will be considered for regulatory follow-up.	FDA will consider action against:	The American Association of Homeopathic Pharmacists supports a risk-based enforcement approach but finds that several of the stated FDA priorities are vague and unsupported by any evidence of a suggested safety issue.
	• Products with reported safety concerns;	
	• Products that contain or purport to contain ingredients associated with potentially significant safety concerns;	
	• Products for routes of administration other than oral and topical;	
	• Products intended to be used for the prevention or treatment of serious and/or life threatening diseases and conditions;	
	• Products for vulnerable populations;	
	• Products deemed adulterated under section 501 of the FD&C Act.	

Below, AAHP provides its specific comments on FDA's proposed enforcement priorities.

Lines 139-141:

> **Products with reported safety concerns.** For example, MedWatch reports or other information submitted to the Agency can indicate or signal a potential association between the product and an adverse event, medication errors, or other safety issues.

As FDA well knows, MedWatch can at best serve as a signal of an issue. While FDA believes that MedWatch underreports issues, it can also over report concerns since no causal relation between the adverse event and the drug is required. This is commonly seen when FDA issues a press release or other public warning and many new reports suddenly appear. Further, how does FDA plan to distinguish genuine safety signals from background data, especially when the Agency has little data on homeopathic use and appears to have shown little interest in examining the data presented by industry?

The draft guidance would benefit from a statement describing how FDA will determine if there is a real safety issue. At what point does a safety signal require follow-up? What processes will be used to validate safety signals and determine the quality of safety data?

Lines 143-156:

> **Products that contain or purport to contain ingredients associated with potentially significant safety concerns.** For example, potentially significant safety concerns are raised by products that contain or purport to contain:
>
> - An infectious agent with the potential to be pathogenic;
> - A controlled substance, as defined in the Controlled Substances Act, 21 USC 812;
> - Multiple ingredients that, when used in combination, raise safety concerns due to possible interactions, synergistic effects, or additive effects of the various ingredients; and,
> - Ingredients that pose potential toxic effects, particularly when those ingredients are concentrated or in low dilution presentations (e.g., 1X, 2X, or 1C), or are not adequately controlled in the manufacturing process.

Any drug product can contain ingredients with potentially significant safety concerns. One need only review the Warnings section of common OTC product labels and the package inserts of Rx products to see an array of potential safety issues. Three of the four categories cited by FDA above are largely mitigated by the fact that the active ingredients in homeopathic drugs are typically so dilute as to render them extremely safe. The HPUS, in setting its guidelines for maximum permitted OTC dilutions, uses a safety factor of 100 based on the available evidence. Potentially toxic active ingredients are typically present in dilutions on the order of one part per million or less. Homeopathic drug products containing controlled substances are limited by the HPUS to Rx use only, and are also regulated by the Controlled Substances Act.

Many OTC homeopathic products are combination products, containing more than one active homeopathic ingredient. There is a long history of safe use of homeopathic combinations and simply suggesting that there may be additive effects is hardly a sound basis for setting enforcement priorities. Given the long history of safe use of combinations of homeopathic active ingredients, AAHP is unaware of any interactions, negative synergistic effects, or additive effects of these combinations.

Even FDA's focus on ingredients present in "low dilutions" offers little useful guidance to industry or FDA personnel.

AAHP is unaware of any OTC homeopathic product which contains a controlled substance. It has long been the position of AAHP members that any homeopathic products containing controlled substances would, irrespective of any degree of homeopathic dilution, be available on an Rx-only basis.

Lines 156-160:

> **Products for routes of administration other than oral and topical.** For example, unapproved injectable drug products and unapproved ophthalmic drug products pose a greater risk of harm to users due to their routes of administration (e.g., bypassing some of the body's natural defenses, differences in absorption) and the potential risk of harm from contamination.

The sterility of injectable and ophthalmic drug products should be a matter of cGMP compliance, not enforcement priority. AAHP is unaware of any homeopathic OTC products which are offered in injectable form. Injectable homeopathic products offered only by prescription can and should be produced with the same care as comparable allopathic drugs.

Many OTC homeopathic drugs are offered for ophthalmic use and AAHP believes that is entirely appropriate. There are numerous allopathic OTC ophthalmic products which are sold pursuant to OTC monographs rather than premarket approval. Homeopathic ophthalmic products are subject to the same sterility and cGMP requirements as their allopathic counterparts. AAHP believes there is no basis for singling them out for special attention beyond what any ophthalmic product receives.

Lines 162-166:

> **Products intended to be used for the prevention or treatment of serious and/or life threatening diseases and conditions.** Unapproved products for serious and/or life threatening diseases and conditions raise public health concerns, in part, because they may cause users to delay or discontinue medical treatments that have been found safe and effective through the NDA or BLA approval processes.

Under the FDCA, products intended to be used for the prevention or treatment of serious and/or life threatening diseases and conditions are by definition offered only by prescription, a position restated in the CPG 400.400. There is a relatively small universe of Rx homeopathic drugs and AAHP believes that licensed homeopathic physicians should be permitted to use Rx homeopathic drugs in their practices subject to appropriate standards of care and patient consent. Thus, AAHP is concerned that lacking any additional direction, the above blanket statement

could lead agency personnel into inappropriate attempts to limit physicians from using homeopathic drugs that are labeled for Rx-only sale under any circumstances. This could be an unintended consequence of the vagueness in the proposed guidance.

Lines 168-175:

> **Products for vulnerable populations.** For example, patient populations such as immunocompromised individuals, infants and children, the elderly, and pregnant women may be at greater risk for adverse reactions associated with a drug product, even if it contains only small amounts of an ingredient, due to their varying ability to absorb, metabolize, distribute, or excrete the product or its metabolites. These populations may also be at greater risk of harm as a result of foregoing the use of medical treatments that have been found safe and effective through the NDA or BLA approval processes or under the OTC Drug Review.

A large number of OTC homeopathic products are labeled for use by children and infants and have been for a hundred years. Indeed, the stellar safety record of homeopathic products is one reason that parents of young children seek out these products. The proposed new guidance could be read as meaning that all of these products are now considered "high risk" for enforcement action. There is no regulatory or scientific justification for this outcome.

Lines 177-183:

> **Products deemed adulterated under section 501 of the FD&C Act.** For example, if a product purports to be or is represented as a product recognized in an official compendium but its strength, quality, or purity differs from the standards set forth in that official compendium (defined by 21 U.S.C. 321 as the official United States Pharmacopeia, official Homoeopathic Pharmacopoeia of the United States, official National Formulary, or any supplement to any of them), or if there are significant violations of current good manufacturing practice requirements.

AAHP agrees that products which are adulterated should be considered for regulatory action.

AAHP finds it difficult to understand why the Agency would choose to adopt new guidance which, on the one hand, adds a great deal of unnecessary confusion to the regulation of homeopathic drugs, while, on the other hand, the proposed guidance gives FDA no new authority or ability to regulate these drugs. Indeed, as the proposed guidance proclaims on its first page, because it is a guidance document, it binds no party, neither FDA nor industry. Any enforcement action must still allege and prove a violation of underlying statutory or regulatory requirements. One would think that the Agency would prefer guidance that helps industry comply.

VI. Proposed Solutions

AAHP believes that the Agency can satisfy its desire for enforcement flexibility and the industry and the public's desire for relative certainty by combining the two guidance documents.

Since the Agency conceded that the new guidance would have little impact on most of the homeopathic drugs on the market, AAHP believes that the Agency has an obligation to the

public as well as to industry to assure that the available homeopathic drugs are appropriately homeopathic, and manufactured and labeled in compliance with the HPUS and applicable FDA regulations. The proposed new guidance would not accomplish that. Indeed, by removing the definition of homeopathy and reference to the HPUS from the guidance, the Agency would make it quite simple for fraudulent products to be offered for sale so long as they steered clear of the stated enforcement priorities. Further, deleting the relative certainty in the current guidance would mean that many mass market sellers might find it difficult to decide which products they could and should sell. Reducing the sale of homeopathic drugs by established mass marketers would simply drive consumers, who clearly want these products, to online sellers who generally escape routine FDA inspection.

AAHP has outlined above many of the ambiguities of the proposed guidance which need clarification if the document is to be useful to the Agency, the industry or the public. In addition, AAHP believes that key components of CPG 400.400 should become part of any final guidance:

A. Require that homeopathic active ingredients be the subject of an approved monograph in the HPUS.

The HPUS has a vigorous program to review the safety and homeopathic efficacy of new and existing homeopathic active ingredients. (A summary of this process is contained in the separately filed comments of the HPUS.) AAHP believes that compliance with an applicable HPUS monograph should be a requirement for FDA exercise of its enforcement discretion. In the existing Compliance Policy Guide, the existence of an HPUS monograph basically provides prima facie evidence that the active ingredient is homeopathic. A manufacturer of an active ingredient which is not in the HPUS bears the burden of demonstrating, if asked, the homeopathic nature of the ingredient. Since 1988, the HPUS has added numerous monographs. AAHP now believes that the burden on the industry of a monograph requirement is outweighed by the greater certainty created by a monograph requirement. AAHP thus supports requiring that any OTC drug marketed directly to the public be the subject of an HPUS monograph.[1]

B. Prohibit combinations of homeopathic and other ingredients.

The revised guidance should definitively state that combinations of homeopathic active ingredients with dietary supplements or allopathic active ingredients are not homeopathic products.

C. List sources for traditional homeopathic use.

CPG 400.400 provided guidance on sources of traditional homeopathic use, a resource lacking in the proposed new guidance. Just as reliance on the HPUS could provide metes and bounds to the products claimed to be homeopathic, so could the traditional homeopathic literature.

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[1] AAHP does not believe that a monograph requirement is either necessary or appropriate for homeopathic drugs which are not marketed directly to the public. The market for homeopathic drug products marketed directly to professionals is small and the cost of developing and gaining HPUS monograph status is likely high in relation to the sales of any given product. Rather than deprive physicians and other homeopaths of the full complement of homeopathic drugs, AAHP believes that no HPUS requirement should be imposed on products not marketed to the public.

D. Identify active ingredients names in Latin.

When the CPG was issued in 1988, it contained a requirement that the names of homeopathic active ingredients be listed on product labels in English, rather than the traditional Latin. In response to industry comments that the use of Latin names for the many plants used as homeopathic active ingredients provided far greater accuracy and eliminated potential confusion and/or adulteration by the use of different plant species having the same common English name, FDA informed the industry by letter that it had changed its mind and would permit the continued use of Latin names. FDA said that it would make this change the next time the CPG was revised. While there has been one minor revision to the CPG since then, the English name requirement, while not enforced, lives on in the CPG. The Agency should clarify that Latin names for active homeopathic ingredients are acceptable; this has been the Agency's position since 1991 and the sound scientific and public health reasons for this choice have not changed by the passage of time.

In addition to including these elements of CPG 400.400, AAHP believes that the following new elements should be part of any new guidance.

E. Identify product as homeopathic on principal display panel.

While AAHP does not believe that this has been an issue, the existing CPG and the proposed guidance nowhere explicitly require that the label of a homeopathic drug disclose the fact that it is homeopathic. AAHP believes that a requirement that the word "Homeopathic" prominently appear on the PDP of any product which is homeopathic. This disclosure is already part of the labeling guidelines of the HPUS.

F. Require disclaimers on label.

AAHP believes that consumers have the right to know that homeopathic drugs are not the same as allopathic drugs. AAHP labeling and advertising guidelines have proposed the disclosure of the homeopathic nature of the products on labels and in advertising. In 2012, AAHP, adopted a voluntary advertising disclaimer program to further educate consumers about the homeopathic nature of these products.

In 2016, the Federal Trade Commission issued a guidance document on the marketing of homeopathic products. In response to that guidance, AAHP engaged an academic expert in consumer perception studies to help it design and test a new disclaimer that would be used in advertising, labels, and labeling. Based on extensive testing, AAHP in 2017 adopted the following disclaimer statement:

> Claims based on traditional homeopathic practice, not accepted medical evidence. Not FDA evaluated.

AAHP believes that all products labeled as homeopathic which do not have product-specific efficacy substantiation should bear this disclaimer and urges the Agency to make its use a condition of Agency enforcement discretion.

G. Establish an FDA point of contact on homeopathic issues.

Finally, the AAHP believes that restoring the prior cooperative working relationship between the Agency and industry would materially advance the Agency's consumer protection objectives. The AAHP believes that this could best be achieved by the Agency designating someone to serve as the point of contact between industry and the Agency.

VII. Conclusions

At the 2015 public hearing, Daniel L. Michels, CDER's Director of Compliance at the time the 1988 CPG was adopted, testifying on his own behalf, said the following:

> But the reality is, to me, the bottom line is, what has changed in your regulatory environment, what has changed in the community, the public health arena, which causes us to be concerned that the conditions and the policies by which the Agency has been operating for lo (sic) these many years, need changing?
>
> And I'm not smart enough to know, because I've not been patched in, but I think to the extent that there are changes appropriate, then they become ones of, all right, let's be careful, let's work together, and not have the classic Washington unintended consequences as a result of doing the obvious thing and having it blow up in your face.

AAHP agrees with Mr. Michels's conclusions. For the reasons discussed above, FDA should revise its draft homeopathic enforcement guidance to include the key elements of CPG 400.400.

Respectfully submitted.

Mark Land

Mark Land
President
American Association of
Homeopathic Pharmacists