
Drug Products Labeled as Homeopathic Guidance for FDA Staff and Industry

DRAFT GUIDANCE

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

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**Drug Products Labeled as
Homeopathic
Guidance for FDA Staff and Industry¹**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This draft guidance describes how we intend to prioritize enforcement and regulatory actions for human drug products² labeled as homeopathic and marketed in the United States without the required FDA approval. As discussed below, FDA has developed a risk-based approach under which the Agency intends to prioritize enforcement and regulatory actions involving certain categories of such products that potentially pose a higher risk to public health. However, the Agency also recognizes that many products labeled as homeopathic will fall outside the risk-based categories described below.

Simultaneous with the issuance of the final guidance, we will withdraw Compliance Policy Guide (CPG) 400.400, *Conditions Under Which Homeopathic Drugs May be Marketed* issued on May 31, 1988.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Homeopathy is an alternative medical practice that has a historical basis in theory and practice first systematized in the late 1700s. Homeopathy is generally based on two main principles: (1) that a substance that causes symptoms in a healthy person can be used in diluted form to treat

¹ This guidance has been prepared by the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

² For the purposes of this guidance, all references to *drugs* and *drug products* refer to human drugs, including drugs that are biological products, regulated by CDER or CBER, unless otherwise specified.

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41 symptoms and illnesses (known as “like-cures-like”); and (2) the more diluted the substance, the
42 more potent it is (known as the “law of infinitesimals”). Proponents claim that a significantly
43 diluted aqueous solution, consisting mainly of water molecules, retains therapeutic properties
44 due to a “memory” of the substance diluted in it. Historically, homeopathic drugs have been
45 identified through “provings,” in which substances are administered to healthy volunteers in
46 concentrations that provoke overt symptoms. Symptoms experienced by volunteers are recorded
47 to indicate possible therapeutic uses for the substances. In other words, if a substance elicits a
48 particular symptom, individuals experiencing that symptom would be treated with a diluted
49 solution made from that substance.

50
51 In 1938, when the Federal Food, Drug, and Cosmetic Act (FD&C Act) was enacted, the bill’s
52 senatorial sponsor, Dr. Royal Copeland, himself a homeopathic practitioner, added a provision to
53 the law recognizing the Homeopathic Pharmacopoeia of the United States (HPUS) alongside its
54 counterparts, the U.S. Pharmacopeia and the National Formulary.³ Recent years have seen an
55 increase in the sale of products labeled as homeopathic. In the past, these products were mostly
56 prepared by homeopathic physicians for individual patients. Today they are frequently mass
57 manufactured and widely marketed as over-the-counter (OTC) products.

58
59 The definition of “drug” in section 201(g)(1) of the FD&C Act (21 U.S.C. 321(g)) includes
60 articles recognized in the HPUS or any of its supplements. As such, homeopathic drugs are
61 subject to the same regulatory requirements as other drugs. Generally, a drug, including a
62 homeopathic drug, is considered a “new drug” if it is not generally recognized as safe and
63 effective (GRAS/E) by qualified experts for use under the conditions prescribed, recommended,
64 or suggested in the labeling (section 201(p) of the FD&C Act) (21 U.S.C. 321(p)). FDA makes
65 GRAS/E determinations for OTC drugs marketed under the OTC Drug Review.⁴ The FDA has
66 not reviewed any drug products labeled as homeopathic under the OTC Drug Review, because
67 the Agency categorized these products as a separate category and deferred consideration of them.
68 (37 FR 9464, 9466 (May 11, 1972)). Under section 505(a) of the FD&C Act (21 U.S.C. 355(a)),
69 before any “new drug” is marketed, it must be the subject of an approved application filed
70 pursuant to section 505(b) or section 505(j) of the FD&C Act; however, a biological product
71 with an approved license under section 351(a) of the Public Health Service Act (PHS Act) (42
72 U.S.C. 262(a)) is not required to have an approved application under section 505 of the FD&C
73 Act. Accordingly, absent a determination that a drug product labeled as homeopathic is not a
74 “new drug” under section 201(p), all drug products labeled as homeopathic are subject to the
75 premarket approval requirements in section 505 of the FD&C Act or section 351 of the PHS Act.
76 There are no drug products labeled as homeopathic that are approved by FDA.

77
78 The FDA’s evidence-based systems for the review of drugs under new drug applications
79 (NDAs), biologics license applications (BLAs), and the OTC Drug Review play an essential role
80 in ensuring that drugs are both safe and effective.⁵ Drugs marketed without required FDA
81 approval may not meet modern standards for safety, effectiveness, quality, and labeling. The

³ Section 201(g)(1) of the FD&C Act.

⁴ See 21 CFR part 330.

⁵ For instance, during the new drug application approval process the applicant must demonstrate that its manufacturing processes can reliably produce drug products of expected identity, strength, quality, and purity. 21 CFR 314.50(d)(1)(ii)(a).

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82 continued marketing of products that have neither been approved by FDA nor found to be
83 GRAS/E is a public health concern.

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A. Compliance Policy Guide 400.400

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87 In May 1988, the Center for Drug Evaluation and Research issued Compliance Policy Guide
88 400.400 entitled “*Conditions Under Which Homeopathic Drugs May be Marketed.*” As stated in
89 the 1988 CPG, it delineates the conditions, including ones regarding ingredients, labeling,
90 prescription status, and current good manufacturing practice, under which homeopathic drug
91 products may ordinarily be marketed.

92

B. FDA’s Reexamination of its Enforcement Policies

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95 In light of the growth of the industry and passage of more than 2 decades since the issuance of
96 the 1988 CPG, FDA announced on March 27, 2015, that it was evaluating its regulatory
97 framework for these products.⁶ In April 2015, FDA held a public hearing to obtain information
98 and comments from stakeholders about the current use of drug products labeled as homeopathic,
99 as well as the Agency’s regulatory framework for such products.⁷ FDA sought broad public
100 input on its enforcement policies related to drug products labeled as homeopathic in an effort to
101 better promote and protect the public health. As a result of the Agency’s evaluation, including
102 consideration of the information obtained as a result of the public hearing, FDA has determined
103 that it is in the best interest of public health to issue a new guidance that applies a risk-based
104 enforcement approach to drug products labeled as homeopathic and marketed without the
105 required FDA approval, consistent with FDA’s risk-based regulatory approaches generally.

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C. FDA’s Risk-based Approach

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109 In many instances, FDA uses a risk-based approach to carry out its mandates. For
110 example, FDA has generally employed a risk-based enforcement approach with respect to
111 marketed unapproved new drugs.⁸ The Agency historically has prioritized compliance
112 actions involving unapproved new drug products that have potential safety risks, lack
113 evidence of effectiveness, are health fraud products, present challenges to the new drug
114 approval or OTC drug monograph systems under the OTC Drug Review, are violative of
115 the FD&C Act in other ways, or that are reformulated to evade an FDA enforcement
116 action.

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118 The Agency generally intends to apply a risk-based enforcement approach to the manufacturing,
119 distribution, and marketing of drug products labeled as homeopathic, as described below.

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⁶ 80 FR 16327, *Homeopathic Product Regulation: Evaluating the Food and Drug Administration’s Regulatory Framework After a Quarter-Century.*

⁷ Docket No. FDA-2015-N-0540; available at <https://www.regulations.gov/docket?D=FDA-2015-N-0540>.

⁸ See *Marketed Unapproved Drugs - Compliance Policy Guide*, Section 440.100, September 19, 2011. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

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III. FDA’s ENFORCEMENT POLICY

The issuance of this guidance, when finalized, is intended to provide notice that any product labeled as homeopathic that is being marketed illegally is subject to FDA enforcement action at any time. FDA is not required, and generally does not expect, to give special notice that a drug product may be subject to enforcement action. However, in the listing that follows, we clarify our approach to prioritizing our enforcement actions with regard to drug products labeled as homeopathic and marketed in the United States without the required FDA approval.

Enforcement and Regulatory Priorities

In developing a risk-based approach, FDA has identified certain categories of drug products labeled as homeopathic and marketed without the required FDA approval as potentially posing higher risks to public health. FDA intends to prioritize enforcement and regulatory actions involving drug products labeled as homeopathic and marketed without the required FDA approval in the following categories:

- ***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.
- ***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 U.S.C. 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.
- ***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.
- ***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

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166 effective through the NDA or BLA approval processes.

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

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

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