



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-N-4611]

Compliance Policy Guide Sec. 400.400 Conditions Under Which Homeopathic Drugs May Be Marketed; Withdrawal of Guidance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; withdrawal.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the withdrawal of Compliance Policy Guide Sec. 400.400 (CPG 400.400) entitled “Conditions Under Which Homeopathic Drugs May be Marketed,” which was issued in 1988.

DATES: The withdrawal is applicable [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

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SUPPLEMENTARY INFORMATION: FDA is withdrawing CPG 400.400, entitled “Conditions Under Which Homeopathic Drugs May be Marketed,” which was issued in 1988. CPG 400.400 described an enforcement policy regarding homeopathic drug products.

Under section 505(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(a)), before any “new drug” is marketed, it must be the subject of an approved application filed pursuant to section 505(b) or section 505(j) of the FD&C Act. The requirements in section 505 of the FD&C Act apply to biological products regulated under

section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262); however, as stated in section 351(j) of the PHS Act, a biological product with an approved license under section 351(a) of the PHS Act is not required to have an approved application under section 505 of the FD&C Act. Accordingly, absent a determination that a homeopathic drug product is not a “new drug” under section 201(p) of the FD&C Act (21 U.S.C. 321(p)), all homeopathic drug products are subject to the premarket approval requirements in section 505 of the FD&C Act or section 351 of the PHS Act. There are currently no homeopathic drug products approved by FDA.

Since the issuance of CPG 400.400, the Agency has encountered multiple situations in which homeopathic drug products posed a significant risk to patients. There is a broad misconception that all homeopathic products are highly diluted and generally composed of “natural” ingredients, and that they are therefore incapable of causing harm. However, as with all drugs, the safety of homeopathic drugs depends upon many factors, such as the product’s intended use, dosage form, frequency of use, manufacturing quality, intended patient population, and the quantity and combination of ingredients. CPG 400.400 does not directly address all these important considerations.

For example, FDA has encountered situations in which homeopathic products either caused or could have caused significant harm, even though the products, as labeled, appeared to meet the conditions described in CPG 400.400. In 2016, FDA’s search of the FDA Adverse Event Reporting System database identified 99 cases of adverse events consistent with belladonna toxicity, including reports of infant deaths and seizures, possibly related to teething products. Multiple homeopathic drug products were identified as associated with this safety concern. Further investigation revealed that the poisonous belladonna alkaloids in some of the products far exceeded the labeled amounts, raising a serious safety concern. As another

example, by 2009, FDA had received more than 130 reports of anosmia (loss of the sense of smell) associated with the use of Zicam homeopathic intranasal zinc products. FDA determined that if the products were used as labeled, a user would receive significant daily intranasal exposure to zinc, raising a serious safety concern. These are only two examples among many. FDA has also, for example, documented many serious violations of current good manufacturing practice (CGMP) requirements by manufacturers of homeopathic drug products, raising significant concerns about the safety of the products made with inadequate process controls.

The homeopathic drug industry has grown significantly since FDA issued CPG 400.400 in 1988. According to the National Health Interview Survey, conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics, between 2007 and 2012 the use of homeopathic products increased by approximately 15 percent in U.S. adults. This growth, and the increased population exposure that it apparently represents, has contributed to FDA's enhanced focus on the safety of homeopathic drugs in recent years and the evaluation of the CPG, which was issued over three decades ago.

In light of the growth of the industry and passage of time since the issuance of CPG 400.400, FDA announced on March 27, 2015, that it was evaluating its regulatory framework for homeopathic drug products. In April 2015, FDA held a public hearing to obtain information and comments from stakeholders about the current use of homeopathic drug products, as well as the Agency's regulatory framework for such products (Docket No. FDA-2015-N-0540; available at <https://www.regulations.gov/docket?D=FDA-2015-N-0540>). FDA sought broad public input on its enforcement policies related to homeopathic drug products to better promote and protect the public health. On December 18, 2017, FDA issued a draft guidance entitled "Drug Products Labeled as Homeopathic; Guidance for FDA Staff and Industry." The draft guidance detailed a

risk-based enforcement policy, prioritizing enforcement and regulatory actions for certain categories of homeopathic products that potentially pose higher risk to public health.

In response to comments received, we have revised the draft guidance and are announcing the reissue of it elsewhere in this issue of the *Federal Register* to enable the public to review and comment before it is finalized. In particular, we have added a definition of “homeopathic drug product” for purposes of the guidance, added an additional explanation of some of the safety issues that contributed to the development of the draft guidance, and clarified the intent to use risk-based factors to prioritize enforcement and regulatory actions involving homeopathic products that are marketed without required FDA approval. In addition, the revised draft guidance removes the statement that the Agency will withdraw the CPG simultaneous with the issuance of the final guidance.

As a result of the Agency’s ongoing evaluation of its regulatory framework, including consideration of the public input received on this issue and the recent growth of safety concerns associated with homeopathic drug products, FDA believes that it is appropriate to withdraw CPG 400.400 at this time, rather than waiting for the issuance of the final guidance. Because CPG 400.400 is inconsistent with the Agency’s risk-based approach to enforcement generally, it does not accurately reflect the Agency’s current thinking. When the draft guidance is finalized, it will specify the categories of products that the Agency intends to prioritize for enforcement. In the interim, before the draft guidance is finalized, FDA intends to apply its general approach to prioritizing regulatory and enforcement action, which involves risk-based prioritization in light of all the facts of a given circumstance. Risk-based enforcement best reflects FDA’s public health priorities.

We note that withdrawing the CPG does not represent a change in the legal obligations that apply to homeopathic drugs under the statutes FDA administers. The definition of a “drug” under section 201(g)(1)(A) through (C) of the FD&C Act includes: (1) articles recognized in the official United States Pharmacopoeia or the official Homoeopathic Pharmacopoeia of the United States; (2) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (3) articles (other than food) intended to affect the structure or any function of the body of man or other animals. As such, homeopathic drugs are subject to the same regulatory requirements as other drugs; nothing in the FD&C Act exempts homeopathic drug products from any of the requirements in the FD&C Act, including those related to approval, adulteration, and misbranding.

Generally, a drug, including a homeopathic drug, is considered a “new drug” if it is not generally recognized as safe and effective by qualified experts for use under the conditions prescribed, recommended, or suggested in the labeling (section 201(p) of the FD&C Act). CPG 400.400 did not, and legally could not, provide a path for legal marketing of unapproved new drugs, including those that are homeopathic. Rather, the CPG merely described an enforcement policy regarding homeopathic drug products. The Agency does not have authority to exempt a product or class of products that are new drugs under the FD&C Act from the new drug approval requirements of the FD&C Act. (See *Cutler v. Kennedy*, 475 F. Supp. 838, 856 (D.D.C. 1979); *Hoffman-LaRoche v. Weinberger*, 425 F. Supp. 890, 892-894 (D.D.C. 1975). See also *Util. Air Regulatory Grp. v. EPA*, 573 U.S. 302, 327 (2014) (“An agency confronting resource constraints may change its own conduct, but it cannot change the law.”).)

The Agency’s interest in its general risk-based enforcement approach also justifies withdrawing an outdated policy that does not reflect that approach. Additionally, withdrawal of

the CPG is appropriate given the recent growth of safety concerns associated with homeopathic drug products--including concerns regarding products associated with serious adverse events and otherwise presenting significant safety risks and serious violations of CGMP requirements--and the increasing number of consumer exposures due to the continued expansion of the homeopathic industry since issuance of the CPG.

Dated: October 22, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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