AMERICAN ASSOCIATION FOR HOMEOPATHIC PRODUCTS

AAHP

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CHAPTER THREE:

Regulatory Framework for Homeopathic Medicines

REGULATORY FRAMEWORK

Introduction

The principal federal regulators of the manufacture, sale, and marketing of homeopathic drug products are the Food and Drug Administration (FDA) and the Federal Trade Commission (FTC). Both agencies recognize the drug status of homeopathic products and believe that the regulatory requirements for drugs in general apply to homeopathic drug products. However, owing to the uniqueness of homeopathic drug products, both FDA and FTC have chosen to use guidance and enforcement policy statements to state their view of how the law applies to homeopathic drugs.

United States Food and Drug Administration

STATUTORY RECOGNITION OF HOMEOPATHIC DRUGS

Since the passage of the 1938 Federal Food, Drug, and Cosmetic Act (FDCA), homeopathic drugs are the only form of alternative or complementary medicine which is explicitly recognized by FDCA. Section 201(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 Homœopathic Pharmacopœia of the United States (HPUS)." Section 501(b) of 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 HPUS.[1]

Given its prominence in both law and regulation, the HPUS is an invaluable reference for both FDA and industry. The HPUS is the legally recognized source of identification and quality standards for the 1,300 homeopathic active ingredients which are the subject of HPUS monographs. In addition to containing specific monographs, the HPUS also contains manufacturing protocols and other information applicable to homeopathic drugs generally.

HOMEOPATHIC DRUGS CLASSIFIED AS PRESCRIPTION

The 1951 Durham-Humphrey Amendment[2] to the FDCA created a statutory distinction between over-the-counter (OTC or nonprescription) and prescription (Rx Only) drugs. FDA had previously enforced this distinction by a regulation which relied upon its view that the statutorily required "adequate directions for use" could not be written for certain drugs because of their toxicity or the need for physician supervision. Although the amendment did "not appear to directly encompass homeopathic preparations as prescription drugs," FDA was persuaded by the American Institute of Homeopathy to categorize virtually all homeopathic drugs as prescription due to the individualized nature of treatment. This view was tempered, however, in that the agency noted it would not act against homeopathic products "without the prescription legend which are offered to the laity or minor ailments."[3]

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HOMEOPATHIC DRUGS EXCLUDED FROM OTC DRUG REVIEW

The 1938 FDCA required only that "new drugs" be examined by FDA for safety. In the Drug Amendments of 1962 (aka Kefauver-Harris Amendment), Congress added a statutory requirement that "new drugs" must also be shown to be effective.[4] That law also required FDA to re-review all previously approved "new drugs" for effectiveness. The agency created two separate structures for this review of existing drugs: the 1967 Drug Efficacy Study Implementation (DESI) system, under contract to the National Academy of Sciences/National Search Council for prescription drugs, and the 1972 OTC Drug Review for OTC drugs.

Neither the 1962 Drug Amendments nor the two FDA-created review processes included homeopathic drugs. In a consumer paper published by FDA 26 years later, the agency implied the reason for this exemption was similar to the exclusion from the FDCA safety review: [homeopathy] "was of little concern at the dilution being used".[5] The exemption might also have been due to the therapy's dwindling popularity at the time, as another 1988 FDA consumer publication implied action might not have been taken until "a growing problem."[6]

Due to low safety risks, no homeopathic drugs had undergone the "new drug" approval process prior to 1962, so they were not included in the prescription-only DESI Review.

When it created the 1972 OTC Drug Review, FDA decided it would be more efficient to review OTC drugs by active ingredient category rather than review drugs individually, as it had in the as-yet unfinished DESI Review. In announcing the procedures for that review, FDA stated: "Because of the uniqueness of homeopathic medicine, the Commissioner has decided to exclude homeopathic drugs from this OTC drug review and to review them as a separate category at a later time after the present OTC drug review is complete."[7]

More than a half century later, FDA had not completed the review of allopathic OTC drugs nor indicated any interest in starting the promised homeopathic OTC review.

CPG 400.400

As previously stated, while implementing the Durham-Humphrey Amendment, FDA categorized homeopathic products as prescription drugs, but the agency seldom enforced this against homeopathic OTCs and almost never against domestic manufacturers. FDA did, however, episodically and inconsistently enforce the Rx Only requirement against imported homeopathic drugs, including seizures of imported homeopathic drugs not labeled as Rx Only.

In the mid-1980s, AAHP took the lead in working with FDA to solve this inequitable situation. The result was the 1988 issuance of Compliance Policy Guide (CPG 400.400) "Conditions Under Which Homeopathic Drugs May be Marketed."[8] This CPG allowed homeopathic products to be marketed as OTC drugs for mild and self-limiting conditions as well as prescription drugs that must be dispensed under the care of a licensed practitioner for the treatment of serious disease conditions.

CPG 400.400 restated the existing statutory or regulatory requirements for marketing homeopathic drug products. It also provided educational information on homeopathic products for FDA personnel and key definitions, including:

- A definition of "homeopathic";
- Reference resources for traditional uses of homeopathic drugs;
- How to handle instances in which the active ingredient was not in the HPUS;

- Recognition of the different way in which the strength of homeopathic active ingredients is declared (e.g., 10X, 20X, 10C); and
- A recitation of statutory and regulatory labeling requirements.

CPG 400.400 led to major changes in the homeopathic industry and the marketing of homeopathic drugs. Prior to the CPG, the only indication on the label of most homeopathic drugs was, "Use according to standard homeopathic indications." While that fit well with the symptom-based approach central to the practice of homeopathy, FDA insisted in the CPG that the statute required a specific indication. The addition of familiar indications to homeopathic labels aided many consumers as they sought alternatives to other available medicines.

GUIDANCE CHANGE FROM COMPLIANCE TO RISK-BASED ENFORCEMENT

In 2015, 27 years after publishing CPG 400.400, FDA conducted a public hearing to evaluate its enforcement policies for drug products labeled as homeopathic from scientific, risk, and process perspectives.

The result of the hearing and subsequent multiple engagements between FDA and multiple stakeholders was the revocation of the compliance-based guidance in 2017 and the finalization of a risk-based enforcement priority guidance on Dec. 7, 2022.[9] Homeopathic Drug Products Guidance for FDA Staff and Industry contains many important policy considerations, including several recommended by AAHP. It also reiterates FDA's position that homeopathic drugs are unapproved new drugs and lists the agency's six categories of enforcement priorities. In the guidance's introduction, FDA states, "The agency anticipates that many homeopathic drug products will fall outside the categories of drug products that FDA intends to prioritize for enforcement and regulatory action."

FDA's view is any drug that does not have an approved New Drug Application, or which is not subject to an OTC monograph, is an "unapproved new drug." Despite its language, the new guidance does not change the legal status of homeopathic drugs. AAHP's position is that FDA's failure to fully implement the Drug Amendments of 1962 does not make homeopathic drugs illegal; FDA's inaction does not determine the legal status of these products.

Given the inherent safety of this class of drugs and remarkably low enforcement history against the category, AAHP believes that regulation via guidance is an effective way for FDA to protect the public health while preserving the agency's resources. The newly-stated risk-based approach is, in fact, simply a recognition of how FDA regulated homeopathic drugs under CPG 400.400.[10] However, guidance needs to be clear and complete enough to provide adequate direction to both industry and agency staff.

Recognizing FDA's reliance on risk-based enforcement, AAHP and the homeopathic community's future focus should be on addressing the issues outlined below.

FUTURE

Guidance documents are subject to interpretation by various FDA staff conducting facility inspections and as well as thousands of industry staff trying to comply with the guidance every day. An incomplete guidance compounds this problem and facilitates uneven enforcement. Unpredictable enforcement is resource intensive and distracts both FDA and industry from more important priorities. The current guidance and regulation fail FDA and industry alike. AAHP proposes the homeopathic community focus on advancing the following areas to ensure the reputation of homeopathic products.

Quality Gaps in Regulatory Guidance: While homeopathic products are part of the pharmaceutical industry in the United States, there are significant differences between homeopathic and allopathic drug products

that require specific attention. Most of the differences relate to the nature of homeopathic active ingredients, which are often below the limit of detection of most modern analytical instrumentation in the final drug product. This reality impacts many facets of manufacturing and quality control of these products. Despite analytical challenges associated with homeopathic active ingredients, AAHP believes that every attempt should be made by industry and FDA to effectively establish the identity and quality of homeopathic drug products.

Specific guidance related to the unique characteristics of homeopathic drug products is necessary for both industry and FDA to meet expectations and ensure public safety Specifically:

- Starting materials: Clear guidance for the identification, inspection, and receipt of homeopathic starting materials from many varied sources.
- Dilution validation: Practical methodology to apply validation principles to the homeopathic dilution manufacturing process.
- Discrete dosage forms: Testing objectives related to content uniformity of discrete dosage forms.
- Finished products: Sound strategies for quality testing of final homeopathic products across the range of dosage forms.

Recognition of Safety Evaluation: A key consumer benefit of homeopathic products is the remarkable safety record of this class of drugs. The safety of homeopathic products is primarily due to the products being labeled for self-limiting conditions (with limited duration of use) and the extremely low level of active ingredients in the products. With adequate safety limit testing, diluted starting materials attenuate any potential toxicity of the active homeopathic ingredient.

Most jurisdictions and regulatory authorities around the world have adopted this foundational attribute of homeopathic products. The European Union (EU) has adopted a methodology for establishing the first safe dilution for homeopathic starting materials.[11] HPCUS also calculates the lowest permissible (or first safe) attenuation.

These methodologies are powerful tools to establish safe dilution levels for all age groups, which should be recognized by U.S. regulators when evaluating the safety of homeopathic medicines. FDA's acknowledgement of these methods would be an effective way to protect the public and further preserve the agency's resources.

Recognition of Medical Literature to Substantiate Efficacy: The clinical use of homeopathic drugs by generations of physicians and consumers has been carefully recorded within homeopathic medical literature. This collection of data documents the symptoms associated with a given homeopathic active pharmaceutical ingredient (symptom picture) and corresponding clinical application. The rich literature base provides the justification for doctors to determine treatments for patients and supports claims made on product labels.

The literature serves as the basis for approval of homeopathic drugs in most jurisdictions around the world. Acceptable references of traditional homeopathic use were included in previous guidance in the U.S. but not the current guidance. Establishing reference to homeopathic literature would not only recognize the homeopathic clinical tradition, but also establish metes and bounds for claims on product labels.

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United States Federal Trade Commission

Section 5 of the Federal Trade Commission Act of 1914 prohibits "unfair or deceptive acts or practices in or affecting commerce," and Section 12 prohibits the dissemination of false advertisements for foods, drugs, devices, services, or cosmetics.[12] Section 15 of the FTC Act defines "false advertisement" as "advertising that is misleading in a material respect".[13]

FTC's authority extends to claims made for health care products, including homeopathic drugs. Given the overlapping authority for health care products, FDA and FTC adopted a Memorandum of Understanding in 1971 that allocates primary jurisdiction for advertising to FTC and primary jurisdiction for labels and labeling to FDA.

Due to increasing consumer interest in homeopathic products, FTC conducted a workshop in 2015 to investigate the policies and practices of the industries and its own enforcement policies related to substantiation of claims made in advertising of homeopathic drugs. At that time, FTC staff asserted in comments to FDA that there was a "potential" conflict between the requirements of CPG 400.400 and the FTC Act's advertising substantiation requirement: "the requirement that labeling for homeopathic drugs display an indication for use, even when the product has not been demonstrated to be efficacious for that indication, creates a potential conflict with the FTC's requirement that health claims be substantiated by competent and reliable scientific evidence."[14]

In 2016, FTC published its Enforcement Policy Statement on Marketing Claims for OTC Homeopathic Drugs that stated: "The FTC Act does not exempt homeopathic products from the general requirement that objective product claims be truthful and substantiated."

"However," the Commission added, " FTC has long recognized that marketing claims may include additional explanatory information in order to prevent the claims from being misleading. Accordingly, the promotion of an OTC homeopathic product for an indication that is not substantiated by competent and reliable scientific evidence may not be deceptive if that promotion effectively communicates to consumers that: (1) There is no scientific evidence that the product works and (2) the product's claims are based only on theories of homeopathy from the 1700s that are not accepted by most modern medical experts."[15]

While AAHP disagrees with the factually incorrect language of FTC's proposed disclaimer, the association generally believes that FTC struck a good balance by encouraging explanatory information on product labels to minimize risk of consumer confusion. AAHP hired an acknowledged university expert in consumer perception to conduct extensive research to develop a disclosure statement that met FTC's communications objectives. Based on that research, AAHP recommends that product labels and advertising for homeopathic drugs not supported by clinical research prominently bear the following disclosure: "Claims based on traditional homeopathic practice, not accepted medical evidence. Not FDA evaluated."

FTC's Health Products Compliance Guidance, published in 2022, reinforced the Commission's position that health claims should be supported with adequate, competent, and reliable scientific evidence. Homeopathic products are specifically named among categories of health products covered by the guidance. This reiterates, but doesn't replace, FTC's expectation stated in its 2016 Enforcement Policy Statement.[16]

AAHP believes that products bearing health claims supported by the homeopathic literature for reasonable self-limiting conditions and prominently bearing the disclaimer developed by the association are non-deceptive and well labeled.

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AAHP calls on the research community to continue the work of advancing the knowledge of the mechanism of action of the category of products related to their clinical application to the satisfaction of the consumers and regulatory authorities alike.

To that end, the association has sponsored more than one public virtual presentation by the Homeopathic Research Institute (HRI) regarding the current research situation and the need for duplication of research to meet accepted standards expected by the greater research community. AAHP also encourages both industry and the homeopathic research community to conduct trials on actual product formulations to support label claims based on historical homeopathic literature.

Conclusions

There is a well-established framework of guidelines, regulations, and quality standards for homeopathic drugs. There are still some gaps in cGMP requirements and possibilities for varying interpretations of the guidance documents; thus while the situation is relatively stable, AAHP and the homeopathic community can help fine tune the regulatory environment to minimize misunderstandings and inconsistent compliance activity. Compliance is enforced by FDA through routine pharmaceutical manufacturing site inspections and surveillance of product labels marketed to consumers. This process safeguards public safety while ensuring consumer access to this drug class, which is known for its safety and medical-economic value.

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