

February 27, 2019  
The Honorable Scott Gottlieb, M.D.  
Commissioner, U.S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

Dear Commissioner Gottlieb:

I am writing to offer the support of the United States Pharmacopeia (USP)<sup>1</sup> on the Food and Drug Administration's (FDA's) recent announcement that it will modernize policies to help ensure the availability of safe, well-manufactured, and appropriately labeled dietary supplements, and to address noncompliant products, including unsafe products illegally marketed as supplements.<sup>2</sup> USP shares the public health goals of this initiative and would welcome the opportunity for collaboration with the Agency as this effort moves forward.

As a result of USP's longstanding work setting standards for dietary supplements, we have gained an appreciation of the complexity of these products and the regulatory challenges—including the task of overseeing the broad range of ingredients covered by the Dietary Supplement Health and Education Act (DSHEA) that are placed into the global supply chain; and the significant problem of tainted products marketed as dietary supplements that are instead unapproved or misbranded drugs under the law.<sup>3</sup>

USP has established over 500 science-based public quality standards for dietary supplements and ingredients in the *United States Pharmacopeia-National Formulary (USP-NF)*<sup>4</sup>, which is an official compendium<sup>5</sup> of national standards for both drugs and dietary supplements. While *USP-NF* standards are voluntary for supplements,<sup>6</sup> they assist manufacturers in supporting product authenticity and quality by providing specifications for identity, purity, and contaminant limits, through analytical procedures and tests.<sup>7</sup> We have worked with FDA to identify supplements and ingredients whose quality has raised particular concerns with the FDA, and have prioritized the creation and revision of monographs accordingly. We would welcome the opportunity to continue this dialogue and further leverage USP's standard setting capabilities to help advance FDA goals.

We have also been closely involved with scientific experts and stakeholders on methods for testing the quality of botanical supplements,<sup>8</sup> and would welcome collaboration with the Botanical Safety Consortium.

In an effort to deploy USP capabilities to help ensure greater quality under the framework established by DSHEA, we have developed the USP Dietary Supplements Verification program. In this program, USP verifies supplement manufacturer adherence to Good Manufacturing Practices and quality standards. We believe this program helps to advance the quality goals in DSHEA but recognize a variety of opportunities exist to improve upon the statutory framework. As part of the broader public dialogue about whether additional steps to modernize DSHEA are necessary - including whether potential changes to the law might be helpful - USP wants to participate and support the advancement of a risk-based approach that provides consumers with the confidence to trust the quality and safety of supplements marketed in the United States.

To raise awareness and create more stakeholder dialogue on supplements quality, USP spearheaded the creation of the *Dietary Supplements Quality Collaborative (DSQC)*. The DSQC meets at least quarterly and has made progress in both building awareness of the

practices of responsible supplement manufacturers, as well as raising awareness of the dangers of adulterated, tainted and/or illegal products. The group has also developed multi-stakeholder responses to these issues.<sup>9</sup> The Collaborative includes industry associations, standards setting organizations, patient groups, practitioner associations and other interested parties. DSQC membership can be found here: <https://www.dsgcollaborative.org/about-us>

We would welcome an opportunity to further discuss dietary supplement quality issues, reform initiatives, and ways that USP can support FDA efforts to ensure the safety and quality of supplements. We look forward to hearing back from you. In the meantime, please feel free to contact me, or Elizabeth Miller, Vice President, US Regulatory Affairs, at [EHM@usp.org](mailto:EHM@usp.org); (240) 221-2064, if you have questions.

Sincerely,



Ronald T. Piervincenzi, Ph.D.  
Chief Executive Officer

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<sup>1</sup> USP is an independent, scientific, nonprofit organization dedicated to improving health through the development of public standards for medicines, foods and dietary supplements. We are governed by the USP Convention, comprising over 450 academic institutions, healthcare practitioners, industry groups and governmental organizations. Our public quality standards are developed through an open, transparent process with participation and input from stakeholders including academic, industry, and government representatives.

<sup>2</sup> The enactment of DSHEA more than 20 years ago created a framework intended to regulate supplements as category separate from drugs and other foods while also protecting the public from unsafe or adulterated products. A recently renewed focus on dietary supplement quality and safety has generated a discussion around public health implications surrounding products marketed as dietary supplements, while also prompting enhanced regulatory interest and scientific and industry initiatives.

<sup>3</sup> DSHEA covers a broad range of dietary ingredients, including vitamins, minerals, herbs or other botanicals, and amino acids, or combinations of these ingredients. Adding a layer of complexity is the issue of tainted products marketed as dietary supplements that are instead unapproved or misbranded drugs under the law (Federal Food, Drug, and Cosmetic Act (FDCA) § 201(g)(1)(B) (defining drugs with respect to intended use); and §§ 301(d) and 505(a) (prohibiting the introduction of new drugs into interstate commerce without FDA approval)). The concern of tainted products requires the Agency's meticulous coordination of regulatory, compliance, and enforcement activities through an involved framework spanning multiple FDA offices and Centers.

<sup>4</sup> Separately, the *Dietary Supplements Compendium* is a compilation of monographs and General Chapters relevant to dietary supplements: it is sourced from *USP-NF* and other sources.

<sup>5</sup> *USP-NF* is an official compendium of the United States (FDCA, §§ 201(j)).

<sup>6</sup> A supplement failing to meet USP specifications is considered misbranded under Federal law, but only if represented as conforming to USP specifications (FDCA §403(s)(2)(D)).

<sup>7</sup> Many supplement manufacturers choose to use *USP-NF* monographs, along with physical reference standards, to help ensure the quality of their products and ingredients. In addition to USP monographs, USP General Chapters provide information or guidelines on common methods and procedures that help ensure quality and consistency. Several USP General Chapters specifically address the dietary supplements industry, for example, the detection of undeclared prescription drugs and their analogues (General Chapter <2251> *Screening for Undeclared Drugs and Drug Analogues*); and procedures to assist manufacturers in applying appropriate GMPs (General Chapter <2750> *Manufacturing Practices for Dietary Supplements*). See also, Sarma, N., Giancaspro, G., & Venema, J. (2016). Dietary supplements quality analysis tools from the United



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States Pharmacopeia. Drug testing and analysis, 8(3-4), 418-23, available at:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5072169/>.

<sup>8</sup> USP's physical reference standards for botanical ingredients, along with compendial analytical procedures and acceptance criteria, help manufacturers of dietary supplement ingredients and finished products meet established quality specifications for identity, strength, purity, and performance. Recent workshops have focused on development and application of DNA-based methods for determining the identity of botanicals, and we have also collaborated on toxicologically-based safe limits for pesticides that may occur unintentionally during harvesting or processing of botanical ingredients.

<sup>9</sup> Dietary Supplements Quality Collaborative, Briefing Paper on Products Illegally Marketed as Dietary Supplements and Proposed Multi-Stakeholder Responses,

[https://www.dsqualitycollaborative.org/sites/default/files/dsqualitycollaborative/PDF/dsqualitycollaborative\\_tainted\\_products\\_briefing\\_document.pdf](https://www.dsqualitycollaborative.org/sites/default/files/dsqualitycollaborative/PDF/dsqualitycollaborative_tainted_products_briefing_document.pdf)

