VIA ELECTRONIC SUBMISSION

March 9, 2020

Food and Drug Administration
Division of Dockets Management
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2019-N-5711 for "Importation of Prescription Drugs"; Proposed Rule

Dear Sir/Madam,

The United States Pharmacopeia (USP)[1] appreciates the opportunity to provide comments to the Food and Drug Administration (FDA or Agency) on the "Importation of Prescription Drugs" proposed rule.

The current U.S. distribution system for prescription drugs ensures the quality and safety of medicines sold in the United States and is predicated on a strong foundation of FDA's review and evaluation supported by the availability of USP's quality standards. Allowing the importation of numerous prescription drugs into the United States makes the consistent application of FDA requirements and USP quality standards all the more important.

Through a longstanding collaboration with FDA, USP has worked continuously to support public health through facilitating the development of accessible quality medicines. As described in more detail below, USP is providing comments on the importance of quality standards, and the labeling and laboratory testing requirements for imported drug products.

Quality Standards

Public quality standards play a role throughout the entire lifecycle of a drug product. There is a critical need for a common public standard to assure the quality and consistency of medicines moving in national and international commerce. Public quality standards allow independent determination that a product has been made according to regulatory expectations for identity, strength, and purity regardless of the manufacturer or manufacturing process. They often cover multiple manufacturers and change over time as science and regulations evolve.

[1] USP is an independent, scientific, nonprofit organization dedicated to improving public health for medicines, foods, and dietary supplements. USP compendial standards are recognized in the Federal Food, Drug, and Cosmetic Act and have helped ensure the quality of medicines in the United States for over 200 years. USP public standards are developed through an open, transparent, expert-based process, offering the ability to confront public health emergencies, adapt to new industry practices, and support evolving science and technology.

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Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), a drug with a name recognized in the *USP–NF* must comply with the current version of compendial standards deemed official by USP, or risk being deemed adulterated, misbranded, or both.[2] Specifically, a drug with a name recognized in the *USP–NF* must comply with the identity requirements of its monograph. Drugs also must comply with compendial standards for strength, quality, and purity (tests for assay and impurities), unless labeled to show all respects in which the drugs differ.

The proposed rule states that the eligible prescription drug, specified by a Section 804 Importation Program (SIP) sponsor, needs to meet the conditions of an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA) including those relating to the drug substance, drug product, production process, quality controls, equipment, and facilities.[3] Because the proposed rule allows the potential for each State, including entities within the same State, to submit different SIP proposals for the same drug, it is important to have clear and consistent quality standards to help ensure that medications have the correct identity, strength, and purity when consumed by patients.

USP agrees with the Agency's recommendation for a SIP to have at least one sponsor that is a State, tribal, or territorial governmental entity. We believe this involvement is critical to facilitate a prompt response in the case of a recall or other event that requires a quick coordinated response from practitioners, pharmacies, wholesalers, or other entities to protect the public health.

Labeling Requirements

The proposed rule requires that a drug covered by section 804 of the FD&C Act meet all labeling requirements of the FD&C Act. The importer must ensure the eligible prescription drug for importation is relabeled with the required U.S. labeling.[4] The proposed rule also states that relabeling and associated limited repackaging activities must meet applicable requirements including current good manufacturing practice requirements.[5]

Under the FD&C Act, a drug with a name recognized in the *USP–NF* must be packaged and labeled in compliance with compendial standards, or risk being deemed misbranded.[6] If a USP monograph exists for the eligible prescription drug, the labeling requirements in such monograph play a role in ensuring that the drug is labeled according to U.S. labeling requirements. Even if a monograph does not exist

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[2] *See* sections 501(b) and 502(e)(3)(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); 21 CFR 299.5(a) and (b).

[3] *See* proposed 21 CFR 251.2.

[4] *See* proposed 21 CFR 251.12(a)(4).

[5] *See* proposed 21 CFR 251.13(c).

[6] *See* section 502(g) of the FD&C Act.

for an eligible prescription drug, USP *General Chapter <7> Labeling* includes information on labeling requirements that manufacturers may find helpful.

Laboratory Testing Requirements

Under section 804 of the FD&C Act, the manufacturer or importer is required to conduct "statutory testing" of an eligible prescription drug for authenticity, degradation, and to ensure the drug is in compliance with established specifications and standards.[7] USP monographs include standards to establish authenticity and control degradation. If a monograph does not exist for a particular eligible prescription drug, USP general chapters, including <11> *USP Reference Standards*, <232> *Elemental Impurities—Limits*, <233> *Elemental Impurities—Procedures*, and/or <467> *Residual Solvents*, as well as other applicable general chapters, can help ensure the quality of the imported drug product.

Regarding sampling requirements, the proposed rule requires that a statistically valid sample of the drug be tested to confirm it meets FDA-approved drug specifications, including analytical procedures and methods and acceptance criteria.[8] Further, a stability-indicating assay provided by the manufacturer must be conducted on the sample.[9] The *USP-NF* contains general chapters on product quality tests that discuss stability-indicating assays used to determine the potency, or strength, of the drug product.[10] These general chapters are specific to oral drug products, topical and transdermal drug products, mucosal drug products, and inhalation and nasal drug products.[11] Other *USP-NF* general chapters also describe stability-indicating procedures, including *General Chapter <1225> Validation of Analytical Compendial Procedures*.

The Federal Register Notice states that a stability-indicated assay developed by USP or the manufacturer would have to be conducted. We appreciate the reference to USP. In order for USP to develop a stability-indicating assay for a product-specific monograph, we partner with manufacturers to facilitate a monograph donation. This enables USP to work with our volunteer scientific experts to develop a public standard for the drug product.[12]

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[7] *See* sections 804(d)(1)(J) and (L) of the FD&C Act.

[8] *See* proposed 21 CFR 251.61(d).

[9] *See id*.

[10] *See General Chapter <2> Oral Drug Products – Product Quality Tests*, *General Chapter <3> Topical and Transdermal Drug Products – Product Quality Tests*, *General Chapter <4> Mucosal Drug Products – Product Quality Tests*, and *General Chapter <5> Inhalation and Nasal Drug Products – General Information and Product Quality Tests.*

[11] We note that drugs inhaled during surgery are excluded from the definition of "prescription drug" under section 804(a)(3) of the FD&C Act.

[12] USP has created Submission Guidelines on how to submit information to support creation of a new monograph or a revision to a proposed or existing official monograph in the *USP-NF.* For more information, see https://www.usp.org/get-involved/donate/submission-

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USP is committed to continued partnerships with key stakeholders, including FDA and the manufacturing industry, in helping to facilitate access to quality medicines in the United States. In the announcement of the proposed rule, it is suggested that strengthened regulatory harmonization between the United States and Canada be pursued, particularly through the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). USP is an observer to the ICH Assembly and look forward to the opportunity to be part of discussions on this topic.

We thank the Agency for the opportunity to provide comments on this proposed rule and welcome further dialogue with the Agency to support the quality of medicines and patient safety when importing prescriptions drugs under section 804 of the FD&C Act.

For more information, please contact Marissa Chaet Brykman, Director, U.S. Regulatory Engagement, at marissa.brykman@usp.org; (301) 692-3660.

Sincerely yours,

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