VIA ELECTRONIC SUBMISSION

January 27, 2020

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

Re: Docket No. FDA-2019-N-5464 for Novel Excipient Review Program Proposal; Request for Information and Comments

Dear Sir/Madam,

The United States Pharmacopeia (USP)[1] appreciates the opportunity to provide comments on a potential FDA novel excipient review program. USP is supportive of a novel excipient review program. Establishing new pathways for the development and regulatory review of novel excipients is critical in facilitating innovation for the advancement of new medical products.

USP has many existing and developing mechanisms to help support a novel excipient review program. In our comments below, we focus on a novel excipients survey conducted by USP, a discussion on novel excipient naming, USP's Pending Monograph Process, and the relevance of public standards in this space.

USP developed and launched a novel excipients survey in March 2019, the goal of which was to better understand the current drug approval pathway's impact on novel excipient innovation. The purpose and objectives of the survey were to identify if any challenges are being experienced by stakeholders related to novel excipients and to better understand views of stakeholders on the current state of innovation in excipients development. The survey results indicated that the current regulatory approval pathway for excipients creates a challenge for the use of novel excipients. Based on the survey results, USP is supportive of a novel excipient review program since it provides a pathway for excipients outside of the normal application review process. The full survey results are targeted to be published in the spring of 2020.

The Federal Register Notice proposing a potential novel excipient review program states FDA's expectation that any excipients that undergo complete review would be listed in the Inactive Ingredients Database (IID) after they are used in approved formulations. As recommended by FDA for single substance ingredients, USP proposes using the Global Substances Registration System (GSRS) to promote

[1] USP is an independent, scientific, nonprofit organization dedicated to improving health through the development of public standards for medicines, foods, and dietary supplements. Through a longstanding collaboration with FDA, we have worked continuously to benefit public health through accessible quality medicines.

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consistency of the official names for novel excipients evaluated by FDA.[2] Through extension of our current collaboration efforts with FDA on data exchange, we can assist in establishing these names for listing in GSRS. As stated in the FDA draft guidance, "Using the Inactive Ingredient Database,"[3] the IID displays the preferred term for the excipient as it appears in GSRS to promote consistency in nomenclature in the IID. As further detailed in our comments in response to this draft guidance on the IID,[4] USP continues to support the Agency's efforts to provide a clearer understanding of the information and terminology provided in the IID. To that end, a USP Expert Committee[5] is developing an excipient nomenclature guideline. The Expert Committee intends to include standardized approaches for naming complex excipients, including mixtures and polymers in the guideline, and to publish the guideline on USP's website.

Once a novel excipient becomes part of an application for FDA approval, which may result in the listing of the excipient in the IID, USP could utilize its Pending Monograph Process (PMP) for the development of monographs or monograph revisions.[6] The PMP is currently used to expedite revision of an existing *USP–NF* monograph or the creation of a new monograph for a drug product or active pharmaceutical ingredient. USP can explore modifying the PMP to clarify how the process could be utilized to facilitate revision of existing *USP–NF* excipient monographs and potential new monographs for excipients that are being reviewed as part of an FDA drug application. Using the PMP for the creation of an excipient monograph would provide a mechanism for determination of the appropriate identification, compositional, and purity specifications for the novel excipient that coincides with FDA's review and approval of the associated application. We welcome discussions with the Agency on how the PMP can be used to reduce burdens on both industry and FDA.

Furthermore, USP is working on developing a general chapter that focuses on quality information including chemistry, identity, and other specifications for excipients that will support industry and FDA's review as part of the novel excipient review program. USP is interested in discussing approaches with FDA on how to establish identity specifications for novel excipients that have been evaluated by FDA. The availability of standardized identity information for a novel excipient could help industry and FDA in its establishment and evaluation of quality specifications for novel excipients.

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[2] *See* FDA draft guidance, "Using the Inactive Ingredient Database," https://www.fda.gov/media/128687/download (July 2019).

[3] *Id*.

[4] *See* USP comments on FDA's draft guidance, "Using the Inactive Ingredient Database" (Docket No. FDA-2019-D-2397), submitted Sept. 25, 2019.

[5] The full name of the Expert Committee is: Excipient Monographs Expert Committee, Excipient Nomenclature Joint Subcommittee, which includes an FDA government liaison.

[6] For more information on USP's Pending Monograph Program, *see* https://www.uspnf.com/pending-monographs. *See also*, FDA's draft guidance, "Harmonizing Compendial Standards With Drug Application Approval Using the USP Pending Monograph Process," https://www.fda.gov/media/128689/download (July 2019).

Additionally, updating USP General Chapter <1074> *Excipient Biological Safety Evaluation Guidelines* could facilitate and enhance the industry's ability to develop safety information that will support the Agency's nonclinical review during the drug application review process. A revised chapter <1074> could potentially help stakeholders by including information on developing toxicological studies supporting the safety of the novel excipient at anticipated levels and duration of exposure by anticipated routes of administration. The scope of revision would be aligned with FDA's guidance for industry, "Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients" from 2005.[7]

We note the success of the 2017 FDA/USP workshop on excipients[8] and look forward to further discussion with FDA and stakeholders on how to best support the pilot novel excipient review program using the proposals discussed above or others. USP's existing and developing programs and expertise can help address gaps and support continuous innovation in the novel excipients space.

Again, thank you for the opportunity to comment. For more information, please contact Elizabeth Miller, Pharm.D., Vice President, U.S. Public Policy and Regulatory Affairs, at ehm@usp.org; (240) 221-2064.

Sincerely yours,

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[7] FDA guidance, "Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients," https://www.fda.gov/media/72260/download (May 2005).

[8] "FDA and USP Workshop on Standards for Pharmaceutical Products-Critical Importance of Excipients in Product Development – Why Excipients are Important Now and In the Future" took place in Feb. 2017, https://www.fda.gov/drugs/news-events-human-drugs/fda-and-usp-workshop-standards-pharmaceutical-products-critical-importance-excipients-product.