VIA ELECTRONIC SUBMISSION

October 14, 2020

U.S. Hemp Authority
250 West Main Street, Suite 2800
Lexington, KY 40507

Re: U.S. Hemp Authority® Certification Program Standard v3.0 DRAFT: INITIAL DRAFT FOR PUBLIC CONSULTATION

Dear Sir/Madam,

The United States Pharmacopeia (USP) appreciates the opportunity to comment on the U.S. Hemp Authority® Certification Program Standard v3.0 DRAFT.[1]

USP is an independent, scientific, nonprofit public health organization devoted to improving health through the development of public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods. We are governed by the USP Convention, comprising over 450 academic institutions, healthcare practitioner organizations, industry groups and government representatives.

USP develops and publishes its official standards for drugs, excipients, and dietary supplements in the *United States Pharmacopeia-National Formulary (USP-NF)*. We also publish a compendium of food ingredient standards, the Food Chemicals Codex (*FCC*). USP develops public quality standards for the identity, strength, and purity of medicines, foods, and dietary supplements through an open, transparent process, with participation from stakeholders including representatives from academia, industry, and government.[2] We also develop reference standards[3] for analytical

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[1] USP's submission of comments does not indicate an endorsement of public policy statements made by the U.S. Hemp Authority® or the U.S. Hemp Roundtable. Additionally, USP's submission of comments does not imply approval or endorsement of U.S. Hemp Authority's certification program, nor does it imply that its certification program is the best available or that any other program was judged to be unsatisfactory or inadequate. USP's comments are not intended as an exhaustive review of the U.S. Hemp Authority® Certification Program Standard v3.0 DRAFT.

[2] Our standards are developed by Expert Committees and Expert Panels. USP formed an Expert Panel with representation from academia and industry, and government representatives from U.S. states and Canada to develop scientifically based specifications for cannabis inflorescence. For more information on the Expert Panel and our comments on products containing cannabis or cannabis-derived compounds, *see* USP's comments to FDA at, https://www.regulations.gov/document?D=FDA-2019-N-1482-3122 (submitted July 5, 2019). In 2016, USP convened a dialogue with interested stakeholders to evaluate which scientific tools and approaches would be advisable and feasible in support of protecting patients' health regarding the use of cannabis for medical purposes. *See* USP's stimuli article, "The Advisability and Feasibility of Developing USP Standards for Medical Cannabis," at https://www.uspnf.com/notices/stimuli-article-advisability-and-feasibility-developing-usp-standards-medical-cannabis-posted-comment (Feb. 26, 2016).

testing. One of USP's areas of expertise and focus is the development of standards for articles of botanical origin, including analytical procedures and acceptance criteria to help ensure their identity, purity and strength.

With respect to the legal and regulatory status of cannabis and cannabis-derived compounds, USP defers to federal law and the Food and Drug Administration (FDA) and other appropriate government authorities' regulatory actions. At the same time, from our interactions with various stakeholders throughout the last several years, we have learned of the critical and growing need for scientific articulation of quality attributes for cannabis and related products to help protect patients and consumers from harm.

The U.S. Hemp Authority® Certification Program Standard v3.0 draft expects hemp growers, processor/manufacturers, and brand owners to comply with applicable regulations, and notes that "[i]t is therefore not the intention of the U.S. Hemp Authority Standard to explicitly repeat in detail all such common requirements, but rather contains provisions to assure that operators have systems in place to adhere to relevant industry norms."

Whatever regulations are applicable, USP believes that product-specific public standards are essential for monitoring product quality. Therefore, we suggest incorporation of hemp-specific quality attributes for the hemp certification program.

Public quality standards help monitor product quality so that adulterants, including contaminants, can be identified and controlled so that they are absent or below the level of concern. Public standards are essential to help prevent harm to patients and consumers, they facilitate the manufacture of products that are not adulterated, and help limit exposure to toxic substances, pathogenic microorganisms, and harmful additives. As such, we suggest consideration of the following USP guidelines, general chapters and reference standards in developing hemp-specific specifications.

Nomenclature

Federal regulations define hemp as *Cannabis sativa* L., including its extracts, with a delta-9 tetrahydrocannabinol (THC) concentration of not more than 0.3 percent on a dry weight basis. Several varieties of hemp, ranging from fiber-type to those that are bred for cannabinoid content, meet the regulatory requirement, but contain differing levels of cannabinoids and are labeled by several common names. Similarly, the terminology used to describe processed extracts, such as full spectrum, broad spectrum, and isolates, may mean different things to different people.

USP believes that more guidance is needed on adequate descriptions and appropriate nomenclature to describe hemp and its extracts, such as the plant part, method of extraction, and percentage of critical cannabinoids, to adequately reflect in

[3] USP reference standards are highly characterized chemical specimens—pure materials or mixtures of chemicals that have been tested in multiple laboratories—intended for quality control use in conducting assays and tests in USP's documentary standards for drugs in the *USP–NF*, for dietary supplements in the *USP–NF* and *Dietary Supplements Compendium*, and for foods in the *FCC*.

the nomenclature used to describe the material. In alignment with FDA's draft guidance on dietary supplements,[4] USP developed a nomenclature guideline for the naming of botanical dietary supplement products.[5] This guideline may help U.S. Hemp Authority® in establishing appropriate nomenclature for the hemp extracts.

Analytical Testing Methods

Recognizing the federal requirement to limit the THC content in hemp at not more than 0.3 percent on a dry weight basis, the use of an appropriate test method is critical to differentiate between hemp (an agricultural commodity) and marijuana (a Schedule 1 controlled substance).[6] The use of orthogonal analytical procedures and acceptance criteria can help identify hemp and differentiate it from other cannabis varieties that contain more than 0.3 percent THC. USP's Cannabis Expert Panel is working on providing appropriate analytical methods in this regard.

The U.S. Hemp Authority® may also find useful the following comments from USP to the United States Department of Agriculture (USDA) for the Certification Program Standard v3.0. In particular, USP comments to USDA's docket on the "Establishment of a Domestic Hemp Production Program" explain USP's perspective regarding the quality considerations for hemp.[7] We highlight below the relevant parts:

- USP's publication on quality attributes for cannabis inflorescence provides science-based chromatographic methods and reference standards to help ensure resolution (separation) of THC from its carboxylated form and from other cannabinoids.[8] We also emphasized the procedures for sampling and testing cannabis varieties grown and harvested to ensure hemp does not exceed the acceptable THC level.

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[4] FDA Draft Guidance, *Dietary Supplement: New Dietary Ingredient Notifications and Related Issues*, at https://www.fda.gov/media/99538/download.

[5] Guideline for Assigning Titles to *USP* Dietary Supplement Monographs, at https://www.usp.org/sites/default/files/usp/document/get-involved/submission-guidelines/guideline-for-assigning-titles-to-usp-dietary-supplement-monograph.pdf.

[6] *See* 7 CFR 990.1, for definitions of hemp and marijuana. Marijuana remains classified as a Schedule I controlled substance regulated by the Drug Enforcement Administration (DEA) under the Controlled Substances Act.

[7] USP comments to USDA dated December 19, 2019: Docket No. AMS–SC–19–0042; SC19–990–2 IR; 84 FR 58522 (Oct. 31, 2019); 7 CFR part 990; Establishment of a Domestic Hemp Production Program; Interim final rule with request for comments, at https://www.regulations.gov/document?D=AMS-SC-19-0042-1518.

[8] *See* Sarma ND, Waye A, ElSohly MA, Brown PN, Elzinga S, Johnson HE, Marles RJ, Melanson JE, Russo E, Deyton L, Hudalla C, Vrdoljak GA, Wurzer JH, Khan IA, Kim N-C, Giancaspro GI. *J Natural Products 83* (4), 1334-1351, 2020, at https://pubs.acs.org/doi/10.1021/acs.jnatprod.9b01200.

- The analytical procedures to determine the content of THC on "dry weight basis," since plant material can contain volatile constituents, impact the determination of water by loss on drying, and drying at high temperature may lead to loss of mass due to decarboxylation and other degradation not related to water loss. We suggested that the methods for determining the dry weight basis be clearly defined. Specifically, for cannabis, we proposed to standardize the definition of "dry weight basis" as a material that has a water activity of not more than 0.65.

- Regarding the testing of samples using "postdecarboxylation or other similarly reliable analytical methods" (7 CFR 990.3(a)(3)), and considering that the carboxylic acid form of THC, tetrahydrocannabinolic acid (THCA), is the precursor for THC, and the THC is the cannabinoid predominantly responsible for the psychoactive properties of cannabis, we suggested that the analytical methods ensure resolution (separation) of peaks for THC and THCA from other cannabinoids. The methods should be appropriate to characterize varieties of cannabis that produce elevated content of minor cannabinoids, such as cannabigerol (CBG), cannabigerolic acid (CBGA), cannabichromene (CBC), cannabichromenic acid (CBCA), and cannabidivarin (CBDVA), among others. We recommended that any cannabinoids above 10 mg/g (1% w/w) should be clearly disclosed in labeling.

- Regarding the "Measurement of Uncertainty"[9] to ensure that the THC concentration level is accurately measured, we would like to highlight a possibility that some test methods might have a larger range of uncertainty, potentially resulting in the passing of controlled substance lots with high THC content. We suggested consideration of *USP-NF General Notices* section *7.20. Rounding Rules* in establishing whether the actual THC concentration level meets the specification of not more than 0.3 percent THC on a dry weight basis.

- Regarding sampling, we suggested consideration of USP General Chapter <561> *Articles of Botanical Origin* which describes the sampling procedures applicable to vegetable drugs, including procedures for gross sampling from multiple batches and the test sampling methods.

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[9] The USDA Interim Final Rule (IFR) defines "measurement of uncertainty" as "the parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the particular quantity subject to measurement." According to the Federal Register Notice, when the measurement of uncertainty, normally expressed as a +/- with a number (*e.g.*, +/- 0.05), is combined with the reported measurement, it produces a range, and the actual measurement has a known probability of falling within that range (typically 95%). The IFR also includes a definition of "acceptable hemp THC level" to account for the uncertainty in the test results. According to the IFR, the reported THC concentration level of a sample may not be the actual concentration level in the sample and that the actual THC concentration level is within the distribution or range when the reported THC concentration level is combined with the measurement of uncertainty.

Scientifically Valid Specifications

We suggest consideration of the following USP compendial procedures to establish the suitability of analytical methods and limits on contaminants:

- USP General Chapter <1225> *Validation of Compendial Procedures* and appropriately characterized reference standards could be used to develop validated test methods that accurately determine the content of THC. USP General Chapter <1225> provides principles for validation of analytical procedures. The chapter describes the data elements required for validation of an analytical method for quantitative limit test, including establishing the accuracy, precision, specificity, quantitation limit and linearity. USP reference standards, with established suitability for use in analytical methods, can help ensure comparability of results and traceability to Système International d'Unités (SI) units.
- USP General Chapter <563> *Identification of Articles of Botanical Origin.*
- USP General Chapters <2021> *Microbiological Enumeration Tests-Nutritional and Dietary Supplements*; <2022> *Microbiological Procedures for Absence of Specified Microorganisms-Nutritional and Dietary Supplements.*
- USP General Chapters <232> *Elemental Impurities—Limits,* and <2232> *Elemental Contaminants in Dietary Supplements.*

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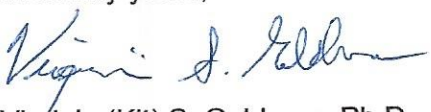
Thank you for the opportunity to discuss the importance of quality products and how USP compendial approaches, including documentary and reference standards, can help ensure the quality of hemp products, as it relates to the U.S. Hemp Authority® Certification Program Standard v3.0 draft. For more information, please contact me at (301) 692-3597 or kit.goldman@USP.org.

Sincerely yours,



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