USP Dietary Supplement Stakeholder Forum
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Standards and Information for Hemp and CBD

Robin J. Marles, Ph.D.
Chair, Botanical Dietary Supplements and Herbal Medicines Expert Committee (2015–2020 and 2020–2025)
Member, Cannabis Expert Panel
Hemp: Definition and Regulatory Status

- The plant *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 % on a dry weight basis.
- FDA has completed the evaluation of three Generally Recognized as Safe (GRAS) notices for hemp ingredients.
- “No questions” letters issued in response to GRAS notices for:
  - hulled hemp seed (GRN765)
  - hemp seed protein powder (GRN771)
  - hemp seed oil (GRN778)

\[ FCC \text{ monographs under development} \]
Hemp and CBD Quality Attributes

Pain points:
- No public standards for the widely available foods and dietary supplements
- Need to differentiate hemp from cannabis containing >0.3% THC
- Consumer Lab report: 10-fold variability of CBD levels (2.5 mg to 25 mg CBD/serving)
- Health concern from parents using large volumes of DS products to achieve ~800 mg CBD/dose from Epidiolex
- CBD: “FDA has determined that products that contain THC or CBD cannot be marketed as dietary supplements”; enforcement is focused on disease claim

USP and FCC admission criteria will determine admissibility:
- Hemp: GRAS or NDI ingredients would meet USP DS Admission Criteria and monograph standards could be introduced to USP and DSC
Major Considerations for Quality

- Nomenclature
- Fingerprint based on naturally-occurring cannabinoid profile (characteristic ID for hemp)
- Limit for $\text{D}^9$-THC (NMT 0.3% on a dry weight basis, inclusive of THCA)
- Test for CBD – minimum content or % of label claim? Consideration of the FDA decisions or Congressional actions about levels allowed in non-drug products
- Specific tests for terpene profile
- Limits for contaminants:
  - Pesticide residues (<561>)
  - Microbial load (<2022> and <2023>)
  - Elemental contaminants (<561> and <2232>)
  - Residual solvents (<467>)

- Labeling
Nomenclature

Complex names:
- Full-spectrum extract
- Broad-spectrum extract
- Distillates
- Isolates
- Decarboxylated versus Non-decarboxylated extracts

Variables:
- Solvents
- Enrichment processes
- Degradants and impurities
USP Cannabinoids Reference Standards

#1651621 ∆⁹-Tetrahydrocannabinol (∆⁹-THC, or Dronabinol)
#1089149 Cannabidiol (CBD)
#1089161 Cannabidiol Solution

USP Cannabinoids Mixture RS
1 mL (1 mg/mL in methanol) [Catalog # 1089183]:
- 0.075 mg Delta-9-Tetrahydrocannabinol (∆⁹-THC)
- 0.025 mg Delta-8-Tetrahydrocannabinol (∆⁸-THC)
- 0.050 mg Cannabidiol (CBD)
- 0.025 mg Cannabinol (CBN)
- 0.025 mg Cannabichromene (CBC)
- 0.025 mg Cannabigerol (CBG)
- 0.025 mg Tetrahydrocannabivarin (THCV)
- 0.025 mg Cannabidivarin (CBDV)

USP Cannabinoid Acids Mixture RS
1 mL (1 mg/mL in acetonitrile and trimethylamine with stabilizer) [Catalog # 1089172]:
- 0.25 mg Tetrahydrocannabinolic Acid (THCA)
- 0.25 mg Cannabidiolic Acid (CBDA)
- 0.025 mg Tetrahydrocannabivarinic Acid (THCVA)
- 0.050 mg Cannabidivarinic Acid (CBDVA)
- 0.025 mg Cannabigerolic Acid (CBGA)

Clear Mandate from USP 2020 Convention Members

Resolution 10 – Cannabis

USP will leverage its scientific expertise and convening power to collaborate with stakeholders and develop fit-for-purpose scientific resources and solutions that will help address quality-related concerns as well as support additional scientific research on cannabis, cannabis-derived products, and cannabis-related compounds.
USP public policy statement:

“The complexity and the challenge of ensuring safe products demand efforts by all concerned organizations. USP encourages all interested stakeholders and organizations committed to quality such as AOAC, AHP and ASTM, to support the exploration of science-based standards to help ensure product quality, and thereby advance our common goals of protecting and promoting public health.”

https://www.usp.org/dietary-supplements-herbal-medicines/cannabis
ASTM Standards

Scope:

The development standards and guidance materials

Subcommittees:

- Indoor and Outdoor
- Horticulture and Agriculture
- Quality Management
- Systems
- Laboratory
- Processing and Handling
- Security and Transportation
- Personnel Training,
- Assessment, Credentialing
- Terminology
AOAC Activities

CASP Objectives

• Facilitate a forum where the science of cannabis analysis can be discussed.
• Provide a home for the development and maintenance of cannabis standards and methods.
• Develop reference materials.
• Establish a proficiency testing program.
• Provide analytical and laboratory management training, in particular ISO accreditation training.
Proposed Comprehensive Safety Review – Oral CBD

Impetus for proposing to perform the review:

- In their March 2020 report to the U.S. House and Senate Committees on Appropriations, FDA stated that, “FDA is actively considering potential pathways for certain CBD products to be marketed as dietary supplements and is interested in data on safety of CBD.”

- USP is seeking stakeholder perspectives about forming an Expert Panel to perform a comprehensive safety review of oral CBD

- USP proposes to take the following points into consideration:
  - Only orally ingested CBD to be included in the review (criterion for dietary supplements)
  - Properties of different formulations that are available
  - Variable quality and grades available: CBD in “full-spectrum” cannabis extract; “broad-spectrum” extract, CBD distillate, CBD in oil, pure CBD isolate
  - Evaluate assessments done by others and liaise with interested parties in industry, academia and regulatory bodies
Thank You

Empowering a healthy tomorrow