USP Dietary Supplement Stakeholder Forum
Thursday, May 28, 2020

Standards and Information for Hemp and CBD

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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 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

Supplement Facts
Serving Size: 15 Drops (1mL)
Servings per container: 30

Amount per serving		
Calories		8
		%DV
Total Fat	0.9g	2%
Hemp seed oil	876mg	**
Omega-3 fatty acids	158mg	**
Omega-6 fatty acids	551mg	**
Omega-9 fatty acids	105mg	**
Cannabidiol (CBD) (from hemp extract)	20mg	**

**Daily Value not established

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 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 Δ^9-Tetrahydrocannabinol (Δ^9-THC, or Dronabinol)
#1089149 Cannabidiol (CBD)
#1089161 Cannabidiol Solution

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)

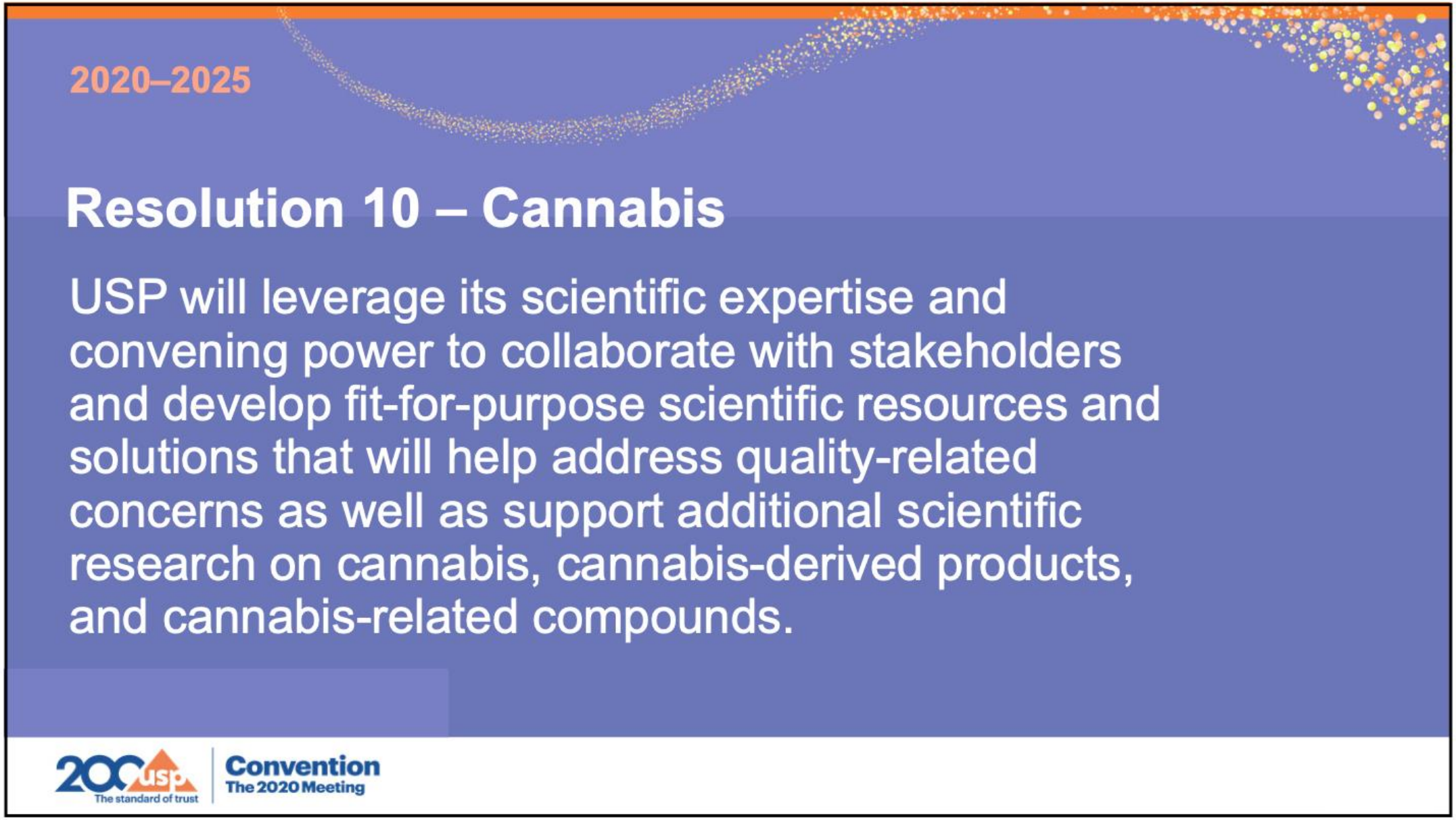
USP Cannabinoids Mixture RS

1 mL (1 mg/mL in methanol) [Catalog # 1089183]:

- 0.075 mg Delta-9-Tetrahydrocannabinol (Δ^9-THC)
- 0.025 mg Delta-8-Tetrahydrocannabinol (Δ^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)

Sarma et al. 2020. Cannabis inflorescence for medical purposes—USP considerations for quality attributes. *Journal of Natural Products* 83: 1334-1351.Open access, with 31 pp. of additional supporting information, available at: https://pubs.acs.org/doi/abs/10.1021/acs.jnatprod.9b01200

Clear Mandate from USP 2020 Convention Members



Need for Collaborative Work

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

STANDARDIZATION NEWS

UPDATE
TECHNICAL COMMITTEES AT WORK

D37/Cannabis

Industrial Hemp

A new ASTM International subcommittee will focus on industrial hemp. The group (D37.07) is part of ASTM's newly formed cannabis committee (D37).

According to organizers, the subcommittee plans to develop practices and guides relevant to industrial hemp, a variety of the cannabis sativa plant species. Industrial hemp is used for many applications, including food, natural health products, animal feed, and nonconsumable products such as insulation, fabrics, and concrete.

"The cannabis committee is excited to expand our existing portfolio and begin developing standards in a new area of need identified by our members," said committee chairman Ralph M. Paroli, Ph.D., director of R&D in metrology at the National Research Council of Canada.

The next meeting of the committee on cannabis is Jan. 27-29, 2019, in Houston, Texas.

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6 ASTM Standardization News www.astm.org/sn

D37/Cannabis

Proposed Cannabis Standards Under Development

ASTM International's committee on cannabis (D37) is currently developing several proposed standards, including the following.

Corrective Action/Preventive Action
Proposed standard WK60084 will help organizations in the industry to develop their own internal corrective action/preventive action processes and procedures. CAPA systems are a key part of quality management, according to committee members.

Specifically, CAPA systems focus on investigating, understanding, and correcting discrepancies to prevent recurrence of undesired issues such as laboratory testing failures, product complaints, and product non-conformance.

CAPA systems support formalized quality management systems that document processes, procedures, and responsibilities for achieving key objectives. These systems also help coordinate and direct an organization's activities to meet customer and regulatory requirements.

Laboratories in the Cannabis Industry
WK63913 will provide recommendations for laboratories involved in the industry.

According to members, the proposed standard will outline best lab practices, recommended certifications, various types of analyses, and the quality assurance functions for labs working with cannabis. Cary Black, consultant for Orion GMP, added that the standard will address issues that may be unique to such labs, including personnel, security, sample handling and disposal, and data management and reporting.

"Whether it be the determination of purity, levels of pesticides or terpenes, or other analytes, consistent procedures across the industry are required," says Black.

Laboratories analyzing products the cannabis industry will find the standard useful as it aims to repr best practices across the industr with strategies that are consisten with various regulatory agencies governing bodies.

Industry Guidelines for Cannabis Recalls
WK63546 will outline how producers can respond when products need to be recalled or removed from the market.

ASTM International member Cary Black, a consultant at Orion GMP, notes that many cannabis products are designed for human consumption, so product safety and quality are critical to doing business in the industry.

"We want this standard to provide clear, step-by-step guidelines as a protocol for effective recall or removal," says Black. "This could help us address compliance with various regulatory agencies."

Quality Management Systems
WK61355 will be a guide for quality management systems that provide a framework for organizations dealing with cannabis consumer products.

The proposed standard will be a guideline to show an organization's ability to provide cannabis-related products or services that meet consumer safety standards along with local and state regulatory requirements.

"This guide is meant to foster strong quality management systems regarding cultivation, processing, packaging, labeling, testing, and distribution activities in both the medicinal and recreational industries," says James Gianoutsos, president of the Emerald Regulatory Group.

Regulatory bodies could potentially use this standard to ensure organizations that are involved with cannabis-related consumer products abide by guidelines to produce quality-first products, he says.

The next meeting of ASTM International committee on cannabis is Jan. 27-29, 2019, in Houston, Texas.

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September/October 2018 September/October 2018 www.astm.org/sn ASTM Standardization News 7

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