



The Supplement Fall Newsletter 2018



New Online Dietary Supplements Compendium Coming in 2019!

[Dietary Supplements Compendium 2019 Edition](#)

To align with user needs and expectations, the Dietary Supplements Compendium (DSC) 2019 Edition will be an online platform, similar to *USP-NF*. The redesigned, intuitive interface will give users access to the most comprehensive collection of quality standards for dietary supplements. Click on the [link](#) for more details.

The new edition of the DSC will be available in the second half of next year. **Please check back at <https://www.usp.org/products/dietary-supplements-compedium> and [sign up](#) for the latest information about upcoming enhancements and availability!**

In addition to selected new and revised monographs and general chapters from the USP-NF and Food Chemicals Codex issued over the last three years, the DSC 2019 will feature:

- 24 new and 45 revised Admission Evaluations documents

New Dietary Supplements Reference Standards:

Below is a list of recently released Reference Standards:

Botanicals

- [European Elder Berry Dry Extract](#)
- [Coffee Fruit Dry Extract](#)

Non-Botanicals

- [Cobamamide](#)
- [Citicoline Sodium](#)

Reference Standards Coming Soon:

Botanicals

- *Angelica sinensis* Root Powder
- Baicalein
- Baicalein 7-O-Glucuronide
- *Scutellaria baicalensis* Root Dry Extract

- 21 new and 12 revised sets of data in support of the dietary supplement monographs with dozens of new chromatograms and color photomicrographs
- A total of 59 new, updated and supplementary High-Performance Thin-Layer Chromatographic sets of data for the botanical monographs in full color and high resolution
- A new edition of the USP Dietary Supplements Verification Program (DSVP) manual
- Revised and updated Dietary Intake comparison tables
- New and updated guidance documents contributed by the DS industry associations
- An extensive collection of FDA documents relevant to the dietary supplement industry

USP is working with an Advisory Board of fourteen USP volunteers, chaired by Dr. Craig Hopp, to understand the needs of our customers and stakeholders to develop a comprehensive and user-friendly standards resource. The new edition reflects our commitment to high-quality public standards for dietary supplements, and ongoing efforts keep our monographs and general chapters up to date. For questions or more information, please contact DietarySciStaff@USP.org.

Upcoming Events and Meetings

If you're attending SupplySide West from November 6-10, 2018, please stop by USP's booth (#3428) to learn about our tools for GMP compliance which include USP's documentary and Reference Standards as well as audit and ingredient verification services. Not attending SupplySide West? No worries. Just visit <http://www.usp.org/dietary-supplements-herbal-medicines> to learn about USP products and services for dietary supplements.

Quality Leadership

USP & FDA Co-Sponsored Workshop on DNA Standards for Botanical Identification

The FDA and USP co-sponsored a [workshop on DNA Standards for Botanical Identification](#) on August 21-22

- Senkyunolide A
- Z-Ligustilide

Non-Botanicals

- Annatto Seed Tocotrienols Extract
- beta- Glycerylphosphoryl choline
- L-alpha-glycerophosphoryl ethanolamine
- L-alpha-Glycerylphosphoryl-choline
- L-alpha-Glycerylphosphoryl-choline Solution

Reference Standards in Development

Botanicals

- Aegle marmelos Fruit Dry Extract
- Broccoli Seed Dry Extract
- *Chrysanthemum indicum* Flower Dry Extract
- *Chrysanthemum x morifolium* Flower Dry Extract
- *Coptis chinensis* Rhizome Dry Extract
- Coptisine Chloride
- Cranberry Fruit Juice Dry Extract
- Epicatechin
- Ginger Rhizome Carbon Dioxide Soft Extract
- Glucoraphanin
- Guarana Seed Dry Extract
- Isochlorogenic Acid A
- *Ligusticum chuanxiong* Rhizome Powder
- Linarin
- Maca root

that was attended by participants from academia, industry, testing labs and regulators. The objective of this workshop was to discuss current DNA-based technologies useful for botanical identification, stakeholder experiences and needs for implementing DNA methods as a routine quality assurance tool. Discussions at USP events in 2014 and 2016 suggested that DNA-based methods could be used for identification of botanical articles if “validated” and that orthogonal botanical or chemical methods should be used to complement the DNA-based methods.

At the 2018 workshop, speakers presented current technologies, their capabilities and limitations, and ways to appropriately interpret the outcomes. There was robust discussion about potential paths forward for appropriate use of the DNA-based methods. The need for transparency and guidelines was reiterated throughout the meeting. The keynote speakers shared insights on the botanical systematic classifications and implications for proper validation of methods, and the value of appropriate positive and negative controls. Some of the discussion points included the following:

1. The questions “Is this species X?” and “What is this ingredient?” are two different questions that call for different methods and different validation requirements. USP’s compendial approach would provide specific methods and acceptance criteria to determine if an ingredient meets the identity requirements for the species claimed on the product label. DNA-based methods may help with species identification, depending on the nature of the matrix (fresh raw material, powdered material or an extract).
2. DNA-based methods have promise in identifying botanicals with the analytical attributes of specificity and sensitivity in discriminating between closely related species, known adulterants (such as *Digitalis lanata*), and allergens (such as nuts).
3. FDA Regulations (21CFR111.75) require that at least one scientifically valid test is used to identify dietary ingredients, but more than one method is often required since no single method can measure enough attributes to identify a complex botanical material. The speakers discussed the validation requirements (specificity, sensitivity and precision) and the challenges of potentially conflicting results from the

- Maca root extract
- Pomegranate Fruit Dry Extract
- Procyanidin A2
- Procyanidin B2
- Punicalagin
- Senkyunolide A
- Z-Ligustilide
- *Angelica sinensis* Root Powder
- *Berberis aristata* Stem Dry Extract
- Chebulagic Acid
- Isorhamnetin-3-O-Rutinoside
- Marmelosin
- Palmatine Chloride
- *Sophora japonica* Flower Dry Extract
- *Terminalia chebula* Fruit Dry Extract

Non-Botanicals

- Choline Citrate
- Citicoline
- Conjugated Linoleic Acids--Triglycerides
- Docosahexaenoic Acid
- Eicosapentaenoic Acid
- Omega-3 Free Fatty Acids
- Pyrroloquinoline quinone

[Find a Reference Standard](#)

[Suggest a Reference Standard](#)

Monographs

Standards Open for Public Comment until November 30, 2018

The standards below were published in PF 44(5) for public comment on September 1, 2018 and will receive and are open for comments until

“orthogonal” methods. Speakers stressed the need for appropriate guidelines to conduct out-of-specification (OOS) investigations in using DNA-based methods to avoid inaccurate outcomes.

4. Case studies illustrated the promises and challenges in using new targeted and non-targeted technologies such as adapter ligation – PCR amplification, meta barcoding using next-generation sequencing, mobile platforms for genetic testing, multiplex PCR, droplet digital PCR, and whole genome sequencing. The studies indicate that DNA methods alone cannot provide definitive identification and that additional testing methods are needed.

5. The workshop session on solutions to the challenges discussed guidelines for appropriate vouchered samples and reference materials for validation of the DNA-based methods. Speakers suggested an update to the USP General Chapter <563> *Identification of the Articles of Botanical Origin* to provide transparent public standards.

6. Appropriate use of data in the GenBank database and the need for transparency of acceptance criteria were emphasized. Correct sequence data and curated databases help ensure accurate identification.

7. The participants highlighted the need for collaborative studies for validation of the DNA-based methods that consider the complexities of the botanical ingredients. The challenge with lack of data for validation of DNA-based methods was discussed.

By bringing together speakers and participants from academia, industry, testing labs and regulators, the workshop offered the opportunity for participants to hear about the challenges and promises associated with DNA methods for botanical identification. The learnings from the workshop will help USP develop transparent, science-based public standards in the form of species-specific methods, guidelines and suitable genomic or botanical Reference Standard Materials.

The speaker presentations and the notes from the 2-day workshop are available at <http://www.usp.org/events-training/workshops/dna-standards-botanical-identification>

November 30, 2018. To comment, please visit: <http://www.usp.org/usp-nf/pharmacopeial-forum>

New Monographs

- Bael Tree Fruit
- Bael Tree Fruit Dry Extract
- Bael Tree Fruit Powder
- Cobamamide
- *Coptis* Species Rhizome
- *Coptis* Species Rhizome Dry Extract
- *Coptis* Species Rhizome Powder
- Indian Barberry Stem
- Indian Barberry Stem Dry Extract
- Indian Barberry Stem Powder
- *Terminalia chebula* Fruit
- *Terminalia chebula* Fruit Dry Extract
- *Terminalia cheubla* Fruit Powder

Revised Monographs

- Cystine

Standards Open for Public Comment until January 31, 2019

The standards below were published in PF 44(6) for public comment on November 1, 2018 and are open for comment until January 31, 2019. To comment, please visit: <http://www.usp.org/usp-nf/pharmacopeial-forum>

New Monographs

- Japanese Sophora Flower
- Japanese Sophora

USP Botanical ID Methodology Tests

The USP Education course on Botanical ID Methodology Tests took place on August 22, 2018 at USP headquarters in Rockville, MD. This course offered an overview of the identification methodologies included in USP General Chapters <563> *Identification of Articles of Botanical Origin* and <203> *HPTLC Procedure for Identification of Articles of Botanical Origin*, which in turn are referenced in proposed USP monographs. The module focus on the orthogonality of the different identification methodologies and the applications of the various types of USP Botanical Reference Standard Materials (powered plants, fractions, extracts and pure compounds) in chromatographic fingerprinting, system suitability, and purity and limit tests. This course is also offered online. [Click here to register to view this on-demand course.](#)

Topics covered were:

- Botanical identification, including illustrated examples of the macroscopic and microscopic identification of different plant parts
- Chemical identification, including HPTLC and HPLC chromatographic examples of specific botanical monographs that allow species differentiation and other anti-adulteration provisions
- Adulteration of botanical articles, describing the different types of adulteration, detection methodologies, cases of botanical adulteration (i.e., boosting, substitution and marker compound addition), as well as different cases and examples of functional adulteration (e.g., erectile dysfunction, weight loss and sports supplementation)

USP at AOAC 132nd Annual Meeting and Exposition (August 24-30, 2018, Toronto, Canada)

USP Dietary Supplement colleagues and volunteers were key participants at the 132nd AOAC International Annual Meeting in Toronto, which was held August 24-30. Gabriel Giancaspro, Ph.D., Vice President of Dietary Supplements and Herbal Medicines at USP, co-chaired and spoke at a symposium on Protein Qualitative and Quantitative Analysis, discussing USP's approach to development of a soy protein monograph. Dr. Giancaspro also presented at a

Flower Dry Extract

- Japanese Sophora Flower Powder

Revised Monographs

- Cholecalciferol
- Ergocalciferol
- Calcium with Vitamin D and Minerals Tablets
- Calcium with Vitamin D Tablets
- Oil- and Water-Soluble Vitamins Tablets
- Oil- and Water-Soluble Vitamins with Minerals Tablets
- Oil Soluble Vitamins Tablets
- Oil Soluble Vitamins with Minerals Tablets
- Vitamin A Tablets– in progress
- Water-Soluble Vitamins Tablets
- Water-Soluble Vitamins with Minerals Tablets

Standards Open for Public Comment until March 31, 2019

The standards below will be published in PF 45(1) for public comment on Jan 1, 2019 and will receive and consider feedback until March 31, 2019. To comment, please visit:

<http://www.usp.org/usp-nf/pharmacopeial-forum>

Revised Monographs

- Chrysanthemum Flower
- Chrysanthemum Flower Powder
- Chrysanthemum Flower Dry Extract
- Wild Chrysanthemum Flower
- Wild Chrysanthemum

symposium on Qualification of Certified and In-House Botanical Reference Materials for Intended Use in Botanical Identification. The two-day pre-conference session addressed SMPRs (Standard method performance requirements) for the following ingredients: Echinacea, ginseng, kavalactones, skullcap, ginger, *Aloe vera*, SAMe, and vitamin B12. Drs. Paula Brown, and Aniko Solyom and Anton Bzhelyansky participated on the Expert Panel Reviews.

USP Admission Evaluations of Articles Prior to Monograph Development

Before a dietary ingredient is considered for the development of quality standards, it undergoes a USP Admission Evaluation, performed by the USP Dietary Supplements Admission Evaluations Joint Standard Setting Subcommittee (DSAE JS3). The DSAE JS3 reviews information related to the ingredient's safety, relevance in the market, regulatory status, and presence in other pharmacopeias and whether the article poses any serious risk to health when used as a dietary supplement.

If the article does not pose a serious risk to health, or poses a minor safety concern that can be mitigated by a label caution statement in the monograph, the article is placed in class A, meaning that it is admitted for monograph development. If the article poses a serious risk to health, it is placed in class B and is not admitted for monograph development.

The DSAE JS3 held a working meeting on Thursday, August 23, 2018 where members considered and admitted Wild Chrysanthemum Flower and Omega-3 Free Fatty Acids for monograph development. The committee recommended that the USP monographs include a cautionary labeling statement stating that "Dosage forms prepared with this article should bear the following statement: Wild chrysanthemum flower and extract may cause rare allergic reactions, rashes, or aggravate asthma, especially in those who are allergic to other members of the daisy family."

Adam Hussein a Pharm.D candidate from Howard University was in the department as a summer intern and completed the admission evaluation of Chinese Skullcap Root which will be considered for admission

- Flower Powder
- Wild Chrysanthemum Flower Dry Extract
- Glycine

New Monographs under Development

Botanicals

- Ajowan Fruit
- Ajowan Fruit Powder
- Ajowan Fruit Dry Extract
- Broccoli Seed Dry Extract
- Cranberry Fruit Juice Dry Extract
- Cranberry Fruit Juice Concentrate
- Cranberry Fruit Dry Juice
- Feverfew leaf extract
- Pomegranate Fruit Dry Extract
- Pummelo Peel
- Pummelo Peel Flavonoids Dry Extract
- Pummelo Peel Powder
- Red Clover Tablets
- Sour Jujube Seed
- Sour Jujube Seed Dry Extract
- Sour Jujube Seed Powder
- White Peony Root
- White Peony Root Powder

Non-Botanicals

- 3-hydroxy-3-methylbutyric acid (HMB)
- Calcium 3-hydroxy-3-methylbutyrate
- Calcium Magnesium Citrate
- Choline Citrate
- D-*chiro*-Inositol
- Lutein Esters
- Native Collagen
- Oil- and Water-Soluble Vitamins Premixes
- Oil-Soluble Vitamins

at the next meeting on November 30 2018.

For more information, please contact Hellen Oketch-Rabah, Ph.D., at hao@usp.org

Nomenclature of Dietary Supplements

Updates from the Dietary Supplements and Herbal Medicines (DSHM) Nomenclature Subcommittee

The Dietary Supplements and Herbal Medicines Nomenclature Joint Subcommittee (DSHM Nom JSC)

held a working meeting on August 7th, 2018 recommended to the USP Nomenclature and Labeling EC the following monograph titles for approval.

- Cranberry Whole Fruit Powder
- Cranberry Fruit Pomace Dry Extract
- Cranberry Fruit Pomace Powder
- Indian Elecampene (Root, Root Powder and Root Dry Extract)
- Chirata (Whole Plant, Whole Plant Powder and Whole Plant Dry Extract)
- Indian Kudzu (Tuber, Tuber Powder and Tuber Dry Extract)
- White Peony (Root, Root Powder and Root Dry Extract)
- Feverfew Leaf Dry Extract and Green Tea Leaf Dry Extract

The following monograph titles were changed: Cranberry Liquid Preparation changed to Cranberry Fruit Juice; Asian Ginseng Extract changed to Asian Ginseng Root and Rhizome Dry Extract.

For more information on dietary supplements nomenclature, please contact: Hellen Oketch-Rabah, Ph.D., at hao@usp.org

USP Answers Your Questions

Q. How does USP define **Temperature and Storage** conditions?

A. Conditions related to appropriate temperature and storage are defined in USP General Chapter <659> *Packaging and Storage Requirements*. Below are some definitions of key terms related to this area:

Freezer: A place in which the temperature is controlled between -25° and -10° (-13° and 14° F). It is noted that, in some instances, articles may have a recommended storage condition below -20° (-4° F). In such cases, the temperature of the storage location should be controlled to $\pm 10^{\circ}$.

Refrigerator: A cold place in which the temperature is controlled between 2° and 8° (36° and 46° F).

Cold: Any temperature not exceeding 8° (46° F).

Cool: Any temperature between 8° and 15° (46° and 59° F). [Note—An article for which

Premixes

- Oil-and Water-Soluble Vitamins with Minerals Chewable Gel
- Phytosterol Esters
- Plant sterols
- S-Adenosyl-L-Methionine 1,4-Butanedisulfonate
- Tocotrienols
- Water-Soluble Vitamins Premixes
- Zeaxanthin Preparation

storage in a cool place is directed may, alternatively, be stored and shipped as refrigerated, unless otherwise specified by the individual monograph.]

Room temperature (also referred to as Ambient temperature): The temperature prevailing in a working environment.

Controlled room temperature: The temperature maintained thermostatically that encompasses the usual and customary working environment of 20°–25° (68°–77° F). The following conditions also apply:

- Mean kinetic temperature not to exceed 25°.
- Excursions between 15° and 30° (59° and 86° F) that are experienced in pharmacies, hospitals, and warehouses, and during shipping are allowed.
- Provided the mean kinetic temperature does not exceed 25°, transient spikes up to 40° are permitted as long as they do not exceed 24 h.
- Spikes above 40° may be permitted only if the manufacturer so instructs.

Articles may be labeled for storage at “controlled room temperature” or at “20°–25°”, or other wording based on the same mean kinetic temperature [see also [Good Storage and Distribution Practices for Drug Products](#) § 1079, [Quality Management System](#), [Environmental Management System](#), [Mean Kinetic Temperature \(MKT\) Calculation](#)].

An article to be stored at *Controlled room temperature* may be stored and shipped in a cool place or refrigerated, unless otherwise specified in the individual monograph or on the label.

Warm: Any temperature between 30° and 40° (86° and 104° F).

Excessive heat: Any temperature above 40° (104° F).

Dry place: A site that does not exceed 40% average relative humidity at 20° (68° F) or the equivalent water vapor pressure at other temperatures. The determination may be made by direct measurement at the site. Determination is based on NLT 12 equally spaced measurements that encompass a season, a year, or, where recorded data demonstrate, the storage period of the article. There may be values of up to 45% relative humidity, provided that the average value does not exceed 40% relative humidity. Storage in a *Container* validated to protect the article from moisture vapor, including storage in bulk, is considered a *Dry place*.

Protect from freezing: The *Container* label will bear an appropriate instruction to protect the article from freezing in cases where freezing exposes an article to loss of strength or potency or to destructive alteration of its characteristics. These risks are present in addition to the risk that the *Container* may break if exposed to freezing temperatures.

Protect from light: Where light subjects an article to loss of strength or potency or to destructive alteration of its characteristics, the *Container* label bears an appropriate instruction to protect the article from light. The article must be packaged in a light-resistant *Container*.

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