



# The Supplement Summer Newsletter 2018



## Coming Soon!

### The 2018 Edition of the USP *Dietary Supplements Compendium*

The 2018 edition of the *Dietary Supplements Compendium (DSC)* will be available by the end of this year. Please keep checking back at: <http://www.usp.org/products/dietary-supplements-compendium> to order. It is being offered as a searchable, downloadable file for a reduced rate of \$150 and precedes a new online platform to be available after mid 2019. Should you still be interested in purchasing a print edition, copies of the 2015 *DSC* remain and will be available to order for \$425 until the new edition is launched

In addition to the new and revised monographs and general chapters from the *USP-NF* (First Supplement to USP41-NF36) and *Food Chemicals Codex (FCC)* (11th Edition), the new *DSC* 2018 includes:

- 24 new and 45 revised Admission Evaluations documents
- 21 new and 12 revised sets of data in support of the dietary supplement monographs with dozens of new chromatograms and color photomicrographs
- 59 new, updated and supplementary high-performance thin-layer chromatographic sets of data for botanical monographs in full color and high resolution
- A new edition of the revised USP Dietary Supplement Verification Program (DSVP) manual
- Significantly revised and updated Dietary Intake comparison tables
- New and updated guidance documents contributed by dietary supplement industry associations
- A substantial collection of FDA documents relevant to the dietary supplement industry

Led by an advisory board of fourteen USP volunteers, chaired by Dr. Craig Hopp, USP staff assembled this comprehensive resource with our customers and stakeholders in mind. Issuance of the new edition demonstrates USP's commitment to the development of high-quality public standards for dietary supplements, and an ongoing effort from USP to keep its monographs and general chapters current and relevant. The *DSC* is

#### New Dietary Supplements Reference Standards:

##### Botanicals

- [Ashwagandha Aerial Parts Dry Extract](#)
- [Kaempferol-3-O-Robinoside-7-O-Glucoside](#)

##### Non-Botanicals

- [Carotenes](#)

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#### Reference Standards Coming Soon:

##### Botanicals

- [Angelica sinensis Root Powder](#)
- [Senkyunolide A](#)
- [Z-Ligustilide](#)

##### Non-Botanicals

- [Annatto Seed Tocotrienols Extract](#)
- [beta-Glycerolphosphorylcholine](#)
- [Cobamamide](#)
- [L-alpha-glycerophosphorylethanolamine](#)
- [L-alpha-Glycerolphosphorylcholine](#)
- [L-alpha-Glycerolphosphorylcholine Solution](#)

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#### Reference Standards in Development

##### Botanicals

expected to be available by the end of this year. Keep checking [the website for availability information](#).

## Upcoming Workshops and Courses

### USP & FDA Co-Sponsored Workshop on DNA Standards for Botanical Identification – Register Today!

USP Rockville, MD | August 21-22, 2018

Join USP and the U.S. Food and Drug Administration (FDA) for this co-sponsored event which will bring together industry experts at USP headquarters for a two-day workshop on botanical identification techniques using DNA methods.

Keynote speakers include Dr. Damon Little with the New York Botanical Gardens and Dr. Caroline Howard with the British Pharmacopeia – National Institute for Biological Standards and Control.

Drs. Sara Handy and Caroline Puente-Lelievre with the FDA, will discuss genomic approaches to botanical identification and development and validation of real time PCR assays for allergen detection.

Topics will include:

- New developments in DNA technologies for botanical identification
- Using DNA testing as routine QA methodologies
- Regulatory approaches and industry experiences with DNA botanical identification techniques
- Challenges with the varying outcomes from use of multiple genomic identification methods and guidelines to compare results from these technologies
- Possible solutions to the challenges associated with voucher specimens and public databases
- Performance requirements for validation of DNA methods
- Potential development of reference standards for identification of botanical articles using DNA technologies

In addition, USP is offering a training course on USP botanical ID methodology tests immediately following the workshop. Participants will gain an overview of the botanical identification methodologies codified in the USP monographs and General Chapters.

Don't miss this opportunity and save your seat by [registering now!](#)

### Botanical ID Methodology Tests (Classroom and Online) – Education Course

USP Rockville, MD | August 22, 2018

This course offers an overview of the botanical identification methodologies codified in USP's General Chapters and will also explore the importance of

- Baicalein
- Baicalein 7-O-Glucuronide
- Broccoli Seed Dry Extract
- *Chrysanthemum indicum* Flower Dry Extract
- *Chrysanthemum x morifolium* Flower Dry Extract
- *Coptis chinensis* Rhizome Dry Extract
- Coptisine Chloride
- Cranberry Fruit Dry Juice
- Cranberry Fruit Juice Dry Extract
- Epicatechin
- Ginger Rhizome Carbon Dioxide Soft Extract
- Guarana Seed Dry Extract
- Isochlorogenic Acid A
- Ligusticum chuanxiong Rhizome Powder
- Linarin
- Maca root
- Maca root extract
- Pomegranate Extract
- Procyanidin B2
- *Scutellaria baicalensis* Root 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

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#### Monographs

#### Standards Open for Public Comment until September 30, 2018

The standards below were published in PF 44(4) for public comment on July 1, 2018, and will receive and consider feedback until September 30, 2018. To

macroscopic and microscopic assessments. Numerous USP monograph examples and case studies in which incomplete compendial evaluation could invite adulteration will be examined.

[Click to register for the course today!](#)

## Quality Leadership



### 2018 Dietary Supplements Stakeholder Forum

Stakeholder input is essential to the development of USP dietary supplement standards. USP convenes stakeholder fora to facilitate interactions between USP and representatives from the industries that utilize the standards. These fora improve USP's ability to understand and address stakeholder needs, and offer opportunities to discuss compendial scientific and process topics.

On May 15, 2018, over 140 stakeholders attended the USP Dietary Supplements Stakeholder Forum. Participants representing manufacturers, trade associations, service providers, and other interested parties who work with dietary supplements shared perspectives and provided direct feedback on priority standards issues. USP staff provided updates to the action items from the **2017 meeting**, which include the ongoing work on the development of a glossary of commonly used USP terms, flexible adoption of modern procedures in USP standards, continued engagement with industry and regulators to advocate for broader adoption of limits for pesticide residues in General Chapter <561> ARTICLES OF BOTANICAL ORIGIN, and USP's engagement with the **Dietary Supplements Quality Collaborative** (DSQC).

Participants were informed about recently proposed new monographs, revisions and omissions in *Pharmacopeial Forum*. USP's prioritization algorithm and upcoming standards were also discussed.

USP staff and stakeholders presented updates and perspectives on the ongoing standards development activities related to cranberry, Quantitative Nuclear Magnetic Resonance (qNMR), probiotics, challenges for standards development using DNA-based methods for botanical identification, proteins, chewable gels (gummies), residual solvents and bioavailability.

comment, [please click here](#).

#### Revised Monographs

- Ascorbic Acid Chewable Gels
- Cholecalciferol Chewable Gels

#### General Chapter Revision

- <2091> Weight Variation of Dietary Supplements

#### Standards Open for Public Comment until November 30, 2018

The standards below will be published in PF 44(5) for public comment on September 1, 2018 and will receive and consider feedback until November, 2018. To comment, [please click here](#).

#### 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 chebula Fruit Powder

#### Revised Monographs

- Cystine

#### Standards Open for Public Comment until January 31, 2019

The standards below will be published in PF 44(6) for public comment on November 1, 2018 and will receive and consider feedback until January 31, 2019. To comment, [please click here](#).

Stakeholders were also encouraged to apply as expert volunteers through USP's Call for Candidates process for the 2020-2025 cycle of **USP Council of Experts**.

Detailed notes from the meeting and the speaker presentations **[are available here](#)**.



## GMP Compliance Workshop

On May 11, 2018, USP conducted a GMP workshop in Orem, UT, focused on the use of USP compendial tools and resources in facilitating compliance with dietary supplement GMP regulations. The class was conducted by Dr. John Atwater and Dr. Kit Goldman from USP, and Larissa Pavlick from the United Natural Products Alliance (UNPA). Attendees learned about the importance of FDA GMP regulations and the relatively new FDA Food Safety Modernization Act (FSMA) requirements for dietary supplements and dietary ingredients.

Attendees learned how USP compendial resources can be beneficial to their GMP quality control laboratory operations in establishing ingredient and dietary supplement specifications, qualifying analytical instrumentation, validating analytical test procedures, skip-lot testing (i.e. reduced) determination and implementation, and qualifying suppliers of components.

Click **[here to learn more about USP resources and services](#)**, including the USP verification services.



## USP in China at CPhI and

### New Monographs

- Citicoline
- Fish Oil Omega-3-Acid Concentrate–Ethyl Esters
- Japanese Sophora Flower
- Japanese Sophora 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
- Water-Soluble Vitamins Tablets
- Water-Soluble Vitamins with Minerals Tablets

### New Monographs under Development

#### Botanicals

- Broccoli Seed Dry Extract
- Cranberry Juice-Derived Powder
- Pomegranate 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

#### Non-Botanicals

- 3-hydroxy-3-methylbutyric acid (HMB)
- Calcium 3-hydroxy-3-methylbutyrate

## SupplySide

In June, USP exhibited at trade shows in China at both the Convention on Pharmaceutical Ingredients (CPHI) and the new SupplySide China. Dr. John Atwater, Sr. Director of Verification Services, conducted a workshop on “Verification of Dietary Supplements Quality” at CPHI and presented on “Compendial Tools for GMP Compliance” at SupplySide China.

USP’s suite of tools and services including our supplement and ingredient verification programs, GMP audit program, and Dietary Supplements Compendium and Reference Standards were featured prominently at both exhibitions.

## USP Admission Evaluations of Articles Prior to Monograph Development

Before a dietary ingredient is considered for the development of quality standards, it must undergo 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 via WebEx on Monday, May 21, 2018 where members considered and admitted Citicoline and Citicoline Sodium for monograph development. Members also considered Chrysanthemum Flower, Chrysanthemum Flower Powder and Chrysanthemum Flower Dry Extract, and determined these ingredients may be allergenic to some individuals. Therefore the committee recommended that the USP monographs include a warning label statement that reads as follows: Dosage forms prepared with these articles should bear the following statements: *“Chrysanthemum flower and extract may cause rare allergic reactions, rashes, or aggravate asthma, especially in those who are allergic to other members of the aster family.”*

This summer Adam Hussein, a Pharm.D. candidate from Howard University, will be working as an Intern on the admission evaluation of dietary supplement ingredients slated for monograph development.

For more information, please contact Hellen Oketch-Rabah, Ph.D., at [hao@usp.org](mailto:hao@usp.org).

- Calcium Magnesium Citrate
- Choline Citrate
- D-*chiro*-Inositol
- Lutein Esters
- Oil- and Water Soluble Vitamins Premixes
- Oil Soluble Vitamins 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

## Nomenclature of Dietary Supplements

### Updates from the Dietary Supplements and Herbal Medicines Nomenclature Subcommittee

In the period from March 31, 2018 to May 31, 2018, the Dietary Supplements and Herbal Medicines Nomenclature Joint Subcommittee (DSHM Nom JSC) held a working meeting on Tuesday, April 3, 2018 where the following monograph titles were discussed and recommended to the USP Nomenclature and Labeling EC for approval: Pummelo Peel, Pummelo Peel Powder and Pummelo Peel Flavonoid Dry Extract.

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

## USP Answers Your Questions

**Q.** We are an herbal extracts manufacturer and I have a question regarding the calculation for pesticides limits in herbal extracts. According to USP General Chapter <561> ARTICLES OF BOTANICAL ORIGIN, when establishing the limits of pesticides in botanical products: “If the article is intended for the preparation of extracts, tinctures, or other pharmaceutical forms of which the preparation method modifies the content of pesticides in the finished product, calculate the limits by the formula:

$$\text{Limits (mg/kg)} = \text{AME}/100\text{B}$$

where E is the extraction factor of the preparation method determined experimentally; and A, M, and B are as defined above.” What is the “extraction factor” and how can I determine it experimentally?

**A.** Factor E is calculated as the ratio between the content of the pesticide in the starting plant material/content of pesticide in the extract. Suppose that your extract manufacturing process enriches the content of pesticide in a ratio of 4:1. That is, your extract contains 4 times more pesticides than the original plant material. In this situation, the limit of pesticide for the starting plant material should be 4 times lower than the acceptable limit in the extract. Accordingly, if the safe limit for pesticide A in the extract is NMT 0.03 ppm, this value should be multiplied by  $E = 0.25$  and the suitable content of pesticide in the plant material should be NMT 0.0075 ppm. On the other hand, if your extraction process removes the pesticide in a ratio of 1:4, then you can multiply the safe limit by 4 to obtain the suitable limit of the pesticide in the plant material intended for extract preparation.

**Q.** In USP’s monographs for vitamins, why are there multiple test procedures listed for the determination of certain active ingredients?

**A.** A test in a monograph may contain and require multiple procedures. However, multiple procedures may be included in particular monographs, specifically for the purpose of assuring the availability of an appropriate procedure for a particular product. In such cases, a labeling statement to indicate the appropriate application of the procedure(s) will be included in the monograph. A labeling statement is not required if Test 1 is used.

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