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USP Dietary Supplements Stakeholder Forum  
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# Dietary Supplements Monographs Modernization Plan 2015-2020

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- General Guidelines
- Examples of Non-Botanicals
- Examples of Botanicals
- General Chapters

*In general, the modernization of a monograph can include:*

- The replacement of outdated technology with more current procedures,
- The addition of missing and the deletion of non-value added tests

*More specifically:*

- Removing tests that are now considered hazardous (odor tests and the use of toxic solvents),
- Ensuring the inclusion of secondary identification tests,
- Reducing the use of non-specific assays that yield weak identity data (titration, UV-Vis, wet chemistry, microbial assay),
- Replacing outdated technologies (TLC impurity process, packed column GC),
- Removing older procedures (melting point, pH) that are no longer considered to add value.



# Monograph Modernization: Examples of Non-Botanicals

## AMINO ACIDS

Monograph Title	Assay	Related Compounds/ Organic impurities	Identification Test	Others
ARGININE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	Remove Melting Range
ARGININE HYDROCHLORIDE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
LYSINE ACETATE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
LYSINE HYDROCHLORIDE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
CYSTEINE HYDROCHLORIDE	Titration to HPLC	add HPLC	Add HPLC ID test	
PHENYLALANINE	Titration to HPLC	add HPLC	Add HPLC ID test	Remove pH test
TYROSINE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
THREONINE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	Remove pH test
PROLINE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
SERINE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
CYSTINE	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
TAURINE	Nitrogen<461> to HPLC	TLC to HPLC	Add HPLC ID test	



# Monograph Modernization: Examples of Non-Botanicals

## VITAMINS

Monograph Title	Assay	Related Compounds/Organic impurities	Identification Test	Others
CHOLECALCIFEROL	HPLC (normal phase) to HPLC(reverse phase)	Add HPLC	Remove TLC test	
ERGOCALCIFEROL	HPLC (normal phase) to HPLC(reverse phase)	Add HPLC	Remove TLC test	
CYANOCOBALAMIN	UV to HPLC	n/a	Add HPLC ID test	
ASCORBIC ACID	Titration to HPLC	Add HPLC	Add HPLC ID test	
CALCIUM PANTOTHENATE	n/a	Add HPLC		
RACEMIC CALCIUM PANTOTHENATE	Nitrogen<461> to HPLC	Add HPLC	Add HPLC ID test	
FOLIC ACID	HPLC to UPLC	HPLC to UPLC	Add HPLC ID test	
RIBOFLAVIN	Fluorescence spectroscopy <853> to HPLC	Limit of Luviflavin, UV to HPLC	Add HPLC ID test	
DEXPANTHENOL	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
DEXPANTHENOL PREPARATION	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
PANTHENOL	Titration to HPLC	TLC to HPLC	Add HPLC ID test	
THIAMINE HYDROCHLORIDE	HPLC Hilic HPLC	HPLC to Hilic HPLC	Add HPLC ID test	Remove pH test
THIAMINE MONONITRATE	HPLC Hilic HPLC	HPLC to Hilic HPLC	Add HPLC ID test	Remove pH test
NIACINAMIDE	n/a	n/a		Remove Melting Range
ADENINE	HPLC to UPLC	HPLC to UPLC	n/a	
CALCIFEDIOL	n/a	add HPLC	Add HPLC ID test	



# Monograph Modernization: Examples of Non-Botanicals

## MINERALS

Monograph Title	Assay	Related Compounds/ Organic impurities	Identification Test	Others
SODIUM ASCORBATE	Titration to HPLC	add HPLC	Add HPLC ID test	Remove pH test
CALCIUM ASCORBATE	Titration to HPLC	add HPLC	Add HPLC ID test	Remove pH test
CALCIUM GLUCEPTATE	Titration to HPLC	n/a	Add HPLC ID test	Remove pH test
CALCIUM GLUCONATE	Titration to HPLC	n/a	Add HPLC ID test	
CALCIUM LACTATE	Titration to HPLC	n/a	Add HPLC ID test	
CALCIUM LACTOBIONATE	Titration to HPLC	n/a	Add HPLC test; remove TLC test	Remove pH test
CALCIUM LEVULINATE	Titration to HPLC	n/a	Add HPLC retention time	Remove Melting Range and pH tests
CHROMIUM PICOLINATE	UV to HPLC	n/a	Add HPLC ID test	
COPPER GLUCONATE	Titration to HPLC	n/a	Add HPLC test; remove TLC test	
FERROUS FUMARATE	Titration to HPLC	n/a	Add HPLC ID test	
FERROUS GLUCONATE	Titration to HPLC	n/a	Add HPLC ID test	
MAGNESIUM GLUCONATE	Titration to HPLC	n/a	Add HPLC ID test	
MAGNESIUM GLYCINATE	Titration to HPLC	n/a	Add HPLC ID test	
MANGANESE GLUCONATE	Titration to HPLC	n/a	Add HPLC ID test	
MANGANESE GLYCINATE	Titration to HPLC	n/a	Add HPLC ID test	
POTASSIUM CITRATE	Titration to HPLC	n/a	Add HPLC ID test	
POTASSIUM GLUCONATE	AA to HPLC	n/a	Add HPLC ID test	Remove TLC ID test
ZINC CITRATE	Titration to HPLC	n/a	Add HPLC ID test	
ZINC GLUCONATE	Titration to HPLC	n/a	Add HPLC ID test	



# Monograph Modernization: Examples of Botanicals

	<b>Conceptually</b>	<b>Monographs / Monograph Families</b>	<b>Assay</b>
<b>Powdered Ginkgo Extract</b>		Introduce a fast HPLC ID method for flavonols and flavonol glycosides conducted before and prior to hydrolysis.	Use a single HPLC method to quantitate flavonol aglycones, and the limit of rutin and quercetin. Ideally, using the same LC protocol as that used for Identification.
<b>St. John's Wort monograph family</b>	Evaluate the utility of using oxybenzone as a quantitative standard.	Enhance HPTLC identification to enable detection of dyes occasionally used as adulterants of SJW products.	
<b>Ginger family of monographs</b>	Re-evaluate the role and significance of shogaols in the total make-up of ginger 'bitter principles'.		Better and faster LC method.
<b>Saw Palmetto, Powdered Saw Palmetto</b>		Evaluate the significance and utility of the current TLC-GC identification procedure.	



# Monograph Modernization: Examples of Botanicals

Monographs / Monograph Families	Conceptually	Identification	Assay
<b>Ganoderma lucidum family of monographs</b>	Introduce methodologies for qualitative and quantitative assessment of beta-glucans	Presence and characterization of intact beta-glucans, without hydrolysis	Quantitative analysis of beta-glucans.
<b>Ginsengs (American Ginseng, Asian Ginseng, Tienchi Ginseng)</b>		Harmonize monographs and HPTLC methods	Harmonize HPLC methods
<b>Powdered Horse Chestnut Extract</b>			Quantitative HPLC method for content of Escins (Escin IA, Escin IB, Isoescin IA and Isoescin IB) against an Escin IA reference standard.
<b>Cinnamon, Maritime Pine Bark, Grapeseed Extract monographs</b>	Further investigation of qualitative/quantitative methodologies with a potential to address proanthocyanidins in numerous species.		





# Monograph Modernization: General Chapters

- **BOTANICAL**

<2030> SUPPLEMENTAL INFORMATION FOR ARTICLES OF BOTANICAL ORIGIN

<2232> ELEMENTAL CONTAMINANTS IN DIETARY SUPPLEMENTS

<2250> DETECTION OF IRRADIATED DIETARY SUPPLEMENTS

<203> HIGH PERFORMANCE THIN-LAYER CHROMATOGRAPHY PROCEDURE FOR IDENTIFICATION OF ARTICLES OF BOTANICAL ORIGIN

<1064> IDENTIFICATION OF ARTICLES OF BOTANICAL ORIGIN USING HIGH-PERFORMANCE THIN-LAYER CHROMATOGRAPHY PROCEDURE

<561> ARTICLES OF BOTANICAL ORIGIN

<563> IDENTIFICATION OF ARTICLES OF BOTANICAL ORIGIN

<565> BOTANICAL EXTRACTS

<2091> WEIGHT VARIATION OF DIETARY SUPPLEMENTS

<2750> MANUFACTURING PRACTICES FOR DIETARY SUPPLEMENTS

- **NON- BOTANICALS**

<115> DEXPANTHENOL ASSAY

<531> THIAMINE ASSAY

<171> VITAMIN B12 ACTIVITY ASSAY

<551> VITAMIN E ASSAY

<411> FOLIC ACID ASSAY

<571> VITAMIN A ASSAY

<441> NIACIN OR NIACINAMIDE ASSAY

<581> VITAMIN D ASSAY

<481> RIBOFLAVIN ASSAY

<91> CALCIUM PANTOTHENATE ASSAY

1. Prioritization of monographs and chapters in need of modernization
2. Obtaining procedures, impurity profiles and acceptance criteria from sponsors
3. Balancing the need to introduce modern methodology with the feasibility for global implementation

## Prioritization of monographs and chapters in need of modernization

USP has about 515 monographs for both non-botanicals and botanicals and about 23 general chapters related to Dietary Supplements. Prioritization is a challenge as we need to go through individual monographs, decide which monograph or group of monographs should be modernized first; review each test in the monograph and decide which test is outdated and need to be replaced, which test should be omitted, which test should be added, etc. Our Dietary Supplements Expert Committee has been involving in this prioritization task.

### Obtaining procedures, impurity profiles and acceptance criteria from sponsors

- For multiple manufacturer products, process-related impurities are often numerous and vary widely from manufacturer to manufacturer due to different starting materials and synthesis routes
- - Not all product-related impurities are captured in current monographs

Balancing the need to introduce modern methodology with the feasibility for global implementation

- TLC vs. HPTLC
- HPLC vs. UHPLC
- Traditional ID tests vs. NMR
- HPLC-UV non-derivatized samples vs. Amino Acid Analyzer for amino acid analysis



## What Should Industry Do?

1. Pay close attention to the monograph update process and raise concerns with USP
2. Enrolling in USP's compendial updates
3. USP is offering a new, free feature, PF Alert bimonthly webinars, issued in conjunction with the PF. The publication and the webinars are free



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A light gray world map is centered in the background of the slide, showing the continents of North America, South America, Europe, Africa, Asia, and Australia.

# Discussions



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# Thank You