Global Expertise
Trusted Standards
Improved Health

U.S. Pharmacopeial Convention

USP Dietary Supplements Standards Up-to-Date

Roundtable Meeting Report

Huy Dinh, MS.
Senior Scientific Liaison
Dietary Supplements

Roundtable's objectives

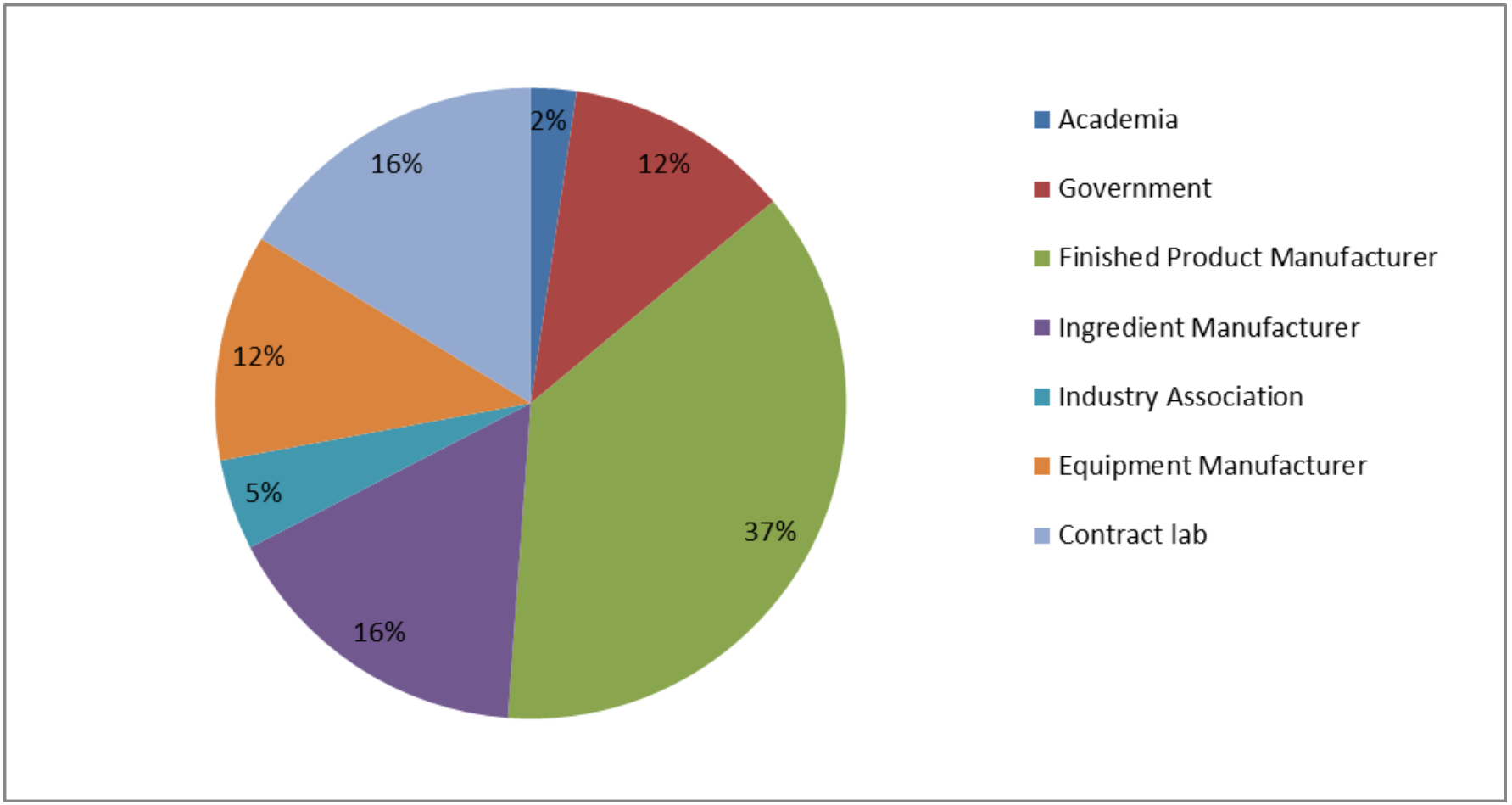
- Foster discussion among the participants to ensure that USP standards for dietary supplements are up-to-date, using current analytical procedures that are affordable, relevant, and can be effectively carried out by dietary supplement stakeholders in the next five years and beyond.

Roundtable Up-to-Date meeting

- Date: October 25, 2016
- Place: USP Headquarters, Rockville, MD
- Co-chairs:
  - Paula Brown (BCIT, BDSHM)
  - Aniko Solyom (GAAS Analytical, NBDS)
- USP staff:
  - Huy Dinh
  - Marie Temple

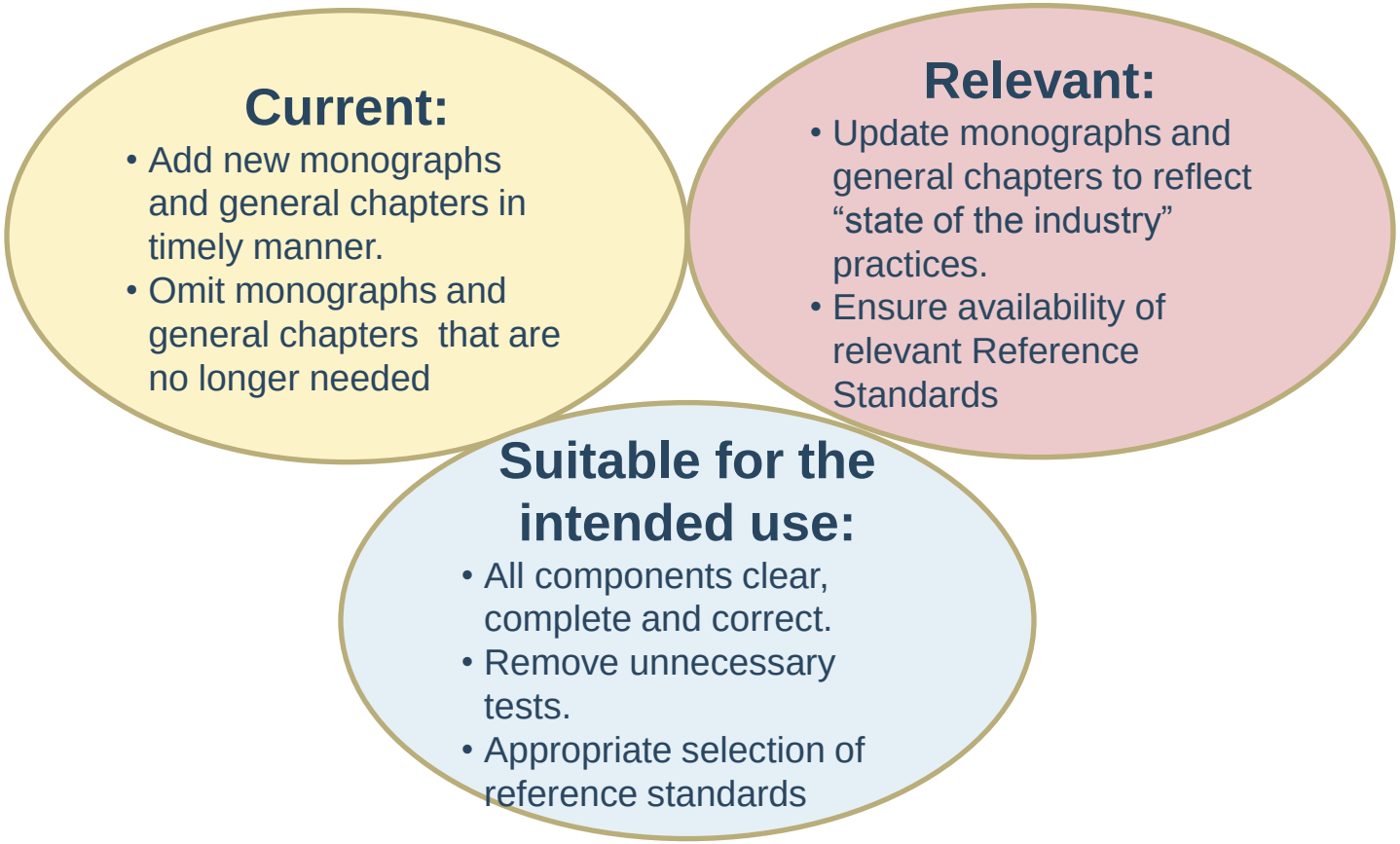
Roundtable Up-to-Date meeting

40+ invited, 27 attended (5 EC member)



Roundtable Up-to-Date Meeting

What is “Standards Up-to-Date”?



Roundtable Up-to-Date Meeting

Up-to-Date monographs would involve:

1. Replacing titration and UV based assays
2. Eliminating hazardous reagents and solvents
3. Replacing organoleptic tests
4. Replacing flame tests
5. Updating chromatography methods
    - TLC to HPTLC
    - HPLC vs. UHPLC
    - Packed GC columns vs. capillary GC
    - Obsolete columns vs. core-shell columns
    - Long running time
    - MS friendly mobile phases

Discussion Points

1. General chapters and monographs
   - Fit for purpose and aligned with regulatory requirements
   - Include modern methods using current science
   - Omission of old methods (wet chemistry, organoleptic)
   - Retain relevant old technologies while introducing new

2. Adulteration, consumer protection
   - UV methods vs. HPLC methods (specificity)
   - Adulteration with synthetic pharmaceuticals
   - Methods for pesticides, residual solvents
   - Adulteration Potential Database

Discussion Points

3. Communication

- Modernization efforts were mostly unknown
- How USP prioritize monographs?
- What is the role of EC-s?
- How USP handles comments submitted by the public?
- Differences between an official monograph and monograph under review

4. USP standards

- Share characterization and stability information with the public
- Include certified concentration values, potencies and chromatograms with peaks identified
- ISO certification of the USP standards

Discussion Points

5. New technologies
   - Replace wet chemistry tests
   - TLC to HPTLC
   - ICP for metal analysis
   - HPLC to UHPLC
   - DNA analysis
   - MS, LC-MS, QTOF, ATR-FTIR, NMR, chemometrics – very limited enthusiasm

Planning the compendial future for dietary supplements

- Increase transparency in the standards revision process
- Include validation data with a method
- Include HPLC chromatograms, pictures of HPTLC plates, fragmentation patterns, DNA information
- Consider providing RS-s in smaller quantities
- Seek existing methods adopted by other organizations and trade associations
- Reach out to companies and organizations to harmonize/integrate their own methods with those of USP

Ongoing DS Up-to-Date work at USP

1. Non-Botanicals

- Vitamins:
  - Cyanocobalamin, Hydroxocobalamin,Beta Carotene: added organic impurities test
  - Biotin: replaced titration with HPLC
  - Vitamin E: replaced packed column with capillary column
  - Calcium Pantothenate: replaced Nitrogen determination by Kjeldhal with HPLC Assay

Ongoing DS Up-to-Date work at USP

1. Non-Botanicals (continued)
   - Vitamins:
     - Niacin: replaced UV + TLC with HPLC Assay and organic impurities
   - Amino acids
     - Alanine, Methionine, Glycine, Aspartic Acid, Valine, Leucine, Isoleucine: the TLC for the Related compounds test has been replaced with HPLC. Other amino acids are in the works.

Ongoing DS Up-to-Date work at USP

2. Botanicals (cont'd)

- Identification tests
  - In agreement with Authorized Title, Definition, and Labeling
  - Must distinguish the plant material from related species that may pose potential for species substitution or adult
  - Use of new techniques
    - ✓ DNA method
    - ✓ HPTLC new chapters <203> and <1064>
    - ✓ Chromatographic and Spectroscopic procedures
- Assay/Content of marker constituents

DS Standards Up-to-Date– a continuous process

- **Public standards should evolve with scientific knowledge**
- **For Non-Botanicals Dietary Supplements**
  - Better and more specific separation methods
  - Impurity determinations
  - Isomerism
  - Performance Tests
- **For Botanicals Dietary Supplements**
  - DNA
  - Complementary tests,
  - HPTLC standardization
  - Fingerprinting
  - Chemometric/metabolomic techniques (MS, NMR, IR)

U.S. Pharmacopeial Convention

Global Expertise
Trusted Standards
Improved Health

QUESTIONS?