Title I (CQA)-Review of Quality Standards for Compounders

Jennifer Devine, Vice President, Global Legal Affairs, Standards, USP
Ruey C. Ju, Senior Advisor for Compounding Compliance and Enforcement, CDER, FDA

Caroline D. Juran, Executive Director, Virginia Board of Pharmacy
Alexander Pytlarz, Owner/Director of Pharmacy, The Compounding Center

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Working Toward Quality Compounded Drugs: Update on USP Compounding Standards

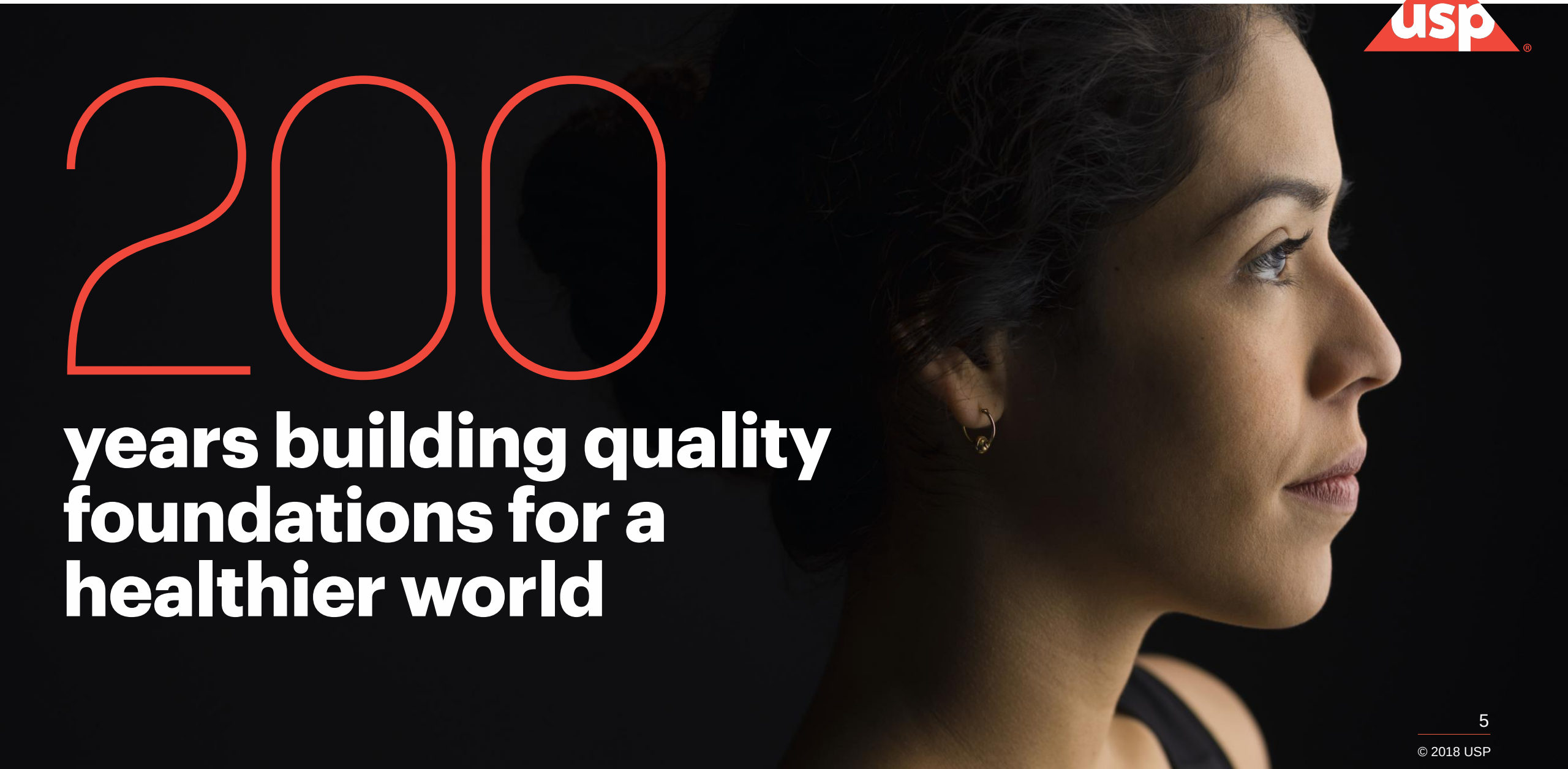
Jennifer Devine, J.D., Vice President, Global Legal Affairs

Mission

To improve global health through public standards and related programs that help ensure the quality, safety and benefit of medicines and foods

200

years building quality foundations for a healthier world



1,100+

employees worldwide

800

external experts

from industry, governments, nonprofits and academia

The experts behind our standards

2015–2020 Council of Experts

Healthcare Quality Standards Collaborative Group

- Nomenclature & Labeling
- Compounding
- Healthcare Quality

Chemical Medicines Monographs Collaborative Group

- Chemical Medicines Monographs 1
- Chemical Medicines Monographs 2
- Chemical Medicines Monographs 3
- Chemical Medicines Monographs 4
- Chemical Medicines Monographs 5
- Chemical Medicines Monographs 6

Biologics Collaborative Group

- B101 Peptides
- B102 Proteins
- B103 Complex Biologicals
- BIO4 Antibiotics
- GC Biological Analysis

Excipient Monographs Collaborative Group

- Excipient Monographs 1
- Excipient Monographs 2

Dietary Supplements/ Herbal Medicines/Foods Collaborative Group

- Non-Botanical Dietary Supplements
- Botanical Dietary Supplements & Herbal Medicines
- Food Ingredients

General Chapters Collaborative Group

- Chemical Analysis
- Physical Analysis
- Statistics
- Microbiology
- Dosage Forms
- Packaging & Distribution

2015 – 2020 Compounding Expert Committee

Chair: Gigi Davidson, B.S. Pharm, DICVP, NC State College of Veterinary Medicine (retired)
Vice Chair: Connie Sullivan, B.S. Pharm, National Home Infusion Association

Member	Affiliation
Lisa Ashworth, B.S. Pharm	Children's Health System of Texas
Gus Bassani, Pharm.D.	PCCA
Edmund Elder, Ph.D. , B.S. Pharm	University of Wisconsin-Madison
Ryan Forrey, Pharm.D., M.S.	Becton Dickinson
Deborah Houston, Pharm.D.	Novant Health - Kernersville Medical Center
Brenda Jensen, M.A.	Compounding Consultants, LLC
Patricia Kienle, MPA, B.S. Pharm	Cardinal Health

2015 – 2020 Compounding Expert Committee

Chair: Gigi Davidson, B.S. Pharm, DICVP, NC State College of Veterinary Medicine (retired)
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Member	Affiliation
William Mixon, B.S. Pharm	The Compounding Pharmacy
John Musil, Pharm.D.	Avella, Inc
David Newton, Ph.D.	Shenandoah University (retired)
Alan Parr, Pharm.D., Ph.D.	BioCeutics, LLC
Abby Roth, B.Sc.	Clinical IQ
Robert Shrewsbury, Ph.D.	UNC Eshelman School of Pharmacy
James Wagner	Controlled Environment Consulting
Brenda Yuzdepski, B.S. Pharm	Saskatoon Medical Arts Pharmacy

2015 – 2020 Compounding Expert Committee

Expert Consultants

Expert Consultants	Affiliation
Jane Axelrad	Axelrad Solutions, LLC
Dennis E. Doherty, MD, FCCP	University of Kentucky College of Medicine
Andrew Murphy, MD	Asthma Allergy and Sinus Center
Elizabeth Rebello, MD, FASA	The University of Texas MD Anderson Cancer Center
Allison T. Vidimos, R.Ph., M.D.	Cleveland Clinic

USP quality standards for compounded preparations

There are 3 types of standards for compounding:

- Monographs for ingredients used in compounded preparations
  - USP–NF Drug Substance Monographs
- Monographs for compounded preparations
  - Compounded Preparation Monographs
- Practice standards
  - General Chapters (e.g., <795> and <797>)

⟨797⟩ PHARMACEUTICAL COMPOUNDING–STERILE PREPARATIONS

INTRODUCTION

The objective of this chapter is to describe conditions and practices to prevent harm, including death, to patients that could result from (1) microbial contamination (nonsterility), (2) excessive bacterial endotoxins, (3) variability in the intended strength of correct ingredients that exceeds either monograph limits for official articles (see "official" and "article" in the *General Notices and Requirements*) or 10% for nonofficial articles, (4) unintended chemical and physical contaminants, and (5) ingredients of inappropriate quality in compounded sterile preparations (CSPs). Contaminated CSPs are potentially most hazardous to patients when administered into body cavities, central nervous and vascular systems, eyes, and joints, and when used as baths for live organs and tissues. When CSPs contain excessive bacterial

Public quality standards for compounded preparations

- <795> *Pharmaceutical Compounding – Nonsterile Preparations*
- <797> *Pharmaceutical Compounding – Sterile Preparations*
- <800> *Hazardous Drugs – Handling in Healthcare Settings*
- <1163> *Quality Assurance in Pharmaceutical Compounding*
- <1160> *Pharmaceutical Calculations in Prescription Compounding*
- <1168> *Compounding for Phase I Investigational Studies*
- <1176> *Prescription Balances & Volumetric Apparatus*

USP anticipated timeline for general chapter revisions

Note: The current version of General Chapters <795> and <797> published in USP-NF are official.

FDA-USP-stakeholders – developing standards

Stakeholders

USP actively seeks engagement with stakeholders throughout the standard-setting process through stakeholder meetings, advisory roundtables, and open-microphone webinars.

- Healthcare Practitioners
- Patients
- Academicians
- Healthcare Industry
- Regulatory Authorities
- Manufacturers

USP Process

1. Public Health Need
- Need identified by any stakeholder or USP
- Need evaluated for possible standard development

2. Draft Standard
- Best practices and scientific information collected

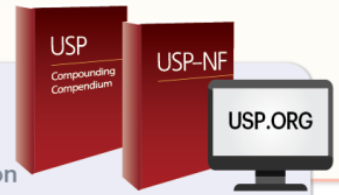
3. Public Comment Period
- Draft standard published for stakeholder input

4. Review & Approval
- Comments evaluated and addressed <or> Comments evaluated and further revision and comment needed

Revision Continues

Approved

5. Publication
- Final standard published with official date at least 6 months after publication



USP Expert Committee

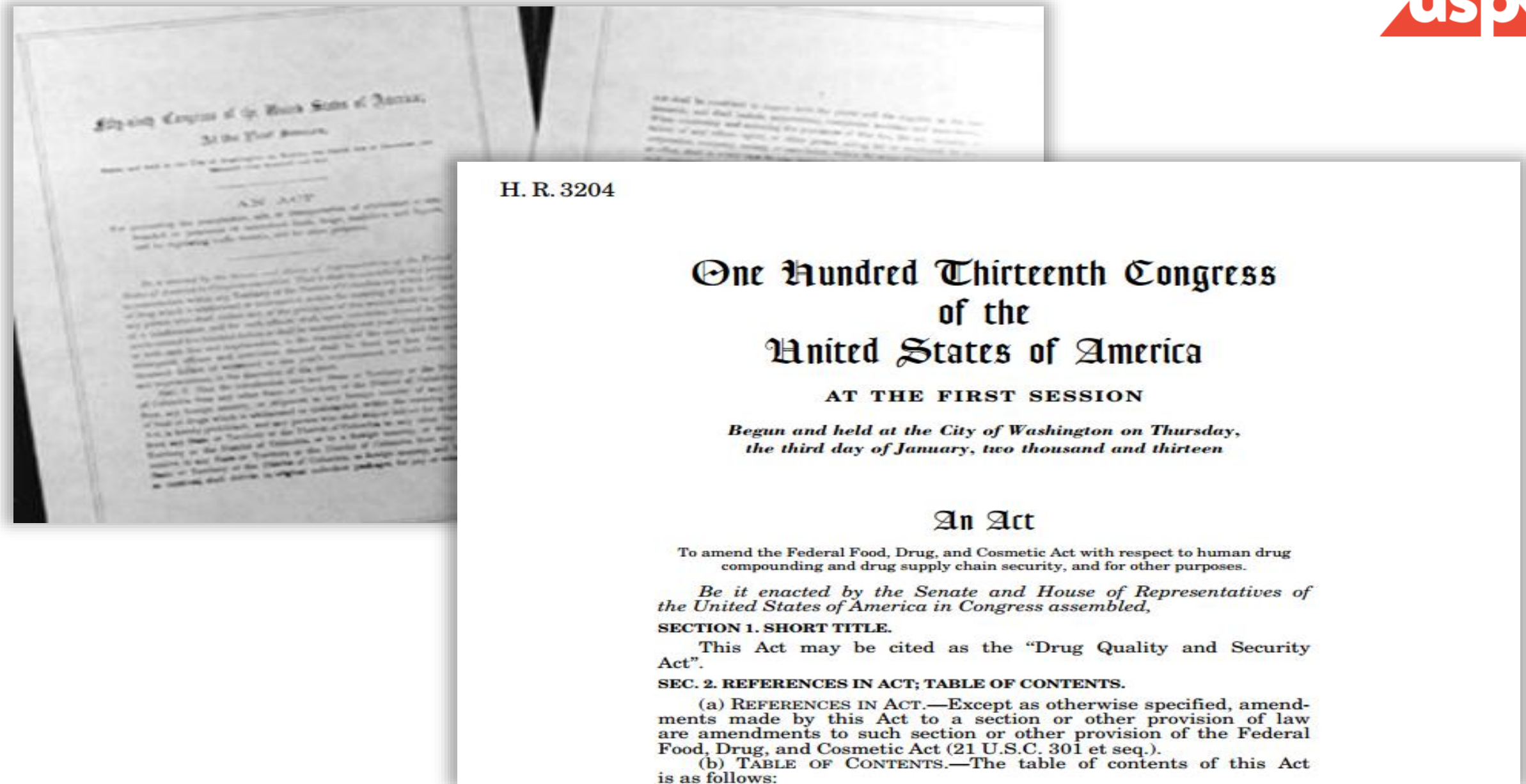
USP convenes a committee of independent experts that are knowledgeable on the public health issue to develop the standard.

- Healthcare Practitioners
- Academicians
- Healthcare Industry
- Regulatory Authorities (Non-voting Liaisons)
- Manufacturers

Stakeholder Implementation

Regulatory Authorities, State Practice Boards, Healthcare Industry, Healthcare Practitioners and other stakeholders utilize USP Healthcare Quality & Safety standards within their specific authority to help ensure public health.

USP standards in federal law



H. R. 3204

One Hundred Thirteenth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Thursday, the third day of January, two thousand and thirteen

An Act

To amend the Federal Food, Drug, and Cosmetic Act with respect to human drug compounding and drug supply chain security, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Drug Quality and Security Act".

SEC. 2. REFERENCES IN ACT; TABLE OF CONTENTS.

(a) REFERENCES IN ACT.—Except as otherwise specified, amendments made by this Act to a section or other provision of law are amendments to such section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

USP standards in federal law

- USP quality standards for drugs are recognized in the Federal Food, Drug & Cosmetic Act (FD&C Act) and have a longstanding role in FDA's determination of whether drugs are adulterated or misbranded
- Enforcement of USP standards is the responsibility of FDA, states, and other regulatory authorities. USP has no role in enforcement

USP standards in federal law

Naming and Identity

Drug deemed *misbranded* unless its label bears the established USP name

FDCA 502(e)

Strength, Purity, and Quality

Drug deemed *adulterated* if strength or quality or purity falls below standards set forth in compendium [USP]

FDCA 501(b)

Packaging and Labeling

Drug deemed *misbranded* unless it is packaged and labeled as prescribed in official compendium [USP]

FDCA 502(g)

Compounding

Traditional Compounding [**503A**]- applicable nationwide; creates **safe harbor** – falls under state law and enforcement; USP chapters must be followed

DQSA, 2013: FDCA 503A

USP standards in federal law

- **1997 FDA Modernization Act** Section 503A states that a compounder must use bulk drug substances and ingredients that comply with the standards of an applicable *USP–NF monograph* and the *USP chapter on pharmacy compounding*

- **2013 Drug Quality and Security Act** clarified FDA's authority over drug compounding, and reaffirmed USP's role under Section 503A.
  - The DQSA reaffirmed that **ingredients in compounded preparations intended for human use must adhere to USP standards**

USP standards in federal law

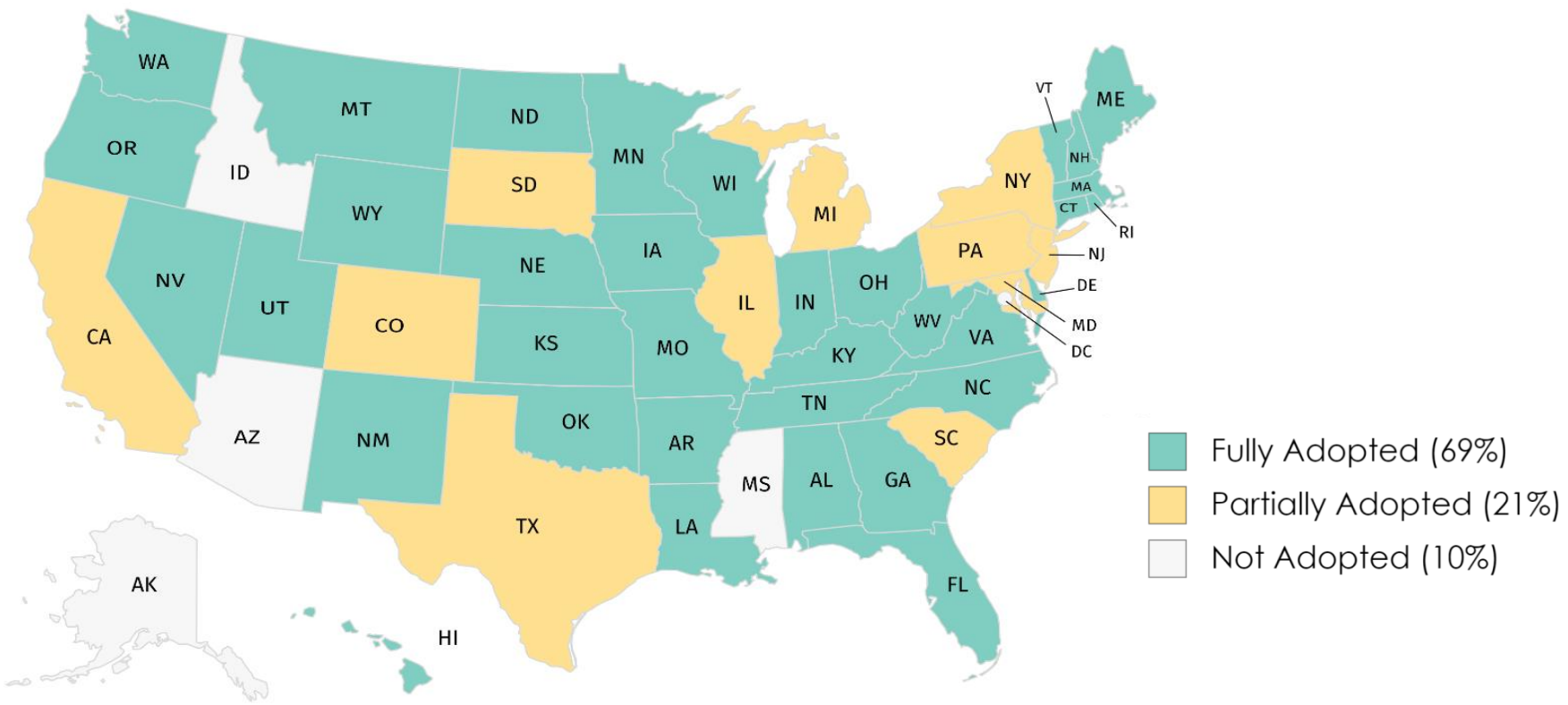
- **FDA guidance** further clarified that traditional compounders must compound preparations intended for human use in compliance with USP's chapters on pharmacy compounding, including General Chapter <795> on nonsterile compounding and General Chapter <797> on sterile compounding in order to meet the "safe harbor" exemption of 503A and fall under state law and enforcement

- **CMS Conditions of Participation for Hospitals**: CMS has issued revised hospital guidance for pharmaceutical services and expanded guidance related to compounding of medications, including a requirement to adhere to Chapters <795> and <797>

FDA Guidance: *Pharmacy Compounding of Human Drug Products under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

USP standards in state law

State Boards of Pharmacy that recognize or adopt <797>



Adopted from NABP Survey of Pharmacy Law. 2016;127.

Questions

Empowering a healthy tomorrow

Title I (CQA) – Review of Quality Standards for Compounders

December 4, 2018

Caroline D. Juran, Executive Director
Virginia Board of Pharmacy

FDLI

Virginia Compounding Requirements for Pharmacies

- USP adopted by reference in Code – §54.1-3410.2
- Sterile and non-sterile
- Applies to pharmacists and practitioners compounding for administration or dispensing
- Physicians “mix, dilute, and reconstitute” unless have license from Board of Pharmacy to dispense
- Limited compounding for office use (human) permissible
- Office use for veterinarians for administration and limited dispensing permissible

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Virginia Compounding Requirements for Pharmacies

- Guidance Document 110-36 and 110-9: http://www.dhp.virginia.gov/pharmacy/pharmacy_guidelines.htm
- Revised routine pharmacy inspection form: http://www.dhp.virginia.gov/Enforcement/enf_guidelines.htm

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Virginia Compounding Requirements for Pharmacies

- Blueprint state
- Nonresident pharmacy current inspection report:
  - Within 6 months for initial application;
  - Within 2 years for annual renewal
- Guidance Document 110-38

Virginia Compounding Requirements for Outsourcing Facilities

- Require FDA registration, compliance with cGMPs
- §§54.1-3434.05, 54.1-3435.5
- Current inspection report:
  - Within 1 year for initial application;
  - Within 2 years for annual renewal
- FDA inspection or board-approved entity
- None currently located in Virginia

FDLI

Contact Information

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pharmbd@dhp.virginia.gov - General board questions

cbd@dhp.Virginia.gov – CBD/THC-A oil, pharmaceutical processor questions

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