Ensuring Quality Hand Sanitizer Production During COVID-19 Seminar

Formulating Quality Alcohol-Based Hand Sanitizer

Brian Serumaga, Ph.D.

Agenda

1. Overview of USP Compounding Standards
   - General Chapters
   - Compounded Preparation Monographs

2. Recommendations from the Compounding Expert Committee for Compounders during COVID-19 Pandemic public health emergency
   - Resources for compounding Alcohol-based hand sanitizer

1.Overview of USP Compounding Standards

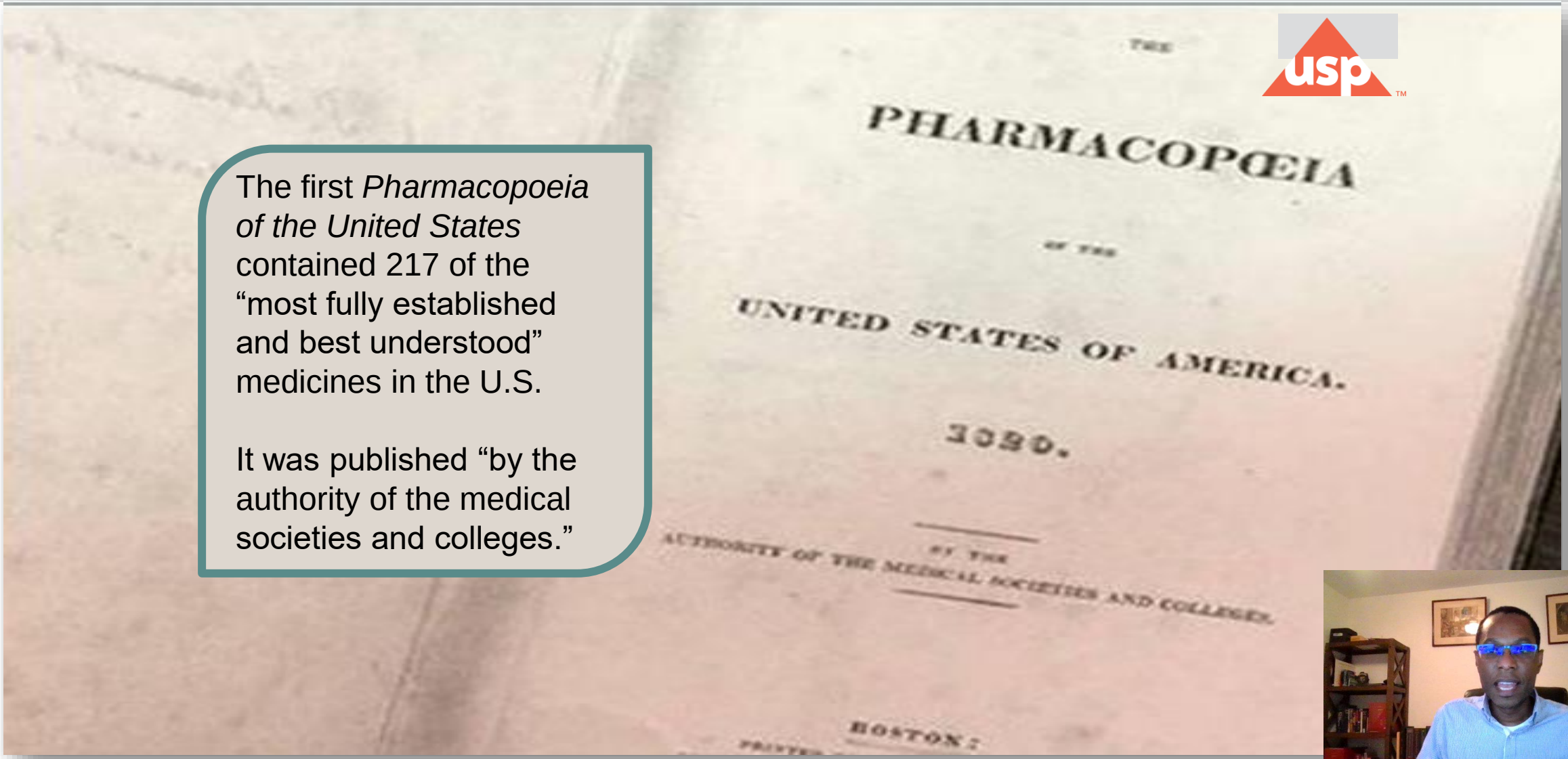
USP's Beginning

USP was founded in 1820 by
11 physicians, in Washington, D.C.

The First Pharmacopeia (1820)

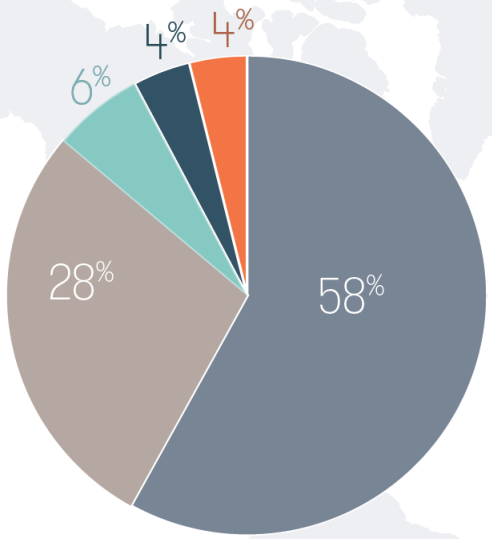
The first *Pharmacopoeia of the United States* contained 217 of the "most fully established and best understood" medicines in the U.S.

It was published "by the authority of the medical societies and colleges."



Our people – USP's global staff and volunteers

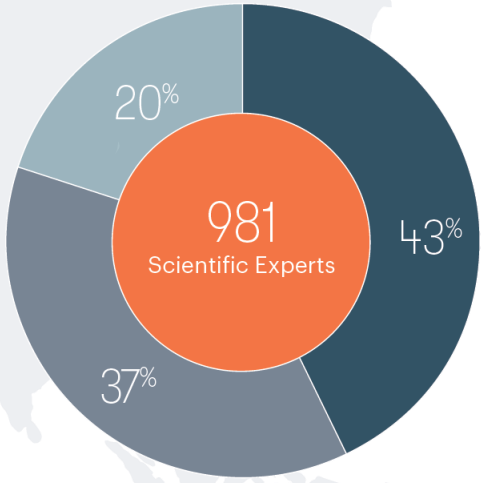
1200+ Staff



- United States
- India
- China
- Brazil
- Other global sites: Ethiopia, Europe, Ghana, Indonesia, Nigeria, Singapore

981 Scientific Experts—

Volunteers and Government Liaisons



- 428 EC Members
- 362 EP-Only Members
- 191 Government Liaisons

The 2020 – 2025 Council of Experts

Collaborative Groups

Biologics

Biologics Monographs 1–Peptides & Oligonucleotides
Michael De Felippis

Biologics Monographs 2–Proteins
Wendy Saffell-Clemmer

Biologics Monographs 3–Complex Biologics & Vaccines
Earl Zablackis

Biologics Monographs 4–Antibiotics
Matthew Borer

Biologics Monographs 5–Advanced Therapies
Mehrshid Alai

Small Molecules

Small Molecules 1
Mary Seibel

Small Molecules 2
Justin Pennington

Small Molecules 3
Eric Kesslen

Small Molecules 4
Kim Huynh-Ba

Small Molecules 5
Amy Karren

Over-the-Counter (OTC) Methods & Approaches
Raphael Ornaf

Excipients

Simple Excipients
Eric Munson

Complex Excipients
Otilia Koo

Excipients Test Methods
Chris Moreton

General Chapters

General Chapters–Dosage Forms
Martin Coffey

General Chapters–Chemical Analysis
Nancy Lewen

General Chapters–Microbiology
Donald Singer

General Chapters–Packaging & Distribution
Renaud Janssen

General Chapters–Measurement & Data Quality
Jane Weitzel

General Chapters–Statistics
Charles Tan

General Chapters–Physical Analysis
Xiaorong He

Healthcare Quality & Safety

Nomenclature & Labeling
Stephanie Crawford

Healthcare Safety & Quality
Melody Ryan

Compounding
Brenda Jensen

Healthcare Information & Technology
Jeanne Tuttle

Dietary Supplements & Herbal Medicines, Food Ingredients

Botanical Dietary Supplements & Herbal Medicines
Robin Marles

Non-botanical Dietary Supplements
Guido F Pauli

Dietary Supplements Admission Evaluation & Labeling
Tieraona Low Dog

Food
Jo

How we work

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 for Compounding

USP provides 3 types of public standards for compounding

USP General Chapters

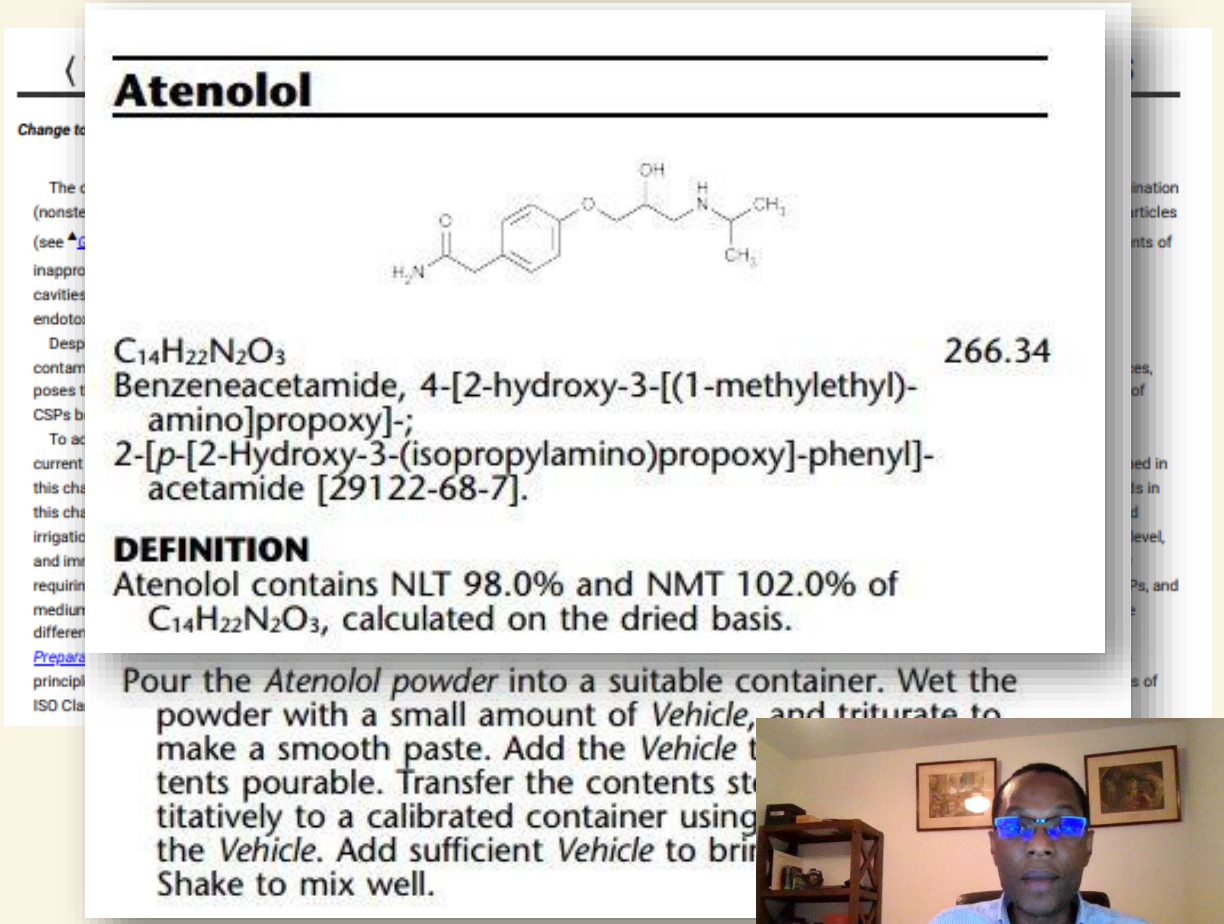
- establish practice standards to help ensure the quality of compounded preparations.

USP Compounded Preparation Monographs

- contain formulations for specific preparations for which there is no suitable commercially available product.

USP Monographs for Bulk Substances and Other Ingredients

- provide standards for identity, quality, purity, strength, packaging and labeling for bulk substances and other ingredients that may be used in compounded preparations.



Atenolol

$C_{14}H_{22}N_2O_3$ 266.34

Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)-amino]propoxy]-;
2-[*p*-[2-Hydroxy-3-(isopropylamino)propoxy]-phenyl]-acetamide [29122-68-7].

DEFINITION

Atenolol contains NLT 98.0% and NMT 102.0% of $C_{14}H_{22}N_2O_3$, calculated on the dried basis.

Pour the *Atenolol powder* into a suitable container. Wet the powder with a small amount of *Vehicle*, and triturate to make a smooth paste. Add the *Vehicle* t tents pourable. Transfer the contents st titatively to a calibrated container using the *Vehicle*. Add sufficient *Vehicle* to bri Shake to mix well.

Relevant Compounding General Chapters

USP standards help promote public health, protect patients and healthcare workers, and address public health challenges.

- <795> *Pharmaceutical Compounding – Nonsterile Preparations*
- <797> *Pharmaceutical Compounding – Sterile Preparations*
- <800> *Hazardous Drugs – Handling in Healthcare Settings*
- <825> *Radiopharmaceuticals – Preparation, Compounding, Dispensing, And Repackaging*
- <1163> *Quality Assurance in Pharmaceutical Compounding*
- <1160> *Pharmaceutical Calculations in Prescription Compounding*
- <1168> *Compounding for Phase I Investigational Studies*
- <1176> *Prescription Balances & Volumetric Apparatus Used in Compounding*
- <1191> *Stability Considerations in Dispensing Practice*

History of <795>

- **First Nonsterile Compounding Standard**
  - USP <1161> *Pharmacy Compounding Practices* **(1996)**

- **General Chapter <795>**
  - Published in USP 24–NF 19 **(2000)**
  - Revised in USP 27–NF 22 **(2004)**
  - Revised in USP 34–NF 29 **(2011)**
    - Incorporated USP <1075> *Good Compounding Practices*
  - Revision Bulletin **(2014)** CURRENTLY OFFICIAL
    - Clarified that the BUDs in <795> are specific for nonsterile preparations and do not apply to sterile preparations

Compounded Preparation Monographs

Metronidazole Benzoate Compounded Oral Suspension

DEFINITION
Metronidazole Benzoate Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of metronidazole ($C_6H_9N_3O_3$).
Prepare Metronidazole Benzoate Compounded Oral Suspension containing 50 mg/mL of metronidazole as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Metronidazole (as the Benzoate) powder	5 g (8 g)
Ora-Blend•, a sufficient quantity to make	100 mL

• Perrigo, Minneapolis, MN.

Place the *Metronidazole Benzoate powder* into a suitable mortar. Wet the powder with a small amount of *Ora-Blend*, and triturate to make a smooth paste. Add the *Ora-Blend* in small portions almost to volume, and mix thoroughly after each addition. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated container. Add sufficient *Ora-Blend* to bring the preparation to final volume. Shake to mix well.

ASSAY
- **PROCEDURE**
  Solution A: 0.1% (v/v) glacial acetic acid in water
  Mobile phase: Acetonitrile and *Solution A* (40:60). Filter, and degas.
  Standard solution: 0.4 mg/mL of metronidazole prepared from USP Metronidazole Benzoate RS in *Mobile phase*. Mix well until dissolved.
  Sample solution: Shake thoroughly each bottle of Oral Suspension. Transfer 0.8 mL of the Oral Suspension into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix well.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 316 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L1
  Column temperature: 30°
  Flow rate: 1.0 mL/min
  Injection volume: 5 µL
  System suitability
  Sample: *Standard solution*
  [NOTE—The retention time for metronidazole is about 7.7 min.]
  Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0% for replicate injections
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of metronidazole ($C_6H_9N_3O_3$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of metronidazole in the *Standard solution* (mg/mL)
C_U = nominal concentration of metronidazole in the *Sample solution* (mg/mL)

SPECIFIC TESTS
- **pH** ⟨791⟩: 3.6–4.6

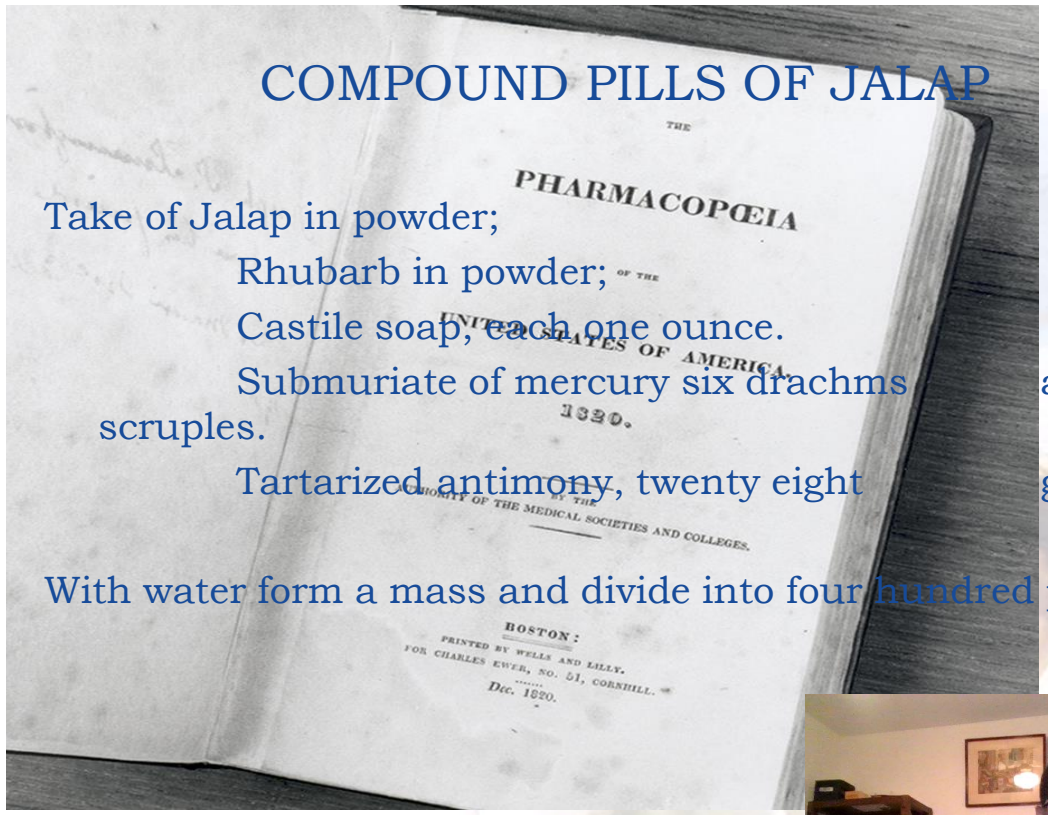
ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store at 2°–8° or at controlled room temperature.
- **BEYOND-USE DATE:** NMT 90 days after the date on which it was compounded when stored at 2°–8° or controlled room temperature.
- **LABELING:** Label it to indicate that it is to be well-shaken before use, and to state the *Beyond-Use Date*.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Metronidazole Benzoate RS

Metronidazole Capsules

DEFINITION
Metronidazole Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of metronidazole ($C_6H_9N_3O_3$).

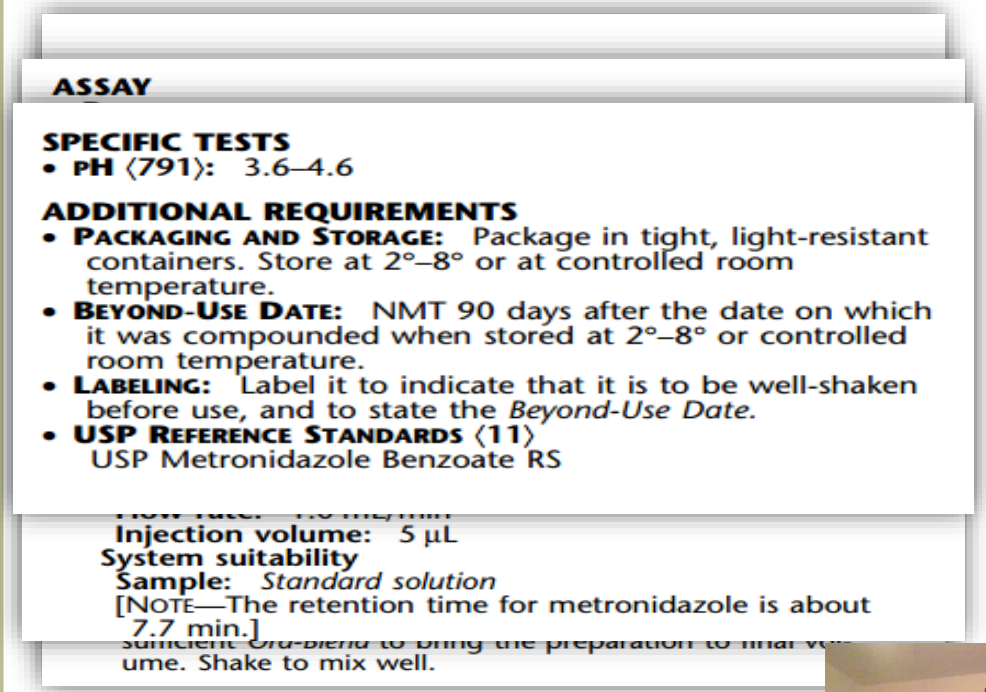
IDENTIFICATION
- **A. INFRARED ABSORPTION** ⟨197K⟩
  Wavelength range: Between 1600 and 1000 cm^{-1}
  Acceptance criteria: Capsule contents show maxima only at the same wavelengths as those of similarly prepared USP Metronidazole RS.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **PROCEDURE**
  Mobile phase: Methanol and water (1:4)
  Standard solution: 0.03 mg/mL of USP Metronidazole RS in *Mobile phase*
  Sample stock solution: Nominally 1 mg/mL of metronidazole prepared as follows. Mix the contents of Capsules (NLT 20). Transfer an amount equivalent to 100 mg of metronidazole to a 100-mL volumetric flask, add 80 mL of *Mobile phase*, and sonicate with intermittent shaking for 10 min. Shake for 30 min, and dilute with *Mobile phase* to volume. Centrifuge a portion of the solution.
  Sample solution: 0.03 mg/mL of metronidazole in *Mobile phase*, from the *Sample stock solution*. Pass a portion of the solution through a nylon membrane filter of 0.45-µm or finer pore size. Discard the first 10 mL of the filtrate, and use the remainder.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 319 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L7
  Column temperature: 30°
  Flow rate: 1 mL/min
  Injection volume: 30 µL
  Run time: 2 times the retention time of the metronidazole peak
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0% for five replicate injections



Components of a Compounded Preparation Monograph

- **Title**
- **Definition**
  - Lists the range of labeled amount of active ingredient
- **Formula**
  - Ingredients and quantities
- **Compounding Procedures**
- **Stability-indicating Assay**
- **pH**
- **Packaging and Storage**
- **Labeling**
- **Beyond-use dates**
  - Stability studies
  - General Chapters <795> or <797>



ASSAY

SPECIFIC TESTS
- **pH** ⟨791⟩: 3.6–4.6

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Package in tight, light-resistant containers. Store at 2°–8° or at controlled room temperature.
- **Beyond-Use Date:** NMT 90 days after the date on which it was compounded when stored at 2°–8° or controlled room temperature.
- **Labeling:** Label it to indicate that it is to be well-shaken before use, and to state the *Beyond-Use Date*.
- **USP Reference Standards** ⟨11⟩
  USP Metronidazole Benzoate RS

Injection volume: 5 µL
System suitability
Sample: *Standard solution*
[Note—The retention time for metronidazole is about 7.7 min.]

ume. Shake to mix well.

2. Recommendations from the Compounding Expert Committee for Compounders during the COVID-19 pandemic

Compounding Expert Committee COVID-19 Activities

- The CMP EC prepared resources as **recommendations** during the COVID-19 pandemic public health emergency
- These documents are for informational purposes only for healthcare practitioners and scientific professionals and are intended to address specific challenges during the COVID-19 pandemic.
- These documents do not reflect the Compounding Expert Committee's opinions on future development or revisions to official text of the USP-NF.
- Parties relying on the information in these documents bear independent responsibility for, awareness of, and compliance with, any applicable federal, state, or local laws and requirements.
- Developed outside the standard setting process = Not compendial standards
- Based on expertise of the Compounding Expert Committee and Input received from stakeholders and

Compounding Alcohol-based Hand Sanitizers

- Stimulated by increased demand for hand sanitizers
- Based on CDC recommendations and WHO formulas
- Provided formulas with compounding instructions for:
  - Ethanol Antiseptic 80% Topical Solution
  - Isopropyl Alcohol Antiseptic 75% Topical Solution
- Provided recommendations for:
  - substitutions
  - calculations
  - addition of denaturants
- USP Compounding hand sanitizer toolkit

Need More Information?

Questions:

CompoundingSL@usp.org

Additional information:
https://go.usp.org/quality_hand_sanitizer

Thank You

Empowering a healthy tomorrow