



The
Microbiology
NETWORK

USP as a Resource for Compounding Pharmacies

Scott Sutton, Ph.D.
scott.sutton@microbiol.org

47

www.Rx-GCP.com

Material in this presentation copyright 2014 Microbiology Network Inc. All rights reserved.

Disclaimer

- I am making this presentation as an independent agent
- I am not making this presentation as a representative of USP, PDA, ASM, USA, BSA, or any other organization with which I am currently associated.
- The views expressed in this presentation are offered as mine alone.



The
Microbiology
NETWORK

© 2014 Microbiology Network

2

Overview of Presentation

- What's in this for Me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- Conclusions/Summary

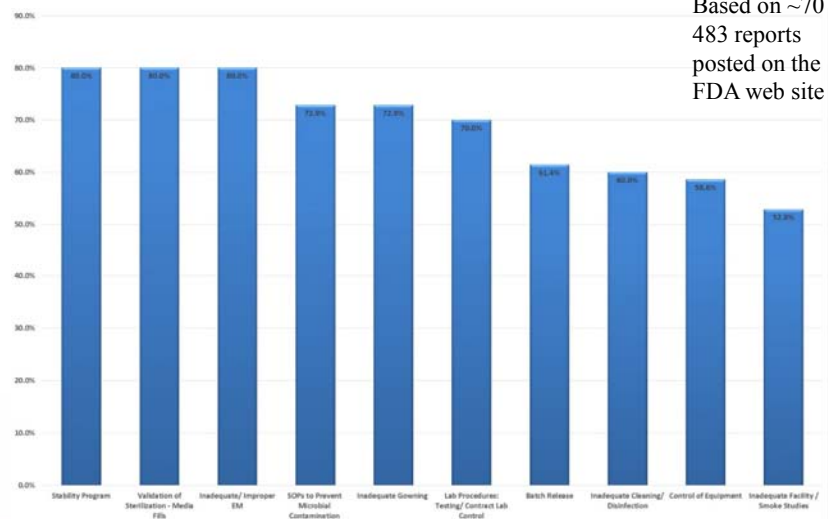


The
Microbiology
NETWORK

© 2014 Microbiology Network

3

FDA 483 Observations



The
Microbiology
NETWORK

© 2014 Microbiology Network

4

Common 483 Topics

483 Topic	Percentage of Occurrence
Stability Program	80.0%
Validation of Sterilization - Media Fills	80.0%
Inadequate/ Improper Environmental Monitoring	80.0%
SOPs to Prevent Microbial Contamination	72.9%
Inadequate Gowning	72.9%
Lab Procedures: Testing/ Contract Lab Control	70.0%
Batch Release	61.4%
Inadequate Cleaning/ Disinfection	60.0%
Control of Equipment	58.6%
Inadequate Facility / Smoke Studies	52.9%
Investigations	48.6%
Control of Pyrogenic Contamination	44.3%
QAU Not Effective/ Production SOPs not followed/effective	42.9%
Separation of Clean and Dirty Operations/Storage of Materials	30.0%



© 2014 Microbiology Network

5

Common 483 Topics

USP has information helpful for:

Stability Program	80.0%
Validation of Sterilization - Media Fills	80.0%
Inadequate/ Improper Environmental Monitoring	80.0%
SOPs to Prevent Microbial Contamination	72.9%
Inadequate Gowning	72.9%
Lab Procedures: Testing/ Contract Lab Control	70.0%
Batch Release	61.4%
Inadequate Cleaning/ Disinfection	60.0%
Control of Equipment	58.6%
Inadequate Facility / Smoke Studies	52.9%
Investigations	48.6%
Control of Pyrogenic Contamination	44.3%
QAU Not Effective/ Production SOPs not followed/effective	42.9%
Separation of Clean and Dirty Operations/Storage of Materials	30.0%



© 2014 Microbiology Network

6

Overview of Presentation

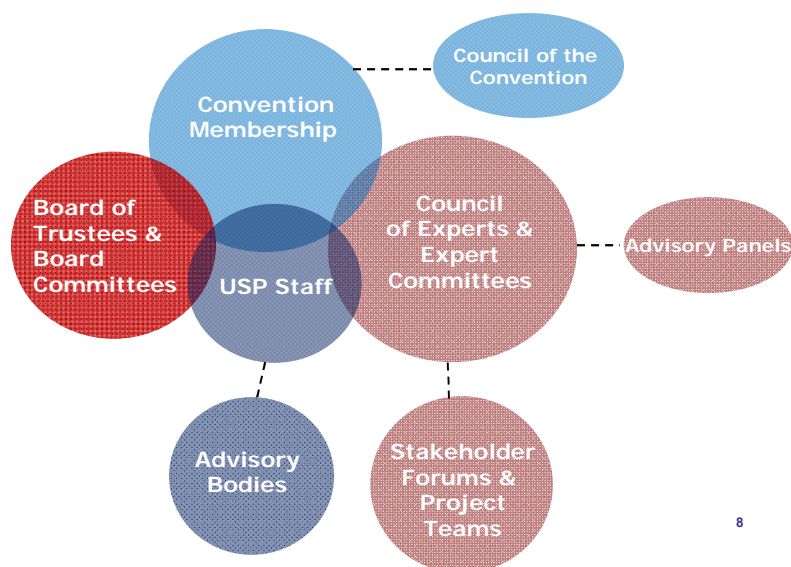
- What's in this for me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- Conclusions/Summary



© 2014 Microbiology Network

7

USP Governing and Advisory Bodies



8

USP Global Laboratory Sites



USP 37–NF 32 (2014)

- ▶ Time-tested, international resource. USP standards are used in more than 130 countries
- ▶ More than 6,000 monographs
- ▶ Continuously updated—published annually in a main edition and two *Supplements*
- ▶ Available in English (print, online, CD) and Spanish (print)



USP's Legal Recognition (FD&C Act)

- **SEC. 201.** For the purposes of this chapter -
 - (g)(1) The term "drug" means **articles recognized** in the official **United States Pharmacopoeia**, official Homoeopathic Pharmacopoeia of the United States, or official **National Formulary**, or any supplement to any of them
 - (j) The term "official compendium" means the official **United States Pharmacopoeia**, official Homeopathic Pharmacopoeia of the United States, official **National Formulary**, or any supplement to any of them.



© 2014 Microbiology Network

11

USP's Legal Recognition: FD&C Act Section 501(b) Adulteration

- A drug or device shall be deemed to be adulterated if it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, **the standards set forth in such compendium**.
- Such determination as to strength, quality, or purity shall be made in accordance **with the tests or methods of assay set forth in such compendium...**



© 2014 Microbiology Network

12

USP for Compounding Pharmacies

USP provides both **general chapters and monographs** for compounded preparations. Compounded preparation monographs may include

- Formulas (ingredients and quantities)
- Specific directions to correctly compound the particular preparation
- Packaging and storage information
- Labeling information
- pH
- Beyond-use dates (BUD) based on stability studies
- Detailed assays (majority of monographs)



The
Microbiology
NETWORK

© 2014 Microbiology Network

13

USP for Compounding Pharmacies

Standards in USP–NF for compounded preparations may be enforced by both

- States - as pharmacy practice/compounding is traditionally regulated by state boards of pharmacy
- FDA - as compounded preparations remain subject to the adulteration and misbranding provisions of the FD&C Act which require conformance to certain USP–NF standards



The
Microbiology
NETWORK

© 2014 Microbiology Network

14

USP-NF

USP–NF is a combination of two compendia, the United States Pharmacopeia (USP) and the National Formulary (NF). Monographs for drug substances, dosage forms, and compounded preparations are featured in the USP. Monographs for dietary supplements and ingredients appear in a separate section of the USP. Excipient monographs are in the NF.



© 2014 Microbiology Network

15

Parts of USP – 2014 (4 volumes)

Volume 1

- Front Matter
- General Notices
- General Chapters
 - Referee Chapters (<1000)
 - Informational Chapters (>1000)
 - Dietary Supplements Chapters (>2000)
- Reagents, Indicators and Solutions
- Reference Tables



© 2014 Microbiology Network

16

Parts of USP – 2014 (4 volumes)

Volume 2

- USP Monographs A-I

Volume 3

- USP Monographs J-Z

Volume 4

- Dietary Supplements



© 2014 Microbiology Network

17

USP *General Notices*

- Title and Revision
- Official Status and Legal Recognition
- Conformance to Standards
- Monographs and General Chapters
- Monograph Components
- Testing Practices and Procedures
- Test Results
- Terms and Definitions
- Prescribing and Dispensing
- Preservation, Packaging, Storage and Labeling



© 2014 Microbiology Network

18

Overview of Presentation

- What's in this for Me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- Conclusions/Summary



© 2014 Microbiology Network

19

For Compounding Pharmacists

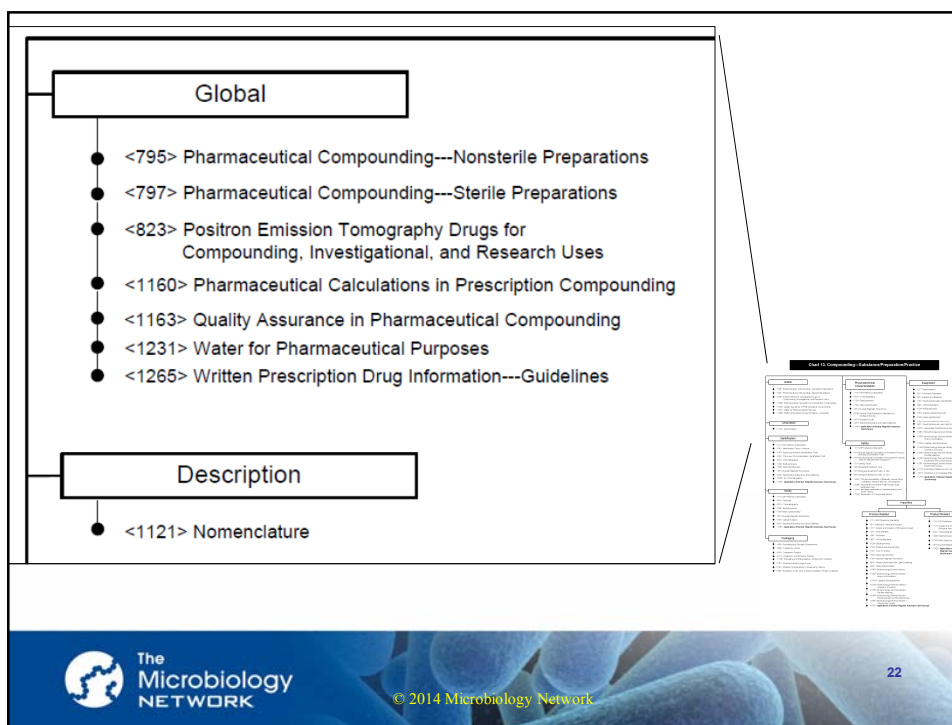
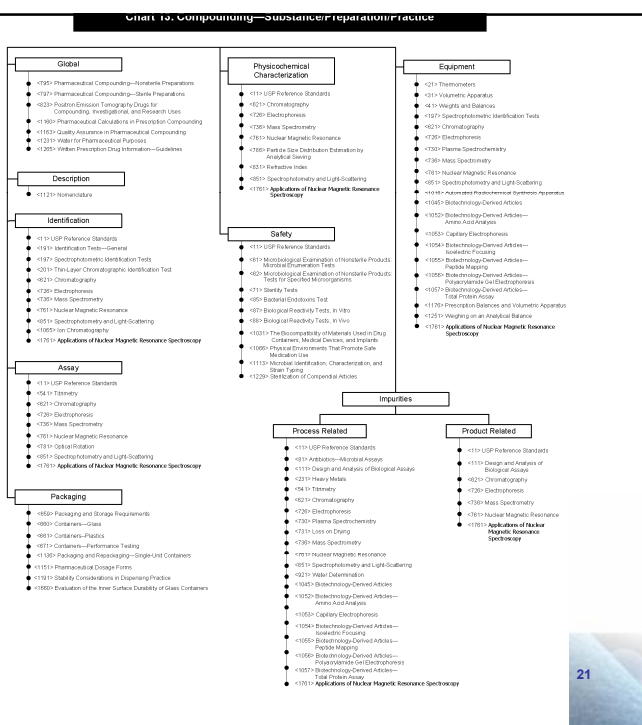
- Monographs
- USP Compounding - Specific Chapters
 - USP <795> *Pharmaceutical Compounding – Nonsterile Preparations*
 - USP <797> *Pharmaceutical Compounding – Sterile Preparations*
 - USP <1163> *Quality Assurance in Pharmaceutical Compounding*
- Others



© 2014 Microbiology Network

20

*From Front
Matter of Volume
1: Guide to
General Chapters*



Identification

- <11> USP Reference Standards
- <191> Identification Tests---General
- <197> Spectrophotometric Identification Tests
- <201> Thin-Layer Chromatographic Identification Test
- <621> Chromatography
- <726> Electrophoresis
- <736> Mass Spectrometry
- <761> Nuclear Magnetic Resonance
- <851> Spectrophotometry and Light-Scattering
- <1065> Ion Chromatography
- <1761> Applications of Nuclear Magnetic Resonance Spectroscopy

© 2014 Microbiology Network
23

Assay

- <11> USP Reference Standards
- <541> Titrimetry
- <621> Chromatography
- <726> Electrophoresis
- <736> Mass Spectrometry
- <761> Nuclear Magnetic Resonance
- <781> Optical Rotation
- <851> Spectrophotometry and Light-Scattering
- <1761> Applications of Nuclear Magnetic Resonance Spectroscopy

Packaging

- <659> Packaging and Storage Requirements
- <660> Containers---Glass
- <661> Containers---Plastics
- <671> Containers---Performance Testing
- <1136> Packaging and Repackaging---Single-Unit Containers
- <1151> Pharmaceutical Dosage Forms
- <1191> Stability Considerations in Dispensing Practice
- <1660> Evaluation of the Inner Surface Durability of Glass Containers

© 2014 Microbiology Network
24

Physicochemical Characterization

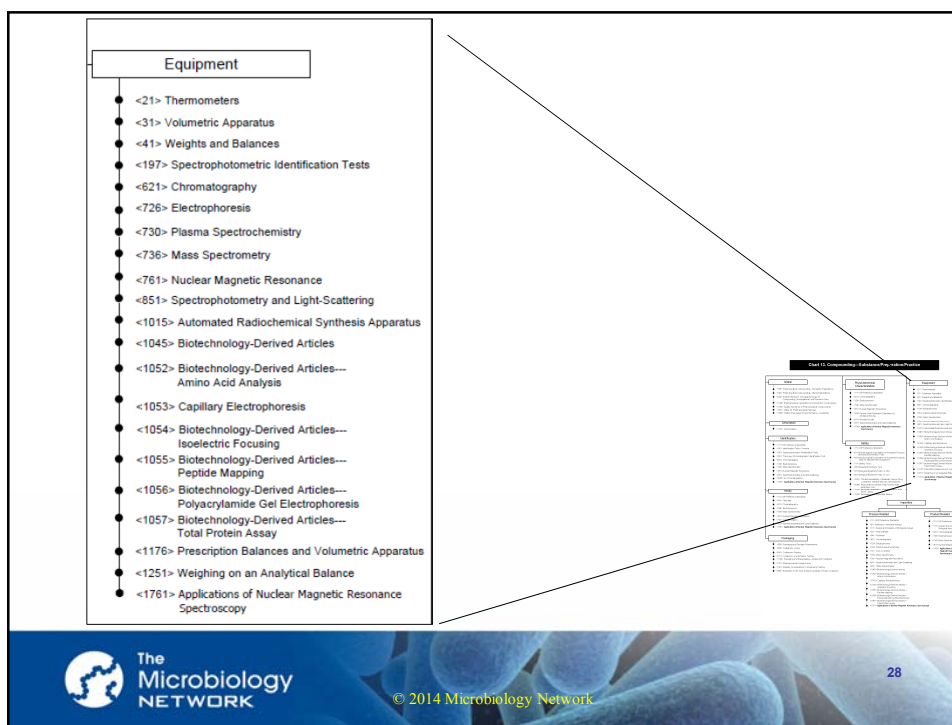
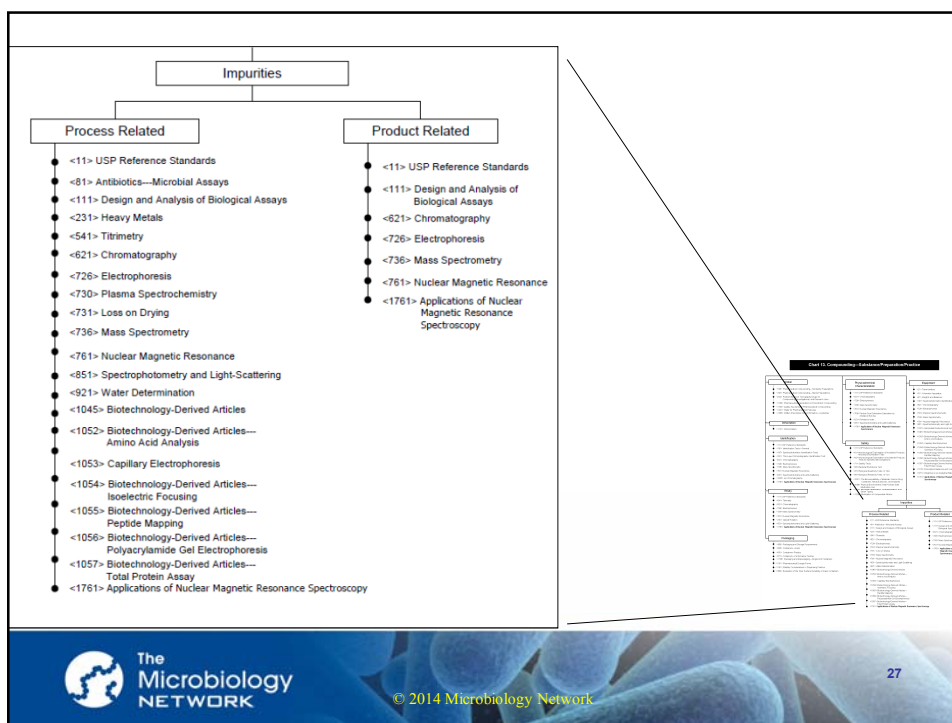
- <11> USP Reference Standards
- <621> Chromatography
- <726> Electrophoresis
- <736> Mass Spectrometry
- <761> Nuclear Magnetic Resonance
- <786> Particle Size Distribution Estimation by Analytical Sieving
- <831> Refractive Index
- <851> Spectrophotometry and Light-Scattering
- <1761> Applications of Nuclear Magnetic Resonance Spectroscopy

The Microbiology NETWORK
© 2014 Microbiology Network
25

Safety

- <11> USP Reference Standards
- <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests
- <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms
- <71> Sterility Tests
- <85> Bacterial Endotoxins Test
- <87> Biological Reactivity Tests, In Vitro
- <88> Biological Reactivity Tests, In Vivo
- <1031> The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants
- <1066> Physical Environments That Promote Safe Medication Use
- <1113> Microbial Identification, Characterization, and Strain Typing
- <1229> Sterilization of Compounded Articles

The Microbiology NETWORK
© 2014 Microbiology Network
26



Overview of Presentation

- What's in this for Me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- Conclusions/Summary



The
Microbiology
NETWORK

© 2014 Microbiology Network

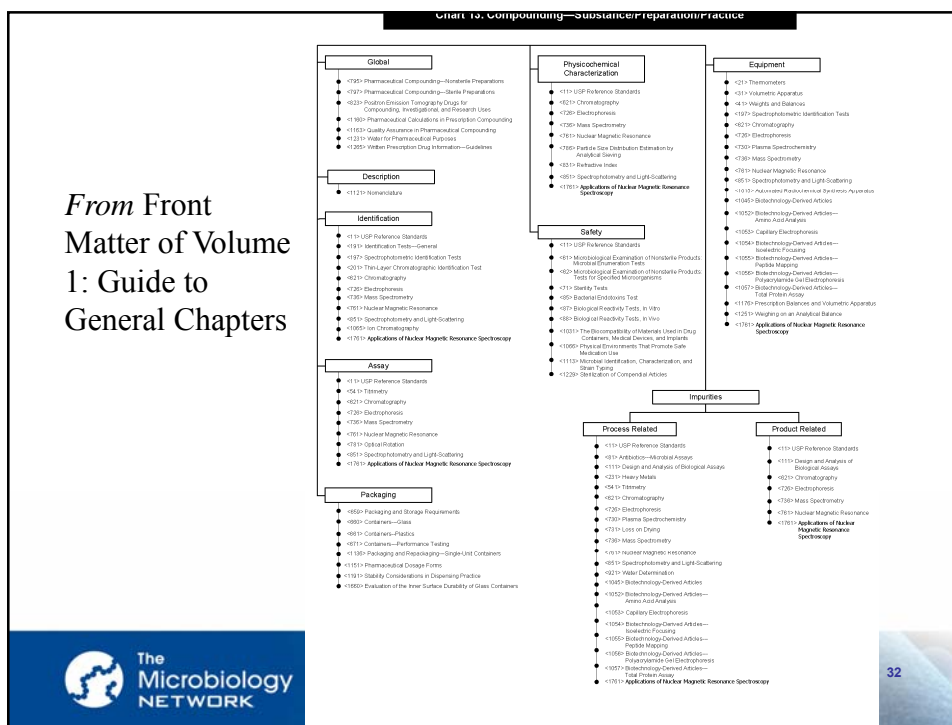
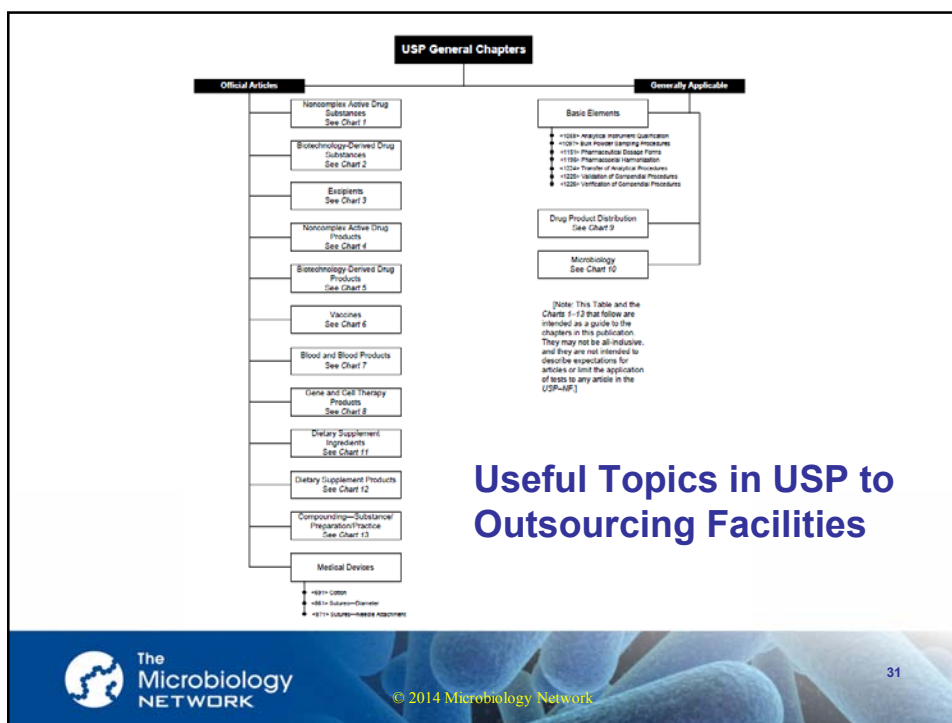
29

24 Outsourcing Facilities (2/7/14)

Advanced Pharma, Inc., Houston, TX	1/22/2014
Allergy Laboratories, Inc., Oklahoma City, OK	12/30/2013
Banner Health, Chandler, AZ	12/26/2013
Cantrell Drug Company, Little Rock, AR	12/16/2013
Edge Pharmacy Services LLC, Colchester, VT	1/21/2014
Infusion Options INC., Brooklyn, NY	1/24/2014
JCB Laboratories, North Wichita, KS	1/21/2014
Kings Park Slope, Inc., Brooklyn, NY	12/23/2013
KRS Global Biotechnology, Inc., Boca Raton, FL	12/15/2013
Leiter's Compounding, (Great Oaks Blvd), San Jose, CA	1/31/2014
Marlborough Hospital, Marlborough, MA	12/26/2013
Medi-Fare Drug & Home Health Center, Inc., Blacksburg SC	12/17/2013
Pharmagen Laboratories Inc., Stamford, CT	1/21/2014
Pharmakon Pharmaceuticals, Noblesville, IN	1/23/2014
PharMedium Services, LLC, Cleveland, MS	12/11/2013
PharMedium Services, LLC, Edison, NJ	12/11/2013
PharMedium Services, LLC, Memphis, TN	12/11/2013
PharMedium Services, LLC, Sugarland, TX	12/11/2013
Region Care, Inc., Great Neck, NY	12/24/2013
SCA Pharmaceuticals, Little Rock, AR	12/13/2013
Triangle Compounding Pharmacy Inc., Cary, NC	1/24/2014
Unique Pharmaceuticals, Ltd., Temple TX	1/24/2014
US Compounding, Inc., Conway, AR	12/20/2013
US Specialty Formulations LLC, Bethlehem, PA	1/31/2014

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm378645.htm#1>

30



Useful for Outsourcing Facilities

Basic Elements

- <1058> Analytical Instrument Qualification
- <1097> Bulk Powder Sampling Procedures
- <1151> Pharmaceutical Dosage Forms
- <1196> Pharmacopeial Harmonization
- <1224> Transfer of Analytical Procedures
- <1225> Validation of Compendial Procedures
- <1226> Verification of Compendial Procedures

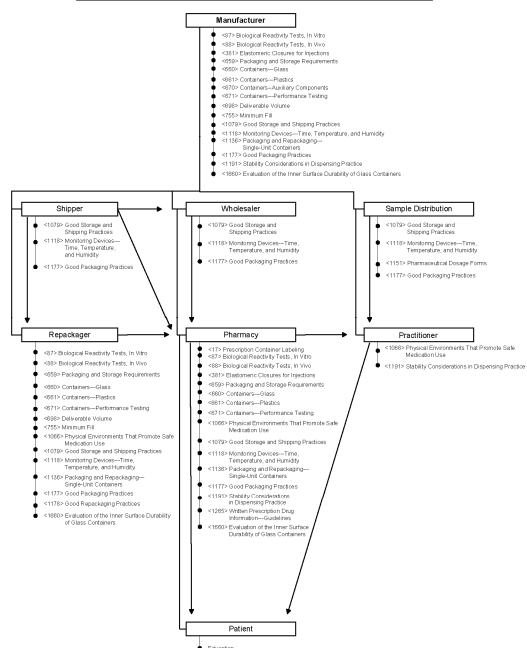


The
Microbiology
NETWORK

© 2014 Microbiology Network

33

Chart 9. Drug Product Distribution



The
Microbiology
NETWORK

34



Common 483 Topics

483 Topic	Percentage of Occurrence
Stability Program	80.0%
Validation of Sterilization - Media Fills	80.0%
Inadequate/ Improper Environmental Monitoring	80.0%
SOPs to Prevent Microbial Contamination	72.9%
Inadequate Gowning	72.9%
Lab Procedures: Testing/ Contract Lab Control	70.0%
Batch Release	61.4%
Inadequate Cleaning/ Disinfection	60.0%
Control of Equipment	58.6%
Inadequate Facility / Smoke Studies	52.9%
Investigations	48.6%
Control of Pyrogenic Contamination	44.3%
QAU Not Effective/ Production SOPs not followed/effective	42.9%
Separation of Clean and Dirty Operations/Storage of Materials	30.0%

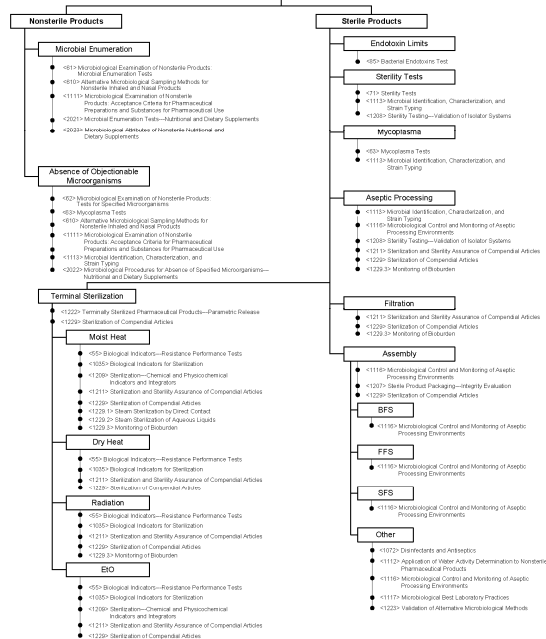


The
Microbiology
NETWORK

© 2014 Microbiology Network

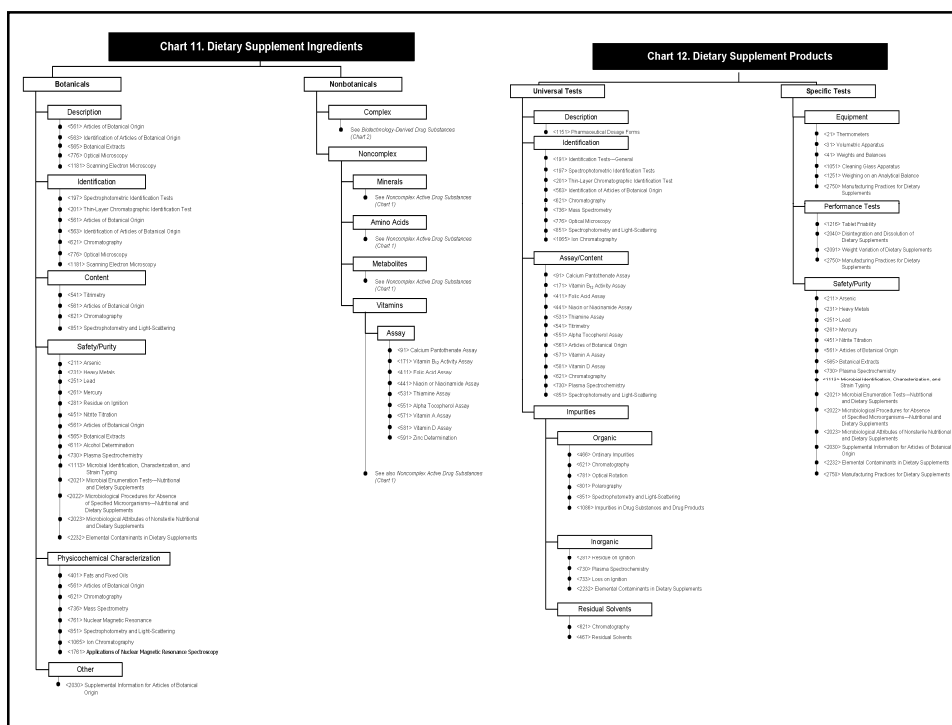
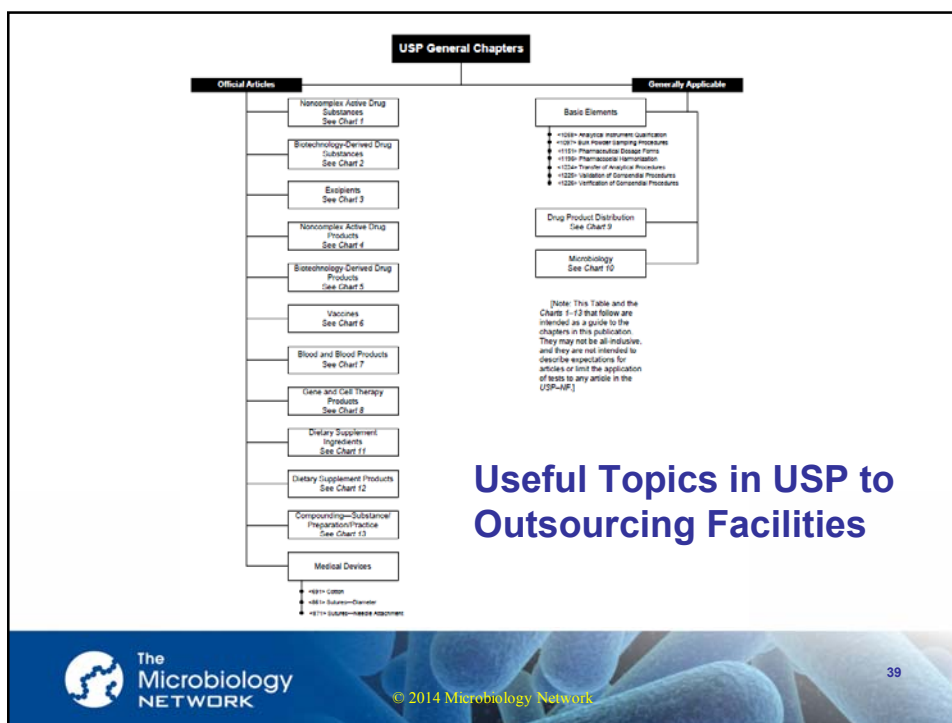
37

Chart 10. Microbiology



The
Microbiology
NETWORK

38



Overview of Presentation

- What's in this for Me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- **Conclusions/Summary**



The
Microbiology
NETWORK

© 2014 Microbiology Network

41

Common 483 Topics

483 Topic	Percentage of Occurrence
Stability Program	80.0%
Validation of Sterilization - Media Fills	80.0%
Inadequate/ Improper Environmental Monitoring	80.0%
SOPs to Prevent Microbial Contamination	72.9%
Inadequate Gowning	72.9%
Lab Procedures: Testing/ Contract Lab Control	70.0%
Batch Release	61.4%
Inadequate Cleaning/ Disinfection	60.0%
Control of Equipment	58.6%
Inadequate Facility / Smoke Studies	52.9%
Investigations	48.6%
Control of Pyrogenic Contamination	44.3%
QAU Not Effective/ Production SOPs not followed/effective	42.9%
Separation of Clean and Dirty Operations/Storage of Materials	30.0%



The
Microbiology
NETWORK

© 2014 Microbiology Network

42

Conclusions

- Difficult for pharmacists to become expert in “GCP” as defined in the current environment
- Outsourcing Facilities are subject to GMP (as per FDA)
- Outsourcing Facilities and Pharmacies have different challenges – both need reliable information
- USP is the primary document to source this information



© 2014 Microbiology Network

43

Overview of Presentation

- What's in this for Me?
- What is the USP?
- Parts of the USP
- Specific Interest for Pharmacists
- Specific Interest for Outsourcing Facilities
- Conclusions/Summary



© 2014 Microbiology Network

44

Microbiology Network

- Consulting
 - Contamination Control/Sterility Assurance
 - Quality Assurance
 - Audits
 - Compounding Facility/Process Contamination Control
 - FDA Mock Systems Audit of Facility (w/team)
 - Laboratory Preparation/Contract Lab Qualification
 - Quality Control
 - Lab Operations/Design
 - Microbiology Process/Procedures
- Training
 - In-house Training
 - Distance Training



© 2014 Microbiology Network

45

Upcoming Webinars

- March 27th - Compounding Pharmacies and the Sterility Test
- April 24th - Compounding Pharmacies and Contract Testing Lab
- May 22nd - Compounding Pharmacies and the Bacterial Endotoxin Test



© 2014 Microbiology Network

46

THANK YOU FOR YOUR ATTENTION

QUESTIONS?

Scott Sutton, Ph.D.
scott.sutton@microbiologynetwork.com
+1 585-298-0767 (cell)
<http://www.Rx-GCP.com>



The
Microbiology
NETWORK

© 2014 Microbiology Network

47