Sterile Compounding Concepts -
a USP <797> approach

NYSCHP Webinar
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Disclosure Statement -

Lou Diorio “declare(s) no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.”

Lou is a Principal and shareholder of LDT Health Solutions, Inc.

Information is known to be accurate at the time of presentation. The compounder is encouraged to consult reference compendia and current USP documentation as information is subject to change.

Honoraria for today’s session is being donated to the NYSCHP’s REF !

Additional Accreditation Information

- Activity Type: Practice-based
- Target Audience: Pharmacists, Pharmacy Technicians
- Release Date:
- Expiration Date:
- For complete ACPE information and disclosures, see the complete program materials

Session Objectives -

- **At the completion of this activity, pharmacists will be able to:**
  - Discuss the Responsibilities of Compounders of Sterile Compounds for "Human Use".
  - Discuss the overlapping regulations that impact the compounding of sterile medications.
  - Describe the professional responsibilities of compounders in meeting the standards described USP General Chapters <797>.
- **At the completion of this activity, pharmacy technicians will be able to:**
  - Discuss the overlapping regulations that impact the compounding of sterile medications.
  - Outline potential compliance strategies for the proper training & evaluation of compounding skills of all personnel.
  - Describe the elements of a comprehensive cleaning & disinfection program for compounding areas.

Question 1 -

- Which of the following is NOT one of the central themes of USP <797> :

a) Control of the compounding environment.
b) Control of the compounding personnel's actions
c) Control of the compounding process.
d) ALL are central safety themes of USP <797>

Question 1 -

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The Responsibility of Compounding Personnel-

- The need to maintain high standards for quality & control of processes, components, and environments and for the skill & knowledge of personnel who prepare CSPs.
- The USP is the National Standard, so compounding personnel must understand the legal risks of non-compliance.
  - Especially for the Pharmacist-in-Charge / “Manager of Record”
  - CMS implications for non-compliance
- To avoid confusion Focus should always be the current USP/NF release

Personal Training and Evaluation in Aseptic Manipulation Skills-

- "Personnel who prepare CSPs shall be trained conscientiously and skillfully by expert personnel and through audio-video instructional sources and professional publications in the theoretical principles and practical skills of aseptic manipulations and in achieving ISO Class 5 environmental conditions before they begin to prepare CSPs."

1-USP<797> Pharmaceutical Compounding-Sterile Preparations Revision Bulletin © USP (emphasis added)

Beyond USP what regulation impacts compounding operations for CSPs -

Since July 2014 the FDA has issued 28 Guidance documents or Regulatory Policy Statements impacting compounding / Pharmacy Practice -

Addressing the following topics:

- Insanitary Conditions at Compounding Facilities
- Pharmacy Compounding of Human Drugs / 503A
- 503B Outsourcing Facilities [Registration, Fees, General Facilities]
- Use of Bulk Drug Substances [503A / 503B]
- Hospital & Health System Compounding
- Compounded Products that are Essentially Copies of Approved Drug Products [503A / 503B]
- Mixing, Diluting, or Repackaging of Biological Products

Beyond USP what regulation impacts compounding operations for CSPs ?

- Local BOP Regulation
- Controlled Substance Regulation
- Voluntary Accreditation Bodies
  - ACHC, TJC, NABP

TJC Hospital Accreditation Program ("HAP") -

- This Sterile Medication Compounding Assessment Cross-walks the TJC Standard to the CMS' "Conditions-of-Participation" (CoP)

- [5-page tool]

Surveyor Guidance Checklist for On Site Activity:
Sterile Medication Compounding Assessment
Hospital Accreditation Program (HAP)

X	Assessment Item	Guidance	Joint Commission Standard	CMS CoP to crosswalk
Certification/Testing Report Evaluation				
	Primary Engineering Control ISO Level	• Must be ISO 5 or less	MM.05.01.07 EP 4	482.23(c)
	Primary Engineering Control Viable Particle Testing *Surface*	• Value must be at or less than 3 CFU/cubic meter	IC.02.01.01 EP 1	482.42
	Primary Engineering Control Viable Particle Testing *Air*	• Value must be at or less than 1 CFU/cubic meter	IC.02.01.01 EP 1	482.42
	Primary Engineering Control HEPA filter leak test	• Must show passed or evidence that holes were patched.	IC.02.01.01 EP 1	482.42
	Secondary Engineering Control Air Exchanges per Hour	• Must have 30/hour. Compounding hood can contribute up to 15 to complete the 30.	EC.02.05.01 EP 15	482.42
	Secondary Engineering Control Air Pressure Differential	• Buffer area= ○ Non-hazardous = + 0.02-0.05" H_2O to unclassified space ○ Hazardous = - 0.01" H_2O • Ante area = positive to unclassified space	EC.02.05.01 EP 15	482.42
	Secondary Engineering Control ISO Level	• Buffer area must ISO 7 or less • Ante area must be ISO 8 or less	EC.02.06.01 EP 1	482.41(a)
	Secondary Engineering Control Viable Particle Testing *Surface*	• Buffer area value must be at or less than 5 CFU/cubic meter • Ante area value must be at or less than 100 CFU/cubic meter	IC.02.01.01 EP 1	482.42
	Secondary Engineering Control Viable particle testing *Air*	• Buffer area value must be at or less than 10 CFU/cubic meter • Ante area value must be at or less than 100 CFU/cubic meter	IC.02.01.01 EP 1	482.42
	Secondary Engineering Control HEPA filter leak test	• Must show passed or evidence that holes were patched.	IC.02.01.01 EP 1	482.42
	Evidence of action taken by organization when any item is out of range	• There must be evidence of remediation actions taken when items do not pass and subsequent testing to ensure compliance. If this is not present then must be scored.	LD.04.01.01 EP 3	N/A
	Primary Engineering Control certification / testing frequency	• Each component listed above must be tested and certified every 6 months. Lack of 6 month interval must be scored • Also any time PEC is moved or relocated	EC.02.04.01 EP 4	483.41(d)(2)
	Secondary Engineering Control certification / testing frequency	• Each component listed above must be tested and certified every 6 months. Lack of 6 month interval must be scored	EC.02.06.01 ep 1	482.41(a)
	Air flow monitoring	• must have continuous monitoring	EC.02.05.01 EP 15	482.42
Compounding Evaluation				
Room Structure				
	Floors	• Must be solid and coved on corners to prevent 90 degree angles where floor meets wall • No rips/tears ; check corners for dust	EC.02.06.01 EP 1	482.41(a)
	Ceiling	• Must be solid material or with sealed drown in ceiling tiles	EC.02.06.01 EP 1	482.41(a)

Medication Compounding Surveyor Onsite Tool Page 1

TJC Hospital Accreditation Program ("HAP") cont. -

- This document covers the following key areas:
  - Certification/Testing Report Evaluation -
    - PECs
    - SECs
  - Compounding Evaluation -
    - Room Structure
    - Handwashing / PPE /Garbing
    - PEC Cleaning [pre-compounding]
    - Sterile Compounding Observation
    - PEC & SEC Cleaning and Maintenance
    - HIGH Risk Level Compounding Additions
    - HD Compounding Additions
    - BUD determinations
  - Compounding Staff Competency Evaluation -

Aseptic Manipulation Skills-

- Aseptic training in pharmacy schools is inadequate or non-existent.
- Most training occurs on-the-job and by “verbal tradition”.
- Training must include thorough didactic instruction in theory and practice of sterile preparation before starting compounding , annually/semi-annually thereafter.
- Evaluations should include a formal written exam, motor-skills assessment and practical evaluation of aseptic technique using growth media.

Personnel Training & Evaluation -

- Training of Compounding Personnel should include:
  - Multi-media Instructional Resources
  - Professional Publications
  - Media-fill testing of work skills
- With Focus on the Critical Areas of:
  - Hand Hygiene
  - Garbing, Gowning & Gloving
  - Cleaning & Disinfection Procedures

Photo © LDT Health Solutions, Inc.

Environmental Quality & Control -

- Aseptic Processing areas must be of proper design -
  - HEPA filtered air introduced at the ceiling
  - Low wall returns
  - Cleanable surfaces, able to stand up to repeated sanitizations
  - Certification of the areas should follow CETA guidance
  - Monitoring of Controls *(Temperature / Humidity / Pressurization)*
- Proper Environmental Monitoring – semi-annually is NOT enough!
- Cleaning cycle must include a sporicidal agent.
- Responses to Viable & Non-Viable contaminations must be appropriate, swift, & measured.

Example – LFWB within a SEC

Engineering Controls -

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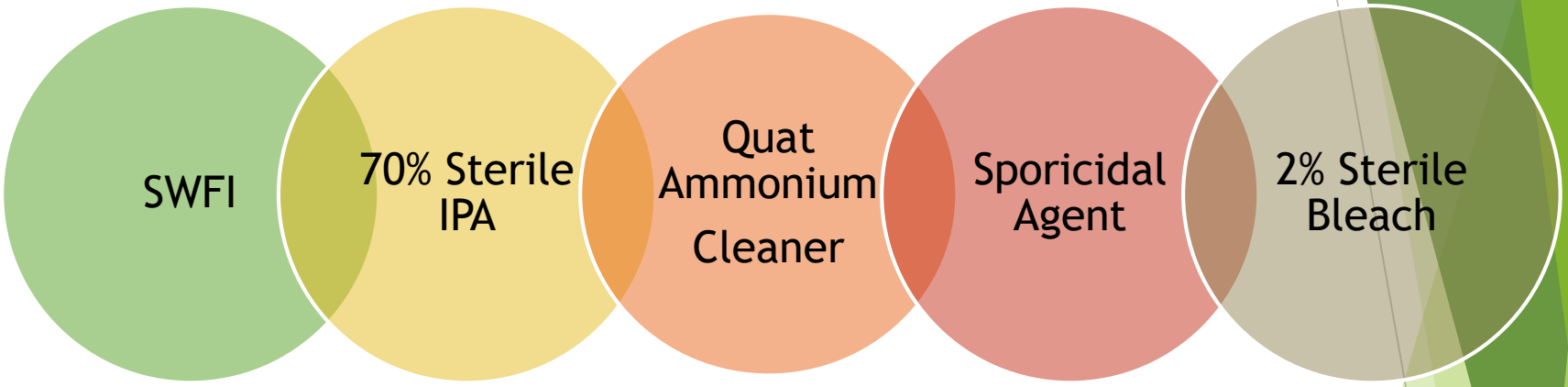
Used with permission from Isotech Design

Cleanroom Cleaning & Disinfecting- for non-HD CSPs

[USP <797>]



Per <797> when dissolution of messy spills is in order

Per <797> this is the primary disinfect agent in your cleanroom

Needed when a germicidal detergent "soap" is indicated. Sticky spills etc.

FDA is advocating the regular use of a sporicidal agent, regardless of ENV monitoring. POINTS to REMEMBER- dilution strength & contact time. [as well as residues]

A good economical disinfectant, especially if a large volume of solution is needed. Can be used to remove Sporicidal residues. OSHA-Corrosive , S Steel could have issues

<797> - Primary concern is Maintaining Sterility

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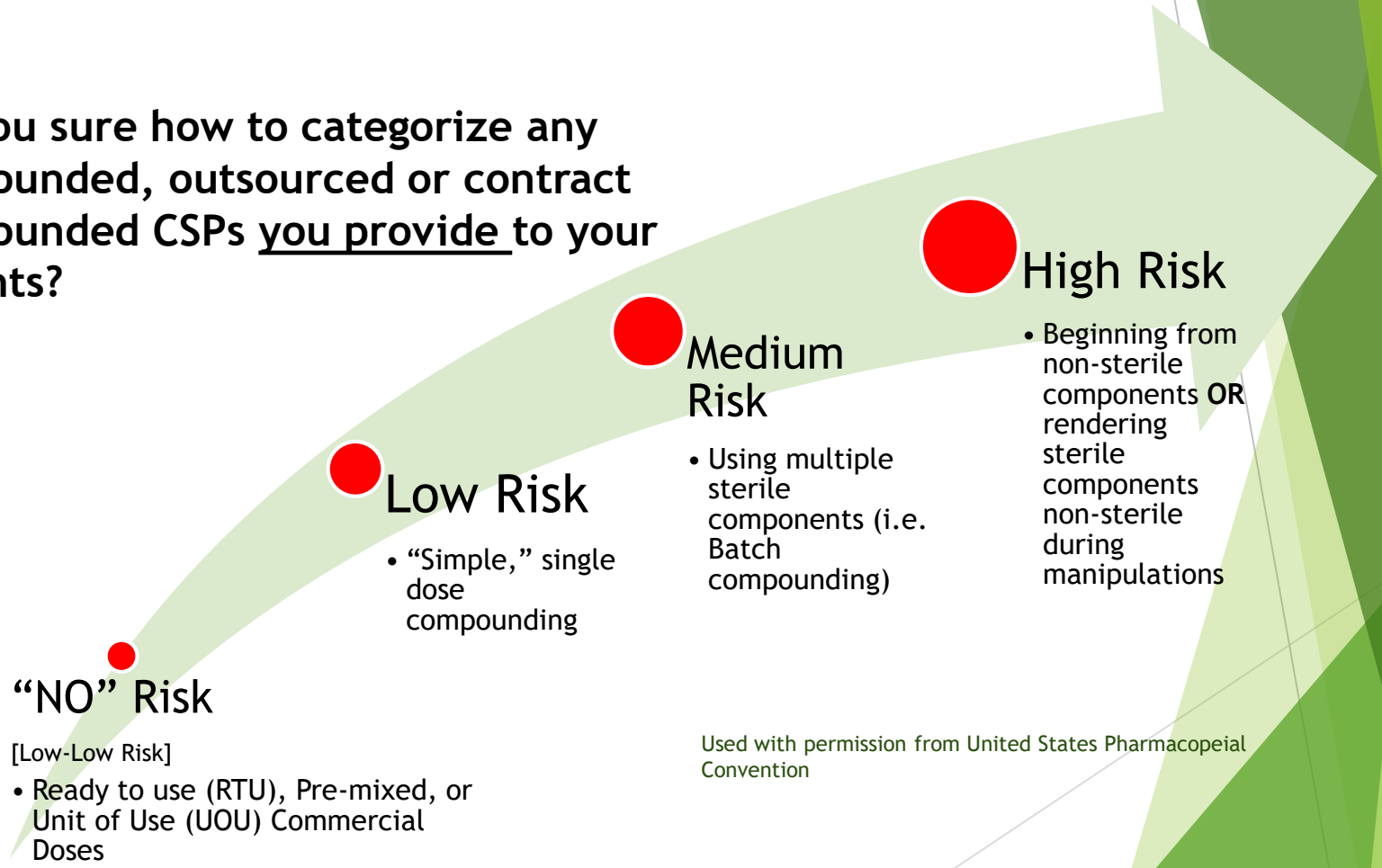
Risk Levels of USP <797>

Are you sure how to categorize any compounded, outsourced or contract compounded CSPs you provide to your patients?



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Risk Levels of USP <797>

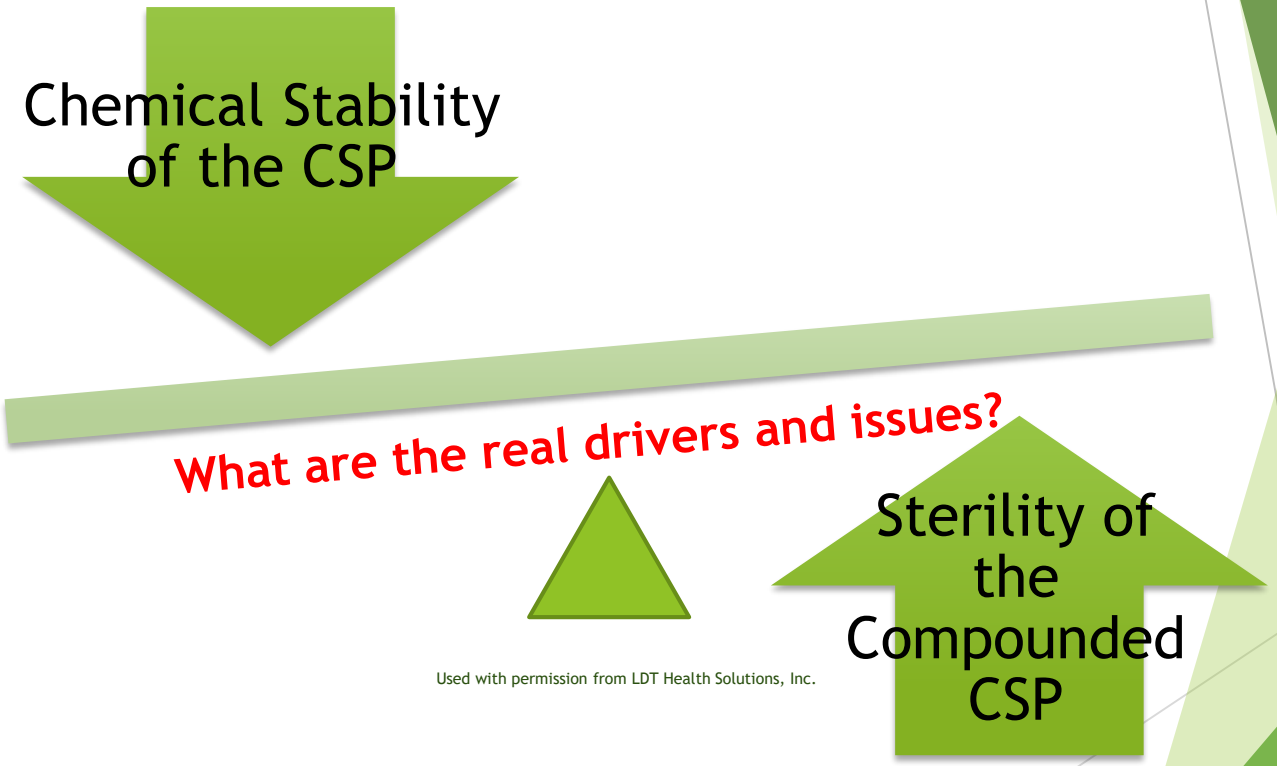
Low Risk Level CSPs	Low risk Level CSPs w/ 12hr or Less BUD	Medium Risk Level CSPs	High Risk Level CSPs
48 Hours Room Temperature	12 Hours Room Temperature	30 Hours Room Temperature	24 Hours Room Temperature
14 Days Refrigerated	N/A	9 Days Refrigerated	3 Days Refrigerated
45 Days Frozen	N/A	45 Frozen	45 days Frozen

Used with permission from United States Pharmacopeial Convention

Beyond-use Dating -

- Applies once a manufacturer's container is opened and the drug product is transferred to another container for dispensing, repackaging, or compounding.
- The USP has developed recommendations for compounders to assign a “BUD” on the label of the new container.
- BUDs cannot exceed the manufacturer's expiration date and often may be much shorter.
- Unlike expiration dating, there is often little scientific basis for the assignment of BUDs.
  - “Theoretical” dating periods exceeding 30 days must be supported by appropriate instrumental analysis.
- Compounders must have their BUD policies in writing!

Finding Balance:
Chemical Stability vs. Sterility -



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Question 2 -

- **TRUE or FALSE** - Determinations of Beyond-Use dating of CSPs are a careful balance of the drug's chemical stability AND its sterility once compounded.

- a) True
- b) False

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Question 3 -

- A compounder should establish a clear & consistent Beyond-Use date (BUD) based upon which of the following criteria:

- a) Established past practice & the experience of the staff.
- b) The recommendation & policy of the largest 503b provider.
- c) Careful examination of available stability data in the literature.
- d) Solely on the BUD guidance within USP <797>.

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Quality Assurance Program-

- Requires formalized policies, controlled processes and clear procedures used in preparing CSPs
- One element of quality that is not routinely performed in pharmacies is documentation, or “written proof” that compounding is occurring properly.

Question 4 -

- **TRUE or FALSE**; USP General Chapter <797> reflects all best practices regarding the compounding of sterile drug for human-use.

- a) TRUE
- b) FALSE

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- b) FALSE

Self-Assessment tools (SAT) or "GAP" Analysis-

- Use a SAT or GAP Analysis to identify organizational points of compliance and operational gaps.
  - High level situational analysis of current state of readiness.
  - Should address-
    - USP <71> <85> <795> <797> <800>
    - FDA CPGs 503A & Hospital and Health System Compounding
    - State and Local Regulation
- SAT or GAP Analysis will serve as a placeholder for regulatory and accreditation agencies.
  - It is only a starting point!
  - But the best place to start is at the beginning!
  - Post-pandemic are you sure that your "temporary" changes have NOT become permanent

Developing an Action Plan-

- Focus should be on:
  - "Changing the culture" -
    - Controlled processes and documentation
    - Competency Based Training and Education
    - Compliance to Local, State, and Federal Regulations
    - Patient Safety is always your goal!

Summary / Conclusions -

- There is no substitute for constant vigilance on the part of any professional, compounder, or healthcare provider of CSPs.
- All professionals must be aware of ALL best practices & prevailing regulation!
- Creation of a “state-of-control” around compounding operations is key to the safety of these essential medications
- A comprehensive situational analysis of the compounders current state of compliance is a good first step in the determination of its long-range compliance plan.

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- QUESTIONS -

Thank You !

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Quality Process-

[Courtesy of LDT]

- Personnel are capable and qualified to perform their assigned duties.
- Ingredients used in compounding have their expected identity, quality, and purity .
- Critical processes are validated to ensure that procedures, when used, will consistently result in the expected qualities in the finished preparation.
- The engineering controls and production environment is suitable for its intended purpose (addressing such matters as environmental cleanliness, control, monitoring, staff attire, and the setting of action limits, as appropriate).
- There is assurance that processes are always carried out as intended or specified and are under control.
- Appropriate stability evaluation is performed or determined from the literature for establishing reliable expiration dating to ensure that finished preparations have the expected potency, purity, quality and characteristics at least until the labeled expiration date.
- Appropriate release checks or testing procedures are performed to ensure that finished CSPs have their expected potency, purity, quality and characteristics at least until the labeled beyond use date.
- Preparation conditions and procedures are adequate for preventing mix-ups.
- There are adequate procedures and records for investigating the product, correcting failures or problems in preparation, testing, or in the preparation itself.