The 2023 USP Chapter Update to USP <797> :

What's in, What's out, What's changed [now] !

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DISCLOSURES -

- Lou Diorio is a shareholder of LDT Health Solutions, Inc., an International Medication Safety and & Quality Management Consultancy.

- The opinions expressed are that of the presenter and based upon the information provided by USP & FDA at the time of the presentation.
  - For the latest USP compendial references go to; www.USP.org
  - The latest FDA information and resources can be found at; www.FDA.gov

Session Objectives-

- **PHARMACISTS-**
  - Describe the expansion in the role of Segrgated Compounding Areas (SCAs) in compounding practice.
  - Describe three attributes of a fully compliant compounding personnel training program.
  - Differentiate between “Compounding” and “Immediate-Use” practices in modern health-system practice.
  - List three differences between a Category I and Category II Cleanroom complex.
- **Technicians-**
  - Describe the role of Restricted Access Barrier Devices (RABs) in compounding operations.
  - List three differences between a Category I and Category II Cleanroom complexes.
  - Describe the difference between “Quality Assurance” & “Quality Control” in everyday compounding practice.
  - Describe the role of Broad-spectrum Sporical use in Secondary Engineering Control Cleaning protocols.

GROUND RULES -

- Please ask questions at any time !
- The “management” reserves the right to defer any questions to the end of the session.

Lets Properly Frame the Conversation -

- Please understand that the USP General Chapters being discussed are being reviewed in the context of the published changes released on 11.1.22 by the USP Expert Committee versus the current, official USP/NF Chapters.
- The proposed changes are scheduled to take effect and become OFFICIAL on 1 November 2023.

- Please remember, these published chapters are not yet part of the compendia and are considered NOT Official until the effective date published in the USP/NF.
- So for now, the following is true;

  - <795> The 2014 revision is Official
  - <797> The 2008 revision is Official
  - <800> The July 1, 2020, is Official
  - <825> The December 1, 2020, is Official

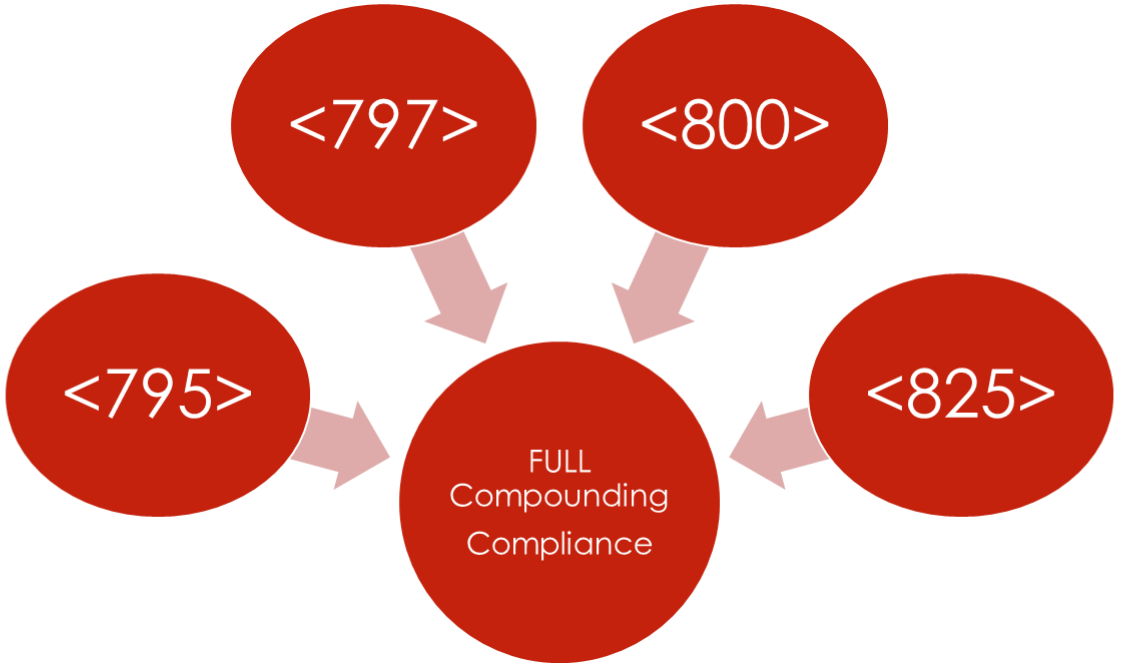
Sterile Compounding <797>

2023 Chapter Revisions

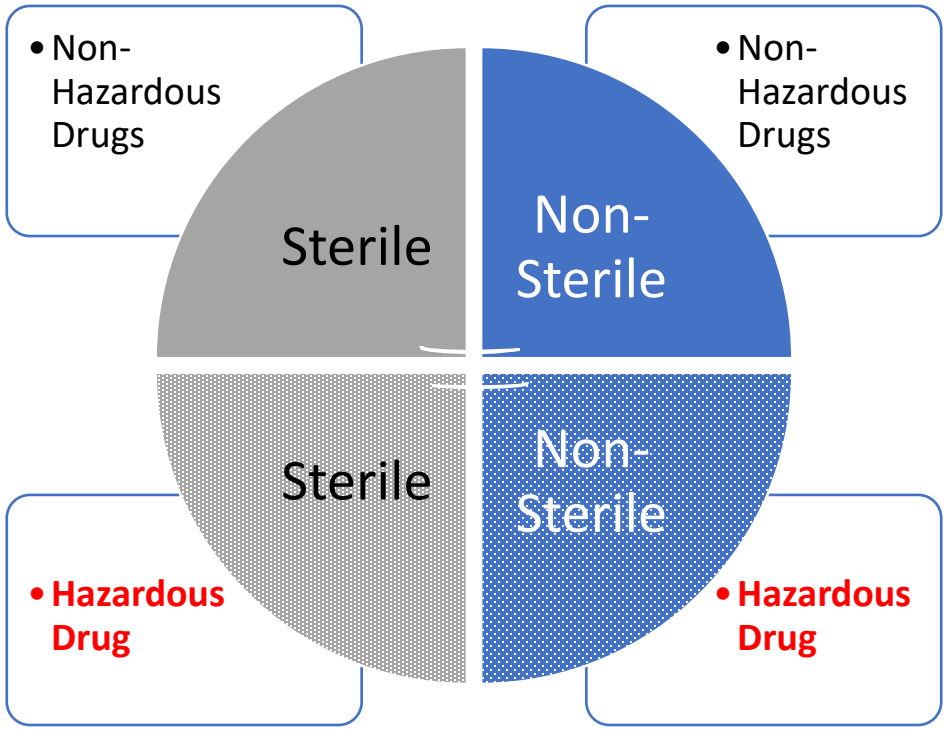
How will these changes to USP <797> impact practice ?

Be aware of the changes to the structure of the compounding chapters -

- The Revised Chapters are both Descriptive and Prescriptive….but could be incomplete if you refer to only one General Chapter, if required.
- Be careful of the “should” “shalls” and the “musts.”
- There are concepts and language that has been harmonized between Chapters.



Assess Your Compounding Operation



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The road to compounding compliance…

People

Places

Practices

USP <797> Sterile Preparations -

- Medicines intended to be Sterile:
  - Injections, including Infusions
  - Irrigations for internal body cavities (e.g., any space that does not normally communicate with the environment outside the body such as the bladder, or peritoneal cavity)
    - *Irrigations for the mouth, rectum, or sinus cavities are NOT required to be sterile!*
  - Ophthalmic Dosage forms
  - Aqueous Pulmonary Inhalation preps
  - Baths and Soaks for live organs and tissues
  - Implants

<797> Major Revisions –

- Change in the definition of “Compounding”
- Creation of THREE Categories (I, II, and III) vs. 3 Risk Levels (L, M, and H)
- Addition of Changes in “Immediate-Use CSPs” (1hr. to 4 hrs. to begin administration)
- Changes in Personnel Qualifications
- PEC changes in terminology – RABS, ISOLATORS, IVLFZ, PHARMACEUTICAL Isolators & ROBOTIC ENCLOSURES
- SEC requirement changes
- Expansion of the role of SCA’s (HD applications)
- Changes in Viable Air & Surface Monitoring (decrease in intervals for this testing)
- Changes in BUD determinations
- Refinement in the role of “QA” & “QC”
- Changes in Cleaning & Disinfection Requirements & Processes
- Changes in Compounding Documentation – Master Formula Docs & Batch Records

USP <797> Sterile Preparations

- NOW Includes standards for these specific practices –
  - Repackaging
  - Allergenic Extracts Prescription Sets
  - Blood derived or other Biological Material (i,.e. Analogous Blood) Compounding
- NOW "re-defines" – Administration and "Preparation" per "Approved Labelling" which could be out of the Scope of **USP <797>** if certain conditions are met.
- Revises the provisions for "Immediate Use" CSPs-
  - No more than **3 different sterile products**
  - Administration **must begin within 4 hours** *(previously 1 hour)* following preparation
- Replaces High / Medium /Low Risk Levels – with
  - **Category I**
  - **Category II**
  - **Category III**
- Carve out of Radiopharmaceuticals to **USP <825>**

Cleaning of Classified Areas / SCAs -

SITE	CLEANING	DISINFECTION	SPORICIDAL
PEC [and equipment within]	Daily [When used]	Daily[When used] 70% S-IPA	Monthly(1,2) Weekly (3)
Removable work tray of PEC (if applicable)	Daily (TOP, When used] Monthly (UNDER tray)	Daily[When used] 70% S-IPA	Monthly
Pass-Through(s)	Daily [When used]	Daily [When used]	Monthly(1,2) Weekly (3)
Work surface(s) outside of PEC	Daily [When used]	Daily [When used]	Monthly(1,2) Weekly (3)
Floors	Daily [When used]	Daily [When used]	Monthly(1,2) Weekly (3)
Wall(s), Door(s), & Door Frame(s)	Monthly	Monthly	Monthly
Ceilings	Monthly	Monthly	Monthly
Storage Shelves & Bins	Monthly	Monthly	Monthly
Equipment Outside the PEC(s)	Monthly	Monthly	Monthly (1,2) Weekly (3)

* From Table 8 - Minimum Frequency for Cleaning and Disinfecting Surfaces and Applying Sporicidal Disinfectants in Classified Areas and within the Perimeter of the SCA - USP <797> © 2021 USP Pharmacopeial Convention

Changes in Personnel Qualifications & Training -

Skill / Competency	Frequency
Hand Hygiene & Garbing	Orientation, then annually
Basic Aseptics	Orientation, then Q6mo (Category I, II) Q 3mo (Category III)
Personnel Media Qualifications	
Fingertip & Thumb Sampling	
Return demonstration of competency	

Is it “Compounding” or Immediate –Use ?

Preparation per Approved Labelling	Immediate-Use CSPs
NOT Compounding -	Compounding for direct and immediate administration to a patient not subject to Category I, II or III. if all of these conditions are met:
“…mixing, reconstitution or other such acts that are preformed in accordance with directions contained in approved labelling and other manufacturer directions consistent with that labelling.”	• Written SOPs are followed (incl. aseptic technique) • Personnel are trained & demonstrate competency • In accordance with approved labelling or stability studies • Not greater than three (3) sterile FDA products • Any remainder from SDVs are discarded • Begin Administration within 4 hours • Conforms to specific Labelling Requirements
OUT of USP <797> Scope if:	
• Prepared as a single dose • For a single Patient • Approved Labelling specifies diluent, resulting strength, container closure system, and storage time.	

Category **ONE** -

A PEC inside a SCA or a C-PEC inside a C-SCA

- BUD
  - 12 hours (or less) at controlled room temperature
  - 24 hours (or less) when refrigerated
  - And ONLY if compounded in accordance with applicable requirements for Category ONE CSPs in the Chapter.
  - NO Requirements for <71> & <85> testing

Category **TWO** -

The Road to Category TWO always goes through an Ante-Room –

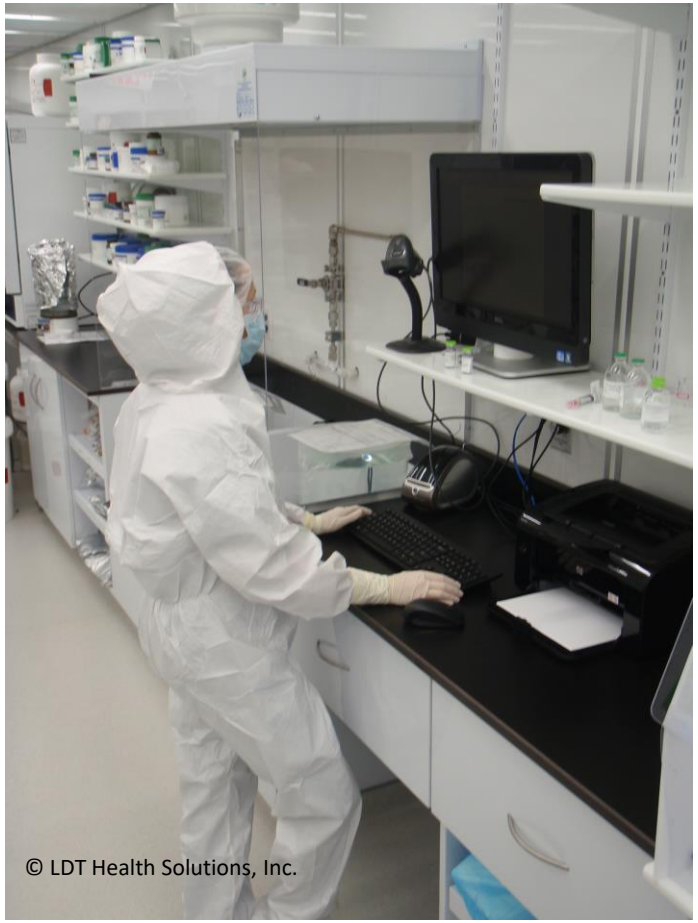
- BUDs-
  - 4 days at controlled room temperature
  - 10 days when refrigerated
  - 45 days when frozen
  - Requirements for <71> & <85> testing based on BUD assigned – See <797> Table 11.
  - And ONLY if compounded in accordance with applicable requirements for Category II CSPs in the Chapter.

BUD Limits for Category TWO CSPs -

CSP Characteristics		Storage Conditions		
Compounding Method	Sterility Test <71> Performed & Passed	Controlled Room Temp (20-25 C)	Refrigerator (2-8 C)	Freezer (-25 to -10 C)
Aseptically Processed CSPs	NO	From one or more non-sterile starting component(s): 1 DAY	From one or more non-sterile starting component(s): 4 DAYS	From one or more non-sterile starting component(s): 45 DAYS
		From only sterile starting component(s): 4 DAYS	From only sterile starting component(s): 10 DAYS	From only sterile starting component(s): 45 DAYS
	YES	30 DAYS	45 DAYS	60 DAYS
Terminally Sterilized CSPs	NO	14 DAYS	28 DAYS	45 DAYS
	YES	45 DAYS	60 DAYS	90 DAYS

* From Table 11 - BUDs for Category 2 CSPs USP <797> © 2021 USP Pharmacopeial Convention

Category **THREE** -



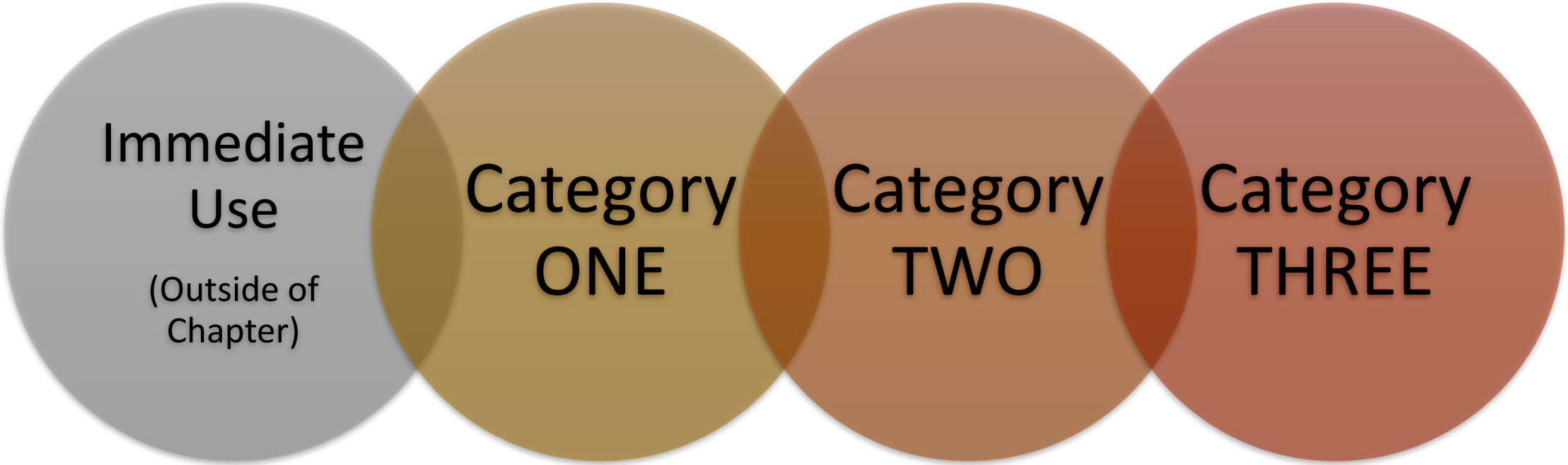
- Category THREE starts with an ISO-classed cleanroom suite, including an ANTE.
- Then, Comply with ALL requirements for Category TWO CSPs, **AND -**
- **Fulfill ALL the additional Category THREE burdens for:**
  - **Sterile Garb**
  - **Use of Sporicidal Disinfectant Agents**
  - **Increased Frequency of Environmental Monitoring**
  - **Stability Determinations (USP Method)**
- **Undergo Sterility testing [<71>].**
  - **Supplemented by Endotoxin testing [<85>] if applicable.**

BUD Limits for Category THREE CSPs -

CSP Characteristics	Storage Conditions		
Compounding Method	Controlled Room Temp (20-25 C)	Refrigerator (2-8 C)	Freezer (-25 C to – 10 C)
Aseptically processed, Sterility tested <71>, and passing all applicable tests for Category THREE CSPs	60 DAYS	90 DAYS	120 DAYS
Terminally sterilized, Sterility tested <71>, and passing all applicable tests for Category THREE CSPs	90 DAYS	120 DAYS	180 DAYS

* From Table 11 - BUDs for Category 2 CSPs USP <797> © 2021 USP Pharmacopeial Convention

“3 Categories + 1”



Summary & Conclusions -

- Full Compliance to the 2023 Revised USP Compounding Chapters will require a multi-pronged approach.
  - Including possible physical plant, PEC, and workflow changes!
- Considerations to FDA Guidance, CETA standards, and Local BOP regulations & requirements will be necessary to assure that compliance gaps are eliminated.
- Patient Safety is the Primary Objective !

QUESTIONS

- Many Thanks !

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Reading List / Bibliography -

- **General Chapter USP <795> <797> <800> - www.usp.org**
- **Controlled Environmental Testing Association (CETA) – www.CETAinternational.org**
- **Centers for Disease Control & Prevention www.cdc.gov**
- **Pharmacy Purchasing and Products Magazine- www.pppmag.com**
- **FDA Website – www.FDA.gov**
  - **Drug Quality & Safety Act -**
    - http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm376732.htm
  - **Guidance – Pharmacy Compounding -**
    - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM377052.pdf
  - **Guidance – Hospital & Health System Compounding-**
    - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM496287.pdf
- **OSHA / NIOSH Resources –**
  - **HD Drug list - http://www.cdc.gov/niosh/docs/2016-161/default.html**
  - **NIOSH Drug Alert- http://www.cdc.gov/niosh/docs/2004-165/default.html**
  - **Workplace Solutions – PPEs- http://www.cdc.gov/niosh/docs/wp-solutions/2009-106/pdfs/2009-106.pdf**
  - **DONNING & DOFFING – (videos) http://www.cdc.gov/vhf/ebola/hcp/ppe-training/**
  - **CSTD- (Draft for comment) - http://www.cdc.gov/niosh/docket/review/docket288/default.html**