Meeting New Requirements for Sterile Compounding Webinar

June 28, 2016
CHA Webinar

Welcome

Liz Mekjavich
California Hospital Association
Continuing Education Requirements

Full attendance, completion of online evaluation and attestation of attendance is required to receive CEs for this webinar. CEs are complimentary and available for the registrant. Post-event survey will be sent this afternoon. Please fill out the survey — we value your input on our programs.

Continuing Education Offered for this Program

**Compliance** — This program has been approved for 2.4 Compliance Certification Board (CCB) Continuing Education Units. Granting of prior approval in no way constitutes endorsement by CCB of the program content or the program sponsor. (Note: CE recipients are solely responsible for retaining a copy for their records and for reporting credits to CCB)

**Health Care Executives** — CHA is authorized to award 2.0 hours of pre-approved ACHE Qualified Education credit (non—ACHE) for this program toward the advancement, or recertification in the American College of Healthcare Executives. Participants in this program wishing to have the continuing education hours applied toward ACHE qualified education credit should indicate their attendance when submitting application to the American College of Healthcare Executives for advancement or recertification.

**Nursing** — Provider approved by the California Board of Registered Nursing, CEP #11924, for 2.4 Contact Hours.

**Legal** — CHA is a State Bar of California-approved MCLE provider. Provider number 1980. This participatory activity has been approved for 2 hours of MCLE credit.
Program Overview and Introductions

BJ Bartleson, RN, NEA-BC
California Hospital Association

Jeannette Hanni, received her Bachelor of Pharmacy degree from Washington State University. She then completed her Master’s degree in Public Administration for Health Services Administration from the University of San Francisco, graduating with honors. Ms. Hanni is currently the Executive Director of Pharmacy for the Bay Area for Sutter Health, West and South Bay. In addition to overseeing the operations of her respective facilities Ms. Hanni has spent the last 10+ years becoming heavily involved in health care policy and medication safety. Ms. Hanni has served as Co-Chair of the very active CHA Medication Safety Committee since its inception in 2009. Through her association with this committee Ms. Hanni has been fortunate to be able to impact the revisions of several important State laws and regulations and to be a part of creating various tools and guidelines to aid the health care community on important medication safety initiatives and challenges. Ms. Hanni has spent many years as an active member of the California Society of Health System Pharmacists, serving as local chapter President, and as a director for the CSHP Board of Directors.
Doug O'Brien received his Doctor of Pharmacy degree from the University of California, San Francisco. He completed his residency in Clinical Pharmacy at Long Beach Memorial Hospital.

Since 2008, has served as the Northern California Regional Director for Inpatient Pharmacy Services for Kaiser Foundation Hospitals. Prior to joining Kaiser Permanente he was the Director of Inpatient Pharmacy Services at Friendly Hills Regional Medical Center in La Habra, California. Dr. O'Brien’s 30 years of professional experience includes roles as Director of Clinical Pharmacy Services at La Habra Community Hospital, and Vice-President of Clinical Pharmacy Consultants, Inc., providing consulting and educational services to various medical centers throughout Southern California. He currently serves as a Member of the California Hospital Association’s Medication Safety Committee.

Michael Ignacio, is a supervising inspector with the California Board of Pharmacy, where he provides guidance, and investigative case plans and assessments to direct investigations. In addition, Mr. Ignacio trains inspector staff, consults with executive staff on complex enforcement and licensing program activities, and has assisted in the development of revisions to California compounding regulations. Prior to joining the Board of Pharmacy, he practiced as a pharmacist, where he was involved with high-risk sterile compounding.
Virginia Herold, became executive officer of the Board of Pharmacy in January 2007. Prior to this appointment, Ms. Herold served as assistant executive officer of the Board for 16.5 years, and interim executive officer for seven months.

As executive officer, Ms. Herold works closely with and advises the 13 Board of Pharmacy members in the development of policy and in the administration of the board’s enforcement, licensing and regulatory programs to further the board’s consumer protection mandate. The Board regulates over 130,000 licensees in 13 separate licensure classifications including pharmacists, pharmacies and drug wholesalers.

Faculty

Lynn Paulsen, is a pharmacist with over 40 years of experience in the spectrum of hospital pharmacy practice; rural, pediatric specialty, community and academic Medical center. She received her Pharm.D. from UCSF after a B.A. from UC Berkeley. The past 5 years have been with UC Health at the University of California in identifying policy, legislation, practice standards and opportunities for the statewide UC system. Patient safety has been her passion throughout her career and translating the complex regulations around sterile compounding into clear and concise guides so that California hospital pharmacies can provide the safest care in the country is her goal. She is moving to be closer to the 3 (soon to be 4) grandsons but will be continuing to work in pharmacy in different capacities.
The Impact of Regulatory Changes on Sterile Compounding

Introduction and Background

Jeannette Hanni, Executive Director of Pharmacy, Sutter Health Bay Area

Goals for the Program

- Become more familiar with the events that led to the increased federal and state oversight and regulation of sterile compounding
- Gain a better understanding of the changes that are being made to USP 797 and 800, and how those changes will directly affect your operations and processes
- Gain a better understanding of the changes that have been made to the California State Board of Pharmacy Sterile Compounding regulations, effective January 1, 2017
- Be introduced to the Board of Pharmacy waiver process that will be available to facilities who have determined that the time needed for local design and construction would not allow them to be compliant on January 1, 2017
- Be introduced to the newly-released crosswalks of the new regulations
- Gain familiarity with the newly-released sterile compounding matrix tools to aid in understanding each regulation at a granular level. These tools and the crosswalks are designed to give each facility a very nuts and bolts method of determining compliance for each major section of the regulations (e.g., facility design, testing, garbing, cleaning, temperature monitoring and documentation)
Early Events

May, 2001, Doc’s Pharmacy in Walnut Creek — Spinal injection of contaminated betamethasone causing acute bacterial meningitis, 13 people hospitalized, three deaths

October, 2001*, The Board of Pharmacy supports the introduction and passage of proposed legislation increasing the standards for pharmacies engaged in sterile compounding

January, 2002*, The Governor signed SB 293 (Torklakson)
1) Requires a separate sterile compounding license for pharmacies engaging in injectable sterile compounding
2) The bill also required that such sterile compounding be performed in a manner consistent with guidelines adopted by the Board
3) Exempted facilities with The Joint Commission accreditation

October, 2013 Governor Jerry Brown signs AB 294 (Emerson), following two incidents of out of state product shipped into California that caused significant harm in June and October, 2012
Hospital exemption for sterile compounding licensure is removed in July, 2014

* “The Script, October, 2001” and “The Script, January, 2002”

The Response to the New England Compounding Center Tragedy 2012 - 2016

New England Compounding Center
- In September of 2012, NECC contaminated spinal preparations sold to hospitals and MD offices
- The NECC tragedy has had profound impact on the practice of sterile compounding in the U.S.

National Response
- On November 27, 2013 President Obama signed the Drug Quality and Security Act (DQSA) into law
- The DQSA contains important provisions relating to the oversight of compounded products
- One provision of the DQSA is mandatory compliance with United States Pharmacopeia standards (USP 797 & 800) in all practice settings
- USP 797 and 800 regulations pertaining to sterile compounding are now legally enforceable in all 50 states

FDA Response
- In February 2016, a new chapter of USP was approved, USP 800. This chapter mandates specific requirements for facilities handling hazardous drugs (e.g., chemotherapy). This chapter is entirely focused on requirements to ensure employee safety
- USP Part III deals with hazardous compounding and storage of drug in negative pressure rooms that are externally vented, effective July 2018
- In September 2015, USP 797 was completely re-written and will most likely have a similar effective date of July 2018

California State Response
- AB 294 signed by Governor Jerry Brown in October, 2013
- In July of 2014, the California State Board of Pharmacy adopted a new licensing requirement for hospital pharmacies who compound sterile injectable products and inspects every licensed compounding facility annually
- In 2016, the State Board wrote a significant revision to their sterile compounding regulations, aligning more closely to the requirements of the Federal law with much stricter language. These regulations were adopted in February, 2016 and currently have an effective date of January, 2017
Federal Changes
Doug O’Brien, PharmD
Kaiser Permanente

The USP and Chapter 797

- The United States Pharmacopeia-National Formulary (USP-NF)
  - Recognized in the 1938 Federal Food, Drug, Cosmetic Act as the official compendia of drug standards in the United States
  - Chapters numbered 1-999 are official monographs and standards, and are enforceable by the FDA

- USP Chapter 797: Pharmaceutical Compounding – Sterile Preparations
  - Intended to protect patients by ensuring compounded sterile preparations (CSPs) are safe for use, including hazardous drugs
  - Applies to all persons who prepare CSPs and all places where CSPs are prepared
  - First published in 2004, subsequently revised in 2008 (current version)
  - New Draft version released in 2015 (comment period ended Jan 31, 2016)
  - Revised Chapter will most likely become effective July 1, 2018
USP Chapter 800

- USP Chapter 800: Hazardous Drugs - Handling in Healthcare Settings
  - Describes practices and quality standards for handling and compounding hazardous drugs
  - Intended to promote patient safety, worker safety, and environmental protection
  - Released Feb 1, 2016 and will become effective July 1, 2018
  - Applies to all healthcare personnel who handle hazardous drugs, and all facilities that store, prepare, transport, or administer hazardous drugs
  - Hazardous drug standards will no longer be included in Chapter 797 when Chapter 800 becomes effective

CMS Conditions of Participation for Hospitals

- CMS State Operations Manual Appendix A – Survey Protocol, Regulations and Interpretive Guidelines for Hospitals
  - Contains the tasks and interpretive guide for conducting surveys in hospitals to validate compliance with all CMS requirements
  - Compliance with USP Chapter 797 was added as a requirement on October 30, 2015
  - Language added to the Pharmaceutical Services section to require compliance with USP Chapter 797 when compounding sterile preparations
  - Language added to the Nursing Services section to require compliance with USP Chapter 797 when compounding sterile preparations outside the pharmacy (“immediate-use CSPs”)
  - Increases the regulatory scrutiny related to the compounding of sterile preparations throughout the hospital by surveyors from CMS and The Joint Commission
2017 Compounding Regulations
Speaker: Michael Ignacio, PharmD
Slides by: Christine Acosta, PharmD

California State Board of Pharmacy
- 141,373 licensees
- Drug rooms (38)
- Hospital pharmacies (485)
- Licensed correctional facilities (53)
- Non-Resident pharmacies (453)
- Non-Resident sterile compounding facilities (91)
- Pharmacies (6,572)
- Sterile compounding facilities (936)
- Centralized Hospital Packaging Pharmacy (5)
Compounding Definitions

- “Potency” active ingredient strength within +/- 10% (or the range specified in USP37-NF32, 37th Revision, Through 2nd Supplement Effective December 1, 2014) of the labeled amount.
- Sterile injectable products compounded solely from commercially manufactured sterile pharmaceutical products in a health care facility licensed under section 1250 of the Health and Safety Code are exempt from this definition. For those exempt, the range shall be calculated and defined in the master formula.
- “Preparation” means a drug or nutrient compounded in a licensed pharmacy; the preparation may or may not be sterile.

Compounding Quality Assurance (1735.8)

- Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug preparations.
- The quality assurance plan shall include written procedures for verification, monitoring, and review of the adequacy of the compounding processes and shall also include written documentation of review of those processes by qualified pharmacy personnel.
Compounding Quality Assurance

The quality assurance plan shall include:

- Written standards for qualitative and quantitative analysis of compounded drug preparations to ensure integrity, potency, quality, and labeled strength, including the frequency of testing.
- All qualitative and quantitative analysis reports for compounded drug preparations shall be retained by the pharmacy and maintained along with the compounding log and master formula document.
- A schedule for routine testing and analysis of specified compounded drug preparations to ensure integrity, potency, quality, and labeled strength, on at least an annual basis.
- Written procedure for scheduled action in the event any compounded drug preparation is ever discovered to be outside minimum standards for integrity, potency, quality, or labeled strength.
- Written procedure for responding to out-of-range temperature variations within the pharmacy and within patient care areas of a hospital where furnished drug is returned for redispensing.

Facility and Equipment Standards for Sterile Compounding

- Viable surface sampling shall be done at least:
  - Every six months for sterile-to-sterile compounding.
  - Quarterly for all non-sterile-to-sterile compounding.
- Viable air sampling by volumetric air sampling procedures under dynamic conditions at least once every six months.
- When the environmental monitoring action levels are exceeded, the pharmacy shall identify the CFUs at least to the genus level in addition to conducting an investigation pursuant to its policies and procedures. Remediation shall include, at minimum, an immediate investigation of cleaning and compounding operations and facility management.
- The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-24 degrees Celsius (68-75 degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.
- A licensee may request a waiver of these provisions as provided in section 1735.6(f).
Sterile Compounding Consultation; Training of Sterile Compounding Staff

Pharmacies that compound sterile drug preparations must comply with the following training requirements:

- Each person engaged in sterile compounding must successfully complete practical skills training in aseptic technique and aseptic area practices using models that are comparable to the most complex manipulations to be performed by the individual.
- Each pharmacist responsible for, or directly supervising and controlling, aseptic techniques or practices, must demonstrate the skills needed to ensure the sterility of compounded drug preparations.
- Evaluation must include written testing and a written protocol of periodic routine performance checks involving adherence to aseptic area policies and procedures.
- Each person’s proficiency and continuing training needs must be reassessed at least every 12 months.
- Results of these assessments must be documented and retained in the pharmacy for three years.

Sterile Compounding Quality Assurance and Process Validation (1751.7)

- Any pharmacy engaged in compounding sterile drug preparations shall maintain, as part of its written policies and procedures, a written quality assurance plan including, in addition to the elements required by section 1735.8, a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities.
- The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications.
- The quality assurance program shall include the following:
  - (1) Procedures for cleaning and sanitization of the sterile preparation area.
  - (2) Actions to be taken in the event of a drug recall.
  - (3) Documentation justifying the chosen beyond use dates for compounded sterile drug preparations.
Sterile Compounding Quality Assurance and Process Validation

- The pharmacy and each individual involved in the compounding of sterile drug preparations must successfully demonstrate competency on aseptic technique and aseptic area practices before being allowed to prepare sterile drug preparations.

- The validation process shall be:
  - Carried out in the same manner as normal production,
  - Be representative of the types of manipulations, products and batch sizes,
  - Shall be as complicated as the most complex manipulations performed by staff and contain the same amount or greater amount of volume transferred during the compounding process,
  - The same personnel, procedures, equipment, and materials must be used in the testing,
  - Media used must have demonstrated the ability to support and promote growth. Completed medium samples must be incubated in a manner consistent with the manufacturer’s recommendations.
  - If microbial growth is detected, then each individual’s sterile preparation process must be evaluated, corrective action taken and documented, and the validation process repeated.

Sterile Compounding Quality Assurance and Process Validation

- Each individual’s competency must be revalidated every:
  - 12 months for compounding from sterile ingredients.
  - 6 months for compounding from non-sterile ingredients.

- The pharmacy’s validation process on aseptic technique and aseptic area practices must be revalidated whenever:
  - Quality assurance program yields an unacceptable result,
  - There is any change in the compounding process, the Primary Engineering Control (PEC), or the compounding environment.

- The pharmacy must document the validation and revalidation process.
Sterile Compounding Quality Assurance and Process Validation

- All sterile compounding personnel must successfully complete an initial competency evaluation.
- Immediately following the initial hand hygiene and garbing procedure, each individual who may be required to do so in practice must successfully complete a gloved fingertip (all fingers on both hands) sampling procedure (zero colony forming units for both hands) at least three times before initially being allowed to compound sterile drug preparations.
- Re-evaluation of garbing and gloving competency shall occur every:
  - 12 months for compounding from sterile ingredients.
  - 6 months for compounding from non-sterile ingredients.

Compounding Requests for Construction Waiver

Virginia Herold
Executive Officer
CA State Board of Pharmacy
Title 16 California Code of Regulations section 1735.6(f);

Where compliance with the amendments to Article 4.5 or Article 7 require physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s).

More 1735.6

Application for any waiver shall be made by the licensee in writing, and the request shall identify the provision(s) requiring physical construction or alteration, and the timeline for any such change(s). The board or its designee may grant the waiver when, in its discretion, good cause is demonstrated for such waiver.
Under Construction

- The Enforcement and Compounding Committee of the board is working to develop the process for submittal and review of waivers
- At early stages of development - completion expected in fall.

Components

The board will seek the assistance of OSHPD in reviewing waivers. OSHPD’s recommendations include such components as:
- Purpose
- Scope of the project
- Project plan
- Definitive dates, including for project completion
- Structural modifications vs. non-structural modifications (remodel)
- Design professionals involved (including the architect of record and the inspector of record)
More to Come

- The next Enforcement and Compounding Committee meeting will further discuss the process for waivers more fully
- Meeting date: August 31

Using the CHA Sterile Compounding Tools

Lynn Paulsen, PharmD
Director, Pharmacy Practice Standards
UC Health, University of California
Why Were These Tools Developed?

- Pharmacists like to do things “right” but the last 10 years has been change by citation
- One goal is to provide everyone information in a more user-friendly format so that each facility does not have to do the difficult work of interpretation and translation
- The **BIG Goal** is to have patients in California experience the safest sterile compounding in the country/world

Does My Hazardous Compounding Space Meet the Requirements?

**Step 1: Do you perform hazardous sterile compounding in your hospital pharmacy?**

- Yes – Proceed to Step 2
- No – Stop here. You don’t need to perform an assessment regarding *hazardous* sterile compounding. However, you will need to assess and compare changes that may be required for *non-hazardous* sterile compounding. Those changes can be found in the “CHA Sterile Compounding Matrices,” included with this packet
Step 2: What engineering controls and hazardous sterile compounding space do you have now? Check all that apply.

- A separate negative pressure room
- International Standard Classification Organization (ISO) class seven or cleaner air
- A negative pressure, unidirectional airflow hood vented to the outside, and at least 30 air exchanges per hour

*If you have checked the previous three boxes above, you will meet the January 1, 2017 requirements for the full Beyond Use Days (BUDs) requirements. Stop here. You have completed the assessment and will meet the regulatory requirements for hazardous compounding for full BUD requirements.*

Step 3: If you don’t have all three of the above, do you have any of the following?

- A separate, negative pressure room
- Unclassified International Organization for Standardization (ISO) and air
- A negative pressure, unidirectional non-turbulent airflow hood, vented to the outside and at least ten air exchanges per hour

*If all three are checked, you will meet the January 1, 2017 requirements for the short BUDs (12 hours) hazardous sterile compounding, without the need for a waiver. Stop here. You have completed the assessment, unless you plan to extend your BUD capabilities, in which case you will need to skip to “Next Steps” (see below).*
More Difficult Situations

Any of the following:

• Negative pressure hood, not uni-directional
• No negative pressure room
• No negative pressure hood
• Hood not vented to the outside

Any of these will **not** meet the requirements and will require reconfiguration or other solution.

One Last Hope

If you have:

• Negative pressure, unidirectional hood
• Vented to the outside
• But, no negative pressure room

Consider a space that could be reconfigured to meet the minimum air exchanges and become negative pressure. This could be a relatively low cost solution for 12-hour BUD.
Next Steps

• Inform your senior management team of your initial assessment and potential changes needed to perform hazardous sterile compounding relative to BUD requirements. Also, inform them that the Board of Pharmacy will require a waiver for planned changes if the proposed facility changes will not meet the January 1, 2017 regulatory deadline
• Meet with appropriate staff and your facilities manager to determine a suitable location that can become a negative pressure room with venting to the outside (one vent per hood)
• If you have a recirculating hood, add a new hood to the budget and or contact the manufacturer for a possible upgrade

Next Steps (cont.)

• Engage an architect, if applicable, for construction plans/modifications
• Confer with your facilities manager to determine a tentative budget and timeline
• Prepare for OSHPD approval process if applicable
• Begin the process for capital budget and seek capital budget approval
• Submit a waiver to the Board of Pharmacy that includes:
  o The assessment
  o The plan
  o The timeline
### Non-Hazardous

- January 1, 2017 vs. July 1, 2018
- Scenario 1
  - ISO Class 7 clean room
  - ISO 8 or better ante-area

#### SECONDARY ENGINEERING CONTROL (Sterile Compounding Space)
<table>
<thead>
<tr>
<th>PRIMARY ENGINEERING CONTROL (PEC-Sterile Compounding Hoods)</th>
<th>Beyond Use Dates</th>
<th>Comments</th>
</tr>
</thead>
</table>
| • Temp 20-24°C (68-75°F)  
• HEPA-filtered air | **LOW RISK**  
• ISO 5 with unidirectional flow  
• HEPA-filtered fine air  
• Non-turbulent | **MEDIUM RISK**  
• Sterile to sterile  
• <= 3 commercial packages  
• <= 2 entries into 1 sterile container | APPLIES TO ALL |

#### ISO Class 7 clean room with ISO 8 or better ante-area
- No sink in clean room
- Sink in ante
- 0.02-0.05" w.c. positive pressure differential relative to all adjacent spaces
- Displacement airflow method: requires air velocity of 40 feet per minute from the clean area across the line of demarcation into the ante area, from floor to ceiling and wall to wall

#### Any ISO Class 5 PEC:
- Laminar Flow Hood
- Biological Safety Cabinet with unidirectional flow
- Compounding automated robots
- Compounding Aseptic Isolators (CAI) with unidirectional flow.
- Air within the CAI shall not be recirculated or turbulent. CAI must meet requirements in 1751.4 (f)(1-3)

|  | 48 hours at Room Temp*  
|  | 14 days at Cold Temp**  
|  | 45 days Solid Frozen State***  
|  | **CCR §1751.8 (a)**  
|  | 30 hours at Room Temp*  
|  | 9 days at Cold Temp**  
|  | 45 days Solid Frozen State***  
|  | **CCR §1751.8 (b)**  

|  |  

* Each ISO environment requires certification at least every 6 months CCR §1751.4(b)(1), 1751.4(f)
* Document data pressure, differential or air velocity, or use continuous recording devices between adjoining ISO rooms. 1751.1(c)(5)
Non-Hazardous

- Scenario 2
  - Segregated sterile compounding area

<table>
<thead>
<tr>
<th>Segregated sterile compounding area</th>
<th>PRIMARY ENGINEERING CONTROL (PEC=Sterile Compounding Hood)</th>
<th>Beyond Use Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Any preparation area that is not ISO classed, exceeds ISO 7 limits, or does not meet pressure or air flow differentials</td>
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<tr>
<td>• PEC within demarcated area (at least 3 ft perimeter/separate room)</td>
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<tr>
<td>• Unidirectional airflow, windows/doors that connect to remainder of building</td>
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<tr>
<td>• Not in high traffic area</td>
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<tr>
<td>• Not adjacent to construction sites, warehouses, or food preparation</td>
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<tr>
<td>• Sink at least 3 ft from PEC</td>
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<td></td>
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<tr>
<td>• Compounding Aseptic Isolators (CAI)</td>
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<tr>
<td>• Manufacturer of CAI must provide documentation for meeting requirements in 21CFR §1751.4(f)(1-3) CAI must be certified part of the certification process</td>
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<tr>
<td>48 hours at Room Temp*</td>
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<tr>
<td>14 days at Cold Temp**</td>
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<tr>
<td>45 days Solid Frozen State***</td>
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<tr>
<td>• Laminar Flow Hood</td>
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<tr>
<td>• Biological Safety Cabinet with unidirectional flow</td>
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<tr>
<td>• CAI where mfg not meeting requirements in 21CFR §1751.4(f)(1-3)</td>
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<tr>
<td>12 hours</td>
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<td>CCR §1751.8 (a)</td>
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<tr>
<td>12 hours</td>
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<tr>
<td>CCR §1751.8 (b)</td>
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<tr>
<td>• No PEC or outside ISO 5 PEC</td>
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<tr>
<td>• Under conditions not meeting all requirements in any subdivision</td>
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<tr>
<td>• Labeled &quot;Immediate Use&quot; and shall be administered as later than 1 hour after mixing</td>
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<tr>
<td>• Requires use of sterile gloves over isolator gloves</td>
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<tr>
<td>• PEC requires certification at least every 6 months CCR §1751.4(f)</td>
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<tr>
<td>• Sink can be within 3 ft of CAI</td>
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<tr>
<td>• Compounded only in limited situations where failure to administer could result in loss of life or intense suffering, and in quantity to meet immediate need</td>
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How is USP 797 Changing?

Category 2

PEC in ISO 7 Buffer room
- With ISO 8 or better ante, separated from
- Buffer and ante must be separate rooms with walls and doors, and controls to prevent low quality air into controlled areas
- Sink in ante
- Buffer and ante must have ACPH ≥ 15, at least 15 must be HEPA filtered fresh air in, recirculated
- Positive pressure differential at least 0.02” wc to separate each ISO classified area and from ante to general pharmacy area

ISO Class 5 PEC:
- Laminar Air Flow System (LAFS)
- Biological Safety Cabinet (BSC)
- Restricted Access Barrier System (RABS), can be CAI or CACI

Sterile to Sterile, No Preservatives, Aseptic Technique

<table>
<thead>
<tr>
<th>Room Temp</th>
<th>BUD</th>
<th>Refrigerated</th>
<th>Freezer</th>
</tr>
</thead>
<tbody>
<tr>
<td>No: 6 days</td>
<td>9 days</td>
<td>45 days</td>
<td>NO 28 days</td>
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</tbody>
</table>

BUD days start after the quarantine period for sterility testing
For: Terminal sterilization, preservatives, non-sterile to sterile compounding
BUDs, please see the USP <797> document

- Recertification every 6 months
- No tacky mats in ISO classified areas
- Document pressure differential or velocity daily in anterooms
- No shipping or external cartons allowed in buffer/ante
- Endotoxin testing required for CSP compounded from non-sterile ingredient(s)

PEC in ISO 8 area
- Sink can be in ISO 8 area 1 meter from PEC
- Must have ACPH ≥ 15, must be HEPA filtered fresh air in, recirculated
- Positive pressure differential at least 0.02” wc to separate each ISO classified area and to general unclassified area

Isolator (must meet standards; see lines 505-511 in proposed USP <797>)

Category 1

Segregated compounding area (SCA)
- Not ISO classified
- Buffer/ante not meeting ISO 7/8 respectively
- Buffer/ante fails surface sampling
- Away from significant traffic flow
- Away from unsealed doors/windows that connect to outdoor
- Perimeter must be defined
- Sink must be 1 meter from PEC (greater than the 3 ft for the BOP requirements)
- Not adjacent to construction, warehouse or food prep

ISO Class 5 PEC:
- Laminar Air Flow System (LAFS)
- Biological Safety Cabinet (BSC)
- Restricted Access Barrier System (RABS), can be CAI or CACI

- Less than or equal to 12 hours at Room Temp*
- Less than or equal to 24 hours at Cold Temp [Refrigerator]**

And This

Category 1

<table>
<thead>
<tr>
<th>Comments</th>
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<tbody>
<tr>
<td>Recertification every 6 months</td>
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<tr>
<td>Endotoxin and sterility testing not required for products</td>
</tr>
<tr>
<td>No shipping or external cartons allowed in SCA</td>
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</table>

And This
Hazardous Drugs 1/1/2018

All the Other Grids are MUCH Easier Temperature

<table>
<thead>
<tr>
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<td>A2</td>
<td>12º</td>
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<td>C1</td>
<td>C2</td>
<td>30º</td>
<td>E1</td>
<td>E2</td>
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<td>E1</td>
<td>E2</td>
<td>32º</td>
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<td>32º</td>
<td>I1</td>
<td>I2</td>
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<td>J1</td>
<td>J2</td>
<td>35º</td>
<td>J1</td>
<td>J2</td>
</tr>
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<td>A2</td>
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<td>D1</td>
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<td>D1</td>
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<td>D1</td>
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<td>D2</td>
<td>-2º</td>
<td>D1</td>
<td>D2</td>
</tr>
</tbody>
</table>

- **All the Other Grids** are MUCH easier temperature.
- Temperature ranges in the table are based on recommendations from the USP <797> and USP <800> guidelines.
- **MDM:** For all medications in MDM use the specific Brand Name, Drug Code and Lot Number on stability charts.
- **USP 39 NF 34 (2016):** Updates to the USP <797> include requirements for pharmaceutical compounding under the Act, storage of hazardous materials, and use of pharmaceutical compounding under the Act.
- **USP <797>:** Proposed for implementation on June 1, 2018.

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**SECONDARY ENGINEERING CONTROL**
- Temperature 20-24ºC (68-75ºF)
- Extensively ventilated
- Negative pressure
- Physically separate rooms

**PRIMARY ENGINEERING CONTROL**
- PEX-80 Class 4 horizontal unidirectional airflow
- Negative pressure
- Sterile packaging
- Pure class ISO 5 PEC

**LOW RISK** Compounding
- Biological Safety Cabinet, Class I Type A2
- Compounding Aseptic Isolator, Class II Type B2

**MEDIUM RISK** Compounding
- Biological Safety Cabinet, Class II Type A2
- Compounding Aseptic Isolator, Class II Type B2

**SECONDARY ENGINEERING CONTROL**
- Biological Safety Cabinet, Class I Type A2
- Compounding Aseptic Isolator, Class II Type B2

**Comments**
- Document daily pressure on differential and air velocity, and at worst-case operating points, between adjoining ISO rooms.
- Automatic monitoring of air pressure and airflow, in addition to the overlap of ISO systems.
- Performance testing of monitoring devices per USP <797>.

**MONITORING REQUIREMENTS**
- All electronic monitoring devices used for temperature monitoring should be calibrated monthly before use, and validated before use.
- Minimum 30 ACPH

**WHAT IS MKT?**
Mean Kinetic Temperature approximates the effects of temperature on drug degradation.
- Higher temperatures result in faster degradation.
- Lower temperatures result in less degradation.

**OPERATIONAL REQUIREMENTS**
- MAAYANA/ASANA/ATANA-MANNA
- Bacterial Spore Test
- Microbiological Air Sampling
- Equipment Monitoring
- Equipment Maintenance

**USP <797>** proposed for implementation on June 1, 2018.
Laboratory Monitoring

<table>
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<tr>
<th>Temperature Monitoring Under Dynamic Conditions</th>
<th>USP &lt;797&gt;</th>
<th>Board of Pharmacy (BOP)</th>
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<tbody>
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<td>Surface Air Sampling</td>
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<tr>
<td>Air Sampling by Microbiological Sampling Methods</td>
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<td>Yes</td>
</tr>
<tr>
<td>High Risk Compounding</td>
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<tr>
<td>Low Risk Compounding</td>
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<td>Yes</td>
</tr>
<tr>
<td>Written Policies &amp; Procedures</td>
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</tr>
<tr>
<td>Process Validation</td>
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<td>Yes</td>
</tr>
<tr>
<td>End-Product Testing</td>
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<td>Yes</td>
</tr>
<tr>
<td>Sterility Testing</td>
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<td>Yes</td>
</tr>
<tr>
<td>Viable Air Sampling</td>
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<td>Yes</td>
</tr>
<tr>
<td>Viable Surface Sampling</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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A Few Words to the Wise

- Remodel once — look ahead and remodel to the highest standards
- This is not a once-and-done. Requirements will continue to evolve
How Do I Use These Grids in Practice?

• One way for the SEC and PEC configurations
  o Identify the configuration of your pharmacy and edit the Grid to that configuration with requirements and BUDs
  o Laminate and post on the wall so there is no question regarding what can be done in your space
  o All staff should be able to identify what kind of sterile compounding space they are working in and what the limitations might be

How To Use The Other Tools

• Flow charts
• Check lists

These are easily turned into QA documents, should drive policy and can be laminated and posted for staff reference.
Will These Requirements Change?

- Oh, yes. Compounding continues to move towards cGMP, so might as well spend $35 for a copy on www.Smile.Amazon.com and ponder where this is going
- Are the cGMP standards changing? Of course!

Tools 2.0

- Will CHA update these tools?
  - If you find them useful, let us know
Thank You

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Questions

Online questions:
Type your question in the Q & A box, hit enter

Phone questions:
To ask a question, hit *1
California Physician Leadership Program
Two days each month:
October 2016 – April 2017

The California Physician Leadership Program is a comprehensive educational program designed to challenge and grow physician leaders and medical executives. Participants will learn to assume greater leadership, serve as a driver of change and achieve better outcomes for patients.

Thank You and Evaluation

Thank you for participating in today’s seminar. An online evaluation will be sent to you shortly.

For education questions, contact Liz Mekjavich at (916) 552-7500 or lmekjavich@calhospital.org.