USP General Chapters and Compounded Monograph Chapters: Best Practices and Regulatory Guidance

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Webinar Q&A - USP <800>

1. **Do you know how much it will cost extra if we are building a new pharmacy building to comply with USP <800>?**
   Due to the number of variabilities that exist, it is very difficult for us to provide a figure. Geographic location, sterile vs. nonsterile or both, size, modular vs. stick framing - these are just a few variables that can significantly impact the quote.

2. **Also, who can my HVAC contractor contact to find the appropriate HVAC equipment needed?**
   USP does not get into specifics about HVAC equipment. A qualified HVAC contractor should be able to interpret the air change requirements provided in USP <800> along with the size of the room and determine equipment needs.

3. **Can we treat all powders as a hazardous drug? Even if it is not hazardous.**
   This is clarified in the USP<800> FAQ #29. Can non-HDs and HDs be compounded in C-PECs located in the same C-SEC?

   Separate rooms (C-SECs) are required for sterile, nonsterile, HD, and non-HD compounding with two exceptions: Per section 5.3 Compounding, for entities that compound both nonsterile and sterile HDs, the respective C- PECs must be placed in separate rooms, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process; and Per section 5.3.2 Sterile Compounding, a BSC or CACI used for the preparation of HDs must not be used for the preparation of a non-HD unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.

4. **Do you have to store premade hazardous drugs in the negative pressure room? Example: we make progesterone caps in bulk. Once they are made, do we have to store them in the lab, or can they be stored in the pharmacy with the other drugs for the techs to count?**
   The best practice would be to store in your hazardous drug room. Due to the uncertainty of residual HD API residing on the capsules, the prudent choice would be to have these handled within your HD room. Refer to the Section 12. Dispensing Final Dosage Forms of USP<800> for additional guidance on counting/repackaging of final dosage forms.

5. **Are plastic drawers/cabinets not acceptable for USP <800>? When it says impervious, does impervious mean stainless steel only?**
   USP does not specify the type of material to use, only that it must be smooth, impervious, free from cracks and crevices and non-shedding. As long as the material meets these requirements, it could be considered for use within the HD room.

6. **Can you address having separate plumbing for a room that will have both USP <795> and USP <800>?**
   You would need to have your USP<800> Hazardous Compounding Lab (fixed walls) separate from your Non-Hazardous Compounding Lab. The only mention of water sources in USP<800> is that water sources and drains must be located at least 1 meter away from the C-PEC. Since the rooms would be separate any supply/return would be separate as well.

7. **What was meant by getting your room certified? Does that apply to strictly non-sterile pharmacies?**
   No - certification would apply to both sterile (HD and Non-HD) and HD nonsterile rooms. This would be part of your validation program to ensure that the room is doing exactly what it was designed to do.

8. **With the USP <800> recommended ebook to purchase, sections are individualized to purchase, do pharmacies need to purchase the whole book or just specific sections?**

   USP has a free download for USP <800>. Click here.

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USP <800> (continued)

9. **How about if it's not a cream concentrate? If it's the final concentration, and we are transferring creams from a large container to the final dispensing container. Does it have to be in the CPEC? If it's in the CPEC, does it have to be in a negative controlled room?**
This is addressed in USP<800> FAQ #51. During nonsterile compounding with HD APIs, are all steps of the compounding process required to be performed in the C-PEC?

   Make special note that USP discusses this in terms of when a process cannot occur in a CPEC. It is believed that the exceptions are based on equipment issues (convection oven, autoclave, etc.…) The transfer of product between containers would be viewed as a step easily achievable within a CPEC. General Chapter <800> states that "bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder)." It is recognized that under some circumstances, it is not possible to perform all steps of the compounding process in the C-PEC (e.g. due to equipment size or function). It is important for the safety of personnel that powdered HDs be weighed and mixed to the wet stage or made into capsules in the C-PEC. Once nonvolatile, non-antineoplastic, powdered HDs are wet, an assessment of risk may be performed to determine alternative containment strategies and/or work practices. The NIOSH list of antineoplastic and other HDs provides general guidance on PPE for possible scenarios that may be encountered in healthcare settings including instances where a C-PEC cannot be used.

10. **Regarding hormone concentrates not being considered the final dosage form. USP<800> Section 2 just after Box 1 indicates that an assessment of risk could be conducted to determine work practices. Could this not be interpreted as if a pharmacy where to perform an assessment of risk for hormone concentrates and determine they do not pose risk of inhaled exposure and could be compounded by a fully garbed compounder outside the hazardous compounding area?**
USP<800> FAQ #55 specifically addresses concentrates. Can an assessment of risk be performed on concentrated solutions of HDs (i.e. hormone concentrates)?

    No, concentrated solutions of HDs (i.e. hormone concentrates) is an HD API that is further manipulated into a final dosage form and is subject to the containment requirements in <800>. General Chapter <800> defines an API as "any substance or mixture of substances intended to be used in the compounding of a drug preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and animals or affecting the structure and function of the body."

11. **Is CAS number enough to match when switching from one supplier to another for API? Considering suppliers are FDA registered and supplying USP/NF or equivalent pharmacopoeial grades?**
USP API monographs provide the primary key information needed to ensure substitutability. The CAS number is one of these factors and is included on the API monograph. However, CAS number alone will not provide everything needed. There are a few molecules/substances that have the same CAS number but are functionally different: Polyethylene Glycols all have same CAS number but PEG 400 is different than PEG 4500 from a formulation standpoint. Compounder must consider all aspects of the official monograph and how the API is used within the specific formulation.

12. **With USP <800>, would you have to be in a CPEC/CSEC to transfer a hormone cream from a 60mL syringe to a 3mL syringe or can that be done in the area where you work with non-hazardous drugs?**
This is addressed in USP<800> FAQ #51. Make special note that USP discusses this in terms of when a process cannot occur in a CPEC. It is believed that their exceptions are based on equipment issues (convection oven, autoclave, etc.…) The transfer of product between containers would be viewed as a step easily achievable within a CPEC located within the CSEC.

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USP <800> (continued)

13. **Can a facility do a risk assessment on using hormone creams outside a containment hood?**
General Chapter <800> states that "bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder)." It is recognized that under some circumstances, it is not possible to perform all steps of the compounding process in the C-PEC (e.g. due to equipment size or function). It is important for the safety of personnel that powdered HDs be weighed and mixed to the wet stage or made into capsules in the C-PEC. Once nonvolatile, non-antineoplastic, powdered HDs are wet, an assessment of risk may be performed to determine alternative containment strategies and/or work practices. The NIOSH list of antineoplastic and other HDs provides general guidance on PPE for possible scenarios that may be encountered in healthcare settings including instances where a C-PEC cannot be used. This is addressed in USP<800> FAQ #51. Make special note that USP discusses this in terms of when a process cannot occur in a CPEC. It is believed that their exceptions are based on equipment issues (convection oven, autoclave, etc....) The transfer of product between containers would be viewed as a step easily achievable within a CPEC.

14. **What's the requirements for compounding autologous seeing drops? What type of hood do we need?**
These are not clearly addressed in chapters but recommend considering this type of compounding as exposure to potential biohazards. Viruses such as HIV and hepatitis have been isolated from tears so the hood used should provide the requisite sterile compounding environment and provide suitable protection from biohazards i.e. biological safety cabinet (BSC). See the following article from PubMed - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2095508/ regarding isolation of various viruses from tears.

15. **If hoods are externally vented, does the pharmacy still need a filter or can they just externally vent?**
The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or have redundant–HEPA filters in series. If the CPEC is the sole source of exhaust for your room the air would pass through a HEPA filter (incorporated in your hood) before exhausting to the outside of your building. If you are using a redundant HEPA filter hood and the room is being exhausted separate from the hood that separate exhaust does not need a HEPA filter (See USP <800> FAQ #27)

USP <795>

1. **Do you need to keep the concentrations also exactly the same as the USP compounding monograph -- no extrapolation?**
Everything needs to be identical to the compounding monograph if you are wanting to use the extended dating provided for in the monograph. If the concentration is changed you would no longer be able to use the published extended BUD but instead would default to the BUD established in USP <795>.

2. **What if I need a concentration higher or lower than USP formula?**
Everything needs to be identical to the compounding monograph if you are wanting to use the extended dating provided for in the monograph. Based on your professional judgment the concentration can be adjusted and the BUD's outlines in USP<795> would be applied.

USP <797>

1. **USP<797> FAQ: Question 69 on BUD extension beyond table 11 if monographic tests are performed? Kindly elaborate.**
At this time USP <797> does not explicitly provide for Extended BUDs in the same manner that USP <795> does via widely accepted industry practice referenced in <795> i.e. stability indicating methods and validation of container/closure system. Based on the distinction made between BUD and Expiration Date in **14. Establishing Beyond Use-Dates > 14.1 Terminology** the use of industry accepted "...analytical and performance testing of sterility, chemical, and physical stability, and packaging integrity of the product" would yield an **expiration date** NOT an **extended BUD**.

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USP <797> (continued)

2. **How many initial media fill tests in required per tech?**
   See <797> section 2. Personnel Training and Evaluation. The number of media fills and frequency should be considered minimums. Operational considerations and difficulty of compounding process may dictate more testing and/or more media fills than what is noted in <797>.

3. **Regarding high risk sterile compounding (i.e. trimix e. d. injections) what are new sterility testing guidelines regarding batches? If 1 vial is made then does an additional vial have to be made and sent off? Or is that only necessary for larger batches. Any recommendations for in house sterility testing?**
   The terminology "high risk" is not used in the new revision of <797>. Instead CSPs are classified as Cat 1 or Cat 2. These categories are well defined in the new chapter and should be thoroughly reviewed. Testing requirements are outlines in section 12. Release Inspections and Testing > 12.2 Sterility Testing. Minimum quantities are further defined in Chapter <71> Sterility Tests table 2 and 3.

4. **Can you tell us again that CE for calculations and potencies for chemical assays?**
   The Practical use of the USP as a Primary Reference Resource in Compounded Formulations webinar recording link is: http://www.arlok.com/Education.

5. **Do you have to have a subscription to the USP to access the USP Compounding Monographs? Is there another source?**
   The USP Compounding Compendium is available for purchase at: https://www.usp.org/products/usp-compounding-compendium

Recommendations represent opinion of presenters based on information available. Individuals should obtain and review relevant chapters to confirm applicability to specific practice sites or procedures. Also, review State Board of Pharmacy rules and federal regulations to ensure compliance.