

Q&A With Eric S. Kastango

Please note: *Although I am a member of the USP Sterile Compounding Expert Committee, I am speaking today in my individual capacity and not as a member of the Committee or as a USP representative. The views and opinions presented are entirely my own. They do not necessarily reflect the views of USP, nor should they be construed as an official explanation or interpretation of <797>.*

Q1. Regarding BUD and sterility testing. I have heard discussions on sending out samples to labs for sterility testing, with the intent to extend BUD to published stability studies. Provided you are following all the guidelines. What sterility testing specifically do you need to do? Can one drug sample per risk level suffice and do you need to do a sample in each type of container you dispense? i.e. Cefazolin in PVC bags, syringes and elastimerics? Do you need to carry out the test for the same length of time as your desired BUD? (I'm assuming, yes) Is there any in house testing that can be done? We do carry out Q.I. Medical, Inc. Quick Test System for TPNs & LVP and incubate for 14 days; does this meet the sterility test cited in 797? What is considered a statistical sample quantity and frequency for any sterility testing or is this a judgment question based on your specific operation?

A1. I have yet to have QI Medical prove that their test kits meet the requirements of USP 71. Please find attached an article to guide you when doing sterility testing. These documents should many of your questions.

http://www.pharmacyonesource.com/images/simplifi797/Sterility_and_BUD.pdf

http://www.rph.com/images/simplifi797/ASHP_SP3_CH13_Verification_Accuracy.pdf

Q2. We need to do both bacterial and fungal for the q6 month viable test, right? Also, we have 90 hospitals in 26 states, so I deal with a number of hood service providers. Regarding the viable testing, many of the providers differ on the idea of a control sample. Any guidance on this?

A2. Yes, you need to do both bacterial and fungal viable air testing every 6 months. That was an oversight in the chapter. There should be a positive and negative control for each lot of media being used for your testing.

Q3. Must the contact plates for gloved-fingertip sampling contain TSA with lecithin and polysorbate 80? Our lab currently stocks TSA with sheep blood for our environmental sampling, and based on the <797> guidelines suspect that we will need to change to TSA with the neutralizing and growth agents as specified. Would you please advise if we do indeed need to change to plates with the exact description "TSA with lecithin and polysorbate 80"?

A3. The lecithin and polysorbate neutralizes any cleaning agent on the surface of the gloves or surface being tested. Gloves should NOT be sprayed prior to testing.

Q4. We prepare fortified eye drops (from sterile ingredients) for both use in single patients and for division into multiple bottles to be used by single patients. Do we need to do sterility testing on all of these ophthalmic preparations? I had not previously

classified these ophthalmic preparations as high risk as they are not from non-sterile ingredients; am I correct or incorrect in my thinking?

A4. As long as you don't exceed the BUD, no sterility testing is necessary. Have the patient refrigerate their eye drops between uses to minimize the risk of growth in the bottle (if it gets contaminated). Are the patients given instruction on how to use the bottle? Wash hands, do not touch the tip of the bottle, etc.?

Q5. Which dating supersedes, the BUDing chart for immediate, low, medium, high-risk at room and refrigerated temperatures, or information from the manufacturer? For example, if data from the manufacturer that says ciprofloxacin in D5W is good for 7 days at room temperature, but the chart for BUD says low risk CSPs at room temperature have a BUD of 48hrs. Would the BUDing of 48hrs supersede the dating of 7 days?

A5. In USP 797, there is specific language that says to follow USP 797 BUD or manufacturers dating, whichever is less! So, 48 hours supersedes 7 days.

Q6. We are getting ready to undergo a construction project in our inpatient pharmacy to be in compliance with 797. We know that there needs to be a designated space for designated cleaning supplies for the ante-/clean rooms (i.e. our housekeeping staff have their clean room dedicated cleaning supplies/mops/etc). Does this designated space need to be its own room with a door/ventilation system within the anteroom, or can it be just that—Space?

A6. It would be better if the designated space for cleaning supplies have its own small room with a door and low-wall return.

Q7. We have purchased spray bottles of sterile 70% IPA to be used in our isolators. The isolators must be opened and cleaned regularly. When the isolators are opened, is the sterile IPA no longer sterile or is sterility restored when the isolator is returned to a class 5 environment?

A7. Since I don't know who the manufacturer of your IPA is, I would ask them since they will most likely have information on packaging integrity of their product/bottle. Good question and one that the vendor should be able to answer.

Q8. Initially each compounding employee must complete 3 samplings. Does this apply to new compounding employees or all (including those already compounding) employees. In other words - do our veteran compounding employees need to do three or just the one annually? For those that must do 3: how are these three samplings separated? Do you do them in a row or wait a time period between all 3? Do they have to regarb if they can do them in a row (on the same day)? Do you have to do sampling for both hands or just one per time? If both hands must be done - can they be done on the same agar plate?

A8. I would like to think that your veteran compounders should be able to demonstrate proficiency in being tested three times. Playing devil's advocate, just because they have

been compounding for 20-30 years, how do you know they know what they are doing? It applies to everyone and USP 797 is not proscriptive on when you do it. Make it a reasonable process where you are evaluating their technique and skills and not a task that needs to be done. Your other questions are answered in policies and procedures that are being sold. Please find attached an article that I think might help.

http://www.pharmacyonesource.com/images/simplifi797/PPP_Fingertip_sampling.pdf
http://www.pharmacyonesource.com/images/simplifi797/PPP_EM_Weissfeld.pdf

Q9. I work in a small hospital and cost containment is a very big issue. I have read studies that compare sterility between using sterile gloves wiped intermittently with sterile IPA vs. regular gloves that were not wiped at all during preparation of CSP's. Are there any studies using either sterile or non-sterile gloves intermittently wiped with regular IPA. We currently use nonsterile gloves, but we wipe intermittently with regular IPA and we have not had any problems. Why is sterile IPA specifically used?

A9. I understand the concern about cost. I am not aware of any studies that looked at the scenarios you posed. If we agree that contamination most likely comes for touch contamination, all materials that come in direct contact with the critical site within the direct compounding area must be sterile. As such, sterile gloves and sterile alcohol for those activities occurring within the DCA is called for. Nonsterile alcohol is not sporicidal and spores/bacillus is a concern when we prepare CSPs. The USP Sterile Compounding Committee had an expert advisory panel (of infection control, microbiology and CDC experts) advise us that sterile gloves and sterile alcohol were required.

Q10. Do we have to put the isolator hood in the cleanroom or can it be located in a different location, i.e. within the general population of the pharmacy? I would prefer in the cleanroom, but because of space limitations, wondering about in the general population of the pharmacy. We also have a separate ante-room that connects to the cleanroom, thus it could go there if needed.

A10. Depending on the type of isolator will determine if it has to go into a cleanroom or buffer area. The chapter has specific language on those requirements. Please find attached a table and article to assist you in this matter.

http://www.pharmacyonesource.com/images/simplifi797/USP_PEC_Table_Labella.pdf
<http://www.pharmacyonesource.com/images/simplifi797/pp12BarrierIsolators.pdf>

Q11. We have a CACI that is vented to the outside and a CAI in the same room that is classified as ISO 8. Do I need to have the CACI in a room by itself or are they both OK in the same big room? They are not right next to each other, they are maybe 6 feet apart from each other.

A11. If you are doing hazardous drug compounding, both the NIOSH Alert and USP 797 specify that these activities occur in a dedicated area. CACIs (for chemo) need to be located in a separate room that has 12 air changes per hour and negative 0.01" w.c. pressure. Please find the attached table for your consideration.

http://www.pharmacyonesource.com/images/simplifi797/USP_PEC_Table_Labella.pdf

Q12. We are a home care company. At all the home care companies I have worked for (3) we sent a week supply of Desferal syringes. Most stability references give the product 8 days. <797> states that room temperature drugs get 30 hours max? Since the drug can not be refrigerated what do we have to do? Making the patients draw up their own seems to be a great step backwards from having it mixed in a clean room.

A12. Can you make the desferal with bacteriostatic water or saline? That would exceed the dating. A study is needed to determine the rate of contamination amongst drugs like desferal, 5FU and other room temp medications. The concern is sterility and having the patient receive a batch of contaminated medication. This issue will require some research.

Q13. When our “new” clean rooms were built in 2006, swing doors were put in between the ante-room and the buffer room as well as between the buffer room and the chemo room. I could not find anything about the doors in <797>, should they be switched to standard steel construction with safety glass doors?

A13. If they cleanable and maintain your pressure differential between your buffer area and chemo room, they you should be good.

Q14. Due to our high volume of ophthalmic surgical patients and the lack of the “old” dropperettes due to bar coding, we have been transferring solutions from larger package sizes to 1or 2ml sterile ophthalmic dropper bottles. What should we use for the BUD; we have categorized it as a low risk; should the BUD be 14 days refrigerated? Can it every be room temperature for 28 days with sterility testing?

A14. I don't know enough about your entire compounding process to assign a BUD. You need to make that decision. In order to extend the dating, you need to test each batch according to USP 71. Also, the integrity of the packaging to maintain sterility is as important as passing the sterility test, so the final container you use will make a big difference.

http://www.pharmacyonesource.com/images/simplifi797/Sterility_and_BUD.pdf

Q15. Is it necessary to wipe down all items when bringing them into the anteroom for storage or just when brought from the ante to the buffer room. Can light sensitive vials of chemo (and other meds) be kept in their paper boxes in the ante room. If chemo can they be kept in the Chemo buffer area? We have our chemo meds sequestered in the chemo prep room.

A15. The principle that we are trying to achieve it to go from dirtiest to cleanest. You can keep "unwiped bags and packaging" on the dirty side of the line of demarcation (LOD) and wipe it down when supplies are moved across to the clean side of the LOD. I would leave individual vials in their immediate shipping container (outer box) within the

negative pressure drug storage area, which can in the negative pressure ISO-Class 7 buffer area. The box should be handled as hazardous material and disposed of properly. http://www.pharmacyonesource.com/images/simplifi797/Sterility_lr.pdf

Q16: We also have two satellites scenarios: In one satellite we have a horizontal BHI and a vertical, vented BHI for the chemo. In the other satellite (oncology) we have 2 vertical flow hoods where we prepare both chemo and nonchemo CSPs. IS this compliant with USP?

A16: No. Chemo drugs cannot be prepared in a satellite that would comply with the requirements in the Low-Risk Level CSP with 12 hour BUD. Refer to the Low-Risk Level CSPs with 12-hour BUD.

Q17: What about the wearing of eye-glasses? Must a face shield be worn? We currently don't.

A17: Eyeglasses are not cosmetics nor known to be a particle generator. If desired, they can be cleaned with IPA prior to wearing in the buffer area.

Q18: We have a vertical flow BSC in our clean room. Is it OK to use it for infrequent (1-5 per week) chemos. This is the same clean room where all other CSP are prepared.

A18: There is a low-volume exception in the chapter for this practice. Preparing hazardous drugs in the same room as non-hazardous drugs would require the use of a closed system transfer device. Refer to the Hazardous Drugs as CSP section of the chapter.

Q19: We are exclusively using CAIs for our compounding. To be compliant with USP 797, should fingertip sampling be done with the gloves inside the isolator, or should it be done with sterile gloves the compounder uses. We have documentation that that gowning and gloving is not necessary with our isolator.

A19: The use of isolators doesn't exempt from any of the testing requirements in the chapter and sterile gloves have to be worn while compounding in an isolator.

Q20: We are in the process of writing PnP's for our barrier isolator. Are there any good sources for proper compounding procedures in a barrier isolator.

A20: Your isolator manufacturer should be able to provide you with PnPs. Policies and procedures are available from a number of vendors and are included in Simplifi 797.

Q21: Will each institution need 30 policies & procedures to cover all of 797 or can these be combined into a fewer number? If they can be combined, what would be the fewest number?

A21: There is no number requirement for PnPs. You can configure your policies and procedures in any manner to make them work for you. Ensure that you meet any and all state board of pharmacy requirements regarding PnPs.

Q22: Add ease made in LFH, not in a clean room, what is the BUD

A22: Please refer to the manufacturer's literature of Add Ease for this information. You can also refer to the Proprietary Bag and Vial System section of USP 797.

Q23: Can you give examples of recommended cleaning agents?

A23: If you work in a hospital, you should contact your Infection Control person and use only approved cleaning agents. Refer to Appendix II in the USP chapter (Common disinfectants)

Q24: How does USP define low volume producer of hazardous drugs? How would I decide if the two tier system would suffice or a separate negative pressure room is required?

A24: The proposed language in the chapter identified 5 or less HD CSPs per week as low volume. Since the Committee could not justify the number, it was eliminated and the final determination must be decided by the pharmacist/organization. The concern is cross-contamination and employee exposure to these agents. The literature is replete with article on exposure. If you visit the ASHP website http://www.ashp.org/s_ashp/doc1c.asp?CID=484&DID=3445, you will find a number of articles of interest.

Q25: Are you aware of any resources for making a hood room structurally compliant with 797? For example, retrofitting an existing hood room to be compliant. Consultant architects with experience in 797 compliance?

A25: There are number of consultants, including myself who do this type of work. Surf the web and Google for USP 797 consultants.

Q26: We use ketamine in the OR. What would you recommend for a BUD for a ketamine syringe?

A26: Your question cannot be answered without more information about how and where it is mixed. The chapter provides good guidance in determine the risk level of a CSP like Ketamine and subsequent BUD.

Q27: Are most hospitals making monoclonals in the Chemo Hood and how are they being transported- like chemos?

A27: It depends on how the manufacturer classifies them in their MSDS documentation.

Q28: Is there an updated gap analysis available? How often should one perform a gap analysis?

A28: At this time, there isn't any updated gap analysis tools. You can use the Shalls and Should section of the USP chapter as a template in performing your gap analysis. Gap analyses are great management and operational tools and can be used at various times (quarterly, semi-annually, annually) to evaluate operational performance.

Q29: With the computers in the cleanroom and they are covered in plastic, is a radio in the cleanroom acceptable if covered in plastic as well?

A29: Your question involves many of the pharmacy urban myths about cleanrooms. The chapter has specific language about the placement of devices in the buffer area being permitted as long as they have not impact of the air quality of the area. Personally, I don't like radios as they are distracting.

Q30: Can I use clear Vinyl Strip Doors with HTP Hardware (Hanging strips) to separate Ante room and clean room? Since space is limited and I can not put real door and also it will help me keeping little different temperature between two rooms.

A30: Strip curtains can be used by need to be cleaned regularly and must be able to maintain the pressure differential between the buffer area and ante area.

Q31: The revised USP 797 guideline is a bit confusing regarding the location of air pressure monitors and velocity meters. Is it correct to interpret that two such devices should be installed: an air pressure monitor should be positioned so as to monitor the pressure differential between the buffer area and the general pharmacy area, and a velocity meter should be installed to monitor sufficient air movement from the buffer area to the ante area? Also, in the case of a line of demarcation between the buffer zone and ante area, can the velocity meter be located in a doorway between the ante area and the general pharmacy, assuming that if the velocity is sufficient at that location, it must be sufficient at the line of demarcation?

A31: Air pressure monitors are used to measure the differential pressure between two physically separated spaces (rooms). The velocity meter is used to demonstrate that air velocity across a line of demarcation between ante area and buffer area is 40 feet per minute if the two areas are not physically separated by a wall.

Q32: Since the presence of a sink could increase the bioburden in the ante-area, we would like to locate our sink just outside of the ante-area, for hand washing to be performed just prior to entering the ante-area for garbing; a disinfectant dispenser can then be located in the ante and buffer areas. Is this an acceptable plan?

A32: The chapter requires a sink to be in the ante area for hand cleansing activity. The sink needs to be away from the entrance of the door to the buffer area and with a proper pressure differential between the buffer area and ante area, the presence of a sink should

not pose a problem. In a GMP environment, there are typically two ante areas, where the sink is located in the outer most ante area.

Q33: Should the non-shedding gowns be front closing?

A33: The garbing requirement calls for a gown closed at the neck and with elastic cuffs. As long as the gown worn properly and these requirements are met, you can use front or back closing gown.

Q34: How do you recommend wiping off manufacturer packaging that has black writing on it? For example, our IV sets are packaged in a plastic bag with black writing. When we wipe these off with alcohol, we have the writing coming off and getting black all over everything.

A34: Not sure how "wet" your wipe is when you handle the packaging. Does it come off if you use hydrogen peroxide or dilute bleach solution? Be as careful as you can.

Q35: Our ceiling tiles consist of inlaid panels impregnated with the impervious hydrophobic polymer. They were sealed above the ceiling level by our architect with the kind of seal that is similar to that on a refrigerator door. Is this acceptable, or would you recommend actually caulking the perimeter of each tile from the inside? Some of the tiles are uncaulked so as to have access to the ventilation above the ceiling.

A35: When the ceiling is cleaned with a mop, do the tiles get pushed up? The language of the chapter calls from them to be caulked in place. The final decision is up to you.

Q36: Is a pressure gauge or velocity meter between buffer/ante and ante/general area REQUIRED in order to meet certification guidelines?

A36: The chapter calls the monitoring of pressure differential between the buffer area and the ante area. Refer to the Pressure Differential Monitoring section that can be found in Viable and Nonviable Environment Sampling (ES) Testing in the Chapter.

Q37: Is it a requirement to have a written procedure for every type product we compound?

A37: If you hired me as a pharmacist, would I know how to prepare every type of CSP you compound?

Q38: Bleach is listed as the only sporicidal agent. We are told that bleach is very destructive to floors, ceilings, walls, and caulking. What cleaning agents do you suggest using on a daily basis? Should we use different agents for the monthly cleaning?

A38: If you follow-up the dilute bleach solution after 30 minutes with a sterile water rinse applied with a mop. There are a number of cleaning agents that can be used. If you work in a hospital or health care facility, check with your Infection

Control/Environmental Services departments. Some institutions' need to approve any cleaning agent brought into the hospital.

Q39: Is it acceptable to wear a face shield if our workers have worn makeup that day? This happens often with our housekeeping staff. They also ask about wearing jewelry as long as it's under the glove. Is that OK? Are our nametags considered OK to wear in the clean room? We had done a culture of this at one time and cultured some pretty disgusting stuff. I would like your opinion as we would like to put the questions to rest.

A39: A study is needed to validate that a face shield can prevent contamination from wearing make-up. Do you routinely observe compounding operations and/or have you observed gloved personnel touching their face?

Q40: What is your opinion on chemo glove boxes rather than a whole clean room environment? How would you suggest storing the chemo meds in a negative pressure environment when our plant operations people tell us that we will be drawing air from the directly-attached chemotherapy infusion room?

A40: Depends on many factors which I do not have, so I cannot comment. There is a requirement for storing the HDs in a negative pressure environment. If the HDs are in the same room as the ISO Class 5 device, the room needs to be ISO Class 7 with a ISO Class 7 ante area.

Q41: 797 Revision states "dispenser shall, when appropriate and practicable, obtain and evaluate results of testing for identity, strength, purity, and sterility before a CSP is dispensed". Are we expected to test each these parameters for every CSP dispensed?

A41: The chapter details when testing is required.

Q42: Regarding Barrier Isolators not located in a cleanroom -- When doing viable testing, is testing the main chamber and transfer chamber sufficient? Does the room air need tested?

A42: Does your isolator isolate? Pharmacy Purchasing and Products magazine has a great article on isolators. There is language in the chapter that answers that question. <http://www.pharmacyonesource.com/images/simplifi797/pp12BarrierIsolators.pdf>

Q43: Do you consider a buffer room designed without low wall returns or ceiling wall returns as a secondary engineering control?

A43: There is a requirement in the chapter for low-wall returns.

Q44: Normal street shoes come in contact with soil, so it must be covered to prevent the introduction of spore-forming Bacillus spp. to IV Admixture Unit . What I know only chlorhexidine is effective against Spore-forming Bacillus spp.. So how I will comply with USP 797 without affecting the sequence of gowning?

A44: The gowning sequence in the chapter has the hand washing after placing shoe covers on. I see no impact based on the information you have provided above.

Q45: I would really like some clarification on the "stat hood" and if gloving and gowning and all of that is necessary (i.e. "sterile" gloves) The way I read it is it is required for all CSP's with a bud longer than 1 hour???

A45: Please refer to the Immediate-Use and Low-Risk CSP with 12 hour BUD sections. You are correct. Would be great if the person mixing a stat could use an alcohol gel before starting compounding.

Q46: Immediately after constructing a new clean room in pharmacy is there a need to fumigate the room before start using it to eliminate the contamination by *Asparagillus* (common in hospitals after constructions) or just mopping with disinfectant to clean room surfaces is enough.

A46: The chapter is not specific on this material. Check with you Infection Control person in your hospital. Ideally, after any work or construction you need to do a complete cleaning. I have done a three-time cleaning, twice with a germicidal detergent and sterile water followed with a third cleaning with a dilute bleach solution and rinsed with sterile water.