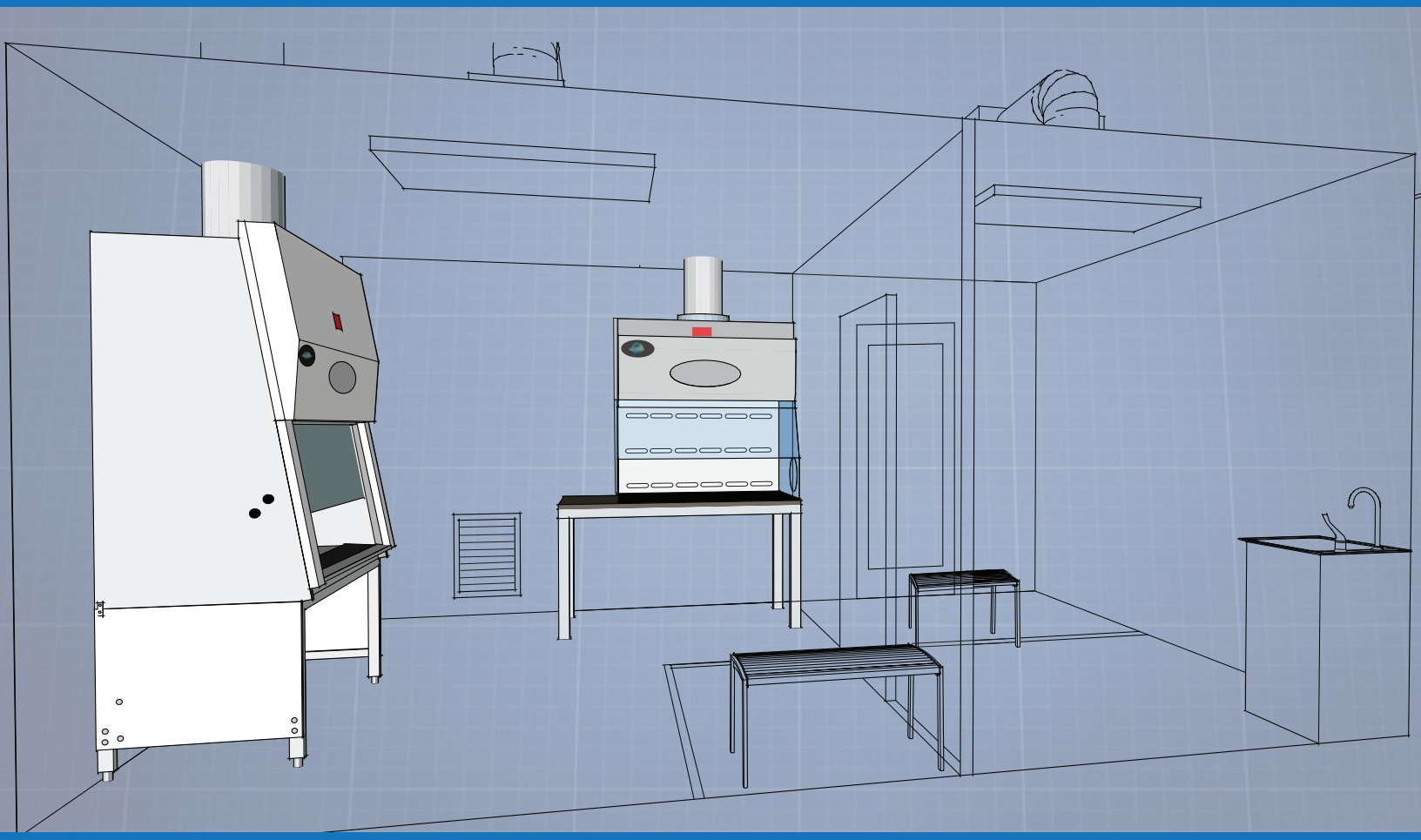
Can a Class I and Class II BSC Be In the Same Sterile HD Room?



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Can a Class I and a Class II Biological Safety Cabinet be in the same Sterile Hazardous Drug Room?

One of the areas that USP Chapter <800> *Hazardous Drugs - Handling in Healthcare Settings* does not directly address is the presterilization process of a sterile preparation, hence the title of the article "Can a Class I and a Class II Biological Safety Cabinet (BSC) be in the same Sterile Hazardous Drug (HD) Room?" This has been a frequently asked question by our pharmacy clients during the USP 800 planning and design phase so we thought it would be wise to address the question.

Presterilization often includes weighing nonsterile dry powders prior to mixing in sterile glassware and liquid solution. Nonsterile powders are usually weighed in a Class I BSC sometimes referred to as a Containment Ventilated Enclosure (CVE) which is a negative pressure hood that provides personnel protection only. The nonsterile powders are then transferred to a Class II BSC that provides both product and personnel protection for the sterile compounding process. In this paper we will be targeting hazardous drugs in sterile preparations and compare current USP 797 workflow processes and future USP 800 workflow options. We will also discuss the engineering merits of the two types of BSC's, which moving forward will be referred to as Containment Primary Engineering Controls (C-PECs), and make a determination as to whether or not a Class I and a Class II BSC should be in the same HD room.

The USP Chapter <800> states this in 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 one meter apart and particle-generating activity must not be performed when sterile compounding is in process."*

So the question and/or debate is not about "can" a Class I and Class II C-PEC be in the same sterile HD room, but "should" it be accepted as a workflow process for presterilization? The main concern for acceptability of placing these two different type and purpose hoods in the same room is maintaining ISO classification in the sterile space because technicians are actively engaging in powder weighing and potentially generating particulates, therefore compromising particle counts and ISO classifications. A bigger concern is that higher particle counts during weighing activities also signals environmental exposure.

Can the C-PEC cause exposure?

Both a Class I and Class II C-PEC with HEPA filtration (single or redundant) do not change the ISO classification in the room. The capture efficiency of HEPA filtration is proven through the initial and bi-annual hood certification which guarantees that the HEPA filter's integrity is not compromised. HEPA filters do not leak over time (sometimes confused with carbon filtration),

instead HEPA filters are more efficient as they load. Particulates are impacted to the filter media as well as other particulates already captured in the filter. HEPA filters don't fail unless touched and punctured by human hands (or foreign objects) causing physical damage to the filter media. These concerns can be put to rest because most manufacture's of hoods and containment equipment strategically place the HEPA filter away from direct contact and personnel exposure.

Where does the Exposure Come From?

Based on years of site observations, below is a brief synopsis of how environmental exposure most commonly occurs in 8 out of 10 compounding pharmacies. All of the exposure points listed incur airborne particulates and surface residue.

1. Technicians consistently breach the face of the hoods while actively weighing or manipulating dry powders and interacting with formulation software.
2. Contaminated weigh boats, wipers, and gloves are disposed in open-face trashcans in the lab environment.
3. Contaminated weighing utensils, glassware and capsule plates are removed from the hood and walked across the lab to the sink.
4. Bulk-chemical containers are not wiped down (with IPA) prior to removing from C-PECs and placing back on shelves.

Presterilization Workflow Past/Present and Future for a Sterile Injectable

Past/Present Workflow: Under current USP chapter <797> *Pharmaceutical Compounding-Sterile Preparations* the accepted workflow for the sterile injectable starts with the nonsterile HD powder being weighed in the cleanroom's positive pressure anteroom (ISO Class 8 or better for high risk Compounded Sterile Preparations-CSP) in a Class I C-PEC and then transferred into the USP 797 positive pressure buffer room, into a Class II C-PEC (or in some cases a Laminar Airflow Workbench-LAFW) for solution, mixing, and filtration.

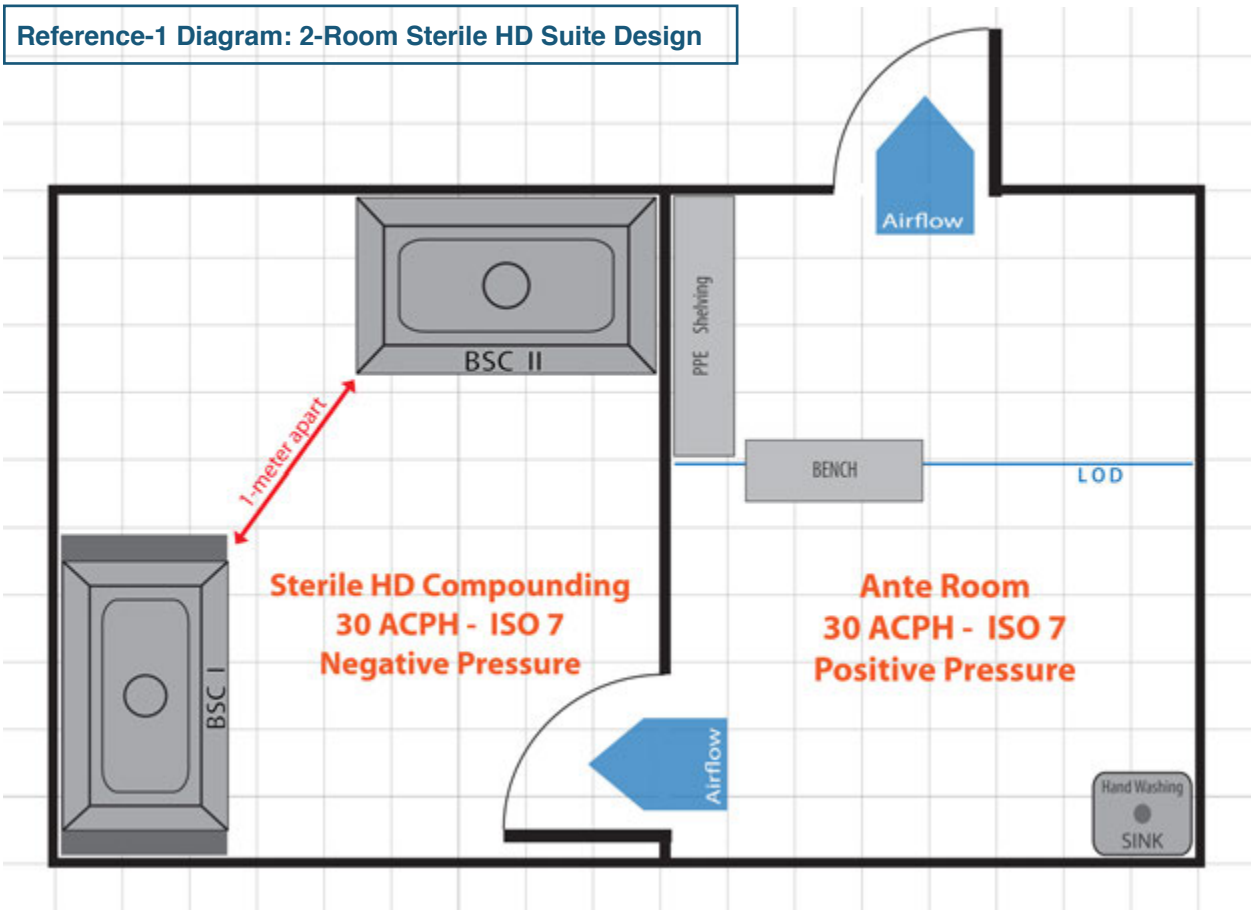
The obvious problem with this current process is no consideration to potential HD particulates released during weighing and mixing. The airborne HDs can be pushed out of the positive pressure ante room into general areas causing environmental and personnel exposure. The presterilization powder handling process in the ante room is the main culprit because it is difficult to manage exposure with positive pressure environments.

Future Workflow: The sterile HD injectable compounding process involves a non sterile powder, so the preparation is still considered a "high-risk" CSP. This means that the presterilization process again has to be accomplished in an ISO 8 or better environment, but now in a negative pressure room. The HD compounding rooms (referred to as Containment Secondary Engineering Controls-CSEC) will still require a positive pressure ante, but only for donning Personal Protective Equipment (PPE) and hand washing, not weighing powders or other presterilization processes.

2-Room Sterile HD Suite Design

The 2-room sterile HD has both the Class I C-PEC for presterilization weighing and the Class II C-PEC for sterile compounding located in the same room. By USP 800 standards, the two C-PECs are separated by no less than one meter (*see Reference-1 Diagram below*). It is important to note that weighing activity (referred in the USP chapter as "particle-generating activity") in the Class I C-PEC cannot occur simultaneously at the same time as sterile compounding in the Class II C-PEC. So one technician multi-tasking between both C-PECs or two technicians working together to speed up production is prohibited as a sterile HD compounding workflow process.

Reference-1 Diagram: 2-Room Sterile HD Suite Design



Why not use the Class II C-PEC for pre-sterilization powder weighing?

There are pros and cons for using a Class II C-PEC as a single containment solution for the sterile HD process. Take into consideration that powder weighing is most effectively accomplished in a “low-flow” and laminar environment which is why the Class I C-PEC, with airflow at 80 feet per minute (fpm) at the face opening, has been proven as a better solution. The Class I C-PEC is available in smaller footprints (3' foot wide hoods) that demand less space in the anteroom. With Class II C-PECs, technicians sometimes complain about powder whisking off the spatula while weighing inside the BSC, of which the air currents and vibration can

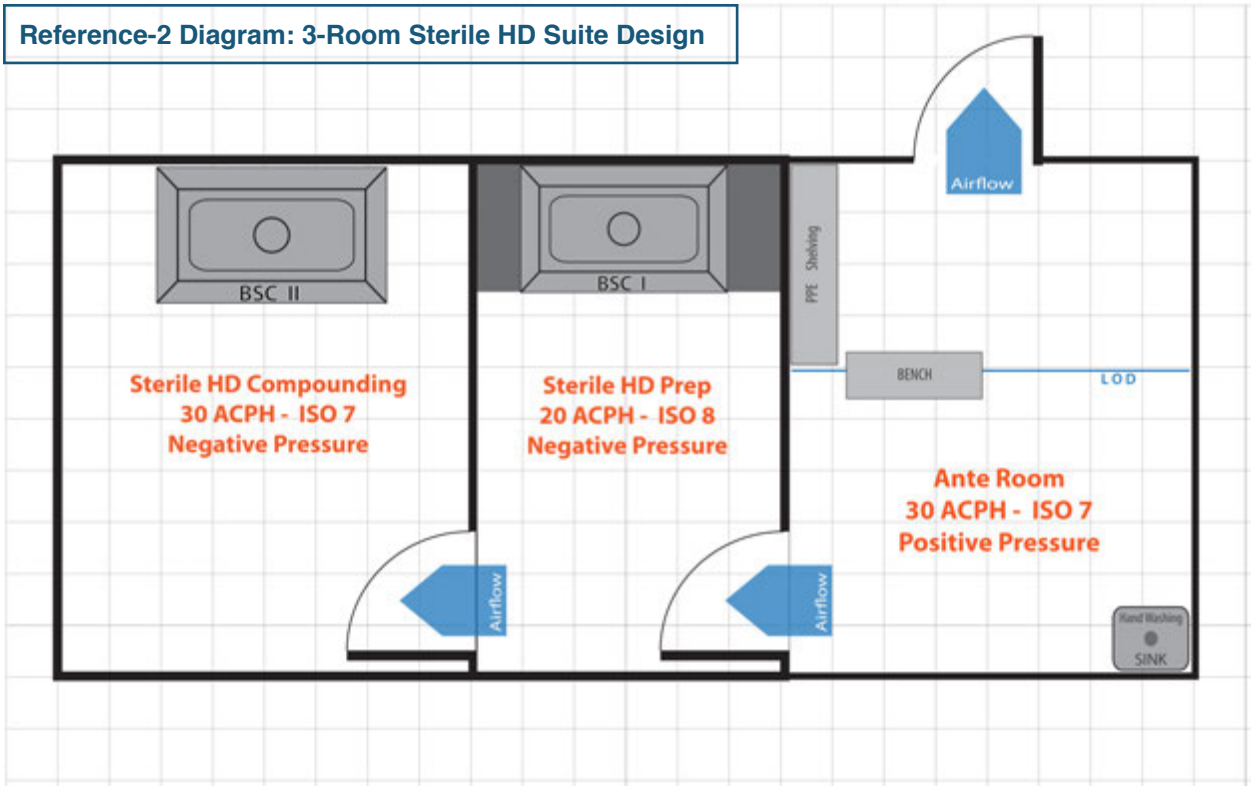
influence electronic balance stability. Class II C-PECs have higher face velocities (105 feet per minute) and additional down-flow air currents recirculating inside the cabinet that make stabilizing a sensitive analytical balance's second or third decimal place somewhat more difficult to achieve, more so with older model BSCs.

Newer model Class II C-PEC designs utilize DC motors for low vibration and improved airflow currents, combined with a fully shielded analytical balance, the Class II C-PEC becomes a viable solution for the presterilization process. There are some pharmacy facilities with real spacial constraints and a having a sterile HD room with both a Class I and Class II C-PEC is not feasible, so the Class II C-PEC will have to be the sole containment solution for the entire sterile preparation workflow process. It is important to remember, if presterilization does occur in the Class II C-PEC, a thorough cleaning procedure must take place prior to engaging in the sterile compounding process.

3-Room Sterile HD Design

For those pharmacies that are concerned about adding additional equipment and processes to the sterile buffer room should consider a 3-room design (*see Reference-2 Diagram below*). The USP Chapter <800> section 5.3.2 states that "All C-PECs used for manipulation of sterile HDs must be externally vented." However, one could make the compelling case that if the Sterile HD Prep room where the Class I BSC resides is classified as an ISO 8, where only nonsterile weighing is

Reference-2 Diagram: 3-Room Sterile HD Suite Design



occurring, then the Class I BSC with redundant-HEPA could be recirculated in that space, potentially saving the cost of an additional roof fan and energy cost.
The USP Chapter <800> does not specifically address all of the issues we have discussed in this paper so we must state a final disclaimer that the State Boards of Pharmacy (SBOP) and other regulatory bodies could feasibly interpret the chapter sections differently than we have. So our final piece of advice is to call your SBOP and discuss with them your intentions and document their response. Additionally, there is no guarantee that additional standards won't be adopted by your SBOP, so clear communication will be a key to your success.

Conclusion

As we are all coming to realize, new regulation is not always clear on every intimate detail and when left to interpretation, has to fit your pharmacy's workflow and spacial needs. So the question of whether or not a Class I and Class II C-PEC should reside together in your pharmacy's sterile HD room is really up to you. The options have all be identified here and you will ultimately make the decision that is best for your facility. With that being said, please remember that there is an extremely important and synergistic relationship between C-PECs and Good Lab Practices (GLP) to maintain low particle counts when weighing powders during the presterilization process. Equally as important is the goal of minimizing or even eliminating personnel and environmental exposure to HDs which requires some additional attention to workflow processes above and beyond the engineering controls. Safe workflow habits start with the pharmacy establishing Standard Operating Procedures (SOPs) that clearly define Good Lab Practices (GLP) during all aspects of the hazardous drug handling process(es) and the end result will be a quality product for your patients and a quality environment for your employees.

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Bryan Prince, MBA is the owner and lead consultant at Lab·Red Pharmacy Consultants (website: http://pharmacyworkflow.com/) His early career in containment technology allowed him access to pharmaceutical labs around the U.S. where he gleaned extensive knowledge of chemical handling technique and safety strategies. In 2012 he started visiting compounding pharmacies to observe workflow habits and share his knowledge, which led to writing articles for the International Journal of Pharmaceutical Compounding (IJPC). Bryan has been invited to speak at conferences on "Quality, Safety, and Workflow in the Compounding Pharmacy" for the American College of Apothecaries and PCCA. He has also contributed to the ACHC as an Expert Panelist on a series of USP 800 webinars. email: bryankprince@gmail.com

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