PASS-THROUGH OPTIONS FOR STERILE COMPOUNDING FACILITIES

ControlledEnvironmentConsulting

Materials must be moved into and out of cleanrooms in a manner that reduces transfer of particulate contamination into the ISO classified suite. Sealed double door pass-through boxes are often used as a convenient and efficient means of transferring directly from the buffer room to an adjacent support room. This often results in a transfer from an unclassified support room to an ISO Classified buffer room. While the FDA has made it clear through their observation reports (form 483) and warning letters that this practice is unacceptable in a GMP manufacturing operation, USP chapters actually promote the practice (see ‹800› section 5.1) as long as appropriate assurances are provided through the certification process that particles are not compromising the air quality of the buffer room.

Pass-through boxes are very commonly used in sterile compounding. What follows is an explanation of the different types and configurations of pass-through systems available.

- There is **NO requirement in USP 797 (2019) for interlocking doors**. It is a "should", however, we strongly recommend the use of pass-throughs with interlocks ONLY.
- There is **NO requirement in USP 797 (2019) or USP ‹800›** for HEPA filtered (purged or recirculating pass-throughs).

CORE RECOMMENDATIONS

I. All Pass-throughs: Requirements

1) The hinged doors must be interlocking and must never be opened at the same time. Note that USP chapters do not say that the doors must be interlocked. However, if they are not, the integrity of the room will be compromised when both doors are opened at the same time.

2) Sliding window or doors are not acceptable.

3) Must have sealed doors on both sides.

II. All Pass-throughs: Best practices recommended by CEC

1) Pass-throughs should have seamless corners and minimal crevices within the chamber. Exposed screws, nuts, bolts, mechanical systems must be avoided.

2) Pass-throughs should be constructed of stainless-steel.

   a) Laminated wood products, acrylic and Plexiglas deteriorate over time.

3) Pass-throughs must have cleanable hinges and are sturdy enough to support the weight of the door over time.

    a) Piano hinges are not easily cleanable.

4) Pass-throughs should have the ability to be flush mounted on the ISO classified room wall. When between two ISO Classified rooms, the cleaner or more critical of the two rooms will be the flush-mount side when possible.

5) Optimum installation location of the pass-through is between the buffer room and non-classified space. By placing pass-throughs in this location, they are positioned to best support efficient material transfer.

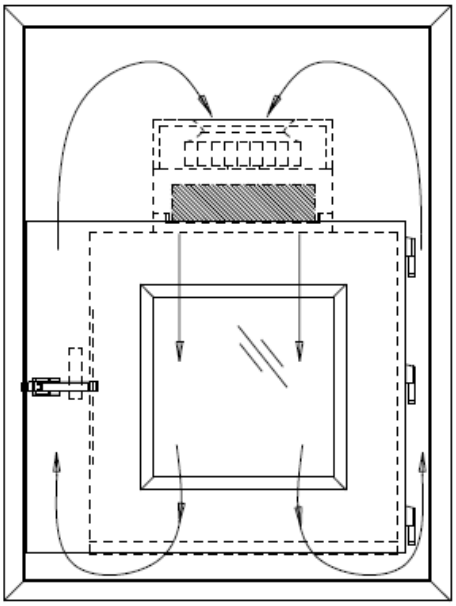
6) Usage

    a) Before any item is placed into the pass-through(s) and when packaging integrity will not be compromised, the materials being transferred must be wiped with a sporicidal agent, EPA registered disinfectant, or sterile 70% IPA using low-lint wipers by personnel wearing gloves.

III. HEPA-filtered Pass-throughs Are Not Required by Chapter ‹797› for 503A Pharmacies

1) Refer to Board of Pharmacy with regard to specific state requirements, if applicable.

IV. Pass-throughs Used Between an ISO Classified Negative Pressure Room and a Non-classified Room: Best Practices Recommendation



1) The pass through has HEPA filtration introduced at the ceiling of the pass-through.

a) This ensures the product being passed into the classified room has been showered with HEPA filtered airflow and particulate contamination brought into the pass-through chamber during loading is removed before opening the clean-side door.

b) The pass-through doors are not perforated.

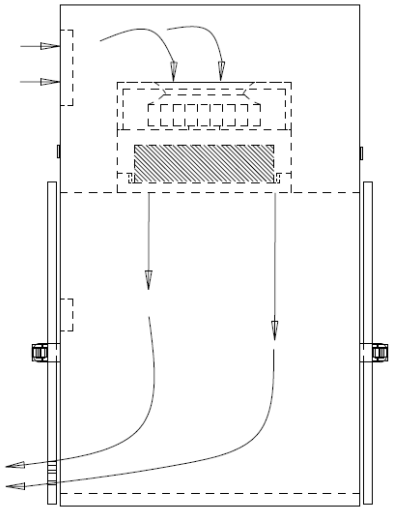
- Perforations may allow unfiltered airflow to be drawn into the room when the door opposite of the perforated door is opened.

2) The supply fan turns on when one door is opened and stays on for the duration that the door is opened and for a suitable duration (60 seconds is typical) after that door is closed.

3) The pass-through has an upstream aerosol introduction and concentration sample port installed to support HEPA filter leak testing.

4) The pass-through has an indicating device (alarm or gauge) demonstrating the pass through is operating within the acceptable parameters as designed.

V. Pass-throughs Between ISO Classified Positive Pressure Rooms and Non-classified Rooms



1) The pass through has HEPA filtration introduced at the ceiling of chamber.

a) This ensures the product being passed into the classified room has been showered with HEPA filtered airflow and that the particulate contamination is removed from the chamber before the opposite door is opened.

2) The pass-through doors may be perforated on the unclassified side.

a) Perforations allow airflow to be pushed into the unclassified room. While the perforation in the outer door will allow air to flow through it when the inner

door is opened, it will be flowing out of the cleanroom into the unclassified room because of the positive pressure in the cleanroom.

b) The pass-through motor/blower has the ability to operate continuously or turn on manually so that the certifier can perform the HEPA filter integrity test.

c) The pass-through has an upstream introduction and concentration sample port installed to support HEPA filter leak testing.

VI. Pass-throughs Between ISO Classified Rooms

1) HEPA filter purge is not necessary as long as the pass-through meets the basic criteria for all pass-throughs.

VII. Environmental monitoring in Pass-throughs

1) USP Chapter ‹797› states that "Surface sampling of all classified areas and pass-through chambers connecting to classified areas for microbial contamination must be conducted at least monthly. The chapter states that "Volumetric active air sampling of all classified areas using an impaction device must be conducted in each classified area [e.g., ISO Class 5 PEC and ISO Class 7 and 8 room(s)] during dynamic operating conditions at least every 6 months. Air sampling sites must be selected in all classified areas".

2) CEC recommends that surface sampling inside the pass-through chamber be included in the monthly surface sample locations.

3) CEC recommends that air sampling be conducted outside of the pass-through chamber in the cleaner room served by that pass-through. When the pass-through chamber is positioned between an ISO classified room and an unclassified room, the pass-through is not considered an ISO classified space. If the pass-through is positioned between two ISO classified rooms, air sample locations outside the pass-through chamber in the cleaner room served by that pass-through will be more indicative of potential contamination to the end-product than samples taken in the pass-through chamber. ***Please note this has been CEC's position, however since November 2020, consideration should be given to the FDA's position as stated in section VIII below.***

VIII. Environmental monitoring in Pass-throughs – FDA Guidance

1) In November 2020, the FDA published *Insanitary Conditions at Compounding Facilities - Guidance for Industry*, which defines a facility designed or operated in a way that permits the influx of lesser quality air into a higher quality air area, as an insanitary condition. This includes, for example:

   a) Material flow directly between an unclassified area and a room in which sterile compounding is conducted (e.g. unclassified pass-through)

CEC recommends if a pass-through is placed between a classified and unclassified room, the pass-through be HEPA filter purged. CEC further recommends the pass-through be

of the internally recirculating type, where the motor operates only during the purge cycle. Technically, environmental monitoring is required to be performed in all ISO classified spaces. Therefore, the pass-through should be classified to the lowest acceptable ISO classification. This is typically one order of magnitude less clean than the buffer room it serves, unless that buffer room is negative pressure, in which case the pass-through would need to be the same ISO classification as the buffer room, typically ISO Class 7. The air sampling device should be placed into the pass-through from the cleaner room. It should further be proven that the pass-through prevents transfer of contamination into the buffer room from the unclassified room by performing an ingress/egress test as described in CAG-002.