Does Your Barrier Isolator Isolate?

The Importance of Eliminating Contamination in Your Barrier Isolator

Barrier isolators are used to compound both hazardous and non-hazardous sterile preparations. USP chapter <797> and the NIOSH Alert for Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings are both based on the assumption that isolators prevent the exchange of unfiltered air between the isolator work chamber and the room in which the isolator is housed. Following is the background you will need to decide whether or not to place an isolator in a cleanroom, and factors to consider when determining your isolator’s ability to actually isolate its work area from the room in which it is placed.

The current version of USP chapter <797> makes the following statements: “A well-designed positive-pressure barrier isolator, supported by adequate procedures for its maintenance, monitoring, and control, may offer an acceptable alternative to the use of conventional LAFWs in cleanrooms for aseptic processing…The contamination-reduction conditions and procedures in this section include LAFWs located within buffer or cleanroom areas that maintain at least an ISO Class 8. It is preferred, but not necessary to locate barrier isolators within such a buffer air quality area.” While we do not yet know the changes to be made to the USP chapter, we can be sure that additional guidance will be forthcoming. In the pharmacy, it seems most people forget the phrase “it is preferred,” and choose to only remember the words “but not necessary.”

Guidance documents have historically required the placement of an isolator in an ISO Class 7 or 8 environment. The most recognized of these is the non-binding FDA document, released in 2004, “Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice,” which states, “The interior of the isolator should meet Class 100 (ISO 5) standards. The classification of the environment surrounding the isolator should be based on the design of its interfaces (e.g., transfer ports), as well as the number of transfers into and out of the isolator. A Class 100,000 (ISO 8) background is commonly used based on consideration of isolator design and manufacturing situations. An aseptic processing isolator should not be located in an unclassified room.” This language is quite clear and strong.

The Importance of Material Transfer Protection

Material transfer in and out of isolators during pharmaceutical manufacturing is recognized as the stage most vulnerable to contamination. The same is true for isolators used in the hospital pharmacy. In fact, material transfer poses a bigger threat to the internal chamber of a compounding isolator than most pharmaceutical manufacturing isolators, because pharmacy isolators typically rely on “pass-through” systems rather than the more robust “direct interface” or “rapid transfer ports” typically associated with pharmaceutical manufacturing.

Pharmaceutical manufacturers place isolators in cleanrooms to reduce the total contamination potential during material transfer. In hospital pharmacies, isolators are often placed in uncontrolled rooms, increasing the susceptibility to transferred contamination, and thus potentially compromising the sterility of the preparations being compounded in the isolator.

Decontamination with a validated system such as Vapor Phase Hydrogen Peroxide or Chlorine Dioxide is considered standard practice in pharmaceutical manufacturing settings. Procedures are developed to ensure full exposure of all isolator surfaces to the chemical decontamination agent. A breach of isolator integrity, such as that caused by entry of room air into the isolator is usually justified for decontamination. Pharmacy isolators, on the other hand, are usually decontaminated by spraying and wiping surfaces with a chemical agent, but the process is seldom validated to be effective. As such, pharmacy assumes substantial risks by rejecting the practice of placing isolators in a cleanroom while not fully embracing all of the other safeguards employed by other industries using isolators. Therefore, it is imperative that we take steps to eliminate the contamination transferred from the room during material transfer, and to maintain strict attention to aseptic technique during product manipulation.

USP Chapter <797> has made us aware of the fact that traditional clean air devices placed outside of a cleanroom are not always adequate protection to sterile products. Cleanroom technology, along with laminar flow equipment, will certainly provide appropriate atmospheres for compounding sterile preparations. In some cases, however, cost or space constraints do not allow for building of proper cleanroom facilities. In these cases, the argument has been made that properly designed positive pressure isolators that prohibit the exchange of unfiltered room air with the isolator are suitable alternatives to the cleanroom option.

Isolators are intended to isolate the work chamber from the room at all times during operation and transfer. However, you cannot simply purchase any system, place it in a room, and then expect it to provide the protection needed for sterile compounding. Understanding the importance of
eliminating contamination, most isolator manufacturers have engineered material transfer protection into their product through the use of airflow and HEPA filtration. In its simplest form, a static pass-through is a box attached to the isolator with two doors. At least one of the doors is closed at all times. While this will prevent the isolator’s working chamber from being directly exposed to the room, it will not prevent the transfer of particulate contamination from the room; room-particulate load enters the pass-through when materials are transferred into the pass-through from the room. Particulate matter is then transferred from the pass-through to the isolator.

To avoid this risk, most isolators utilize HEPA filtration to purge the pass-through. These HEPA-purged pass-throughs are able to eliminate virtually all particle transfer. Furthermore, the use of unidirectional airflow in the pass-through allows for the transfer of materials directly from the room to the isolator chamber with practically no purge time. I do not suggest transferring materials without at least a short purge time, but it is reassuring that the purge times can be short enough that even busy pharmacies will be able to use the system properly.

Laminar Air Flow
When thinking through the process of using the isolator for sterile compounding, remember that we need to prevent the ingress of contamination into the isolator. Your isolator will most likely not be in a cleanroom and the outside of the packages used in the isolator are most likely not going to be sterile. Do you really want to take these packages into the isolator without some type of preparation?

Some isolators are equipped with a laminar air flow pass-through, allowing users to remove the outer packaging or to wipe down the
Waste Containment for Barrier Isolators

By Charlotte A. Smith, RPh, MS

When choosing a new barrier isolator or ensuring the correct usage of your current isolator, proper waste containment must be considered. The type of waste containers needed depends on how the isolator is being used, but it is likely that hazardous waste will be involved, and therefore, will require special handling. Barrier isolators typically have two ports for waste containers, although they can be ordered with additional outlets. Keep in mind that the number of waste containers needed affects the number of ports you should order.

When preparing chemotherapy agents, plan on having a trace chemotherapy container—often yellow or white—for needles, syringes, and trace-contaminated pads, etc. You will also need a hazardous waste container—often black or dark blue—to contain any remaining drug in the vials or ampoules, or any overtly contaminated spill-clean-up materials.

The yellow or white trace chemotherapy containers must be disposed of by a regulated medical-waste vendor through incineration at one of their facilities. The hazardous waste container must be disposed of by a hazardous waste vendor at a federally permitted treatment, storage, and disposal facility. The vendor must be permitted under the Resource Conservation and Recovery Act (RCRA) to dispose of hazardous chemicals. A log detailing which drugs have been placed in the container must be maintained, and the containers must be labeled as hazardous waste while in the pharmacy. Additional labeling and manifesting is required before they are shipped.

For the preparation of non-chemotherapy sterile products, a hazardous waste container must also be available if epinephrine or other drugs considered by the EPA to be hazardous waste are being prepared in the barrier isolator. Since epinephrine is a P-listed hazardous waste, even empty vials and ampoules must be managed as hazardous waste. There is a federal exemption for used epinephrine syringes, but the EPA has not clarified whether that refers to syringes used in drug preparation. Since some hazardous waste vendors cannot take needles, be sure to coordinate between your vendor and your state regulatory authority.

A barrier isolator also needs a red sharps container for needles and syringes. A container must also be considered for empty vials and ampoules. For these products, the pharmacy and health-care organization must make a risk-management decision whether to use a trash container or one that will be incinerated as non-hazardous pharmaceutical waste. Such a white/blue container. In this situation, three isolator outlet ports would be required.

In making a barrier isolator purchase, consider waste needs as part of your analysis and be sure to order the appropriate number of outlets.


Where to find it:

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Compounding Hazardous Drugs

When considering how well the isolator isolates, we must also consider the isolators used for compounding hazardous drugs. Unlike biological safety cabinets, isolators are not certified to an industry standard by an independent agency. Every isolator is tested to criteria established by that manufacturer. The Controlled Environment Testing Association (CETA) is in the final stages of developing a standard that will at least give the end user a method of establishing consistent testing protocols. That should be available by the end of the year. The same concerns that are important for transferring material into an isolator are even more...
important when removing materials from an isolator used to contain hazardous drugs.

Unidirectional isolator airflow will prevent a build up of process-generated aerosols that may provide a risk to the room during material egress. Additional isolation is provided by HEPA-purged pass-throughs. The NIOSH Alert suggests specific isolators for use with volatile drugs. It should be noted that even HEPA-purged pass-throughs will not prevent the transfer of volatile contamination, as HEPA filters do not filter gases and vapors. Isolators and their associated pass-throughs should be vented outside the building if used to contain volatile contamination. Much more work is needed to understand containment isolators and that process has just begun. As such, for now, make sure you look at all the isolator options and understand how they utilize airflow and HEPA filtration to accomplish their stated goals. With a combination of proper aseptic technique and the use of a barrier isolator with a unidirectional pass-through and work area, you will most likely achieve the level of protection your pharmacy needs. However, one should remember that although it is acceptable to use a barrier isolator outside of a controlled environment, to minimize the potential for contamination during material transfer and cross contamination during operation or it should be located in an ISO Class 8 or cleaner environment.

James T. Wagner, principal of Controlled Environment Consulting, has over 25 years’ experience evaluating facilities used for aseptic processing. He has served on many industry-standard writing committees, and is currently a member of the committee revising USP Chapter <797>. 