

By Howard Siegerman, PhD

# Cleaning Compounding Aseptic Isolators and Class II Biological Safety Cabinets

COMPOUNDING ASEPTIC ISOLATORS (CAIs) and Class II biological safety cabinets (BSCs) are used to physically isolate compounded sterile preparations (CSPs) from contamination from the background environment and to protect compounding personnel from contamination from hazardous drugs. Both CAIs and BSCs are rated as ISO Class 5 devices in terms of air particle cleanliness and are maintained as sterile environments to a sterility assurance level (SAL) of $10^{-3}$. Per USP <797>, some form of cleaning and surface sanitization of these engineering controls and their background environments is required to prevent cross-contamination from one CSP to the next, and cleaning is required at the beginning of each shift.

Following is information on how to achieve the cleaning and disinfection requirements of USP <797>, as well as details on product selection, cleaning procedures, protocols, and step-by-step guidelines for effective CAI and Class II BSC cleaning. Both are cleaned the same way, and for simplicity, we will refer to CAIs and BSCs as CAIs for the remainder of this document.

Isolator cleaning tools, such as the one pictured above, can help pharmacy staff efficiently clean the CAI's interior chamber, particularly the areas out of arm's reach.

## Cleaning and Disinfecting CAIs

The cleaning and disinfection activities for CAIs can be separated into three areas: cleaning and disinfecting the CAI at the beginning of each shift, cleaning and sanitizing the interior of the CAI between CSPs, and cleaning the background environment. At the outset, and to state the obvious, it must be emphasized that any cleaning, sanitizing, disinfection or sterilization procedures must never be done while compounding activities are underway.

The cleaning of CAIs requires specialized procedures, or "critical cleaning," for optimum results. These procedures are counterintuitive and differ from the casual, cursory wiping approach that is used to clean a kitchen counter at home. While old and worn cotton dishtowels may be used in a circular motion to clean up spills or soils on kitchen countertops, this approach cannot be employed for CAIs. The wiping action puts the fabric in intimate contact with the surface, allowing the application of strong forces for the removal of contaminants such as bioburden. Wiping has a long and successful history for removal of contaminants from cleanroom surfaces. However, to be successful, the wiper must be used properly. The table on page 26 addresses the primary concerns in the use of wipers and mops for critical cleaning and provides corresponding best practices with explanations.

## Wipers and Mops

Much of the literature on isolator cleaning refers to the need for "low-linting" fabrics that do not shed. However, little guidance is provided as to which fabric types are best. The lint shed from wiping or mopping materials is made up of loose fibers that are not bound to the fabric surface or that break free during the cleaning process. Cleaning and disinfecting solutions can promote this linting or shedding activity if inappropriate fabrics are used.

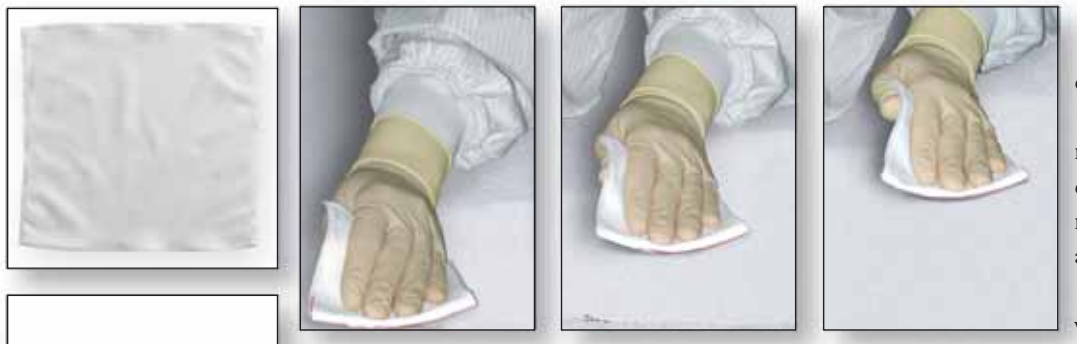
A wide variety of fabrics can be fashioned into wipers or mops for use in cleaning isolators. These include natural materials, such as cotton, rayon, and cellulosics; synthetic materials, such as polyester, nylon, polypropylene, or foams; or blends, such as polyester-cellulose combinations. Of these choices, polyester knit fabrics have the requisite cleanliness, low particle and fiber counts, low endotoxin levels, low extractable residues, durability, and chemical compatibility needed for the cleaning and disinfection of CAIs. Further, polyester knit fabrics can be sterilized by autoclaving or by gamma irradiation to a sterility assurance level (SAL) of $10^{-6}$ without loss of structural stability. The characteristically low levels of releasable particles and fibers associated with polyester knit fabrics are especially important in aseptic applications, since it is well known that particles are potential carriers of bacteria. Some facilities may use blended fabrics of polyester-cellulose to clean their CAIs. If such fabrics are used within the isolator, the pharmacist should recognize that they do carry a risk of higher particle and fiber release. Put simply, polyester knit fabrics represent the best choice for "non-linting" or "non-shedding" materials.

Sterile polyester knit wipers are used before production to clean the isolator and during production to clean spills, to wipe down gloves when wetted with sterile 70% isopropyl alcohol (IPA), or to clean work surfaces. All IPA solutions described here are assumed to be 70% IPA/30% water (v/v), where the "water" is either water for injection (WFI) or deionized water (DIW). Before IPA solutions are used for cleaning, rinsing, or sanitizing isolator surfaces, ensure that the materials of construction in the isolator will withstand repeated exposure to IPA. Some transparent materials, such as polycarbonates, may cloud over or crack when exposed to IPA. These wipers can be wetted with detergents to clean the isolator, deionized water or 70% IPA to remove cleaning agent residues, disinfecting agents to disinfect the isolator, and deionized water or 70% IPA to remove disinfectant residues. Pre-wetted sterile wipers containing 70% IPA are also available for these activities.

## Cleaning and Disinfecting CAIs at the Beginning of Each Shift

Since the isolator is most often cleaned and disinfected while closed, to maintain the sterility of the isolator, sterile cleaning and disinfecting consumables – wipers, pre-wetted wipers, mops, cleaning/disinfecting agents, water, 70% IPA, etc. – must be

All photos courtesy of ITW Texwipe



**In order to prevent re-contaminating surfaces you have already cleaned, use quarter-folded wipers with linear overlapping strokes, wiping from clean areas to dirty, renewing the wiper surface after each stroke.**

introduced through an appropriate transfer device. Even if a facility's standard operating procedure (SOP) calls for the isolator to be opened for cleaning and disinfection, the use of sterile wipers and pre-wetted wipers is recommended, since they can be introduced into the isolator for *in situ* cleaning needs. This also eliminates the confusion of having both sterile and non-sterile wipers on hand and the need to sterilize wipers prior to use within the isolator.

The usual sequence for cleaning and disinfection includes a cleaning step, a rinsing step, a disinfecting step, another rinsing step, and, if needed, a gaseous sterilization step. Wipers can also be used to wipe down hard surface articles that are introduced into the transfer device for use within the isolator. This will remove surface contaminants that might otherwise compromise disinfection or sporicidal treatments.

**Cleaning:** To ensure that each shift begins in a pristine environment, clean the isolator to remove any residues and soils produced from the prior shift's activity. These contaminants, if not removed, would otherwise unnecessarily consume disinfectant and mitigate its application.

Typically, small flat surface mops (isolator cleaning tools), wipers, swabs, and detergents are most commonly employed for these cleaning applications. Detergent selection is based on the type of soil to be removed. Also, cleaning mechanism factors such as wetting, dissolution, oxidation, hydrolysis, enzyme action, emulsification, deflocculation, sequestration, saponification, and rinse-ability can all be important in determining which detergent to use. The detergent is applied to the surface using quarter-folded wipers with linear overlapping strokes – wiping from clean areas to dirty, renewing the wiper surface after each stroke. Wipers are used for all surfaces within arm's reach. Isolator cleaning tools are used for surfaces beyond arm's reach. Detergents also have the benefit of reducing the bioburden level on the surface; this lessens the task somewhat for the subsequent disinfection step. Your pharmacy's quality supervisor should determine which cleaning and disinfecting steps are required for any given circumstance.

**Rinsing Following Cleaning:** After cleaning, detergent residues are removed from the surfaces with wipers or mops wetted with sterile DIW or 70% IPA. This will ensure that disinfectants have the opportunity to contact bare surfaces. Surfaces are considered clean when devoid of visible surface contaminants. Verify visually that the last wiper used to wipe down the surface is also devoid of visible residues.

**Disinfection:** Follow the same procedures as you do for cleaning, substituting liquid disinfecting agents for detergents. Disinfecting agents include pheno-

# Critical Cleaning

## Critical Cleaning with Wipers and Mops

| Concern | Best Practice | Comment |
|---|---|---|
| Effective removal of surface soils | Select wiping material that entraps soils | Soils are collected in the fabric and discarded with the wiper |
| | Fold wiper in quarters | Ensures full contact of wiper to surface |
| | Use appropriate detergent or other cleaning agent | Cleaning agent must be compatible with materials of construction used in isolators or safety cabinets |
| Recontamination of surfaces already cleaned | Select non-linting fabrics | Prevents contamination of wiped surface from particles and fibers from wiper fabric |
| | Wipe in linear, overlapping strokes from clean area to dirty area | Wipe vertical surfaces from top to bottom, as circular wiping will contaminate clean area |
| | Refold wiper to expose fresh wiper surface after each stroke | Prevents re-deposition of contaminants picked up on previous stroke |
| Deposition of residues from cleaning and disinfecting agents | Remove residues with wipers wetted with deionized water or 70% IPA solution | Ensures that bare surfaces are disinfected and that unsightly corrosive residues do not accumulate |
| Cleaning effectiveness | Surfaces should be free from visible contaminants after cleaning | Illuminating surface with high-intensity light at an oblique angle will help to identify soils not removed<br><br>Examine the last wiper in contact with the surface to verify absence of visual contaminants on the wipe |

lics and quaternary ammonium compounds, known as "quats." Use either phenolics or quats – never both together. Aqueous mixtures of IPA provide some measure of disinfection, but they are ineffective against spores. Occasionally, liquid sterilants such as sodium hypochlorite (bleach), peracetic acid, and hydrogen peroxide will be substituted for disinfectants when sporicidal activity is needed. These sterilants can be corrosive to surfaces and are therefore used intermittently.

**Rinsing Following Disinfection:** Disinfecting agent residues are wiped from the surface with wipers or isolator cleaning tools that have been wetted with sterile deionized water or sterile 70% IPA. This will eliminate the buildup of residue deposits that become difficult to remove in subsequent cleaning operations, and that will cause staining of work surfaces.

**Gaseous Sterilization:** Once the cleaning and disinfection steps are completed, if required, the isolator can be sterilized with a suitable sterilant such as vaporized hydrogen peroxide (VHP).

### Cleaning and Sanitizing Between CSPs

To avoid cross contamination between CSPs, the accepted procedure is to wipe the isolator counter with a wiper wetted with 70% IPA. This will remove any residues from the work surface and provide a measure of surface sanitization as well. IPA will remove many types of soils. Some residues may only be water soluble, so wipers wetted with water for injection (WFI) should be used to remove them. A final wipedown with IPA will leave the surface clean for the next CSP. A second IPA-wetted wiper should be used to wipe gloved hands to guard against cross-contamination in the preparation of the next CSP. If the CAI is used for compounding hazardous drugs, swab sampling of the interior surfaces with subsequent analysis may be appropriate to prove that the compound of interest is not present at levels that would constitute an exposure limit danger.

### Cleaning and Disinfection of Background Environments

USP <797> requires that floors in the CAI's background environment to be mopped daily, while walls, ceilings, and shelving are to be mopped monthly. To accomplish these tasks, the following procedure can be employed.

- **Step 1**: Place a clean dry mop cover on the mop head and wet it with a suitable liquid cleaning agent – either detergent or 70% IPA – to clean the ceilings, walls, and floors of the background environment. Use linear, overlapping strokes to ensure all surfaces are cleaned thoroughly. If the mop cover becomes visibly dirty during the cleaning process, replace it.
- **Step 2**: If 70% IPA was used in Step 1, proceed directly to Step 3. If a detergent was used in Step 1,

| Cleaning Task | Recommended Products |
|---|---|
| Cleaning and disinfecting of interior walls, ceiling and deck of closed isolators (Use one or more of the products to the right) | **1. An isolator cleaning tool** to reach all interior surfaces of the isolator<br>Sterilize the isolator cleaning tool and mop covers before introducing them into the isolator. Dampen the mop covers with sterile WFI, sterile DIW, IPA, detergent cleaning solution, disinfectant solution, or liquid sterilant.<br>**2. Polyester knit wipers,** wetted with 70% sterile-filtered IPA and gamma-irradiated<br>**3. Gamma-irradiated polyester knit wipers**<br>Dampen the wipers with the solutions described above, as appropriate for the cleaning task at hand.<br>**4. Swabs,** dampened with one of the solutions described above, for cleaning hard to reach spaces or isolator corners |
| Wiping down isolator deck between CSPs | **Polyester knit wipers**, wetted with 70% sterile-filtered IPA and gamma-irradiated |
| Cleaning up spills while isolator is in use | **Sterile wipers** for absorbing spilled liquid, then **polyester knit wipers**, wetted with 70% sterile-filtered IPA and gamma-irradiated |
| Wiping mating and sealing surfaces between transfer isolator(s) and main isolator | **Polyester knit wipers**, wetted with 70% sterile-filtered IPA and gamma-irradiated |
| Cleaning background environments | **Polyester knit mop covers**, wetted with detergent cleaning agents, disinfectants, and deionized water |

place a clean mop cover on the mop head, then dampen it with either deionized water or 70% IPA. Use linear, overlapping strokes to remove the dried cleaning agent residue. Again, if the mop cover becomes visibly dirty during the cleaning process, replace it.

■ **Step 3**: Place a clean mop cover on the mop head and spray the mop cover with an approved disinfectant – such as phenolic or quaternary ammonium compound – solution. Spread the disinfectant over the ceiling, walls, and floors with linear, overlapping strokes. Alternatively, spray the ceilings, walls, and floors with the disinfectant, and spread the disinfectant solution evenly over the surfaces with the mop. Allow appropriate kill time (10 to 20 minutes) for the disinfectant to do its job.

■ **Step 4**: Place a clean mop cover on the mop head, then dampen it with either deionized water or 70% IPA. Use linear, overlapping strokes to remove the dried disinfecting agent residue. Again, if the mop cover becomes visibly dirty during the cleaning process, replace it.

Establishing a rigorous cleaning program for your CAIs is a relatively inexpensive way to immediately improve the quality of your pharmacy's compounding operations. By following the protocols and procedures outlined in this article, you can ensure the sterility of your compounded preparations, limit your personnel's exposure to hazardous drug agents, and achieve compliance with the standards set forth in <797>. ■

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