

## **Cleaning of Isolators and Bio-safety Cabinets**

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### **1. Introduction**

Isolators (Figures 1 and 2) and bio-safety cabinets<sup>3</sup> (Figure 3) are well accepted as cost-effective, convenient and compact controlled environments to provide product and personnel protection. These devices consist of protective enclosures that physically isolate products from the background environment (the room outside the isolator), either because the product of interest is unsafe and therefore needs containment, or the product cannot tolerate contamination and therefore needs isolation. Collectively, they are known as “separative enclosures”, or more properly “separative devices”.



Figure 1 – Pharmaceutical Isolator (Photo courtesy Geringe, La Calhène)

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<sup>3</sup> Also known as “safety cabinets”, “biocontainment isolators”, “containment isolators” or “barrier isolators”



Figure 2 – Compounding Aseptic Isolator (Figure courtesy of NuAire, Inc.)



Figure 3 – Bio-safety Cabinet (Photo courtesy The Baker Company)

The term “isolator” is usually reserved for pharmaceutical and pharmacy applications, whereas the term “bio-safety cabinet” (BSC) is used in the pharmacy, biotechnology and microbiology industries. For this discussion, we will consider that isolators and Class II bio-safety cabinets (and associated transfer devices) in biotechnology, microbiology, pharmaceutical and pharmacy applications are used as ISO Class 5 devices in terms of air particle cleanliness and are maintained as sterile environments to a sterility assurance level (SAL) ranging from  $10^{-3}$  to  $10^{-6}$  depending upon application.

Some applications, such as the handling of cytotoxic drugs, potent hormones and radiopharmaceuticals require both containment and isolation to achieve both protection of personnel from the product and protection of the product from contamination<sup>4</sup>. These activities would typically be done in a Class II bio-safety cabinet or compounding aseptic containment isolator (CACI), where the necessary levels of air particle control and sterility would be maintained.

In applications where containment only is required, air flow is directed into the enclosure from the outside environment and filtered air is exhausted. This arrangement would suffice for a Class I bio-safety cabinet. Conversely, where product protection is need, filtered air is delivered to isolators which maintain a net positive pressure to the background environment. This arrangement would suffice for a pharmaceutical isolator or a compounding aseptic isolator in which containment is not required, because hazardous products are not involved. Where containment and production protection are required, air flow into and out of the separative enclosure is filtered, ie. BSCs and CACIs.

In order to maintain product quality and integrity, it is necessary to clean isolators and bio-safety cabinets on a regular basis, with appropriate cleaning products, according to established and validated standard operating procedures (SOP's). Some isolators can be cleaned with clean-in-place (CIP) systems using spray wands. Others require manual cleaning with wipers, mops, cleaning agents and if necessary, disinfectants. For the latter category, this paper addresses the wipers and mopping systems that are best used for isolators and bio-safety cabinets and provides recommendations on optimum cleaning techniques. The manner in which pharmaceutical isolators, compounding aseptic isolators (CAI's) and bio-safety cabinets are used is sufficiently different that different cleaning (and disinfection) approaches are needed. Suggested protocols and recommended products are provided for the three applications. The reader may also wish to refer to publications dealing with the cleaning of aseptic pharmaceutical environments for additional background information (1-6)

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<sup>4</sup> Brian Midcalf , Chairman of the Pharmaceutical Isolator Working Party and User Group and Assistant PTQA Course Director, University of Leeds, UK, points out that progression from product isolation to product containment to product isolation and containment represents movement along what could be considered the “separation continuum”.

## 2. Optimum Cleaning Procedures

Cleaning of separative enclosures such as isolators and bio-safety cabinets requires specialized procedures for optimum results – procedures termed as “critical cleaning”. 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 (often not replaced for many days) may be used in a circular motion to clean up spills or soils on kitchen countertops, this approach cannot be employed for separative enclosures. Neither the wiping material nor the wiping action would be appropriate for isolators and safety cabinets. The kitchen counter may look clean – in fact, it may appear clean enough to eat on<sup>5</sup> – but it is still not clean enough for the contamination requirements of a separative enclosure. Fortunately, several sources (7-8) provide guidance for best practices for critical cleaning.

One could well ask, “Why bother with wiping? Why not just spray with alcohol to clean the surface?” The case for wiping as opposed to merely spraying was effectively made by Cockcroft and coworkers (9) who studied disinfection techniques for transfer of components into hospital pharmacy cleanrooms. They stated “...spraying [with alcohol] may reduce the bioburden slightly, but wiping is much more efficient and a combination of spraying and wiping gave the best results”. Further, the following points were made. *“If a disinfectant wipe is used, two modes of action come into play. Particles and micro-organisms are removed from the surface on to the wipe as the fibres pass over the surface, or the micro-organism is killed by the disinfectant. If not killed by the disinfectant, the micro-organisms collected will remain on the wipe unless transferred by contact with another surface such as the hand manipulating the wipe. For this reason, it is recommended that a fresh part of a sterile wipe is used for each wiping action and overlapping strokes are used.”*

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. Table 1 addresses the primary concerns in the use of wipers and mops for critical cleaning and provides corresponding best practices with explanations. This information is also summarized in Figure 4 below.

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<sup>5</sup> This probably speaks more to the tolerance of the human body for environmental bacteria than the apparent cleanliness of the counter.

**Table 1. Critical Cleaning with Wipers and Mops**

<b>Concern</b>	<b>Best Practice</b>	<b>Comment</b>
Effective removal of surface soils	<p>Select wiping material that entraps soils.</p> <p>Fold wiper in quarters</p> <p>Use appropriate detergent or other cleaning agent.</p>	<p>Soils are collected in the fabric and discarded with the wiper</p> <p>Ensures full contact of wiper to surface</p> <p>Cleaning agent must be compatible with materials of construction used in isolators or safety cabinets</p>
Re-contamination of surfaces already cleaned	<p>Select non-linting fabrics</p> <p>Wipe in linear, overlapping strokes from clean area to dirty area.</p> <p>Refold wiper to expose fresh wiper surface after each stroke.</p>	<p>Prevents contamination of wiped surface from particles and fibers from wiper fabric</p> <p>Wipe vertical surfaces from top to bottom Circular wiping action re-contaminates area just cleaned.</p> <p>Prevents re-deposition of contaminants picked up on previous stroke.</p>
Deposition of residues from cleaning and disinfecting agents	Remove residues with wipers wetted with deionized water or 70% isopropyl alcohol (IPA) solution	Ensures that bare surfaces are disinfected and that unsightly 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 Examine the last wiper in contact with the surface to verify absence of visual contaminants on the wiper.

## Wiping Guide

1. Follow relevant site protocol (procedures for safety, contamination, etc.) and wear clean-room gloves.
2. Fold wiper in mid-air into quarter folds (Fig. 1A–1C). This will produce several clean surface areas and allow better contact with the surface to be wiped.
3. When wiping, hold the wiper so that the single-fold edge is outward toward the area to be wiped. Hold the selvages closer to your hand. (Fig. 2)
4. Use either a pre-wetted wiper or a dry wiper moistened with an appropriate cleaning agent.
5. Wipe in one direction, overlapping wiped area by 10% to 25%. Wipe systematically, for example, from top to bottom, far to near. (Fig. 2)
6. Wipe from cleanest to least clean regions of the surface being wiped.
7. Keep track of which surfaces have been cleaned and which wiper areas are unused.
8. Use the cleanest surfaces of the wiper. If re-wiping use clean wiper area, not used wiper area.
9. Dispose of wipers according to site procedures.

### Wiping Wet Spills

1. Identify the spilled liquid. Follow the Material Safety Data Sheet (MSDS).
2. Choose wiper and gloves that will not be degraded by liquid.
3. For hazardous spills, wear two pairs of gloves and try to keep the gloves dry. Wear any other necessary protective gear.
4. Use dry wipers to wipe spills up immediately, then wipe slowly.
5. Dispose of wipers according to site procedures.

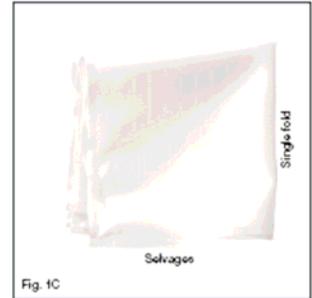
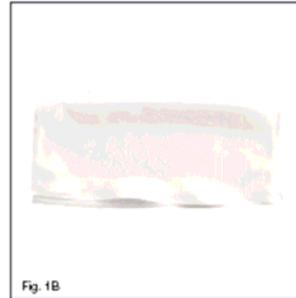
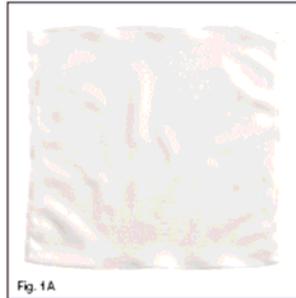


Figure 4 – Wiping Guide

### **3. Cleaning and Disinfection of Pharmaceutical Isolators**

#### **a) Overview**

This section deals with the cleaning and disinfection of pharmaceutical isolators used to conduct aseptic filling operations, sterility testing, cell culturing and purification activities, among others. Section 4 deals with the cleaning and disinfection of compounding aseptic isolators used by pharmacies. Both types of isolators are rated as ISO Class 5 devices in terms of air particle cleanliness and are maintained as sterile environments to an SAL ranging from  $10^{-3}$  to  $10^{-6}$ .

Akers and Agalloco (10) have pointed out that there are no substantial differences between an isolator and a cleanroom as far as the cleaning of product contact surfaces are concerned. Obviously, an isolator is smaller in volume than a cleanroom, with a correspondingly smaller footprint. But both need to be cleaned and disinfected and these processes should be thorough, consistent, convenient and validatable. Previous publications have addressed the general topic of cleaning of isolators (11-16). This section, however, focuses on details such as wiper selection, wiping procedures, protocols and step by step guidelines for isolator cleaning. Commercial training programs for isolator cleaning and use are also available (17-18).

#### **b) Wipers and Mops for Cleaning and Disinfection of Isolators**

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 that is shed from wiping or mopping materials is made up of loose fibers that are not bound to the fabric surface or that are broken 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 cellulose, synthetic materials such as polyester, nylon, polypropylene or foams, or blends such as polyester-cellulose combinations. Of these choices, only polyester knit fabrics have the requisite cleanliness, low particle and fiber counts, low endotoxin levels, low extractable residues, durability, and chemical compatibility that are needed for the cleaning and disinfection of isolators. Further, polyester knit fabrics can be sterilized by autoclaving or by gamma irradiation to an 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 (11).

Put simply, polyester knit fabrics used for wipers and mop covers will not contaminate isolator surfaces when used in cleaning and disinfection operations. Consequently, they represent the best choice for “non-linting” or “non-shedding” materials. The same cannot be said for other fabrics.

Sterile polyester knit wipers are used during production to clean up spills, wipe down gloves (when wetted with sterile 70% IPA), or to provide clean work surfaces. These wipers can be wetted with (i) detergents to clean the isolator, (ii) deionized water or 70% IPA<sup>6</sup> to remove cleaning agent residues, (iii) disinfecting agents to disinfect the isolator and (iv) deionized water or 70% IPA to remove disinfectant residues. Pre-wetted sterile wipers, containing 70% IPA are also available for these activities.

#### c) Cleaning and Disinfecting Frequency

Good contamination control practice would suggest that isolators and associated transfer devices be cleaned and disinfected after a production campaign<sup>7</sup> has been concluded (referred to here as “post cleaning” which includes disinfection) and again before a new production campaign is begun (referred to here as “pre-cleaning” which also includes disinfection). This will avoid cross contamination. If the isolator has not been opened after “post cleaning” and if a new manufacturing campaign starts within short time (say one hour) after “post cleaning”, then an additional “pre-cleaning” step may be unnecessary. In that case, a surface sanitization of the isolator interior with sterile wipers and/or mops wetted with sterile 70% IPA may be sufficient to ready the isolator for production. Decisions on cleaning/disinfecting frequency and procedures are the province of the Quality Supervisor.

#### d) Cleaning and Disinfecting Specifics

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 introduced through an appropriate transfer device. Even if a facility’s 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 eliminates 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 and a cleaning validation step. As a side note, wipers can be used to wipe down any 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.

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<sup>6</sup> All IPA solutions described in this article 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, e.g. polycarbonates, may cloud over or crack when exposed to IPA.

<sup>7</sup> A production campaign is considered a session in which multiple products of the same type are manufactured.

(i) Cleaning

To ensure that each production run will be conducted in a pristine environment, it is necessary to clean the isolator to remove any residues and soils produced from the prior run. These contaminants, if not removed, would otherwise unnecessarily consume disinfectant and mitigate its application (19).

Typically, small flat surface mops known as isolator cleaning tools (Figure 5), 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 rinseability can all be important in determining which detergent to use (20-21). The detergent is applied to the surface in the manner described in Section 2 General Cleaning Techniques – 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.



Figure 5 – Isolator cleaning tool in use (Photo courtesy Getinge, La Calhene)

(ii) Rinsing Following Cleaning

After cleaning, detergent residues are removed from the surfaces with wipers or mops that have been wetted with sterile deionized water or sterile 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.

(iii) Disinfection

The same procedures are followed for disinfection, except that liquid disinfecting agents are substituted for detergents. Disinfecting agents can include phenolics and quaternary ammonium compounds<sup>8</sup> (“quats”). Aqueous mixtures of IPA will 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

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<sup>8</sup> Use phenolics **or** quats, never both together.

sterilants can be corrosive to surfaces and are therefore used intermittently. Again, isolator cleaning tools and wipers are used as described Section (i) above.

(iv) Rinsing Following Disinfection

The same procedure is followed here as in Section (ii) above. 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.

v) Gaseous Sterilization(22)

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).

vi) Cleaning Validation

Surface sampling with swabs to verify the absence of cleaning and disinfecting agents may be required after step (iv). More details can be found in other documents (2, 23-25)

This constitutes the “post clean” described in the Cleaning Frequency Section above. An identical series of steps would be followed for a “pre clean” operation, except that if surfaces have not been contaminated since the “post clean”, only disinfection, rinsing and perhaps gaseous sterilization may be needed. Again, the Quality Supervisor determines what cleaning and disinfecting steps are required for any given circumstance.

e) Recommended Products

Table 2 lists the various cleaning tasks and the products recommended for both pharmaceutical isolators and compounding isolators, since so many of the tasks are common to both. Those tasks that are unique to pharmaceutical isolators are shown in blue; those that are unique to compounding isolators are shown in red.

**Table2. Cleaning Tasks for Pharmaceutical Isolators and Compounding Aseptic Isolators**

<b>Cleaning Task</b>	<b>Recommended Products</b>
Post-clean or pre-clean of interior walls, ceiling and deck of closed isolators	Choose one or more of the following: 1. Isolator cleaning tool with polyester knit mop covers to reach all interior surfaces of the isolator. Sterilize the cleaning tool and mop covers before introducing them into the isolator. Dampen the mop covers with sterile WFI, sterile DIW, sterile IPA <sup>9</sup> , detergent cleaning solution, disinfectant solution or liquid sterilant as described in 3d above. 2. Sterile IPA-pretreated polyester knit wipers. 3. Sterile dry polyester knit wipers. Dampen the wipers with the solutions described in 1 above, as appropriate for the cleaning task at hand. 4. Swabs with polyester knit heads for cleaning hard-to-reach spaces, crevices, nooks, crannies, and isolator corners. These swabs can be dampened with one of the solutions described in 1 above.
Wiping down deck between CSP's	Sterile IPA-pretreated polyester knit wipers.
Cleaning up spills while isolator is in use.	Sterile dry polyester knit wipers for absorbing spilled liquid, then Sterile IPA-pretreated polyester knit wipers for removing surface contamination.
Wiping down gloves while isolator is in use.	Sterile IPA-pretreated polyester knit wipers.
Wiping mating and sealing surfaces between transfer isolator(s) and main isolator	Sterile IPA-pretreated polyester knit wipers.
Wiping down articles before placing them in the transfer isolator	Sterile IPA-pretreated polyester knit wipers.
Validation of isolator cleaning	Total Organic Carbon (TOC) Cleaning Validation kit.
Cleaning Background Environments	Flat surface mop with polyester knit mop covers, wetted with detergent cleaning agents, disinfectants and deionized water as described in Section 4e below.

Text in black refers to tasks for both pharmaceutical isolators and compounding aseptic isolators. Text in blue refers to tasks unique to pharmaceutical isolators. Text in red refers to tasks unique to compounding aseptic isolators.

<sup>9</sup> Again, IPA refers to 70% IPA, 30% DIW (v/v)

#### **4. Cleaning and Disinfection of Compounding Aseptic Isolators(CAI's)**

##### **a) Overview**

This section deals with the cleaning of isolators used in hospital pharmacies and other dispensing facilities to formulate ( i.e. “compound”) individual prescriptions for patient care. As for pharmaceutical isolators, CAI's are rated as ISO Class 5 devices in terms of air particle cleanliness and are maintained as sterile environments to an SAL of  $10^{-3}$ . In the United States, the cleaning and disinfecting of CAI's and the associated background environments fall within the province of the US Pharmacopeia's document USP <797> (12). CAI's are not used in exactly the same manner as the isolators used for pharmaceutical manufacturing. There are few opportunities to run extensive production campaigns with CAI's. A licensed compounding facility producing cancer treatment drugs for example, may produce batches of identical products numbering in the tens or low hundreds, but a typical hospital pharmacy is more likely to have a “manufacturing run” of just a single preparation (or perhaps a few doses of the same drug), transferred aseptically into a vial, intravenous (IV) bag, syringe, infusion device, etc. These are termed compound sterile preparations (CSP's) in the industry. While the extensive cleaning and disinfection procedures previously described for pharmaceutical isolators are unnecessary and obviously impractical here, some form of cleaning and surface sanitization of compounding isolators will be required to prevent cross-contamination.

The cleaning and disinfection activities for CAI's will 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 CSP's
- 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.

Section 3, which covered many of the guidelines for cleaning and disinfection of pharmaceutical isolators, applies here as well. To save space, only specifics that are unique to CAI's will be covered below.

##### **b) Selection of Wipers and Mop Covers**

From a best practice viewpoint, knit polyester wipers and mop covers are again preferred for their low particle and fiber release characteristics for use in these ISO Class 5 isolators. It is recognized that some facilities will consider that blended fabrics of polyester-cellulose (discussed in Section 5 below) may suffice for CAI's. If such fabrics are used within the isolator, the pharmacist should recognize that they do carry a risk of higher particle and fiber release onto the isolator surfaces.

c) Cleaning and disinfecting the CAI at the beginning of each shift.

The procedures here are identical to what is done for pharmaceutical isolators Section 3d (i) through (v).

d) Cleaning and sanitizing the interior of the CAI between CSP's

To avoid cross contamination between CSP's, the accepted procedure is to wipe the counter or "deck" of the isolator with a wiper wetted with 70% IPA. Pre-wetted wipers are most convenient for this task. This will remove any residues from the work surface and will provide a measure of surface sanitization as well. IPA is a versatile cleaning agent and will remove many different types of soils. Some residues may only be water soluble, so in those cases, wipers wetted with water for injection (WFI) should be used to remove the surface soils. A final wipedown with IPA will leave the surface clean for the next CSP. A second IPA-wetted wiper should be used to wipe down the gloves to guard against cross-contamination in the preparation of the next CSP.

If the CAI is used for compounding hazardous drugs, then swab sampling of the interior surfaces with subsequent analysis may be appropriate to prove that the compound of interest is not present at levels which would constitute an exposure limit danger.

e) Cleaning and Disinfection of Background Environments

The USP <797> document requires that floors in the background environment (also termed "buffer or clean area") be mopped daily, while walls, ceilings and shelving are to be mopped monthly. To accomplish these tasks most effectively, the following procedure, utilizing a single flat mop with replacement mop covers can be employed.

- i) 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 (Figure 6). If the mop cover becomes visibly dirty during the cleaning process, replace it.



Figure 6 – Flat surface mop for ceiling, wall and floor cleaning

ii) If 70% IPA was used in step i) proceed directly to step iii). If a detergent was used in part a), 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.

iii) Place a clean mop cover on the mop head and spray the mop cover with an approved disinfectant (e.g. 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 (e.g. 10 – 20 minutes) for the disinfectant to do its job.

iv) 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.

This procedure will ensure that the background environment outside the compounding isolator will meet the requirements for USP <797>.

f) Recommended Products

Refer to Table 2 above for the various cleaning tasks and the associated products recommended for CAI's. Ignore the blue text in Table 2 which refers to tasks unique to pharmaceutical isolators. Tasks relevant to CAI's are in black and red.

## 5. Cleaning Bio-safety Cabinets

### Overview

As stated previously, bio-safety cabinets are used to protect operators from the hazardous materials within the cabinet. Class II bio-safety cabinets (used for handling cytotoxic drugs, potent hormones, active pharmaceutical ingredients, etc) and CACIs that are maintained sterile with ISO Class 5 air particle levels, would be cleaned according to the guidelines laid out previously for pharmaceutical isolators or compounding aseptic isolators. These cabinets require the use of polyester knit fabrics to maintain the necessary particle levels within the separate enclosure.

However, some bio-safety cabinets, such as the Class I category, do not require that the interior of the separate enclosure be kept sterile, do not require that ISO Class 5 air quality be maintained and typically do not incorporate glove ports. For these applications, fabric selection for wipers and mop covers can be relaxed somewhat.

### b) Selection of Wipers and Mop Covers

The blended polyester-cellulose materials that were previously considered too contaminating for pharmaceutical and compounding isolators will be quite suitable for most Class I bio-safety cabinet applications.

### c) Cleaning Specifics for Class I Bio-safety Cabinets

The cleaning specifics for Class I bio-safety cabinets are similar to those for pharmaceutical isolators, except that cleaning activity can be confined to the end of a manufacturing campaign and sterile consumables need not be used. Again, the desire is to prevent cross-contamination from one manufactured product to another. However, since there is no need to maintain sterility, one can reasonably assume that if the bio-safety cabinet interior is cleaned thoroughly and is validated, there should be no need to clean again, prior to the beginning of the next manufacturing campaign. These are broad guidelines, however and the protocols defined by the Quality Supervisor must be observed.

One further cleaning activity bears mention. Since the production activity involves hazardous materials, it may be prudent to wipe down the exterior of the manufactured product to ensure that dangerous substances are removed prior to the product being transferred out of the bio-safety cabinet. These wipers, and those used to clean the interior of the bio-safety cabinet must be appropriately bagged and transferred out of the separate enclosure in a safe manner.

The wipedown procedures follow the same procedures as described in Section 2. Linear wiping patterns from clean to dirty (usually top to bottom, front to back), with overlapping strokes, quarter-folding the wiper after each stroke. Since hazardous materials are being removed from surfaces, consideration should be given to changing the wipers frequently. After cleaning, suitable validation tests should be run to verify the absence of the hazardous material involved. Obviously, the bio-

safety cabinet must be thoroughly wiped down and decontamination procedure verified before the enclosure is opened to the background environment.

d) Recommended Products

Table 3 lists the various cleaning tasks and the products recommended for BSC's.

**Table 3. Cleaning Tasks for BSC's**

<b>Cleaning Task</b>	<b>Recommended Products</b>
Cleaning of interior walls, ceiling and deck of closed BSC's at the beginning of each shift	Choose one or more of the following: 1. Isolator cleaning tool with blended polyester-cellulose mop covers to reach all interior surfaces of the isolator. Dampen the mop covers with DIW, IPA, detergent cleaning solution, disinfectant solution or liquid sterilant as described in 3d above.  2. IPA-pretreated blended polyester-cellulose wipers.  3. Dry blended polyester-cellulose wipers, wetted with the solutions described in 1 above, as appropriate for the cleaning task at hand.  4. Polyurethane foam swabs for cleaning hard-to-reach spaces, crevices, nooks, crannies, and BSC corners. The swab can be dampened with one of the solutions described in 1 above.
Cleaning up spills while BSC is in use	Dry blended polyester-cellulose wipers for absorbing spilled liquid, then IPA-pretreated, blended polyester-cellulose wipers for removing surface contamination.
Wiping down gloves while BSC is in use	IPA-pretreated, blended polyester-cellulose wipers.
Wiping mating and sealing surfaces to BSC	IPA-pretreated, blended polyester-cellulose wipers.
Wiping down articles before placing them in the transfer device	IPA-pretreated, blended polyester-cellulose wipers.
Wiping down manufactured articles before transferring them out of the BSC	IPA-pretreated, blended polyester-cellulose wipers.

## 6. Summary

The manner in which pharmaceutical isolators, compounding aseptic isolators and bio-safety cabinets are used dictate the somewhat varied approach to cleaning and where applicable, disinfection practices. Good contamination control practices and dedicated adherence to established, written SOP's will minimize cross-contamination surprises. For specific product recommendations for the cleaning of isolators and bio-safety cabinets, please contact the authors at [hsiegerman@texwipe.com](mailto:hsiegerman@texwipe.com) or [kbonnell@texwipe.com](mailto:kbonnell@texwipe.com).

## 7. Acronyms

BSC – Bio-safety Cabinet  
CAI – Compounding Aseptic Isolator  
CACI – Compounding Aseptic Containment Isolator  
CSP – Compounded Sterile Pharmaceutical  
DIW – Deionized Water  
IPA – Isopropyl Alcohol (always at 70% concentration)  
SAL – Sterility Assurance Level  
SOP – Standard Operating Procedure  
TOC – Total Organic Carbon  
WFI – Water for Injection

## 8. Acknowledgements

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## 9. References

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