ITW TEXWIPE

TechNote ICT-1

Cleaning of Compounding Aseptic Isolators (CAIs) and Class II Biological Safety Cabinets (BSCs)

I. Overview

Compounding Aseptic Isolators and Class II biological safety cabinets are used in hospital pharmacies and other dispensing facilities to formulate (i.e. "compound") individual prescriptions for patient care. A typical hospital pharmacy utilizing a CAI for contamination control and sterility, will make individual pharmaceutical preparations that are transferred aseptically into vials, intravenous (IV) bags, syringes, infusion devices, etc. These are termed compound sterile preparations (CSPs) in the industry. By contrast, a licensed compounding facility, utilizing a Class II biological safety cabinet for containment, contamination control and sterility, might produce cancer treatment drugs in batches of perhaps tens or a few hundred.

Both CAIs and Class II BSCs are used to physically isolate manufactured products from contamination from the background environment — the room outside the isolator. Class II BSCs provide containment capability not found in CAIs. This is necessary when working with hazardous drugs such as cytoxics, hormones and radiopharmaceuticals. Both 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}. Some form of cleaning and surface sanitization of these separative enclosures is required to prevent cross-contamination from one CSP to the next. Further, cleaning of these devices at the beginning of each shift is required. In the United States, the cleaning and disinfecting of CAIs and the associated background environments fall within the province of the US Pharmacopeia's document USP <797> (USP) General Chapter <797> Pharmaceutical Compounding — Sterile Preparations, U.S. Pharmacopeia, Rockville, MD; see also proposed revisions issued May 2006 at http://www.usp.org/pdf/EN/USPNF/PF797.pdf.

This ITW Texwipe® Technical Note is intended to provide information on how to achieve the cleaning and disinfection requirements of USP <797> and includes details such as product selection, cleaning procedures, protocols and step-by-step guidelines for effective CAI and Class II BSC cleaning. As far as cleaning requirements are concerned, they are both cleaned the same way, and for simplicity, we will refer to CAIs and Class II BSCs as CAIs for the remainder of this document.

Compounding Aseptic Isolator

II. Cleaning and Disinfecting CAIs

The cleaning and disinfection activities for CAIs will be separated into three areas:

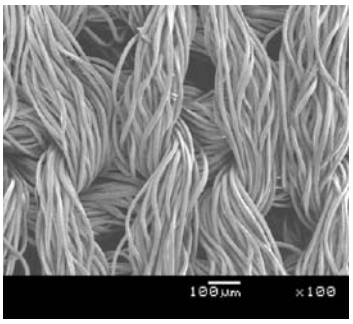
- Cleaning and disinfecting the CAI at the beginning of each shift
- Cleaning and sanitizing the interior of the CAI between CSPs
- Cleaning the background environment

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.

a) 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 cellulosics, 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 CAIs. 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. It is recognized that some facilities will consider that blended fabrics of polyester-cellulose may suffice for 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 onto the isolator surfaces.



Photomicrograph of polyester knit fabric

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 before production to clean the isolator and during production to clean up spills, wipe down gloves (when wetted with sterile 70% isopropyl alcohol (IPA)[1]), or to provide clean work surfaces. These wipers can be wetted with:

(i) detergents to clean the isolator,
(ii) deionized water or 70% IPA 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.

b) Cleaning and disinfecting the CAI 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 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 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. 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.

(i) Cleaning

To ensure that each shift begins in a pristine environment, it is necessary to 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.

Figure 1. *Isolator cleaning tool in use*

Typically, small flat surface mops known as isolator cleaning tools (*Figure 1*), 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. The detergent is applied to the surface in the manner described in Section V — "Optimum Cleaning Procedures" — 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.

[1] 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, e.g. polycarbonates, may cloud over or crack when exposed to IPA.

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

(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

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).The Quality Supervisor determines which cleaning and disinfecting steps are required for any given circumstance.

c) Cleaning and sanitizing the interior of the CAI between CSPs

To avoid cross contamination between CSPs, 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 gloved hands 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.

d) 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 (*Figure 2*) with replacement mop covers can be employed.

Figure 2. *Flat surface mop for ceiling, wall and floor cleaning*

Figure 3. *Mop cover fitted to mop head*

i) Place a clean dry mop cover on the mop head (*Figure 3*) 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.

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

[2] Use phenolics or quats, never both together.

III. Cleaning Tasks and Recommended Products

Following is a table of cleaning and disinfecting activities performed on CAIs and the recommended ITW Texwipe products for those tasks.

Cleaning Task	Recommended Products
Cleaning and disinfecting of interior walls, ceiling and deck of closed isolators	Use one or more of the following: 1. **TX7101 Mini AlphaMop™ Isolator Cleaning Tool** with **TX7114 Mop Covers** to reach all interior surfaces of the isolator. Sterilize the TX7101 isolator cleaning tool and TX7114 mop covers before introducing them into the isolator. Dampen the mop covers with sterile WFI, sterile DIW, **TX3270 Sterile IPA**, detergent cleaning solution, disinfectant solution or liquid sterilant as described in section II. 2. **TX3252, TX3280 or TX3285 Sterile AlphaSats®**, containing sealed-border polyester knit wipers, pre-wetted with 70% sterile-filtered IPA and gamma-irradiated. 3. **TX3215, TX3212 or TX3211 Dry SterileWipes™** containing gamma-irradiated polyester knit wipers. Dampen the wipers with the solutions described in 1 above, as appropriate for the cleaning task at hand. 4. **TX714A Swabs** for cleaning hard to reach spaces or isolator corners. TX714A swabs can be dampened with one of the solutions described in 1 above.
Wiping down isolator deck between CSPs	TX3252, TX3280 or TX3285 Sterile AlphaSats
Cleaning up spills while isolator is in use	TX3215, TX3212 or TX3211 SterileWipes for absorbing spilled liquid, then TX3252, TX3280 or TX3285 Sterile AlphaSats for removing surface contamination.
Wiping mating and sealing surfaces between transfer isolator(s) and main isolator	TX3252, TX3280 or TX3285 Sterile AlphaSats
Cleaning background environments	**TX7108 AlphaMop™ with TX7118 AlphaWipe® Polyester Knit Mop Covers**, wetted with detergent cleaning agents, disinfectants and deionized water.

TX7101 Mini AlphaMop™Isolator Cleaning Tool

TX7114 Mop Covers

TX3270 Sterile IPA

TX3252, TX3280 and TX3285 Sterile AlphaSats®

TX3215, TX3212 and TX3211 SterileWipes™

TX714A Large Alpha® Swab

TX7108 AlphaMop™

IV. Detailed Product Descriptions

TX7101 Mini AlphaMop™ Isolator Cleaning Tool

The ITW Texwipe TX7101 Mini AlphaMop™ Isolator Cleaning Tool is designed to facilitate cleaning of CAIs. The mop head has a low, flat profile, rounded corners and is totally autoclavable. The swivel joint allows the user to reach otherwise inaccessible areas. The replaceable foam pad ensures that the mop cover conforms to the surfaces that are being cleaned. TX7101 includes two handles, 18" and 24" (46 cm and 61 cm), and is easily used with one hand. Changing the mop covers is quick and easy — they are designed to slip on and off, yet remain secure while in use.

Product Number	Description	Packaging
TX7101	Mini AlphaMop™ Isolator Cleaning Tool 1 polyester foam pad 6 TechniCloth® mop covers	1 mop/case 2 handles (18" and 24")
TX7114	Mini AlphaMop™ covers AlphaWipe® replacement mop covers	150 mop covers/case 25 covers/inner bag 6 inner bags/case 6 foam pads/case

TX3270 Sterile 70% IPA — 16-oz. (473 ml) spray bottle

This product is used for convenient dispensing of sterile 70% IPA onto dry sterile wipers or onto mop covers for cleaning and sanitizing activities during production and to remove cleaning and disinfecting agent residues from surfaces. The spray bottle can also be used to sanitize gloves during production.

Sterile Wipers

ITW Texwipe SterileWipe™, incorporating polyester knit wipers gamma-irradiated to an SAL of 10^{-6}, are recommended for the cleaning and disinfection of CAIs. These wipers are used during production to clean up spills, or to provide clean work surfaces. When wetted with sterile 70% IPA, they can be used to clean surfaces or to wipe down gloves during production. These wipers can be wetted with:

(i) detergents to clean the isolator,
(ii) deionized water or 70% IPA to remove cleaning agent residues,
(iii) disinfecting agents to disinfect the isolator and
(iv) deionized water or 70% IPA to remove disinfectant residues.

SterileWipe™ Selection Guide*

Product Number	Product Name	Wiper Characteristics	Selection Criterion
TX3215	SterileWipe™ AS10	12" x 12" (31 cm x 31 cm) two ply, sealed-border polyester knit	Highest absorbency Low particle and fiber levels
TX3212	SterileWipe™ LP10	12" x 12" (31 cm x 31 cm) single ply, sealed-border polyester knit	Moderate absorbency Lowest particle and fiber levels
TX3211	SterileWipe™ LP	9" x 9" (23 cm x 23 cm) single ply, cut-edge polyester knit	Moderate absorbency Cut edges contribute to higher fiber levels Most economical

*Another sterile wiper, TX3210 SterileWipe™ HS II, made of blended polyester-cellulose is also available, but it is not generally recommended for isolator cleaning because of its higher particle and fiber burden compared to the polyester knit wipers shown above.

Sterile Wipers Pre-Wetted with 70% IPA

The following pre-wetted wipers are all polyester knit, laundered, pre-wetted with 0.2 µm-filtered 70% IPA, then gamma-irradiated to a Sterility Assurance Level of 10^{-6}. These wipers eliminate the need to use sterile 70% IPA in the isolator and are used during production to clean up spills or to wipe down gloves. These wipers are also used to remove cleaning and disinfecting agent residues or to sanitize surfaces just prior to production. Note that WFI is used in place of DIW in the TX3280 below.

Sterile AlphaSat® Selection Guide*

Product Number	Product Name	Wiper Characteristics	Selection Criterion
TX3252	Sterile AlphaSat®	Uses TX3215 wiper 12" x 12" (31 cm x 31 cm) two ply, sealed-border polyester knit	Delivers largest amount of 70% IPA of the three choices Low particle and fiber levels
TX3280	Sterile AlphaSat®	Uses TX3212 wiper 12" x 12" (31 cm x 31 cm) single ply, sealed-border polyester knit	Wetting solution is 70% IPA / 30% WFI Lowest particle and fiber levels
TX3285	Sterile AlphaSat®	Uses 9" x 9" (31 cm x 31 cm) version of TX3212 wiper single ply, cut-edge polyester knit	Smallest wiper of the three choices Wipers are individually folded in half, then stacked before pre-wetting and packaging Lowest particle and fiber levels Most economical

*Another sterile pre-wetted product, TX3217 Sterile TechniSat® HS II, incorporating blended polyester-cellulose wipers is also available, but it is not generally recommended for isolator cleaning because of higher particle and fiber burden compared to the polyester knit wipers shown above.

TX7108 AlphaMop™

Flat surface mop with replaceable AlphaWipe® mop covers incorporates a swivel joint to permit ease of handling and to reach into corners. Excellent for routine cleaning of large surface areas such as ceilings, walls, floors, cabinet exteriors, etc.

TX714A Large Alpha® Swab

Incorporates AlphaLite® polyester knit fabric thermally bonded to a polypropylene handle. Ideal for cleaning hard-to-reach spaces, crevices, nooks, crannies and isolator corners. Ideal for performing final wipedown to verify absence of visible residues. Packaged 50 swabs per inner bag; 2 inner bags per outer bag.

V. Optimum Cleaning Procedures

Cleaning of separative enclosures such as CAIs 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[3] — but it is still not clean enough for the contamination requirements of a separative enclosure.

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 below 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 the wiping guide (*Figure 4*).

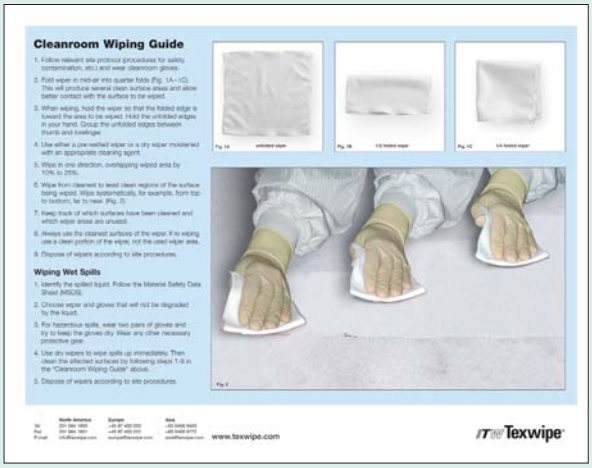


Figure 4. *Wiping Guide*
Wiping Guide posters are available on our website at www.texwipe.com

[3] This probably speaks more to the tolerance of the human body for environmental bacteria than the apparent cleanliness of the counter.

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
Re-contamination 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 Circular wiping action re-contaminates area just cleaned
	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
		Examine the last wiper in contact with the surface to verify absence of visual contaminants on the wiper

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