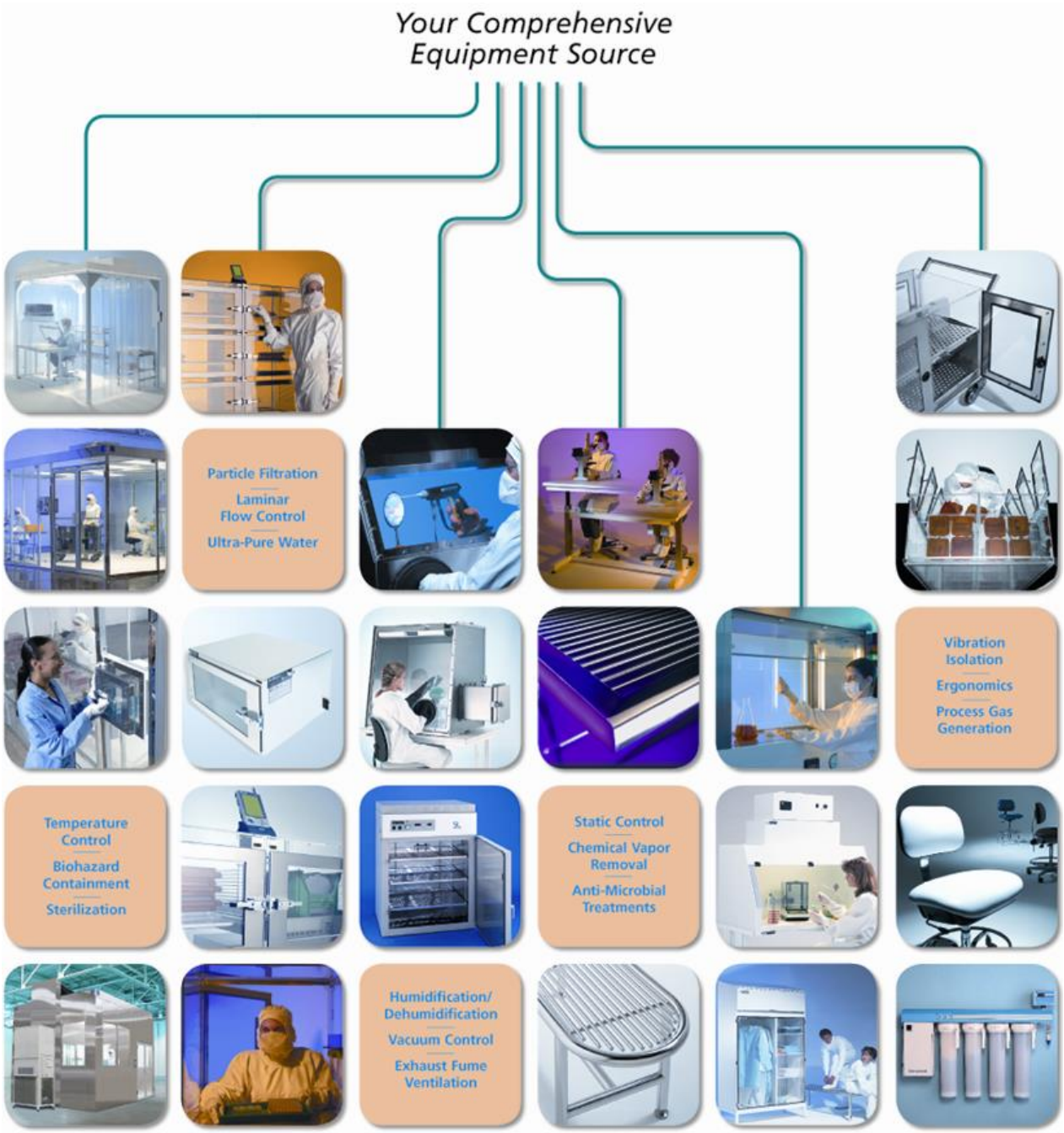
TERRA UNIVERSAL.COM
Critical Environment Solutions

Quick-Start Operating Guide *Document No 1800-35*

Compounding Aseptic Isolator



Quick-Start Operating Guide

Compounding Aseptic Isolator

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Safety Notice

A thorough familiarity with all operating guidelines is essential to safe operation of the product. Failure to observe safety precautions could result in poor performance, damage to the system or other property, or serious bodily injury or death.

The following symbols are intended to call your attention to two levels of hazard involved in operation:

CAUTION — **Cautions are used when failure to observe instructions could result in significant damage to equipment.**

WARNING — **Warnings are used when failure to observe instructions or precautions could result in injury or death.**

The information presented here is subject to change without notice.

1.0 Description

Terra Universal's Compounding Aseptic Isolator (CAI) provides a sterile environment for compounding non-hazardous pharmaceuticals by physically separating the critical compounding areas from the greatest source of contamination: the compounding personnel. Terra's isolator employs a pass-through, HEPA-purged design featuring ISO 5 unidirectional air flow to meet and exceed USP 797 standards for Primary Engineering Controls (PEC).

Photo 1: Polypropylene compounding isolator chamber

WARNING

NOT intended for hazardous drug compounding!
Refer to TerraUniversal.com for information on USP 800 and the Compounding Aseptic Containment Isolator (CACI).

1.1 Processing and Ante Chambers

The compounding chamber is fabricated of clean materials that can be sanitized and sterilized with standard disinfectants, including isopropyl alcohol and hydrogen peroxide. The chamber walls are made of 304/316 stainless steel, or polypropylene with polycarbonate viewing windows and glass antechamber divider, which slides back and forth in a polypropylene track. The main chamber window tilts up to allow full access for easy cleaning or introduction of large processing equipment. The HEPA-purged antechamber allows operators to transfer compounding materials into the sterile environment while minimizing the exposure of the main chamber to contamination.

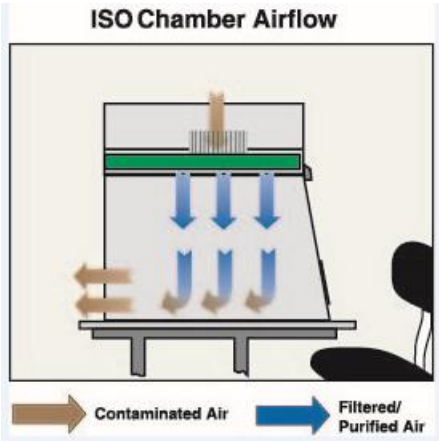

Figure 1: Laminar airflow path – air enters from the top, passes through the HEPA filter, is pushed downward and exits via the rear vent.

1.2 Fan/Filter Unit

The fan/filter unit (FFU) incorporates a 3-speed, direct-drive 1/3 HP electric motor that forces air through a HEPA filter. In conjunction with the system's pre-filters, the HEPA filter removes 99.99% of all particles 0.3 microns and larger from a large volume air stream, and the vertical laminar flow of air to the work surface effectively blocks the inrush of contaminants. Each 2' x 4' FFU provides 644 CFM of filtered air @ 90 FPM. Air is exhausted through the exit filters along

the back wall of the enclosure, which restrict the air flow in order to maintain a positive internal pressure of at least 0.05 inches of water column ("WC). Operators can adjust the speed of the FFU to increase or decrease the internal pressure and air changes per hour to meet the applicable cleanliness standards. See **Appendix I** for more information on USP and cGMP compliance.

1.3 Magnehelic® Pressure Gauge

The CAI includes two 0 – 0.25"WC Magnehelic™ differential pressure gauges that monitor the internal positive pressure of the main chamber and antechamber. This pressure is necessary to prevent unfiltered air from entering the isolator when the antechamber door is opened or if any small gaps exist. See **Appendix V** for recommended differential pressure levels.

Photo 2: (From left) FFU control knob, Magnehelic™ differential pressure gauge, and certifier test ports

1.4 Lighting

The system also features a fluorescent light fixture (T5, 13W bulb) that is externally mounted to eliminate interference with the controlled environment inside the chamber.

1.5 IV Rod

A 0.25"-diameter IV bag hanging rod is mounted 3" from the top (filter face) of the chamber.

Photo 3: Antechamber sliding transfer door

1.6 Waste Chute

A 6"-diameter waste chute is provided for connection to a user-furnished externally mounted waste receptacle bag. The chute includes an external 3" flange for attaching the bag.

1.7 Certifier Test Ports

The FFU is equipped with three test ports that allow the certifier to verify the differential pressures on the gauges.

Photo 4: Rear polyester exit filters

Photo 5: Tilt-up and swing access door

3.0 Initial Operation

WARNING **To prevent dangerously low oxygen levels and risk of asphyxiation, nitrogen-purged systems should only be installed in a well-ventilated area.**

To operate the system:

1. Plug in the power cord to a grounded 115VAC/60Hz or 230VAC/50Hz receptacle.

2. Turn the FFU speed control knob to increase the air velocity and positive pressure within the isolator. To ensure ISO 5 conditions, a differential pressure reading of at least 0.05"WC should be constantly maintained in the main chamber, as well as differential pressure reading of at least 0.035"WC in the antechamber.

3. Use a flexible clamp (1/2" x 20") to attach the lower flange of the waste chute to an appropriate waste receptacle (polyethylene or metalized bag, depending on whether sharp objects are being used).

Refer to **Appendix II** for USP 797-compliant operating and sterilizing protocol.
Refer to **Appendix VI** for Compounding Aseptic Isolator Best Practices.

4.0 Maintenance

Replacing the Fan Filter Unit
As the system HEPA filter clogs, you will notice in increase in blower noise and a reduction in the internal positive pressure. To compensate temporarily, you can increase the FFU speed. The filter should be replaced as soon as you are unable to maintain at least 0.05"WC in the main chamber.

To replace the filter, first disconnect power to the FFU, use a ladder to lift it off of the isolator chamber, and move it to a safe, convenient location.

1. Remove the eight sheet-metal screws from the top perimeter of the FFU.

2. Carefully lift the top of the FFU, including the impeller motor, to expose the HEPA filter.

3. Visually inspect the replacement filter for damage to the filter face and for gaps along the sealed edges. Use care when handling the replacement filter not to damage the filter face. Gently position it inside the filter housing so that it seats against the lower edge of the FFU housing. Make sure that the air-flow arrow points down.

4. Replace the FFU top and blower assembly.

5. Reposition the FFU on top of the glovebox.

6. Perform the Daily Cleaning Procedure and the Sterilization Procedure outlined in **Appendix II** prior to resuming compounding operations.

Replacement 24" x 48" HEPA Filter **Cat. # 6601-25**
99.99% efficient @ 0.3µm particles

Replacement MERV 7 Exit Filters **Cat. # 2900-65**
Processing Chamber

Replacement MERV 7 Exit Filters **Cat. # 2900-66**
Antechamber

Replacing the Fluorescent Light
Simply rotate the fluorescent T5 bulb inside the fixture until it disengages and slides free. Replace with item number below (typical life: two years of continuous operation).

Replacement Fluorescent Tube **Cat. # PA01520**
For 24" fixture

5.0 Specifications and Performance

Exterior Dimensions:	49”W x 29.25”D x 54”H (including filter/fan unit)	
Antechamber:	12.5”W x 19.25”D x 39”H	(Opening: 10”W x 32”H)
Process Chamber:	32”W x 19”D x 39”H	(Opening: 27”W x 32”H)
Housing:	304/16 stainless steel, or polypropylene	
Viewing Windows:	Polycarbonate (1/4” thick) with swing access door	
Glove Ports:	10” diameter (order gloves, sleeves, and connectors separately)	
Waste Chute:	6” diameter, 0.75”H flange (inside glovebox), 3” flange (below glovebox); port cover included	
IV Rod:	0.25” stainless steel rod mounted 3” from the filter face	
Pressure Gauge:	0 – 0.25”WC Magnehelic gauge monitors internal positive pressure	
Lighting:	External-mount fluorescent fixture	

Performance: Meets or exceeds the requirements/specifications of the following industry standards:

ISO 5 (Class 100 (M 3.5)) air per the latest I.E.S.T.

14664-1 (Airborne Particulate Cleanliness Classes)

I.E.S.T. Recommended Practices (Laminar Flow Clean Air Devices)

Airflow Velocity: 90 (±10) FPM (0.45 m/s), when measured using a Velgrid (eight readings) 6 in. (152 mm) below the filter face.

Sound Level: Approximately 53 dBA on low speed measure at 30 in. from the filter face, with the fan delivering an average air flow velocity of 90 FPM (0.45 m/s). Ambient sound level less than 35 dBA

Vibration Level: Will not exceed 0.09 MILS RMS

FFU Housing: Both the fan plenum and filter housing have a mill finish (powder coat paint or stainless steel exterior optional), and sealed airtight

Pre-filter: Furnished with a 16.0 in. x 23.25 in. x 0.25 in. polyurethane foam, washable pre-filter

HEPA Filter: Factory tested and rated 99.99% efficient in removal of particles 0.3 micron and larger; leak free in accordance with the latest I.E.S.T. Recommended Practices

Filter Media: Microglass fiber with hot melt separators, sealed to the aluminum housing

Filter Face Guard: Anodized aluminum plate with perforations

Fan/Motor: Direct drive; forward curve centrifugal type with permanently lubricated sealed ball bearings
Motor: Permanent split capacitor type, rated for continuous duty furnished with thermal overload protection and a three-speed switch

Power Requirements: 120VAC, 50/60Hz, 1 phase

Full Load Nameplate Amps: 4.3 (for 120V, 60Hz)

FFU Performance:	Airflow ft/min (m/s)	Operating Amps/Watts
High Speed	150 (0.77)	2.7/290
Med Speed	120 (0.61)	2.0/210
Low Speed	95 (0.48)	1.5/160
90 fpm*	90 (0.45)	2.8/190
70 fpm*	70 (0.35)	2.5/150

* With solid state speed control. When operating with the speed control, the voltage is reduced and this reduction may result in the amperage exceeding full load amps. This is a safe operating condition

Fan/Motor Unit: Delivers 650 CFM (0.307 m^3/s) of air at a filter pressure drop from 0.25 to 0.75 in. WG (62 Pa to 188 Pa), at 90 FPM (0.45 m/s), based on a useable media area of 7.15 sq. ft.

Lighting: Fluorescent type (T5 bulb), approximately 1,250 lumens; does not disturb the air flow

HEPA Filters
The filtration medium consists of highly efficient micro-fiberglass paper folded over corrugated separators of aluminum which prevent the media from nesting. This design channels air flow with optimal efficiency to reduce resistance.

All filters are tested for air flow resistance and DOP (dioctylphthalate) smoke penetration (with a mean particle diameter of 0.3 microns) by measuring upstream and downstream smoke concentrations with a photometer.

6.0 Warranty

Products Manufactured by Terra: Terra Universal, Inc., warrants products that it manufactures to be free from defects for a period of 12 months for parts and 90 days for labor, commencing from the date of shipment. Terra's sole responsibility is to repair or replace, at its option, any part of the product that proves defective or malfunctioning during this time limit. In some cases, components incorporated in Terra Universal products are covered by additional warranties from component manufacturers; obtain specific information from Terra sales representatives. This warranty is void if the equipment is abused or modified by the customer, is operated outside Terra's operating instructions or specifications, or is used in any application other than that for which it is specified. This warranty does not include routine maintenance or service procedures, breakage of quartz baths after 60 days, shipping damage, nor damage from misuse, intentional or unintentional abuse, neglect, natural disasters, or acts of God.

Products Manufactured by Others: Terra Universal, Inc., warrants that, to the best of its ability, Terra's representations of products that are manufactured by others reflect the manufacturer's representations, subject to change without notice. Sole warranty for these products is the original manufacturer's warranty that is passed forward to the purchaser and constitutes the customer's sole remedy for these products. Detailed warranties for distributed products are available through Terra sales representatives.

Freight Shortage or Damage: Upon receipt of any equipment from Terra Universal, Inc., customer shall immediately unpack and inspect for damage or shortage. The customer shall not accept a damaged package or a short shipment until the carrier makes a "damage or shortage" notation on both the carrier's and customer's copy of the freight bill or delivery receipt. Service title passes when the shipment is loaded, so customer is responsible for filing and collecting a freight claim. Any replacement products must be ordered and paid for separately. For Terra's "Policy and Procedures for Returning Goods," see Terra's Internet site: www.TerraUniversal.com.

Generally, customers can improve the chance of collecting on a freight claim by following these procedures: 1) formally requesting that the carrier inspect the shipment immediately upon suspecting damage or shortage to verify condition; 2) notifying the carrier upon discovery of concealed damage and requesting an inspection within 15 days of receipt, both in person or phone and following up via mail; 3) keeping the shipment as intact as possible, including retaining original packaging materials and keeping the product as close to the original receiving location as possible; 4) holding salvage for disposition by the carrier.

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Warranty Returns: All warranty returns must be authorized in advance by Terra Universal and approved under an RMA. Unless approved in advance for good reason, all returns must be in original condition, including all manuals, and must be packaged in original packaging materials. All returned goods are to be shipped to Terra Universal, freight prepaid at customer's expense. See Terra's "Policy and Procedure for Returned Goods.

Thank you for ordering from
Terra Universal!

Appendix I: USP 797 Compliance Overview

Terra's Compounding Aseptic Isolator is manufactured to comply with the requirements set forth in USP Chapter 797. These guidelines apply to facilities involved in the compounding of sterile preparations (CSPs).

USP 797 specifies that sterile compounding take place in either:

A. An ISO 5 (Class 100) Laminar Air Flow Workstation (LAFW), which includes both hoods and biological safety cabinets, positioned inside an ISO 7 (Class 10,000) cleanroom, or

B. An ISO 5 (Class 100) Compounding Aseptic Isolator (CAI), which is not currently required to be positioned inside a cleanroom if it meets the criteria outlined in USP 797.

Refer to *USP Chapter <797>: Pharmaceutical Compounding—Sterile Preparations* for a more detailed explanation.

NOTE

FDA-issued cGMP guidelines for aseptic compounding require isolators to be installed in AT LEAST ISO 8 conditions. Some State Boards of Pharmacy also enforce this standard, which is not required in the current USP 797.

Compounding Aseptic Isolator Testing and Certification

In addition to environmental monitoring requirements, USP 797 requires testing and recertification of all Primary Engineering Controls (PECs) every six months or when the PEC is moved.

USP 797 allows an isolator to be placed in an unclassified space if it meets the following criteria:

1. The isolator shall provide isolation from the room and maintain ISO Class 5 during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs.
2. Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.
3. Not more than 3520 particles (0.5 µm and larger) per m^3 shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing the transfer.

See **Appendix V** for specific recommendations related to testing your CAI for certification.

Once the isolator is qualified to the above standards by an independent certifying agency, it can be operated in a non-controlled environment as long as proper operation and sterilization protocol are observed (see **Appendix II**).

Operation and sterilization recommendations apply only to aseptic processing of non-hazardous compounded sterile preparations (CSPs).

WARNING

Hazardous drugs, including radioactive materials and cytotoxins, require a negative-pressure processing environment and should never be handled inside Terra's Compounding Aseptic Isolator.

The rest of this appendix provides further explanation of the USP 797 requirements regarding CAIs and how the Terra Compounding Aseptic Isolator meets these requirements.

General Features of the Compounding Aseptic Isolator (CAI)

Terra's Compounding Aseptic Isolator provides a unidirectional vertical flow of HEPA filtered air that sweeps contaminants out of the processing area and through exhaust vents. The effectiveness of the system depends on several critical design features.

First, it employs an industry-leading Filter/Fan Unit that incorporates a HEPA filter rated at 99.99% effectiveness for particles 0.3 µm in diameter and larger. This three-speed FFU provides an average flow of 644 CFM, at 90 FPM air speed, when operated at low speed.

Because the filter covers the entire surface of the ceiling area of the glovebox, this airflow is unidirectional. Any contaminants that enter the processing chamber, either through an access door or on the surface of materials passed into the chamber, are swept out of the processing area and through the exhaust vents almost immediately.

The exhaust vents are restricted by a MERV 7 non-shedding polyester filter that traps the particles and contaminants that are swept downward by the laminar airflow. The exhaust filter enclosure is designed to allow quick access to the exhaust filters for regular sterilization and routine replacement, which is critical for preventing the gradual build-up of microbiological contaminants along the exhaust path. Operators must be sure to properly sterilize the filter and the surfaces of the housing according to the guidelines in **Appendix II**.

The exhaust vent is sized to create a controlled backpressure inside the glovebox, which is measured by the Magnehelic™ pressure gauge mounted above the enclosure. The resulting positive pressure differential helps prevent unfiltered air from entering the isolator when an access door is opened. A slightly greater positive pressure differential in the main chamber relative to the antechamber likewise blocks airborne contaminants from entering the compounding area when transferring compounding materials.

Internal pressure inside Terra's Compounding Aseptic Isolator can be regulated by means of the FFU speed control. The volume of displaced air is approximately 644 CFM, adequate to quickly remove contaminants that enter the chamber.

Air Locks and Antechambers

The Compounding Aseptic Isolator features an antechamber separated from the main processing area by a tempered glass sliding door mounted in a polypropylene track. Because it has a unidirectional flow of HEPA filtered air, the antechamber provides an air-purging effect that prevents cross-contamination during compounding material transfer. This airflow sweeps away any particles passed into the antechamber, minimizing the chance of contaminants reaching the main chamber.

Materials

USP 797 requires that a CAI be regularly sterilized. Terra's isolator features materials of construction that are compatible with common disinfecting agents, including 70% IPA and germicidal detergent solutions (refer to Specifications for details).

Appendix II: Operating Guidelines and Sterilization Protocol

Operators must adhere to the guidelines presented in this appendix to minimize the risk of contaminating the critical areas of the isolator environment when preparing CSPs. These recommendations are based on USP 797, industry best practices, and expert opinion.

Refer to *USP Chapter <797>: Pharmaceutical Compounding—Sterile Preparations* for a more thorough explanation of the standards for compounding sterile drugs.

Transporting Materials into the Compounding Area

To optimize workflow without increasing bioburden, Terra recommends using the "clean cart/dirty cart" system for moving the compounding materials into the anteroom/segregated compounding area. The "clean cart" stays on the "clean side" of the Line of Demarcation (LOD) and the "dirty cart" only transports the compounding materials from the supply room up to the LOD.

The following preparations should be performed prior to gowning:

1. After removing supplies from corrugated cardboard containers, wipe down each item with a sporicidal agent.
2. Use the designated "dirty cart" to transport the compounding materials and any transfer containers/totes up to the Line of Demarcation (LOD) in the anteroom/segregated compounding area.
3. Any items that will be brought into an ISO-classified buffer room must be sprayed with 70% sterile IPA and wiped with a sterile, non-shedding wipe prior to being transferred onto the "clean cart."
4. If a segregated compounding area is used, transfer the items over the LOD, directly onto the "clean cart."
5. Proceed with gowning procedures after loading the "clean cart."

Operator Gowning Requirements


NOTE

The FDA requires all gowning materials to be sterile and completely cover the skin when working in the compounding room. CGMP requires isolators to be installed in at least ISO 8 conditions.


WARNING

The following procedure must be followed to best prevent contamination of the compounding materials prior to transfer into the Compounding Aseptic Isolator:

1. Ensure all gowning materials are of the **non-shedding/non-linting variety**.
2. Verify the anteroom or segregated compounding area features a Line of Demarcation (LOD) for gowning.
3. Beginning on the "dirty side" of the LOD, don a hair net (and/or facial hair net) and facemask.

4. If compounding will occur in an ISO-classified environment, shoe covers will be required. Lifting one foot off of the ground, don a shoe cover, and step onto the "clean side" of the LOD in a single motion. The shoe cover should never touch the "dirty side" of the line of demarcation. Repeat for the other shoe.

5. Perform aseptic hand washing and dry hands using a sterile, lint-free towel. The sink should be located on the "clean side" of the LOD.

6. Proceed into the buffer room or segregated compounding area, pushing the "clean cart" into the room while protecting your hands from any unnecessary surface contact.

7. Position the "clean cart" near the CAI antechamber.

8. Perform antiseptic hand cleansing using a waterless alcohol-based surgical hand scrub and allow hands to air dry completely.

9. Don powder-free sterile gloves.

Transferring Compounding Materials into the Compounding Aseptic Isolator

WARNING

Operators must follow these procedures exactly to best protect compounding materials and the isolator environment from contamination:

1. Operators must wear sterile gloves, a non-shedding hair net, a non-shedding facemask, and a non-shedding gown when opening the antechamber. If the CAI is located in an ISO-classified area, non-shedding shoe covers are required.

2. Make sure that the Fan/Filter Unit is ON and both Magnehelic™ gauges show a positive pressure of **at least 0.05 inches of water column (10 Pa)**.

3. Verify that the internal sliding door between the antechamber and the main chamber is closed. If it is not, use the glove port access to close it.

4. The compounding materials and transfer container must be disinfected before opening the antechamber. Starting with the transfer container, spray sterile 70% IPA onto each item and wait for the recommended dwell time before wiping with a non-shedding sterile wipe.

5. Open the antechamber swing door and place the materials into the antechamber. Do not touch any surfaces within the antechamber, being especially mindful of non-sterile gown sleeves.

6. Close the antechamber door and **wait at least one minute to purge the antechamber, returning the environment to ISO 5 conditions before retrieving the materials.**

7. Insert hands into the glove ports and retrieve the materials through the internal sliding door, closing the sliding door promptly.

Workflow for the Compounding Aseptic Isolator

1. Stage the compounding materials on the left side of the main chamber as they are brought in through the antechamber. Aseptic manipulations should be performed towards the right side of the chamber.

2. Don sterile gloves over the isolator gloves prior to compounding, using aseptic technique.

3. Open all sterile packaging using the "peel-and-present" technique, presenting the sterile materials up towards the filter face to take advantage of the "first air" coming through the HEPA filter. It's preferable to open sterile packaging on the left side of the chamber and complete the manipulation on the right side of the chamber. Remove any trash from the chamber as soon as possible, using the trash chute if applicable.

4. **Wait at least one minute for the main chamber to return to ISO 5 conditions before compounding.**

Cleaning and Sterilization Procedures

USP 797 requires regular sterilization of the isolator's interior surfaces, including gloves and processing equipment used during compounding. The sterilization requirements are the same for any ISO 5 Primary Engineering Control (PEC).

USP 797 Cleaning Requirements	
Daily	**Monthly**
• ISO 5 PEC • All surfaces immediately surrounding the PEC • Easily cleanable horizontal surfaces in the compounding area • Floors	• Ceiling • Walls • Pass-throughs • All other surfaces within the compounding area • All carts • Supply bins • Doors, handles, vents

At a minimum, USP 797 requires that the Compounding Aseptic Isolator be sterilized:

- **Before each work shift**
- **Between batches**
- **After every 30 minutes of continuous compounding operation**
- **After spills**
- **When surface contamination is known or suspected**

The isolator must be **thoroughly cleaned daily using a germicidal detergent diluted in sterile water, followed by sterilization.**

In addition, all work surfaces in the buffer area or segregated compounding area must be **cleaned and disinfected daily.** All floors must be mopped and disinfected daily.

Refer to *USP Chapter <797>: Pharmaceutical Compounding—Sterile Preparations* for a more detailed explanation.

Sterilization Procedure

All cleaning and sterilizing procedures must follow the basic principles of moving from top-to-bottom and from cleanest-to-dirtiest, wiping in one direction (rather than wiping in circles). All surfaces must be visibly wetted, but not dripping. Cleaning agents must be allowed to air dry. All hand and arm motions inside the glovebox chamber or antechamber should be performed slowly and deliberately to minimize air turbulence.

1. Follow all standard garbing and hand cleansing procedures before entering the compounding area.

2. Make sure that the isolator is ON and the Magnehelic™ gauges show a positive pressure of **at least 0.05 inches of water column (10 Pa)** from the main chamber of the isolator to the ambient air. If the isolator was turned OFF, allow the CAI to operate for **at least 10 minutes** before sterilizing.

3. Don powder-free sterile gloves.

4. Transfer a spray bottle of sterile IPA and sterile, non-shedding wipers into the main chamber using the proper transfer procedures described above. If desired, transfer a dedicated ISO 5 isolator cleaning tool into the main chamber to help with hard-to-reach areas.

5. If this will be the final round of sterilization following the daily cleaning, transfer a pair of sterile gloves into the main chamber as well.

6. After all materials have been placed in the antechamber, wait one minute for the antechamber to return to ISO 5 conditions before opening the sliding door.

NOTE

Steps 7 through 10 must be performed through the glove ports, with the isolator sealed.

7. If this will be the final round of sterilization following the daily cleaning, perform the Glove Replacement procedure outlined in **Appendix III** prior to sterilization.

8. Disinfect the isolator gloves with 70% sterile IPA.

9. Use the sterile, non-shedding wipers dampened with 70% sterile IPA to sterilize the main chamber interior, working from top to bottom, back to front, with special attention paid to seams and corners. Do not spray sterile IPA directly onto the surface to be sterilized.

   Surface sterilization order for all PECs:
   1. Ceiling
   2. Back wall
   3. Rear filter
   4. Side walls
   5. IV bar and hangers
   6. Front face and viewing window
   7. Sleeves and gloves
   8. Any devices continuously stationed on the deck of the isolator
   9. Deck (bottom surface)

   Fold a sterile wiper into quarters and use slow, unidirectional motion across each surface, overlapping strokes, folding the wiper to enclose contaminants. Make sure that a clean, unused surface of the wiper is used for each pass along the interior surface, and replace the wiper when all surfaces have been used. Avoid circular wiping motions, and do not flip wiper over to expose a used surface to the controlled environment. Allow the sterile IPA residue on the surface to air dry.

NOTE

To sterilize the filter at the back of each chamber, liberally spray the face of the filter with sterile IPA and allow for the appropriate dwell time for the filter to air dry. If desired, gently wipe the surface of the filter media with a sterile wiper. Discard the sterile wiper immediately after cleaning the filter.

10. Discard used wipers into the interior trash chute. Place any remaining materials back into the antechamber and close the sliding door.

11. Remove hands from the glove ports.

12. Open the antechamber swing door.

13. Perform the same wipe-down procedure described in step 10, sterilizing the antechamber from top to bottom, back to front.

14. Close the antechamber door.

15. **Wait at least one minute for the isolator to return to ISO 5 conditions before compounding.**

Daily Cleaning Procedure

1. Follow all standard garbing and antiseptic hand cleansing procedures before entering the compounding area.

2. Prepare the cleaning solution (germicidal detergent diluted with sterile water) in a container dedicated for use in ISO 5 areas.

3. Don a sterile gown, sterile gloves, and sterile hair net before opening the isolator. The facemask can remain non-sterile.

4. Open main chamber tilt-up door.

5. Inspect sleeves for pinholes as well as breaches at the glove connectors. Repeated exposure to cleaning chemicals can lead to stiffening or cracking.

6. Using the same order and pattern described in step 10 of the sterilization procedure above, wipe down the inside of the main chamber with a solution of germicidal detergent diluted with sterile water.

7. **Every 3-6 months**, replace the filters at the back of each chamber. Prior to installing the new filter, liberally spray the face of the filter with sterile IPA and wipe the filter edges with a sterile wiper. Discard the wiper after cleaning the filter. Allow for the appropriate dwell time for the filter to air dry before installing it in the isolator.

8. **Once a week**, following the Daily Cleaning Procedure, repeat the wipe-down procedure using a sporicidal agent.

9. Close access doors and engage latches.

10. Perform the Sterilization Procedure.

11. Reinstall a clean waste bag on the bottom flange of the waste chute (if equipped), using a 1/2" x 20" clamp.

12. Allow FFU to run for approximately ten minutes before use. At an average flow rate of 644 CFM, this stabilization period will produce approximately 280 air changes.

Appendix III: Glove and Sleeve Replacement

The Compounding Aseptic Isolator should be equipped with Hypalon sleeves and glove connectors (sold separately). This three-piece glove port assembly can withstand the heavy cleaning regimen of a CAI while offering maximum protection for the sterile environment. Each Hypalon sleeve fits the standard 10"-diameter Terra glove ports and includes a stainless steel clamp for connecting to the sleeve to the glove port flange. The FDA-compliant polypropylene glove connectors are designed for simple daily glove replacement, without having to open the isolator and risk contamination.

Photo 6: Hypalon Sleeve

Sleeve Replacement Procedure

The Hypalon sleeve should be replaced every 6 months or if tears/holes are discovered upon inspection. Sleeve replacement should be performed immediately prior to the Daily Cleaning Procedure.

With the isolator turned OFF, follow these instructions to replace the Hypalon sleeve:

1. The sleeve is held in place by a stainless steel clamp (Terra Cat. No. 1689-40). Loosen the clamp and pull the old sleeve off.

2. Insert the new sleeve into the glove box, allowing 2" of sleeve to extend beyond the front edge of the mounting flange.

3. Fold the outside edge of the sleeve over the flange, so that roughly 2" of the sleeve cuff is stretched along the outside perimeter of the flange.

4. Position the clamp along the mounting flange so that about 1" of excess sleeve cuff protrudes on the inside edge of the flange (the edge closest to the front wall of the glove box). Carefully tighten the clamp just enough to hold the sleeve in place.

CAUTION

Over-tightening the clamp could crack or warp the flange and damage the isolator.

5. Fold back the excess sleeve cuff toward the front edge of the flange to cover the clamp. Repeat procedure for the other sleeve.

Glove Replacement Procedure

Important Note: **Sterile** gloves must always be used for the isolator gloves.

The three-channel design of the glove connector allows the gloves to be replaced while the isolator remains sealed.

To replace the sterile isolator gloves:

Photo 7: Polypropylene Glove Connectors with O-rings

1. The Daily Cleaning Procedure and Steps 1 through 6 of the Sterilization Procedure must be completed prior to glove replacement.
2. Disinfect the isolator gloves with 70% sterile IPA.
3. Remove the O-rings attaching the isolator gloves to the connectors and set them down in a clean space within the main chamber.
4. Roll the beaded cuffs of the isolator gloves out of the middle groove of the glove connectors and into the outer groove. Dampen a sterile, non-shedding wiper with 70% sterile IPA and wipe the O-rings and the glove connectors.

   Note: Replace one isolator glove at a time, following Steps 5 through 7 before repeating for the other glove. Be careful to minimize contact with the critical areas of the sterile gloves, preferably manipulating the sterile gloves at the cuff.
5. Open one side of the sterile glove packaging using aseptic technique. Carefully unfold the cuff of the sterile glove, using the paper packaging to hold the glove in place.
6. Take your hand out of the old isolator glove and pinch the sleeve to the connector.
7. Pick up the sterile glove by the bead of the cuff. Use the hand in the sleeve to press the new sterile glove's bead into the middle groove of the connector. Holding the bead in place, stretch the rest of the cuff over the old isolator glove and make sure that it rests securely in the middle groove of the connector before letting go.
8. Gather the old isolator glove in the hand in the sleeve.
9. Working through the cuff of the new sterile glove, roll the old glove's beaded cuff out of the outer groove of the connector and pull the old glove out through the sleeve.
10. Repeat Step 5 through 7 for the other glove.
11. After both gloves have been replaced, secure the new sterile gloves with the O-rings.
12. Continue with the remaining steps of the Sterilization Procedure.

Appendix IV: Environmental and Personnel Monitoring

NOTE

The FDA requires DAILY environmental and personnel monitoring. CGMP requires isolators to be installed in at least ISO 8 conditions.

USP 797 requires that all Primary Engineering Controls (including Compounding Aseptic Isolators) perform routine environmental and personnel monitoring.

Refer to *USP Chapter <797>: Pharmaceutical Compounding—Sterile Preparations* for a more detailed explanation.

Environmental Monitoring Requirements

Environmental Air Sampling Requirements
Both viable and non-viable environmental air sampling shall occur at a minimum under any of the following conditions:
• During certification of new facilities and/or equipment • After servicing facilities and/or equipment • During recertification of existing facilities and/or equipment • In response to any concerns of potential contamination or adverse events

Non-Viable Air Sampling	
Must be performed at least semiannually during certification/recertification of facilities and/or equipment, under dynamic operating conditions.	
Required Sampling Locations	**Recommendations**
• All Primary Engineering Controls • ISO Class 7 buffer areas • ISO Class 7/8 anterooms • Segregated Compounding Areas	• Particle testing should be performed according to CETA guidelines • Follow all standard garbing and material transfer procedures when bringing testing equipment into controlled areas and/or the isolator • Use the carts designated for the compounding area to transport testing equipment into the area • Wipe down testing equipment with 70% sterile IPA before placing it in the compounding aseptic isolator

Viable Air Sampling	
Must be performed at least semiannually during certification/recertification of facilities and/or equipment, under dynamic operating conditions	
Required Sampling Locations	**Recommendations**
Volumetric air sampling of at least 400-1000 liters of air (0.4-1 cubic meter) is required in the following locations: • All Primary Engineering Controls • ISO Class 7 buffer areas • ISO Class 7/8 anterooms • Segregated Compounding Areas **The impaction method of volumetric air sampling is preferred. Sampling should include the use of control plates.**	• Follow all standard garbing and material transfer procedures when bringing testing equipment into controlled areas • Samples should be taken where air turbulence might be expected in the isolator or in the surrounding area • Samples should be taken near doors, passthroughs, corners, staging areas, gowning areas, cart exchange areas, countertops, and the area surrounding the compounding aseptic isolator

USP 797 Viable Air Sample Action Levels	
Air Classification	**Minimum Action Level**
ISO Class 5	> 1 CFUs/1000 liter sample
ISO Class 7	> 10 CFUs/1000 liter sample
ISO Class 8	> 100 CFUs/1000 liter sample

NOTE

Pressure differentials must be verified and documented at least daily.

Personnel Monitoring Requirements

Media-Fill Testing Requirements	
Initial Competency Evaluation: All new compounding personnel must successfully perform an initial media-fill test before being allowed to compound CSPs for human use.	
Risk Level	**Frequency**
Low- and Medium-Risk Compounding	Annually
High-Risk Compounding	Semiannually

Gloved Fingertip Sampling Requirements
Initial Competency Evaluation: All new compounding personnel must complete the gloved fingertip sampling procedure with ZERO CFUs at least three times before being allowed to compound CSPs for human use.
Perform gloved fingertip sampling concurrently with media-fill testing.
After Garbing: Conduct sampling after donning the sterile gloves within the isolator.
After Media-Fill: Conduct sampling after completion of the media-fill preparations.
Do NOT apply 70% sterile IPA to gloves prior to sampling!

Surface Sampling Requirements

USP 797 only requires "periodic" surface sampling and has left the actual frequency up for interpretation. Pharmacists should use their best judgement in establishing a sampling protocol, based on compounding risk levels, past results, staff experience, and other factors that may require more frequent sampling.

Requirements	Recommendations
• Sampling must be performed at the end of the day, to simulate the worst-case scenario • Nutrient agar-filled contact plates should be used for normal surfaces and swabs may be used for irregular surfaces • For all risk levels of compounding, use TSApl medium to neutralize cleaning agents in addition to media that supports the growth of fungi such as malt extract agar	• Surface sampling should occur at least every 6 months; monthly surface sampling is preferred • Surface sampling can be combined with media-fill procedures to enhance personnel traceability • Sampling should be performed at different times and without warning employees • Consider more frequent surface sampling during periods of high volume or to validate the use of new disinfecting solutions

USP 797 Personnel Monitoring Action Levels		
Air Classification	**Gloved Fingertip Sample**	**Surface Sample**
ISO Class 5	> 3 CFUs (except initial testing)	> 3 CFUs/plate
ISO Class 7	> N/A	> 5 CFUs/plate
ISO Class 8	> N/A	> 100 CFUs/plate

Appendix V: Certification Guide for the Compounding Aseptic Isolator

PRINT AND FILL OUT THIS APPENDIX EACH TIME CERTIFICATION IS PERFORMED

According to USP 797, certification of the Compounding Aseptic Isolator will be required:

- At least every 6 months
- When the isolator is relocated
- When the isolator's performance is in question
- After the filter or blower/fan is replaced

USP 797 requires Compounding Aseptic Isolators to be independently certified according to the CETA Guidelines Document (CAG-002-2006) prior to commencing compounding operations and every 6 months thereafter.

Terra Universal's Compounding Aseptic Isolator must be certified using the following CETA-approved tests in order to be considered USP 797-compliant:

1. **Airflow Test**
2. **Chamber Pressure Test**
3. **HEPA Filter Integrity Test**
4. **Particle Containment Integrity and Enclosure Leak Test**
5. **Recovery Time Determination Test**
6. **Airflow Smoke Pattern Test** (*performed under dynamic conditions*)
7. **Preparation Ingress and Egress Test** (*performed during material transfer*)
8. **Particle Count Tests** (*performed under dynamic conditions*)
9. **Pass-Through Particle Purge Time Determination Test** (*performed during material transfer*)

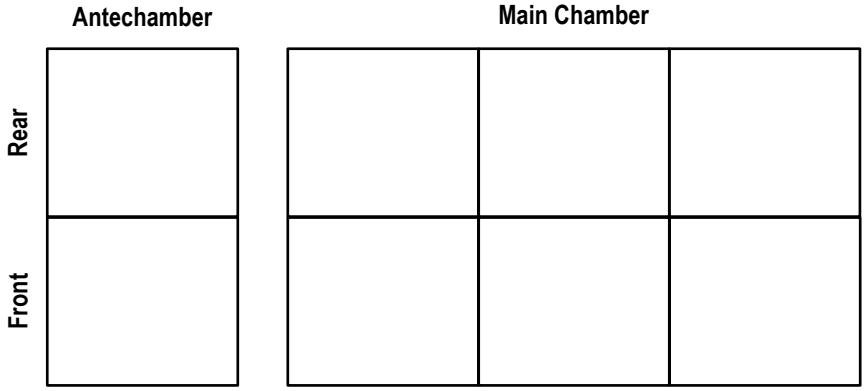
Important Note: Do not assume that the certifier will conduct all of these tests! Specifically request each one and especially take note of any tests that must be performed **"under dynamic conditions."** This statement implies that the typical numbers of personnel are working in the compounding area for the duration of the test, or surrogate manipulations are taking place in the isolator for the duration of the test.

Record each isolator test result in its respective section below. Always request a copy of the test data from your certifier and keep this information for your records. Use the test results to validate your Standard Operating Procedures and establish the optimum settings for the Compounding Aseptic Isolator.

I. Airflow Test

Write in your air speed setting (example: knob at 12 o'clock): _____.

Take air speed measurements in the following eight locations:



Verify that each air speed measurement falls within the following acceptable range:

Minimum Value	65 FPM @ 6" under filter face
Recommended Value[1]	90 FPM @ 6" under filter face
Maximum Value	120 FPM @ 6" under filter face

[1] CETA Doc. CAG-001-2005, Page 5

II. Chamber Pressure Test

Although the current USP 797 does not prescribe a specific internal positive pressure level for isolators, other guidelines do. According to the FDA's Current Good Manufacturing Practices, an isolator typically maintains a positive pressure differential between the main chamber and the ambient air ranging from **0.07 to 0.2 inches of water column (17.5 to 50 Pascals)**. The draft revision of USP 797 requires a **minimum overpressure of 0.05 inches of water column (approximately 12 Pascals)** to qualify a PEC as an isolator.

To confirm the readings of the installed Magnehelic gauges, test the differential pressure of the two chambers compared to ambient/room pressure. To do this, make sure your CAI is operational and chamber doors closed. Record the readings from the two pressure gauges located on the upper-front panel of the glove box isolator. The ambient room air can be measured using the orange valve located on the outer right side of the glove box.

Record the pressure differential measurements in the table below (units are in inches of water column):

	Antechamber to Ambient	**Main Chamber to Antechamber**	**Main Chamber to Ambient**
Minimum Value[2]	0.035"	0.035"	0.07"
Measured Value			
Maximum Value[2]	0.1"	0.1"	0.2"

[2] CETA Doc. CAG-001-2005, Page 6

Verify that each pressure differential reading falls between the minimum and maximum values.

III. HEPA Filter Integrity Test

Sustained aerosol penetration shall not exceed 0.01% of the upstream concentration.

PASS_____ FAIL_____

EXPLANATION_____

IV. Recovery Time Determination Test

Record the amount of time it takes for the main chamber to return to ISO 5 conditions:_____

Acceptance Criteria: A recovery time less than or equal to one minute is acceptable.

PASS_____ FAIL_____

EXPLANATION_____

V. Airflow Smoke Pattern Test

NOTE **Terra Universal recommends recording a video of the smoke visualization test as documentation of the test results (in the absence of numerical data).**

The isolator delivers uniform air flow without any configuration required by the certifier or end user.

Confirm that air movement within the isolator is uniform by performing a smoke visualization test **under dynamic (working) conditions.** During the test, operators must transfer materials through the antechamber and into the main chamber, stage the compounding materials and remove sterile packaging, and perform surrogate manipulations. Smoke must be released throughout the antechamber and main chamber using the following protocol:

1) Starting 1 inch away from all chamber walls and view screens
2) 6 inches below filter face
3) 6 inches above work surface
4) Make sure to pass smoke over the gloves, sleeves, IV rod, and trash chute (if equipped).

Acceptance Criteria: The smoke should demonstrate uniform downward airflow throughout the test. The smoke should demonstrate a particle sweeping action over the critical compounding areas during manipulations.

PASS_____ FAIL_____

EXPLANATION_____

V. Preparation Ingress and Egress Test

Verify the ability of the pass-through system to protect the main compounding chamber from contamination during compounding material transfer.

Be sure to follow the procedures for Operator Gowning and Transferring Compounding Materials into the Compounding Aseptic Isolator as outlined in **Appendix II**.

Acceptance Criteria: Particle counts within the main chamber shall not exceed 3520 particles/m^3 (at 0.5 µm or larger) at any time during the test.

PASS_____ FAIL_____

EXPLANATION_____

VI. Particle Count Tests

The Compounding Aseptic Isolator must be tested during **static** (at rest) and **dynamic operating conditions** to ensure that the isolator is able to maintain ISO 5 conditions during normal operation.

Static Particle Levels
The certifier should determine the particle probe locations per ISO 14644-1:1999. The main chamber should have at least 5 sample locations and the antechamber should have at least 3 sample locations.

Acceptance Criteria: Particle counts within either chamber shall not exceed 3520 particles/m^3 (at 0.5 µm or larger) at any time during the test.

PASS_____ FAIL_____

EXPLANATION_____

Dynamic Operating Particle Levels
Particle counts will be measured in the main compounding chamber **under dynamic (working) conditions.** During the test, operators must transfer materials through the antechamber and into the main chamber, stage the compounding materials and remove sterile packaging, and perform surrogate manipulations.

Prior to the test, be sure to follow the procedures for Operator Gowning, Transferring Compounding Materials into the Compounding Aseptic Isolator, and Workflow for the Compounding Aseptic Isolator as outlined in **Appendix II**.

The particle counter probe should be positioned no more than 12 inches (30.5 cm) away from the location of the Critical Site within the Direct Compounding Area.

Acceptance Criteria: Particle counts near the Critical Site shall not exceed 3520 particles/m^3 (at 0.5 µm or larger) at any time during the test.

PASS_____ FAIL_____

EXPLANATION_____

VII. Pass-Through Particle Purge Time Determination Test

The amount of time required to purge the antechamber must be tested using a particle counter. Materials will be transferred into the antechamber and the certifier will record the amount of time necessary for the antechamber to return to ISO 5 conditions.

Be sure to follow the procedures for Operator Gowning and Transferring Compounding Materials into the Compounding Aseptic Isolator as outlined in **Appendix II**.

Record the amount of time it takes for the antechamber to return to ISO 5 conditions:_____

Acceptance Criteria: A recovery time less than or equal to one minute is acceptable.

PASS_____ FAIL_____

EXPLANATION_____

Appendix VI: Compounding Aseptic Isolator Best Practices

Reduce turbulent air by following these techniques when working in the isolator:

- Be mindful of hand movement. Make slow, controlled motions and complete tasks so as not to obstruct filtered air from washing over other objects
- It's best to complete tasks a few inches away from vents
- Don't place items against the internal hood panels; keep supplies or equipment 3-4 inches out from walls to promote airflow
- When a UV lamp is present for sterilization, be sure to close all doors, set a timer, and leave the area during the cycle
- Install elevated rods for IV bags; space is used efficiently and obstructions are minimized
- Watch the use of lightweight towels or wipes: these items can get sucked up into exhaust systems and block ducting or interfere with filter units
- Keep lab doors and windows closed to cut down on drafts and outside contaminants
- Prior to using the isolator, let the FFU run for 10 minutes to cleanse the internal working space
- When working with liquids (such as ampules) in a horizontal laminar flow cabinet, open *away* from the filter face
- When inserting a sterile needle into a tube stopper, make sure there are no obstructions between it and the filter face
- Only use necessary supplies - everything you add to the work surface is an additional opportunity for turbulence and contamination. The isolator is not a storage area
- When possible, put larger equipment on sturdy blocks/feet when inside the hood. This allows circulating air underneath the instrument. While the item causes some turbulence, the effect is minimized by the airflow