NuAire Model NU-NR800
Negative Pressure Recirculating
Compounding Aseptic Containment Isolator
Performance Evaluation
Compliance to USP797/USP 800

Note: This revision has been updated for the official USP797 and USP800 release of November 1, 2022.

Background

The United States Pharmacopeia (USP) published USP Chapter 797, Pharmaceutical Compounding - Sterile Preparations. The chapter details the requirements of most every aspect of Compounded Sterile Preparations (CSP's) from definitions of quality assurance programs practices and procedures necessary to provide the highest quality CSP's to patients. In addition to the USP chapter 797, USP chapter 800, Hazardous Drugs Handling in Healthcare settings, has been published as additional guidance. Each state board of Pharmacy will determine to adopt this chapter in full, partially or with modifications and provide a timetable to accomplish the task.

Restricted-access barrier systems (RABS), specifically Compounding Aseptic Containment Isolators (CACI's) as Primary Engineering Controls (PEC's)

Within the USP797 and USP800 chapters many aspects of PEC's are discussed. This includes CACI's starting with their definition, design characteristics, placement, performance verification and general use.

In regard to design characteristics, placement, performance verification and general use, the USP797 states that "When a RABS is used, the recovery time after opening the transfer chamber to achieve ISO 5 air quality must be documented (e.g. by the manufacturer), and internal procedures must be developed to ensure that adequate recovery time is allowed after opening and closing the RABS, both before and during compounding operations. Adynamic airflow smoke pattern test must be performed in the PEC under dynamic operating conditions initially and at least every 6 months to ensure that 1) the RABS is properly integrated into the facility and 2) compounders understand how to utilize the unidirectional airflow to maintain first air in the DCA". To assure that NuAire's CACI complies, NuAire has performed various testing to the CETA CAG-002 as well as additional performance testing exceeding the specified requirements. To assure compliance we will review the current version of USP797 chapter on each of the above CACI aspects and reference compliance design and/or product performance verification testing as documented in this technical bulletin.

The USP chapter 797 defines both RABS and CACI as the following:

Restricted-access barrier system (RABS) – A RABS is an enclosure that provides HEPA filtered ISO class 5 unidirectional air. It allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of environmental air contamination and are generally not to be opened during compounding operations. RABS include compounding aseptic isolators (CAIs) and compounding aseptic containment isolators (CACIs). In a CAI or CACI, glove ports are used to provide physical separation between the surrounding area and the aseptic manipulations.

Compounding Aseptic Containment Isolator (CACI) – A CACI is designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to maintain an ISO class 5 environment for compounding sterile HD preparations (see USP800).

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

The USP chapter 800 defines the CACI as the following:

Compounding aseptic containment isolator (CACI):

A specific type of CAI that is designed for the compounding of sterile HDs.
The CACI is designed to provide worker protection from exposure to undesirable levels of airborne drugs throughout the compounding and material transfer processes and to provide an aseptic environment with unidirectional airflow for compounding sterile preparations.

The USP 797 chapter continues to identify design characteristics of PEC's as discussed within the "Facility Design and Environmental Controls" section. This section as stated below provides the following design characteristic requirements for compliance. Alongside the requirements, NuAire compliance is stated if applicable.

Design Requirements to maintain air quality	**NuAire Compliance**
Facilities used for compounding CSP's must be designed so that air quality improved with movement through separate operational areas to the PEC. Classified areas in which the air quality is controlled (see table 4, USP797) include anterooms, buffer rooms and PEC's. • Category 1, Category 2, and Category 3 CSP's must be compounded is an ISO 5 or better PEC. If compounding only Category 1 CSP's, the PEC may be placed in an unclassified SCA.	The NU-NR800 CACI is designed to provide a sterile negative pressure work environment for the compounding of hazardous drugs. The NU-NR800 Isolator creates HEPA filtered unidirectional (laminar flow) supply at 23-29 air changes per minute within both the work zone and interchange areas to assure ISO Class 5 conditions. The airflow pattern is illustrated on Drawing ACD-18093. Utilizing unidirectional (laminar flow) assures a continuous stream of HEPA filtered air across the work zone at a velocity sufficient to sweep particles away from the compounding area and maintain unidirectional airflow during operations. Once the air is through the work area, the airflow is split front to rear. Then proceeds under the work tray, up the rear divider panel and is partially re-circulated again through the supply HEPA or exhausted through the exhaust blower/HEPA filter assembly. The exhaust blower/HEPA filter assembly provides the negative pressure for Isolator containment. The exhaust air is drawn from the re-circulating Isolator airflow as described above. In addition, an intake HEPA filter is located just in front of the exhaust filter-providing make up air for the Isolator. **It is strongly recommended that the exhaust air volume be ducted to the outside per NIOSH guidelines**. NuAire offers a canopy, or air gap exhaust transition as an accessory to connect to the facility exhaust system. The Isolator workzone chamber pressure is always less negative relative to the interchange chamber, which also operates at a more negative pressure relative to the room. This cascade airflow assures of no contamination migration into the workzone during the material movement process. To assure personnel protection from particulates and vapors, the interchange external door is interlocked to the Isolator supply blower. When the external door is opened the supply blower turns off, the exhaust blower remains on providing a negative flow through the interchange chamber providing personnel

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

	protection. Once the external door is closed, the supply blower will turn on providing normal recirculation airflow. **NuAire recommends a minimum of 1 minute pass-through purge or wait time** for material removal and possibly more depending upon volatility and quantity of hazardous drugs compounded. Sufficient airflow velocity particle sweep is verified by the acceptable workzone sterility test results in both static and dynamic conditions. In situ air pattern analysis is also verified by acceptable airflow smoke pattern test results.

The CSP compounding environment
The PEC must be certified to meet ISO class 5 or better conditions (see Table 4, USP797) during dynamic operating conditions and must be designed to minimize the risk of contamination during compounding of CSPs. Unidirectional airflow must be maintained in the PEC. HEPA filtered must be supplied by the PEC at a velocity sufficient to sweep particles away from critical sites and maintain unidirectional airflow during operations. Proper design, control, and use minimizes turbulence and creation of eddy or stagnant air in the PEC.

Placement Requirements of USP797
Proper placement of the PEC is critical to ensuring an ISO class environment for preparing CSPs. Placement Of the PEC must allow for cleaning around the PEC. (See table 5, USP 797) for a summary of minimum requirements for the placement of PECs for preparing CSPs. If used to prepare only Category 1 CSPs, the ISO class 5 environment may be achieved by placing the RABS in an unclassified SCA. If used to prepare Category 2 or Category 3 CSPs, the RABS must be located within a Cleanroom suite with an ISO class 7 or better buffer Room with an ISO class 8 or better anteroom. For placement of a CACI used for the preparation of antineoplastic and/or API HDs (see USP800).

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

The USP chapter 800 is very similar to the above statements from the USP chapter 797.

Engineering Controls for Sterile HD Compounding			
Configuration	**Compounding Primary Engineering Control (C-PEC)**	**Compounding Secondary Engineering Control (C-SEC)**	**Maximum BUD**
ISO Class 7 Buffer Room	• Externally Vented • Examples: Class II BSC or CACI	• 30 ACPH • Externally vented • Negative pressure between 0.01 and 0.03 inches of water column	As described in USP797
Containment Segregated Compounding Area (C-SCA)	• Externally Vented • Examples: Class II BSC or CACI	• 12 ACPH • Externally vented • Negative pressure between 0.01 and 0.03 inches of water column	As described in USP797 for CSPs prepared in a segregated compounding area

Performance verification testing to the CAG-002 on all aspects of the NU-NR800 CACI is recorded on the subsequent pages. Additional testing was performed using biological challenges to demonstrate workzone airflow patterns from a cross contamination perspective. This testing included the sidewall area, just under the IV pole in the direct compounding area with and without TPN bags in place. The results indicate that no cross contamination occurred within 14 inches of the workzone sidewall and 12 inches between work product in the direct compounding area. The results also indicate the importance of using the unidirectional "first air" during the compounding process to assure product sterility.

Cleaning and disinfecting the compounding area should follow the USP chapters for practices and frequencies. These practices shall be included in written Standard Operating Procedures (SOP's) and shall be followed by all compounding personnel.

Personnel Hygiene and garbing should also follow the USP797.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Conclusion

The performance verification test results based on the CETA Testing Guide CAG-002 indicate that the NuAire NU-NR800 Compounding Aseptic Containment Isolator (CACI) meets and exceeds the requirements of the USP chapter 797 for providing an ISO Class 5 environment. The test results also indicate the CACI continues to meet the above requirements for use outside a clean room maintaining ISO Class 5 conditions during product movement in and out of the CACI.

The NU-NR800 CACI testing also indicates the containment performance for both particulates and volatile gases. Through the use of the negative pressure and HEPA filters, particulates are removed from the recirculation and exhaust airstreams. However, volatile gases pass through HEPA filters, so containment of volatile gases depends upon several usages factors.

First, the CACI must be connected to an exhaust system to capture and remove any volatile gases from the CACI's exhaust airflow. Second, perform a risk analysis based on the type and quantity of hazardous drugs used in the CACI. Use the test results of the volatile hazardous drug containment test to determine work practices required based on quantity and volatility (hazardous drug properties should be available on their respective MSDS) of the hazardous drugs being compounded.

NOTE: The NIOSH Alert: Preventing Occupational/Exposures to Antineoplastic and other Hazardous Drugs in Health Care Settings (2004) – has in general terms made recommendations for primary engineering controls used for compounding hazardous drugs. The recommendation states;

- When aseptic technique is required, use one of the following ventilated cabinets:
  - Class II BSC (Type B2 is preferred, but Types A2 and B1 are allowed under certain conditions)
  - Class III BSC
  - Isolators intended for asepsis and containment (aseptic containment isolators) [NSF/ANSI 2002;PDA 2001]

  The recommendation also states:

- Do not use a ventilated cabinet that recirculates air inside the cabinet or exhausts air back into the room environment unless the hazardous drug(s) in use will not volatilize (evaporate) while they are being handled or after they are captured by the HEPA filter. Information about volatilization should be supplied by the drug manufacturer (possibly in the MSDS) or by air-sampling data.

Equating the Isolator to a Class II BSC in terms of internal function, recirculating versus total exhaust, the NU-NR800 would be similar to the Class II, Type A2 BSC. Per the above NIOSH recommendation, a recirculation BSC or Isolator should only be used on hazardous drugs that will not volatilize (evaporate).

However, with proper work practices, the test results indicate that the NU-NR800 does contain volatile gases in similar known quantities. Again, performing a risk assessment, as stated above, based on the type and quantity of hazardous drugs used will determine if the NU-NR800 CACI can be used for a particular application.

The USP chapter 800 reads (see below) similar to the above, performing risk assessment as to the HD volatility.

All C-Pecs used for manipulation of sterile HDs must be externally vented. Sterile HD compounding must be performed in a C-PEC that provides a Class 5 or better air quality, such as a Class II or III BSC, or CACI. Class II BSC types A2, B1 or B2 are all acceptable. For most known HDs, type A2 cabinets offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SEC. Class II type B2 BSCs are typically reserved for use with volatile components.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

In addition to the base product performance and personnel protection testing, cross contamination testing was performed. The cross contamination results indicate the benefit of a full size supply HEPA filter producing vertical uniform laminar airflow. The results can also be used to aid in the generation of efficient and effective work practices. Work practices should always be performed aseptically during the compounding process. Below, briefly reviewed are some base aseptic work practices for hazardous drug preparations. These work practices along with the testing results should provide a base for which to generate standard hazardous drug compounding work instructions.

a. After proper introduction into the Isolator of supply items required for and limited to the assigned operations, they are so arranged that a clear, uninterrupted path of unidirectional (laminar airflow) or "first air" will bathe all critical sites at all times during the planned procedures. That is, **no objects may be placed above an exposed critical site in a vertical position.**

b. If totes, plastic bags, or transport bags are used for material handling, these items should not be brought into the main chamber during the compounding process. These items should be left in the transfer chamber to minimize exposure to hazardous drugs and minimize potential for drag out during the removal process.

c. All supply items are arranged in the Isolator working from dirty (work material entry point) to clean (Direct Compounding Area (DCA)) to reduce clutter and to provide maximum efficiency and order for the flow of work.

d. All procedures are performed in a manner designed to minimize the risk of touch contamination. Sterile double gloves shall be sanitized with adequate frequency with an effective disinfectant.

e. All rubber stoppers of vials and bottles and the neck of ampules are sanitized with 70% isopropyl alcohol before the introduction of a needle or spike for the removal of product.

f. After the preparations of every admixture, the contents of the container are thoroughly mixed and then inspected for the presence of particulate matter, evidence of incompatibility, or other defects.

g. For the transfer process, all compounding should have ceased before the internal transfer chamber door is opened. In particular, a second technician should not add or remove compounding materials from the transfer chamber while active compounding is conducted in the main chamber.

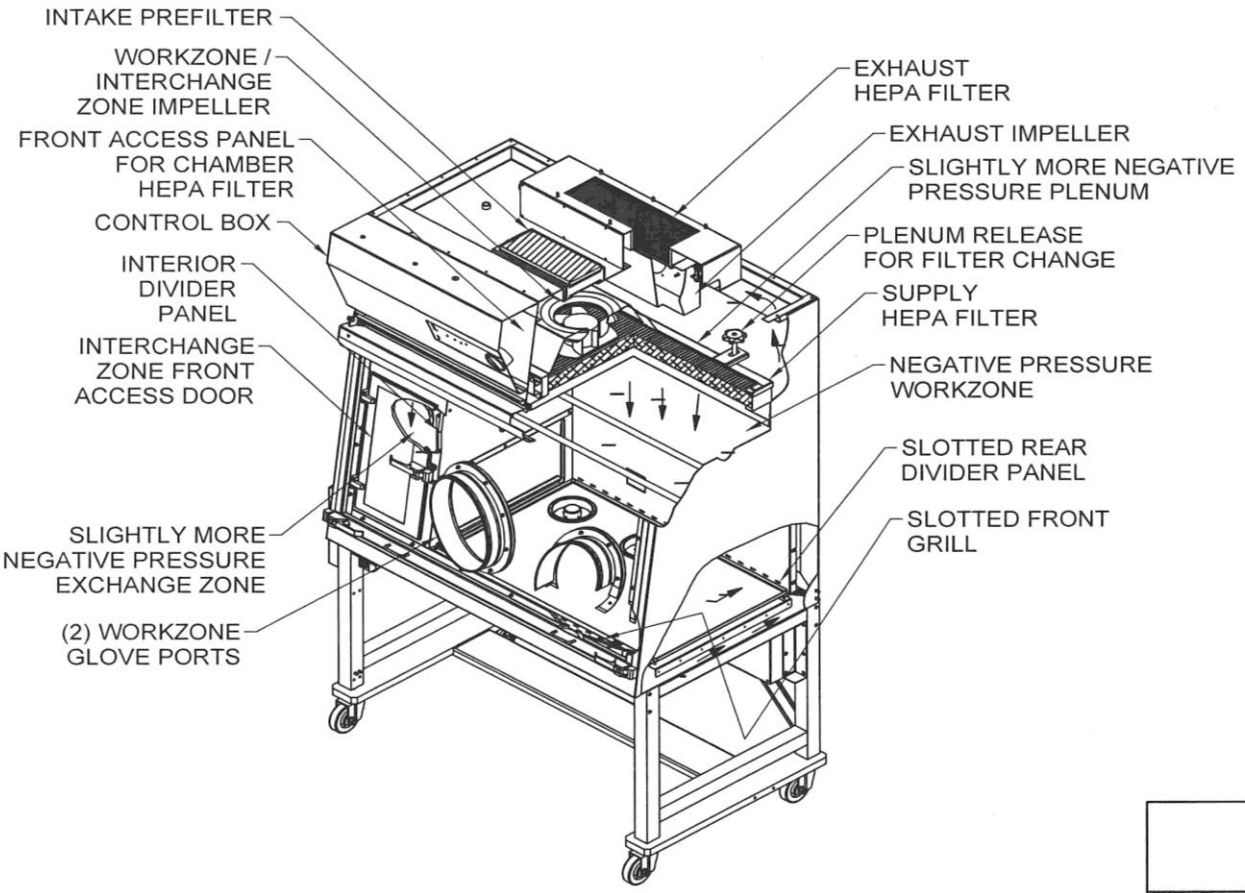
h. Surface decontamination of the preparation before removal from the main chamber should reduce hazardous drug contamination. Surface decontamination may be accomplished using alcohol, sterile water, peroxide, or sodium hypochlorite solution provided the packaging is not permeable to the solution and the labels remain legible and intact.

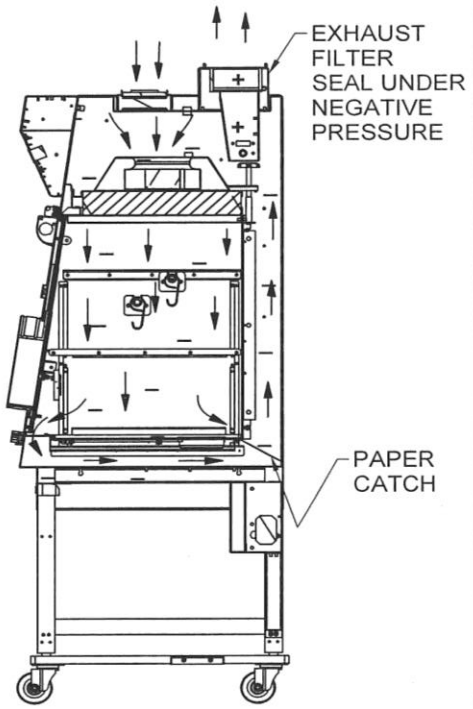
i. After procedures are completed, used syringes, bottles, vials, and other supplies are removed or discarded, but with a minimum of exit and re-entry into the Isolator to minimize the risk of introducing contamination into the septic work space.

The above information along with the various testing results provides location, operation, and usage information required by the USP chapters. Additional work practice information is available from USP, ASHP and NIOSH.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

REVISION HISTORY					
REV	ECO	DESCRIPTION	DATE	DFTM	CHKD
A	12915	RELEASED TO PRODUCTION	01/15/16	LS	DSH





SECTION A-A

ORIGINAL

TITLE	NU-NR800 NEGATIVE PRESSURE RECIRCULATING AIR FLOW SCHEMATIC					
DFTM	DATE	CHKD	SHEET			
LS	01/15/16	DSH	1	OF	1	
DRAWING NUMBER	ACD-18093					A

Supply/Exhaust HEPA Filter Integrity Testing (REF. CETA CAG-002, 2.05)

Purpose:
This test determines the integrity of all HEPA filters, filter housings, and filter mounting frames to the IEST-RP-CC034. The Isolator shall be set at operational airflows for this test.

Instrument:

- ATI TDA-2E Aerosol Photometer
- Sinclair-Phoenix SG-30 Smoke Generator

Procedure:
(Supply)

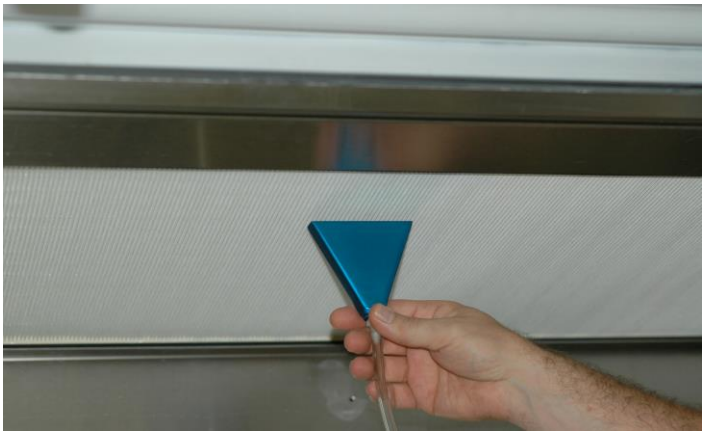
1. Open front hinged window exposing workzone interior.
2. Remove supply HEPA diffusers.
3. Turn on Isolator blower.
4. Polyalphaolefin (PAO) aerosol is introduced upstream of the HEPA filter by placing supply tube in the rear center of the workzone over the intake slots.
5. Sample the upstream challenge using the port provided to verify the challenge requirement of 10 to 90 micrograms per liter is supplied and set the photometer to 100%.
6. The supply HEPA filter and periphery are scanned by passing the photometer probe across the filter, using slightly overlapping strokes. Scanning shall be done at the transverse rate of not more than 2 in. /sec. (51mm/sec).
7. Turn off PAO aerosol after scanning is complete.

(Exhaust)

1. Move photometer upstream challenge tube to the exhaust filter upstream challenge port.
2. Turn on PAO aerosol in same location as before.
3. Sample the upstream challenge using the port provided to verify the challenge requirement of 10 to 90 micrograms per liter is supplied and set the photometer to 100%.
4. The exhaust HEPA filter and periphery are scanned by passing the photometer probe across the filter, using slightly overlapping strokes. Scanning shall be done at the transverse rate of not more than 2 in. /sec (51mm/sec). Turn off PAO aerosol after scanning is complete.

Acceptance Criteria: When scanning, a leakage from any point shall not exceed 0.01% of the upstream concentration.

Conclusion: No leaks were detected exceeding 0.01% of upstream concentration.



NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Airflow Testing (REF. CETA CAG-002, 2.01)

Purpose: This test is performed to verify that the Isolator meets the airflow requirements.

Instrument:

- TSI 8355 Thermo anemometer
- Ring Stand

Procedure:

1. Place Thermo anemometer and ring stand in main chamber and adjust on a horizontal plane 6 inches (152mm) from the supply diffuser.
2. With window closed take readings on the grid provided with no readings taken closer than 6 inches (152mm) from inside perimeter and record results

Acceptance Criteria:

1. Average downflow velocity = **45 to 55 fpm (.23 to .28 m/s)**
2. Individual readings must be within ± 20 (factory) ± 25% (field) percent or ± 16 fpm of the average downflow velocity, whichever is greater.

Test Data:

Inches (mm):

400	7 (178)	14 (356)	21 (533)	28 (711)
600	7 (178)	16 (406)	25 (635)	34 (864
7 (178)	52	55	53	43
12 (305)	45	49	43	36

Average velocity: 47 fpm

Allowable Airflow Range:
31 fpm to 63 fpm

Actual Airflow Range:
36 fpm to 55 fpm

Conclusion: Average airflow velocity and range meets acceptance criteria.

Chamber Pressure Testing (REF. CETA CAG-002, 2.02)

Purpose: This test is performed to verify that the Isolator meets the pressure requirements.

Instrument: Minihelic Gauges on Isolator

Procedure: Review minihelic gauges and record readings.

Acceptance Criteria:

Isolator Pressure Requirements

Workzone	-.15”w.g. +/- 0.05”w.g.
Interchange at least -.05”w.g. lower than the workzone Pressure	≤ -0.15”w.g.
Difference between workzone and interchange	≥ -0.05”w.g.

Test Data:

- Workzone pressure -0.13”w.g.
- Interchange pressure -0.22”w.g.
- Difference between workzone and interchange -0.09”w.g.

Conclusion: Both workzone and interchange chamber pressure meet acceptance criteria.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Airflow Smoke Pattern Testing

(REF. CETA CAG-002, 2.08)

Purpose:
This test is performed to verify the Isolators unidirectional vertical laminar airflow is downward with no dead spots or refluxing in the critical workzone.

Instrument: Smoke Source

Procedure:
A smoke source shall be passed within 1" (25mm) around all main chamber walls and from one end of the cabinet to the other, along the centerline of the work surface, at a height of 4 inches (102mm) above the top of the glove ports.

Acceptance Criteria: The smoke inside the cabinet shall show smooth downward flow with no dead spots of reflux.

Conclusion: All smoke moved downward without refluxing or dead spots meeting the acceptance criteria.

Product Protection Cross Contamination Biological Test

Purpose:
Four different sets of tests were performed to quantify the ability of the Compounding Isolator to provide cross contamination protection of products that are being manipulated within the workzone.

Biological testing was chosen because the test protocol could easily be adapted within the Compounding Isolator. The NSF/ANSI 49:2002 cross contamination test uses a nebulizer to aerosolize bacterial spores (B. Subtilis) into the workzone air stream. The bacterial spores are then either swept away in the workzone laminar airflow to be HEPA filtered or collected by agar plates or vacuum samplers. Analyzing the collected results indicates workzone laminar airflow patterns to aid in understanding Isolator performance and work practices.

The first test is an NSF/ANSI 49:2002 cross contamination test that is performed on the work surface both right and left sides. The second and third test is a modified biological test run at the IV pole height to evaluate cross contamination at a higher level, in addition to downstream airflow patterns with and without IV bags present.
Fourth test with glove/sleeve at manipulation height.

Instrument:

- Nebulizer w/Bacillus Subtilis no less than 5.0×10^4
- Six AGI-30 samplers (flow rate calibrated at 12.5 Lpm) containing 20 mL of sterile diluent.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Procedure, First Test:

1. First cross contamination test, set up and run following NSF/ANSI 49:2002.
2. Route tube for nebulizer through waste/sharps port on worksurface, then seal with plastic and tape.
   Place three control plates around the base of the nebulizer (front and both sides) to collect control quantities of bacteria to verify the challenge.
3. Place two rows of 5 plates, with the first row centered on a line 14" from sidewall and a second row directly behind the first row.
4. Test per NSF/ANSI 49:2002 (run nebulizer for 5 minutes, stop, continue to run the Isolator for 15 minutes, collect plates, and incubate at 99°F (37°C) for 48 hours.

Acceptance Criteria: No more than 2 colony forming units (CFU's) shall be formed on plates other than the control plates.

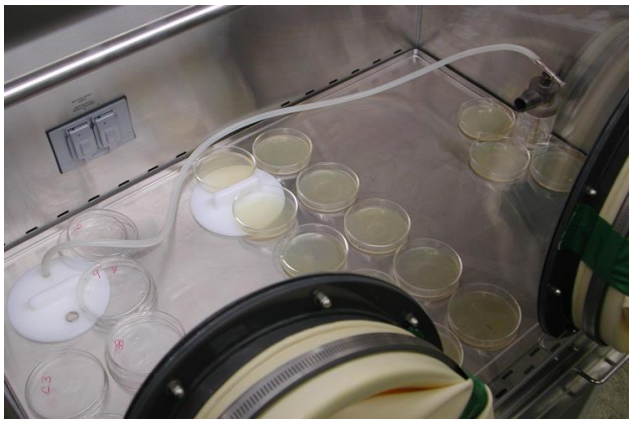
Test Data:

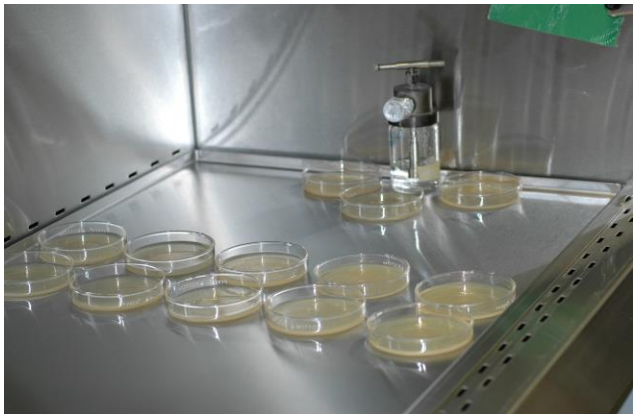
		Run 1 Right Side	**Run 2 Right Side**	**Run 1 Left Side**	**Run 2 Left Side**
Control Plates	Closest to Backwall	1. 50	1. >300	1. 0	1. 90
	Center	2. >200	2. >300	2. >200	2. >200
	Closest to Front	3. 0	3. 0	3. 0	3. 0

	Run #1				**Run #2**			
	Front Row		Back Row		Front Row		Back Row	
Test Plates Right Side	1.	0	6.	0	1.	0	6.	0
	2.	0	7.	0	2.	0	7.	0
	3.	0	8.	0	3.	0	8.	0
	4.	0	9.	0	4.	0	9.	0
	5.	0	10.	0	5.	0	10.	0

	Run #1				**Run #2**			
	Front Row		Back Row		Front Row		Back Row	
Test Plates Left Side	1.	0	6.	0	1.	0	6.	0
	2.	0	7.	0	2.	0	7.	0
	3.	0	8.	0	3.	0	8.	0
	4.	0	9.	0	4.	0	9.	0
	5.	0	10.	0	5.	0	10.	0

Conclusion:
No colonies were found on the plates in either row 14" from sidewalls. Only the control plates surrounding the nebulizer to verify the challenge collected CFU's indicating that there is no lateral airflow movement from either sidewall towards the center of the workzone.





NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Procedure, Second Test:

1. Second cross contamination test is set up and centered in the workzone.
2. The testing area involves 6” on each side of centerline.
3. Three rows, 5 each of plates for control to verify the challenge are set centered beginning on centerline.
4. The nebulizer nozzle is centered 4” below the IV bar, and 6” from center on right side.
5. On the left side of Isolator, 6” from center, a series of 6 AGI-30 samplers are positioned across the depth of the Isolator, three on each side of the IV bar. Position of the two top AGI-30 sampler is 20” above worksurface and 6-1/4” out from IV bar. The middle AGI-30 sampler sits 3” from the IV bar and 19-1/2” above the worksurface at IV bar height. The lower AGI samplers sit ½” from IV bar and 15” above worksurface. AGI-30 samplers openings are all positioned same distance (6”) from center.
6. Test per modified NSF /ANSI 49:2002 (start nebulizer, turn on samplers 1 minute later for 5 minutes, stop nebulizer 30 seconds after Impinger turns off, collect plates, collect samplers and filter individually and plate results). Incubate at 99°F (37°C) for 48 hours.

Acceptance Criteria: Each AGI-30 Sampler shall not have more than 2 CFU’s.

Test Data:

Control Plates on Surface

	Test #1		Test #2	
Closest to Backwall & AGI Samplers	1.	0	1.	0
	2.	0	2.	0
	3.	0	3.	0
	4.	12	4.	11
	5.	9	5.	19
	6.	0	6.	0
	7.	0	7.	0
	8.	15	8.	8
	9.	124	9.	>150
	10.	23	10.	70
	11.	0	11.	0
	12.	0	12.	0
	13.	>200	13.	>100
Closest to Nebulizer & Front of Isolator	14.	>200	14.	>200
	15.	>41	15.	47

AGI Samplers Backwall	1.	0	1.	0
	2.	0	2.	0
	3.	0	3.	0
	4.	0	4.	0
	5.	0	5.	0
Front of Isolator	6.	0	6.	0

Conclusion

The 6 AGI-30 Samplers were individually filtered, plated and incubated. No CFU’s were found indicating that there is minimal lateral airflow movement in the IV pole area. However, the control plates on the worksurface illustrate the airflow pattern showing more CFU’s just under the nebulizer and decreasing CFU’s as you move further away. In addition, all of the CFU’s were directed towards the front of the workzone because the nebulizer was centered under the front IV bar, which is located toward the front of the workzone. The results indicate that no cross contamination occurred when working in the IV pole area at a distance of 12” apart. The results also indicate the importance of using the laminar or first air during the compounding process to assure product sterility.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Procedure, Third Test:

1. Third cross contamination test is set up centered in the workzone.
2. The testing area involves 6” on each side of centerline.
3. Place 2 IV bags from IV bar in the testing area. Gloves pulled back from the workzone area.
4. Three rows, 5 each of plates for control to verify the challenge are set centered beginning on centerline.
5. The nebulizer nozzle is centered 4” below the IV bar and 16”and 6” from center on right side. Its opening is 1/2” from first row of control plates.
6. On the left side of Isolator, 6” from center, a series of 6 AGI-30 samplers are positioned across the depth of the Isolator, three on each side of the IV bar. Position of the two top AGI-30 sampler is 20” above worksurface and 6-1/4” out from IV bar. The middle AGI-30 sampler sits 3” from the IV bar and 19-1/2” above the worksurface at IV bar height. The lower AGI samplers sit 1/2” from IV bar and 15” above worksurface. AGI-30 samplers openings are all positioned same distance (6”) from center.
7. Test per modified NSF/ANSI 49:2002 (start nebulizer, turn on samplers 1 minute later for 5 minutes, stop nebulizer 30 seconds after Impinger turns off, collect plates, collect samplers, filter individually and plate results. Incubate at 99°F (37°C) for 48 hours.

Acceptance Criteria: Each AGI-30 Sampler shall not have more than 2 CFU’s.

Test Data:

Control Plates on Surface

	Test #1		Test #2	
Closest to Backwall & AGI Samplers	1.	0	1.	0
	2.	0	2.	0
	3.	16	3.	0
	4.	114	4.	11
	5.	34	5.	19
	6.	0	6.	0
	7.	0	7.	0
	8.	134	8.	8
	9.	>150	9.	>150
	10.	20	10.	70
	11.	0	11.	0
	12.	0	12.	0
	13.	>150	13.	>100
Closest to Nebulizer & Front of Isolator	14.	>150	14.	>200
	15.	15	15.	47

AGI Samplers Backwall	1.	0	1.	0
	2.	0	2.	0
	3.	0	3.	0
	4.	0	4.	0
	5.	0	5.	0
Front of Isolator	6.	0	6.	0

Conclusion:

Again, the 6 AGI-30 Samplers were evaluated in the same manner as the second test and with the same test results of no CFU’s found. Again, reviewing the control plates, the airflow pattern was slightly different in this third test. The difference is the bacterial spores didn’t travel as far on the worksurface. This seems to be caused by the addition of IV bags that impeded the lateral flow of the bacterial spores illustrating how objects, and work materials, etc., can influence airflow patterns.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Procedure, Fourth Test:

1. Fourth cross contamination test is set up centered in the workzone.
2. The testing area involves 6” on each side of centerline.
3. Place 2 IV bags from IV bar in the testing area. Glove/sleeve extended into the workzone at manipulation height to simulate work in cabinet.
4. Three rows, 5 each of plates for control to verify the challenge are set centered beginning on centerline.
5. The nebulizer nozzle is located 1” above the IV bar (19” above worksurface), and 6” from center on right side. For test 1, nebulizer is sitting in front of IV bar. For test 2, nebulizer is sitting behind IV bar. The opening of the nebulizer is 1/2” from first row of control plates.
6. On the left side of Isolator, 6” from center, a series of 6 AGI-30 samplers are positioned across the depth of the Isolator, three on each side of the IV bar. Position of the two top AGI-30 sampler is 20” above worksurface and 7” from IV bar. The middle AGI-30 sampler sits 17-1/2” above the worksurface and 4” from IV bar. The lower AGI samplers sit 15” above worksurface, and 2” from IV bar. AGI-30 sampler openings are all positioned same distance (6”) from center.
7. Test per modified NSF/ANSI 49:2002 (start nebulizer, turn on samplers 1 minute later for 5 minutes, stop nebulizer 30 seconds after Impinger turns off, collect plates, collect samplers, filter individually and plate results. Incubate at 99°F (37°C) for 48 hours.

Acceptance Criteria: Each AGI-30 Sampler shall not have more than 2 CFU’s.

Test Data:

Control Plates on Surface

	Test #1		Test #2						
Closest to Backwall	1.	0	1.	0	AGI Samplers	1.	0	1.	0
& AGI Samplers	2.	0	2.	0	Backwall	2.	0	2.	0
	3.	0	3.	8		3.	0	3.	0
	4.	5	4.	56		4.	0	4.	0
	5.	1	5.	4		5.	0	5.	0
	6.	0	6.	0	Front of Isolator	6.	0	6.	0
	7.	0	7.	0					
	8.	0	8.	>100					
	9.	99	9.	83					
	10.	20	10.	4					
	11.	0	11.	0					
	12.	0	12.	0					
	13.	0	13.	>200					
Closest to Nebulizer	14.	>150	14.	96					
& Front of Isolator	15.	45	15.	9					

Conclusion:

Again, the 6 AGI-30 Samplers were evaluated in the same manner as the second test and with the same test results of no CFU’s found. Again, reviewing the control plates, the airflow pattern was again slightly different in this fourth test. The difference again is the bacterial spores didn’t travel as far on the worksurface. This seems to be caused by the addition of IV bags and extended glove/sleeve that impeded the lateral flow of the bacterial spores illustrating how objects, and work materials, glove/sleeves, etc., can influence airflow patterns.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Workzone Sterility Test (Static/Dynamic) (REF. CETA CAG-002, 2.10)

Purpose:
This test is performed to determine to verify that the Compounding Isolator main chamber operates within ISO 14644-1 Class 5 at 0.5 micron in both static and dynamic (surrogate compounding process) conditions.

Instrument:
- Met One Laser Particle Counter Model A2408
- Aerosol Generator

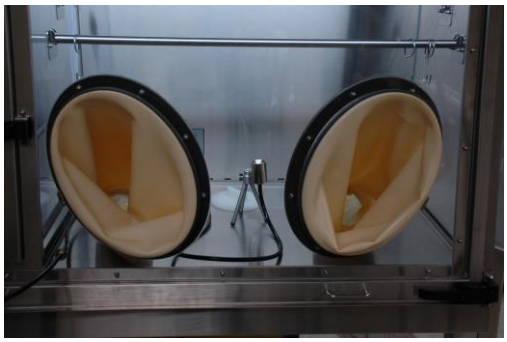
Procedure:
1. Verify the background count in the testing room is at least 100,000 ppcf (ppcf) (3,532,000 particles per cubic meter (ppcm)).
2. If the count is too low, elevate the background levels using an aerosol generator.
3. Connect the particle counter sampling tubing to the workzone test port provided on the Isolator. Connect isokinetic probe to sampling tube within the workzone.
4. Turn on Isolator and let warm up five minutes. Turn on particle counter and flush out sample tubing line to remove latent particles. Set the particle counter to measure 0.5 micron or larger at 1 CFM sampling rate.
5. Take readings at 5 locations sequentially (no particle counter filtering between intervals) in 1-minute intervals on a grid; in a horizontal plane as measured by the center point of the glove ports (approximately 6 inches above the worksurface). The grid location is designated as the workzone center point and each corner measured 6-inches (152mm) from the inside perimeter. For dynamic test, place probe in measurement location, start surrogate compounding process, then start air sampling (NOTE, for center position during surrogate compounding process, probe was raised to stay above the process area).

Acceptance Criteria:
No particle count reading during the 1-minute interval should exceed 100 ppcf. In addition, since we fall within the 2 to 9 sampling locations at 5, the ISO 14644-1 requires a statistical analysis of the upper 95% confidence level to confirm that sample levels measured meet the requirements.

Test Data:
Room background count: > 120,000 ppcf

	Test 1 (Static)	Test 2 (Static)	Test 3 (Dynamic)	Test 4 (Dynamic)
Particle counts for each test point				
Left Rear	0	1	2	1
Left Front	2	0	0	3
Center	0	3	1	0
Right Rear	1	1	1	4
Right Front	0	0	0	1

Conclusion
All 1-minute interval particle counts for both static and dynamic conditions were well below the 100 ppcf level in both measurement and statistical analysis meeting and exceeding ISO Class 5 at 0.5 micron.



NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Interchange Chamber Sterility Test (REF. CETA CAG-002, 2.10)

Purpose:
This test is performed to determine to verify that the Compounding Isolator interchange chamber operates within ISO 14644-1 Class 5 at 0.5 micron.

Instrument:
- Met One Laser Particle Counter Model A2408
- Aerosol Generator

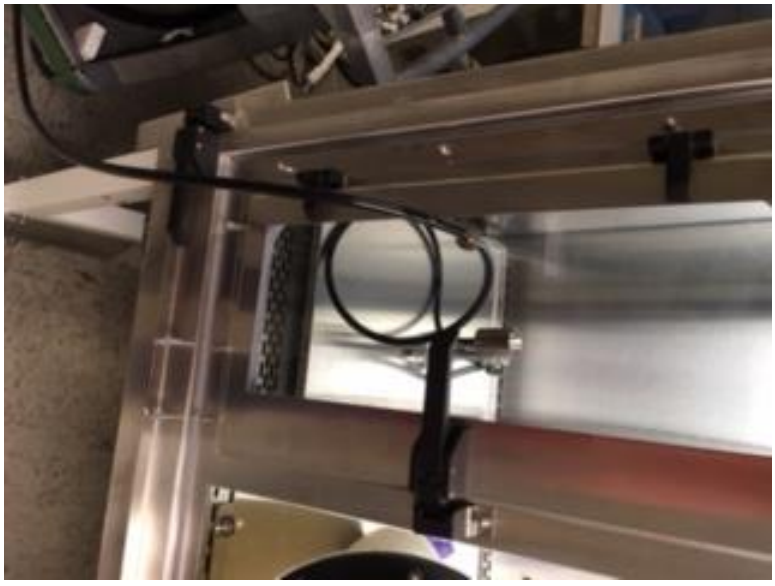
Procedure:
1. Verify the background count in the testing room is at least 100,000 ppcf (ppcf) (3,532,000 particles per cubic meter (ppcm)).
2. If the count is too low, elevate the background levels using an aerosol generator.
3. Connect the particle counter sampling tubing to the workzone test port provided on the Isolator. Connect isokinetic probe to the sampling tube within the workzone.
4. Turn on Isolator and let warm up five minutes. Turn on particle counter and flush out sample tubing line to remove latent particles. Set the particle counter to measure 0.5 micron or larger at 1 CFM sampling rate.
5. Take a reading at one center location for in 1-minute approximately 6 inches above of the work surface.

Acceptance Criteria: No particle count reading during the 1-minute interval should exceed 100 ppcf.

Test Data:
Room background count: > 120,000 ppcf
Particle counts for each test point.

Test 1	**Test 2**	**Test 3**
Center 3	Center 4	Center 4

Conclusion:
All 1-minute interval particle counts were well below the 100 ppcf level meeting and exceeding ISO Class 5 at 0.5 micron.



Product Ingress and Egress Test (REF. CETA CAG-002, 2.09)

Purpose:

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

This test is performed to assure the Isolator workzone can maintain an ISO 14644-1 Class 5 at 0.5 micron environment during material transfers with no wait or purge time during the transfer process when used outside an ISO Class 7 clean room as mentioned in the USP 797 requirements.

Instrument:

- Met One Laser Particle Counter Model A2408
- Aerosol generator or smoke tubes
- Transfer tray or other compounding materials

Procedure:

1. Verify the background count in the testing room is at least 100,000 ppcf (ppcf) (3,532,000 particles per cubic meter (ppcm)).
2. If the count is too low, elevate the background levels using an aerosol generator or smoke tubes.
3. Place the particle counter isokinetic probe in the Compounding Isolator workzone 8 inches above the work surface, and 2 inches outside the normally used path. Probe placement should be so that the operator's arms will not pass directly over the probe when removing material from the pass-through.
4. Verify the particle counts meet ISO Class 5 levels before beginning the test cycle.
5. Set the particle counter for a 1-minute count with no more than a one second hold time.
6. Open the outside pass-through door.
7. Place a transfer tray into the pass-through and close the outer door (no wait or purge time required).
8. Open the interior pass-through door and move the transfer tray from the pass-through to the work area.
9. Close the inside pass-through door.
10. Document the particle counts during the transfer process and for a period of 1-minute after the transfer.

Acceptance Criteria: No particle count reading during the 1-minute interval should exceed 100 ppcf.

Test Data:
Room background particle count: > 100,000 ppcf

Particle Counts (ppcf)	Test 1	Test 2	Test 3
Start	0	0	1
Open/Close Exterior Door	0	2	0
Open Interior Door	0	0	0
Transfer Tray	1	0	0
Close Interior Door	0	0	1
Post Wait Period	0	0	0

Conclusion:
All 1-minute interval particle counts were well below the 100 ppcf level meeting and exceeding ISO Class 5 at 0.5 micron. The results indicate that the Isolator can be used outside an ISO Class 7 clean room with no wait or purge time required during the material transfer process.

Recovery Time Determination (REF. CETA CAG-002, 2.07)

Purpose:

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

This test is performed to determine the amount of time it takes the main chamber to recover to ISO 14644-1 Class 5 at 0.5 micron particle levels after an event such as a full window opening or large scale contamination generated by the compounding process.

Instrument:

1. Laskin Nozzle Aerosol Generator
2. Met One Laser Particle Counter Model A2408
3. Clock w/Second Hand

Procedure:

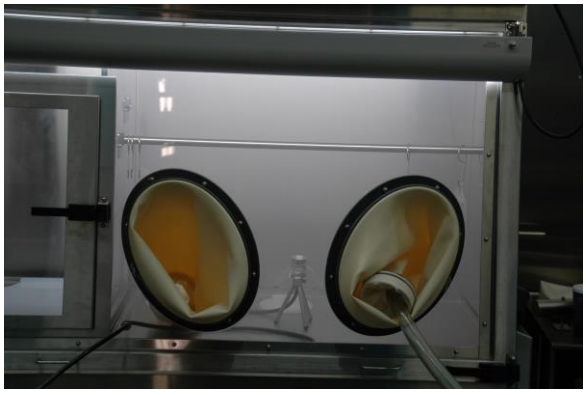
1. Place particle counter isokinetic probe in the Compounding Isolator workzone at a height as measured by the center point of the glove ports directly under the IV pole and centered within the workzone.
2. Set the particle counter sample time to 6-second sample periods in "Concentration" mode to report in ppcf.
3. Insert tube from aerosol generator through glove port and seal around.
4. Turn off Compounding Isolator and fill the chamber with particulate using a Laskin nozzle generator set at 20 psi for 10-seconds.
5. Turn on the Compounding Isolator and start timer.
6. To prevent sampling above the particle counter's coincidence loss rate or damaging the device, wait until the smoke is visibly cleared from the chamber and remove particle counter probe cover and begin sampling.
7. Actuate the particle counter every 8-seconds.
8. Concentration levels are achieved when three consecutive counts are at or below 100 ppcf.
9. Total recovery time is considered from Compounding Isolator blower turn-on time to the first particle count where maintained particle levels were achieved.

Acceptance Criteria: Particle concentration levels to be at or below 100 ppcf in less than 90-seconds.

Test Data:

Test # 1	**Test # 2**	**Test # 3**
35 Seconds	32 Seconds	30 Seconds

Conclusion:
All particle concentration levels were reduced to ISO 14644-1 Class 5 at 0.5 micron conditions well within 90 seconds. The results indicate with an additional safety factor, that the recommended Isolator start up time should be at least 5 minutes to assure ISO Class 5 workzone conditions.



NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Glove/Sleeve Breach Test (REF. CETA CAG-002, 2.04)

Purpose: This test is performed to assure some level of personnel protection in the event of a significant sleeve integrity failure.

Instrument: TSI 8355 Thermo anemometer

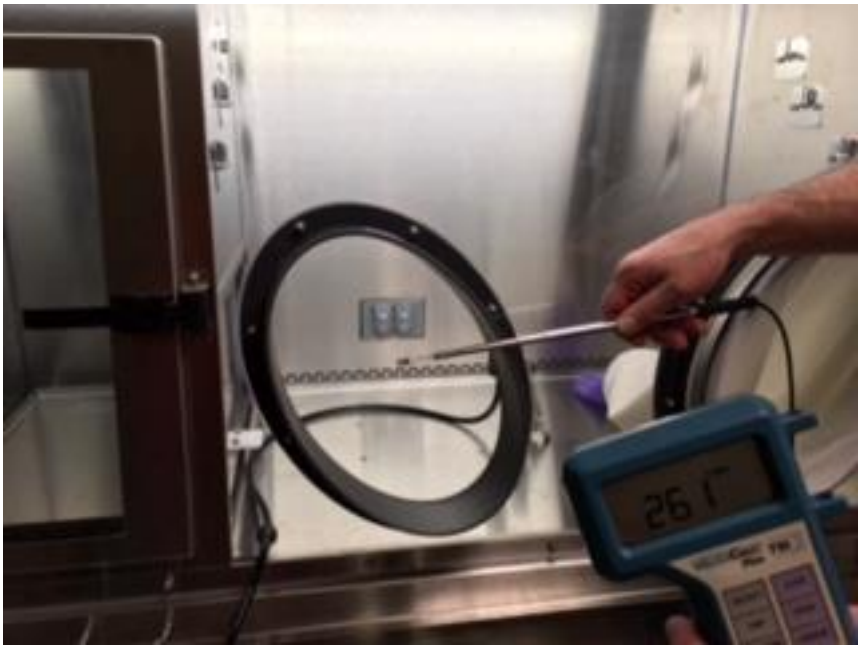
Procedure:

1. Remove one glove/sleeve from the view screen.
2. Measure velocity from the external glove port plane at the center of the opening.

Acceptance Criteria: Velocity shall be equal or greater than 80 fpm.

Test Data: 262 fpm, 258 fpm, 268 fpm Average velocity 263 fpm

Conclusion:
The measured velocity at the center of the opening was greater than 80 fpm. In addition to the airflow, the sleeves are mechanically attached with a band clamp to virtually eliminate the risk of a significant sleeve integrity failure.



NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Glove Port/Sleeve Push/Pull Test

Purpose:
This test is performed to determine that the chamber pressure is adequate to provide Isolator containment while the operator is inserting and removing the glove/sleeve.

Instrument: Magnehelic Pressure Gauge

Procedure:
1. Record pressure level of main chamber with inner door closed and Isolator gloves/sleeves extended into Isolator.
2. Insert hands into gloves in pressure and pull back from Isolator to simulate hand removal.
3. Determine the change in pressure and verify that the pressure does not change from negative to positive.

Acceptance Criteria: The pressure shall not change from negative to positive.

Test Data:
- Initial pressure: -.15”w.g.
- Lowest pressure after pull test: -0.04”w.g.

Conclusion:
The pressure in the Isolator did not increase above 0.00”w.g. therefore did not change to positive pressure when the gloves/sleeves were extended from the main chamber.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Particle Containment Integrity Test (REF. CETA CAG-002, 2.06)

This test is to verify that the CACI provides personnel protection from the escape of volatized hazardous drugs with the workzone as well as providing product protection to ISO Class 5 conditions at all times. This test can aid in determining particle integrity of the cabinet construction joints, seams, access panel and seals, glove ports and entry/exit points into the main chamber or where elevated particle levels have been detected at or near the work surface and where potential leak sources have been eliminated (e.g. damaged HEPA filters, damaged glove/gauntlet, etc.).

Instrument:

- Met One Laser Particle Counter Model A2408
- Aerosol Generator

Procedure:

1. Verify the background count in the testing room is at least 100,000 ppcf (ppcf) (3,532,000 particles per cubic meter (ppcm)).
2. If the count is too low, elevate the background levels using an aerosol generator.
3. Connect the particle counter sampling tubing to the workzone test port provided on the Isolator. Connect isokinetic probe to sampling tube within the workzone.
4. Turn on Isolator and let is warm up five minutes. Turn on particle counter and flush out sample tubing line to remove latent particles. Set the particle counter to measure 0.5 micron or larger at 1 CFM sampling rate.
5. Scan areas as described below within 1-inch of the surface at a scan rate of no more than 2-inches per second.
    - 1-inch from entire perimeter of hinged window gasket area.
    - 1-inch from perimeter of glove ports, sleeves and gloves.
    - 1-inch from internal interchange door perimeter seal.

NOTE: If during the scanning process, the 1-minute interval ends restart the 1-minute interval and record both values as necessary.

Acceptance Criteria:
No particle count reading during the 1-minute interval should exceed 100 ppcf.
Test Data:
Room background count: $\geq$ 120,000 ppcf

Particle counts for each of the above areas

Test 1.	5
Test 2.	2
Test 3.	2

Conclusion
All 1-minute interval particle counts were well below the 100 ppcf level in both measurement and statistical meeting and exceeding ISO Class 5 at 0.5 micron.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Volatile Hazardous Drug Containment Test (REF. CETA CAG-002, 2.11)

Purpose:
This test is to verify that the CACI provides personnel protection from the escape of volatilized hazardous drugs during all aspects of compounding operations. Being this product is a partial recirculation design, any volatile released in the workzone will partially recirculate and partially exhaust. In addition, since the interchange chamber is HEPA filtered with the Isolators recirculation airflow, any released volatiles will also be present within the interchange chamber.

To assure personnel protection, the test below uses a known amount of volatile tracer gas (SF6), releases the volatile into the main chamber airstream, then monitors the material transfer process monitoring for tracer gas just outside the external interchange door. The test is designed to determine the volatile purge time based on the known release value.

With the test results, a risk analysis can be performed for the hazardous drug preparation process equating amount of volatile present to purge time required.

Instrument:

- Miran Infrared Spectrophotometer
- 60 ml syringe filled with tracer gas (SF6) and placed within bag and sealed
- Clock w/second hand

Procedure:

1. Activate air analyzer and allow to warm up per manufacturer's instructions.
2. Place bagged tracer gas filled syringes in main chamber
3. Record room background levels of SF6 (or tracer gas).
4. Open (1) bag and release 60 ml of tracer gas into the workzone.
5. Initiate trace gas measurements along all front panel seams and around glove ports, holding detector inlet approximately 1" from the seams and traveling at a speed of approximately 3" per second.
6. Upon conclusion of seam checks, operator places detector in least favorable position within 1" of exterior pass-through chamber door based on Isolator design. (i.e. measure just below door on static pass-through or measure just above door or integral vertical flow pass-through.
7. Perform surrogate manipulation by opening another bag and release 60 ml of tracer gas into workzone. Place syringe back into bag and seal. Place sealed bag into pass-through chamber, then open outer pass-through door and remove bag.

   NOTE: Either a chamber or pass-through purge time may be required to meet acceptance criteria.
   Repeat above steps 6 & 7 until acceptance criteria are met.

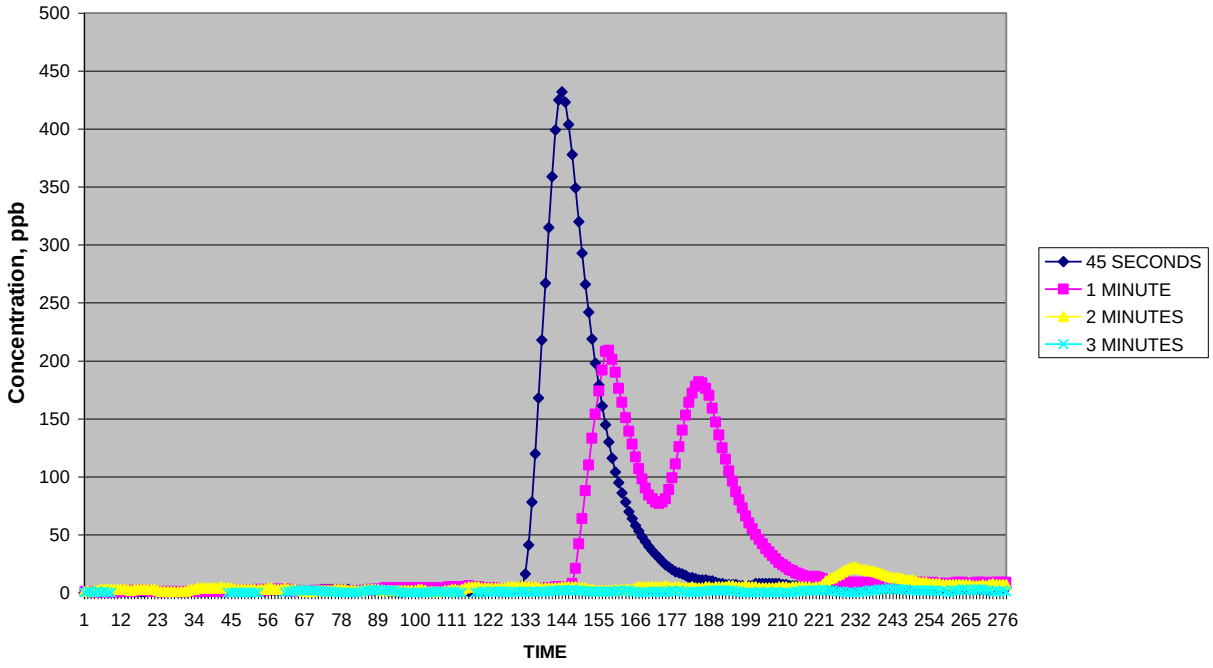
8. Record seam check results, time from discharge of tracer gas and peak detection (ppm) from external pass-through door detector position.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Acceptance Criteria: Tracer gas concentration level shall not exceed .01 ppm at any time during these tests.

Test Data:
Exterior scan peak concentration detection was less than .01 ppm.
Exterior interchange door detection levels:

Figure 1
Transfer Chamber Spillage



Run	Time (seconds) from tracer gas discharge	Peak Concentration
1	45	.43 ppm
2	60	.20 ppm
3	120	.02 ppm
4	180	<.01 ppm

Conclusion: Exterior scan peak concentration meets the acceptance criteria. Exterior interchange door detection levels versus time from gas discharge are recorded above. To achieve the required concentration of <.01ppm for a release amount of 60ml, a 3 minute delay time was required before removal of materials from the Isolator.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com

Interchange Particle Purge Time Determination Test (REF. CETA CAG-002, 2.13)

Purpose:
This test is performed to determine the amount of time it takes the interchange chamber to recover to ISO Class 5 at 0.5 micron particle levels after placing materials into the interchange chamber prior to transfer into main chamber.

Instrument:

- Met One Laser Particle Counter Model A2408
- Clock w/second hand

Procedure:

1. Verify the background count in the testing room is at least 100,000 (ppcf) (3,532,000 particles per cubic meter (ppcm)).
2. If the count is too low, elevate the background levels using an aerosol generator.
3. Place interchange counter isokinetic probe in the geometric center of the interchange chamber at a height of 6 inches.
4. Set the particle counter sample time to 3 second sample periods in "Concentration" mode to report ppcf.
5. Open exterior interchange door and place a transfer basket on the interchange worksurface.
6. Close exterior interchange door and initiate particle counter and clock.
7. Concentration levels are achieved when three consecutive counts are at or below 100 ppcf.
8. Record purge time as determined from initiation of particle counter to where maintained particle levels are achieved.

Acceptance Criteria: Particle concentration levels to be at or below 100 ppcf in less than 30 seconds.

Test Data:

Room background particle count: > 100,000 ppcf

Test # 1	Test #2	Test #3
12 seconds	10 seconds	11 seconds

Conclusion:
All particle concentration levels were reduced to ISO Class 5 at 0.5 micron conditions well within the 30 seconds. In addition, the interchange chamber being slightly more negative than the main chamber will always assure that no contamination will ever enter the main chamber through the Isolator airflow.

NuAire, Inc. | 2100 Fernbrook Lane | Plymouth, MN 55447 | U.S.A | ph: 763.553.1270 | fx: 763.553.0459 | tf: 800.328.3352 | www.nuaire.com