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Worldwide Headquarters • Esco Micro Pte Ltd • 21 Changi South Street 1 • Singapore 486777
Phone +65 6542 0833 • Fax +65 6542 6920 • mail@escoglobal.com • www.escoglobal.com

ROC No. 198400165W

HPI-4P1 POSITIVE PRESSURE COMPOUNDING ASEPTIC ISOLATOR PERFORMANCE EVALUATION

by

Yayi Nestiti and Alexander Atmadi | Esco Micro Pte. Ltd.

Introduction

The United States Pharmacopeias (USP) has published USP Chapter 797-Pharmaceutical Compounding Sterile Preparations. The USP <797>, enacted Jan 1, 2004 was written to improve the compounding of sterile products. It is the first official and enforceable requirement for compounded sterile preparation (CSP).

Specific issues of USP <797> addresses the responsibility of compounding personnel to ensure that CSPs are prepared safely by the means engineering control, which involves primary and secondary control. The primary control can be laminar flow, biosafety cabinet, or isolator, while the secondary control is the room requirement.

Below are the two alternative engineering control requirements:

Alt #	Control	Type of Drugs Being Handled	
		Non-hazardous	Hazardous
1	Primary	Laminar flow or biosafety cabinet	Class II or III biosafety cabinet
	Secondary	ISO Class 7 clean room, ≥ 5 Pa (0.02 "WC) positive pressure, ≥ 30 ACPH	ISO Class 7 clean & ante rooms, ≤ -2.5 Pa (-0.01 "WC) negative pressure, ≥ 30 ACPH
2	Primary	Positive pressure isolator	Negative pressure isolator
	Secondary	Normal room	Normal room, ≤ -2.5 Pa (-0.01 "WC) negative pressure, ≥ 12 ACPH

As can be observed from the table above, the benefit of using the isolator compared to laminar flow or biosafety cabinet is that there is no need to place the isolator inside the costly clean room, provided that the isolator has been validated to meet the USP <797> requirements, with the details being explained in CETA CAG-002-2006.

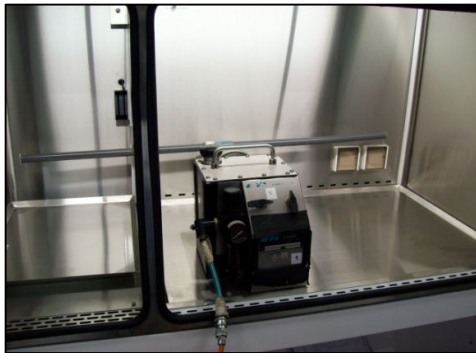
Isolator Validation

To validate that Esco Positive Pressure Hospital Pharmaceutical Isolator (HPI-4P1) can provide the necessary operator and product protection, the following validation tests were performed:

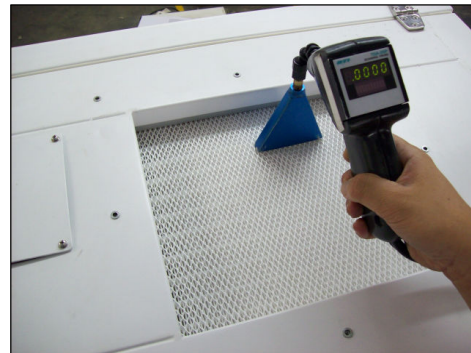
No	Test	Type
1	Filter leak	Mechanical
2	Airflow velocity	
3	Chamber static pressure	
4	Chamber dynamic pressure	
5	Work chamber sterility	
6	Pass through chamber sterility	
7	Product ingress and egress	
8	Recovery time determination	
9	Smoke pattern	
10	Gauntlet breach air velocity	
11	Noise level	
12	Light intensity	
13	Vibration	
14	Cross contamination at work tray	Microbiological
15	Cross contamination at underneath the IV bar	

1. Filter Leak Test

The downflow (supply) and exhaust filters were challenged with PAO aerosol of fixed concentration. The aerosol was evenly distributed throughout the supply (positive) cabinet plenum. An aerosol photometer was used to monitor aerosol penetration downstream of both filters, and to scan for the presence of leaks. Note that the inlet ULPA filter can't be tested.



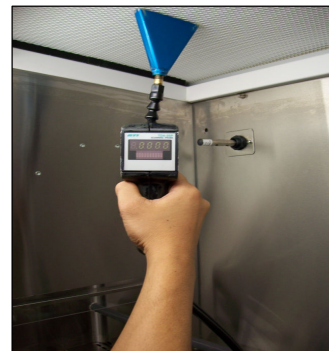
Aerosol injection location



Scanning exhaust filter



PAO sampling tube, located underneath the tray



Scanning downflow filter

PAO concentration : 30 µg/liter (NSF49:2002 requires > 10µg/l, but > 25µg/l is recommended)

Downflow filter

Leaks detected in media : No
 Leaks detected in gasket : No
 Particle penetration : 0.0005 %

Exhaust filter

Leaks detected in media : No
 Leaks detected in gasket : No
 Particle penetration : 0.0005 %

Acceptance : Maximum particle penetration of 0.01% for downflow & exhaust filters; no filters leaks present.
 For HPI-T, maximum total particle penetration is 0.005% for the exhaust filter.

Instrument used : Air Techniques International (USA) Model TDA 2G Aerosol Photometer. Accuracy: ± 1% of reading

Result : **Pass**

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

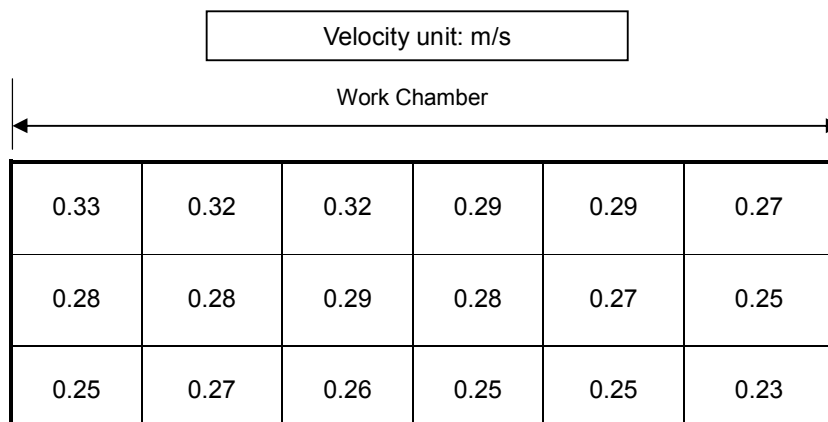
- ★ CETA CAG-002-2006 Section 2.05
- ★ NSF Standard 49:2002 (Section 6.3 and Annex A Section 2)

2. Airflow Velocity Test for Unidirectional Airflow Main Chamber

Purpose : to verify that the airflow in the Main Chamber meets design specification.

Instruments used : 1. TSI Incorporated (USA) Model 8346 Thermo-Anemometer with Pressure, Temp & Humidity Correction
 Accuracy: 3% of reading or $\pm 0.015\text{m/s}$ or $\pm 3\text{fpm}$
 2. Retort stand and clamp

Procedure : 1. Take reading with the front window closed
 2. Place thermo-anemometer and retort stand in main chamber on a horizontal plane that is 15 cm (6 inches) underneath the downflow diffuser and close the front window.
 3. Take readings according to the airflow grid: 15 cm (6") from the walls and $\leq 15\text{ cm}$ (6") apart as below:

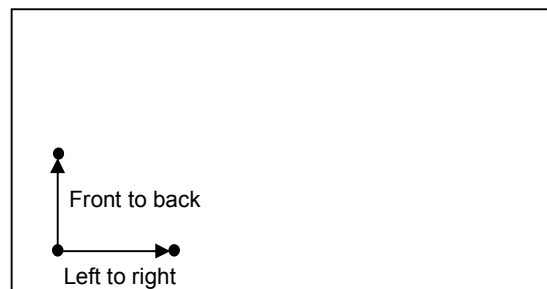


Distance between one measuring point to another:

- Left to Right : 108 mm
- Front to Back : 115 mm

Testing Results:

- Average : 0.28 m/s
- Max Deviation : 0.05 m/s = 17.9 %



Acceptance : Average airflow velocity must be within $\pm 0.025\text{ m/s}$ ($\pm 5\text{ fpm}$) of **0.28 m/s (55 fpm)** (Esco's setpoint).
 All individual airflow velocity readings must be within $\pm 20\%$ or 0.08 m/s (16 fpm) from the average, whichever is larger

Result : **Pass**

Notes : Probe position when performing airflow test:

1. Front row: the probe was pointed to the front
2. Middle and back row: the probe was pointed to the right on the right half of the cabinet, and is pointed to the left on the left half and center of the cabinet
3. The velocity probe must be placed with accuracy within 12.5 mm from the above grid

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the

- ★ CETA CAG-002-2006 Section 2.01
- ★ NSF Standard 49:2002 (Section 6.9 and Annex A Section 9)



3. Chamber Static Pressure Test

Purpose : to verify that the isolator meets the manufacturer’s pressure requirements.

Instruments used : Shortridge Instrument (USA) Model ADM-870 Airdata meter. Use differential pressure (to atmospheric) mode

Procedure : Check the pressure reading of Main Chamber and Pass-Through Chamber and record the data below:



Note:
 Use the ports on the glass to connect the tube to the Shortridge meter



Pressure in Main Chamber (Pa)	Pressure in Pass-Through Chamber (Pa)	Pressure Difference (Pa)
42.76	28.02	14.74

Acceptance for Isolator Type	Main Chamber	Pass- Through Chamber	Pressure Difference	Pass?
Positive Re-circulating	≥ 37 Pa (0.15 “WG)	≥ 25 Pa (0.10 “WG)	≥ 12 Pa (0.05 “WG)	Yes

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the
 ★ CETA CAG-002-2006 Section 2.02

4. Chamber Dynamic Pressure Test

Purpose: to check: 1. Pass-through and main chamber pressures don't change from positive to negative or vice versa (depends on the type of isolator) during dynamic condition.
 2. The pressure displayed on LCD changes in a correct manner during & after dynamic condition.
 3. There is no excessive alarm when the gloves are moved in extreme manner
 4. The LCD warns the user that the outer or inner door is opened.

Instruments used : Cabinet's built-in digital pressure gauge.

Procedure : 1. Ensure that the pressure sensors are properly calibrated, with correct pressure displayed on LCD
 2. Follow the table below, with the underlined part denotes what is changed for each test (1, 2, 3, 4)

Step explanation : 1. Opening and closing the outer pass-through door
 2. Opening and closing the inner pass-through door
 3. Pulling both gloves to the same level as the window, simultaneously, in 1 second.
 4. Start with the gloves outside the isolator, then push both gloves inside, simultaneously, in 1 second.

Test #	Condition-1				Condition-2				Condition-3			
	Outer Door	Inner Door	Gloves	P (Pa)	Outer Door	Inner Door	Gloves	*P (Pa)	Outer Door	Inner Door	Gloves	*P (Pa)
1	<u>Close</u>	Close	Inside	P: 28 M: 43	<u>Open</u>	Close	Inside	0	<u>Close</u>	Extend	Inside	P: 28 M: 43
2	Close	<u>Close</u>	Inside	P:28 M:43	Close	<u>Open</u>	Inside	P:27 M:27	Close	<u>Close</u>	Inside	P:28 M:43
3	Close	Close	<u>Inside</u>	P: 28 M: 43	Close	Close	<u>Pulled</u>	P: 28 M: 40				
4	Close	Close	<u>Pulled</u>	P: 28 M: 38	Close	Close	<u>Inside</u>	P: 28 M: 43				

*) Refer to Acceptance Criteria table below on which pressure to record on the table above.

No	Acceptance Criteria	Pass ?
1	<u>Pass through chamber pressure</u> didn't change from negative to positive or positive to negative between condition 1 to 2 to 3. Pass through chamber pressure become within 5 Pa from zero when the outer door is opened. The LCD displays warning: "Outer Door Opened".	Yes
2	<u>Pass through (P) and Main chamber (M) pressure</u> didn't change from negative to positive or positive to negative between condition 1 to 2 to 3. Pass through and main chamber become within 5 Pa of being equal when the inner door is opened. Pressure returned to original level between condition 1 and 3. The LCD displays warning: "Inner Door Opened".	Yes
3	<u>Main Chamber Pressure</u> didn't change from positive to negative between condition 1 to 2. Pressure alarm is not activated.	Yes
4	<u>Main Chamber Pressure</u> didn't change from negative to positive between condition 1 to 2. Pressure alarm is not activated.	Yes

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

★ CETA CAG-002-2006 Section 2.02

5. Work Chamber Sterility / Particle Count Test

Purpose : To determine to ISO 14644-1 cleanliness classification of the main chamber.

Instruments used : Met One Laser Particle Counter Model A2400

Procedure : 1. Connect the particle counter sampling tubing to the work chamber test port on front window.
 2. Connect the isokinetic probe to work chamber test port on front window.
 3. Make sure front window is closed, gloves are attached, and cabinet has been running ≥ 3 min after that
 4. Set the particle counter to measure 0.3 micron at 1 CFM sampling rate.
 5. Put the isokinetic probe at approximately 15 cm (6") above the work surface using the mini tripod / stand

6. Discharge the first reading because there may be some contamination inside the tube
 7. Take readings at 5 locations: at the 4 corners and center of work zone for 1 minute each as below:

0	-----	0
-----	0	-----
0	-----	0

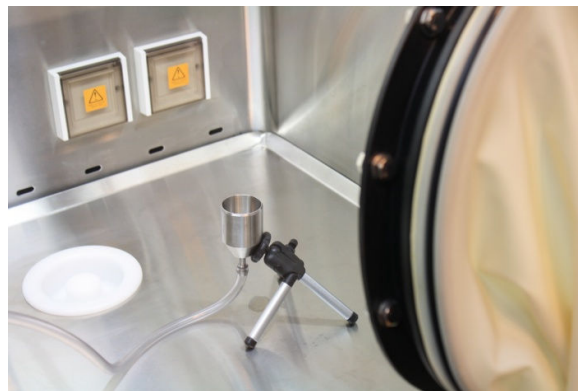
Acceptance : The number of particles on each location ≤ 3 for ISO Class 3, or ≤ 30 for ISO Class 4

Results : **ISO Class 3**

Note : CETA CAG-002-2006 requires minimum cleanliness of ISO Class 5

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

- ★ CETA CAG-002-2006 Section 2.10
- ★ IEST-RP-CC002.2 Section 6.6



Work chamber sterility test using particle counter

6. Transfer Chamber Sterility / Particle Count Test (Required for Field Testing)

Purpose : To determine to ISO 14644-1 cleanliness classification of the main chamber.

Instruments used : Met One Laser Particle Counter Model A2400

Procedure : 1. Use same setting as the Work Chamber Sterility Test, but move the isokinetic probe to transfer chamber
 2. Put the isokinetic probe at the center of the transfer chamber, at height of 15 cm (6”) above the tray
 3. Take 3 readings at the same location and record below:

Reading #1	Reading #2	Reading #3
0	0	0

Acceptance : The number of particles on each location ≤ 3 for ISO Class 3, or ≤ 30 for ISO Class 4

Results : **ISO Class 3**

Note : CETA CAG-002-2006 requires minimum cleanliness of ISO Class 5

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

- ★ CETA CAG-002-2006 Section 2.10
- ★ IEST-RP-CC002.2 Section 6.6



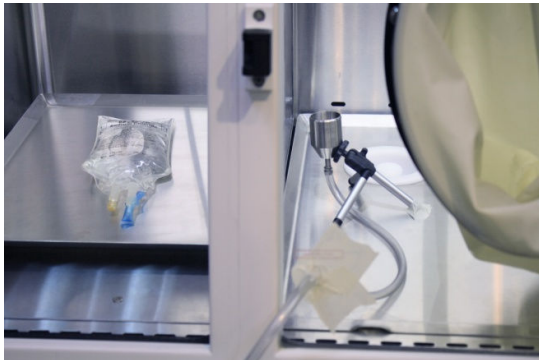
Transfer chamber sterility test using particle counter

7. Product Ingress and Egress Test

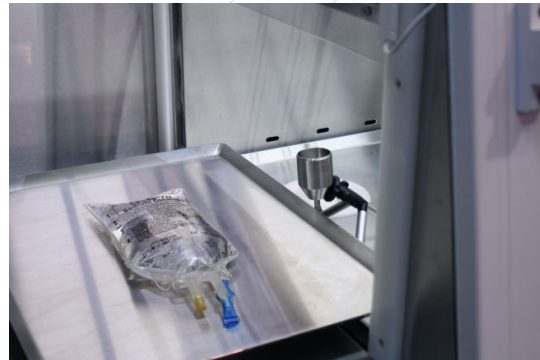
Purpose : To assure the Isolator work chamber can maintain ISO 14644-1 Class 3 at 0.3 micron, during material transfers with no wait or purge time during the transfer process when used outside an ISO Class 7 clean room as mentioned in the USP 797 requirements.

Instruments : 1. Met One Laser Particle Counter Model A2400
 2. Transfer tray or a box to simulate material transfer. This object must be cleaned with IPA before test.

Procedure : 1. Use same set-up from the previous Chamber Sterility Test
 2. Put the isokinetic probe inside the main chamber center, 5 cm (2”) away from transfer tray sliding path
 3. Using the mini tripod like before, put the probe at the height of 15 cm (6”) above the tray
 4. Probe is placed so operator’s arms will not pass above it when moving material through transfer door
 5. Verify the particle count reading meets ISO Class 3 before beginning the test cycle.
 6. Set the particle counter for a 1-minute count with no more than a one second hold time.
 7. Open the outside pass-through door.
 8. Place the transfer tray into the pass-through and close the outer door (no wait or purge time required).
 9. Open the interior pass-through door and move the transfer tray from the pass-through to work area.
 10. Close the inside pass-through door. Document the particle counts during the transfer process



Open the outside pass-through door



Open the interior pass-through door, transfer the material

Operations	Test #1	Test#2	Test#3
Start	0	0	0
Open/Close Exterior Door	0	0	0
Open Interior Door	0	0	0
Transfer Tray	0	0	0
Close Interior Door	0	0	0
Post Wait Period	0	0	0

Acceptance : The number of particles on each location ≤ 3 for ISO Class 3, or ≤ 30 for ISO Class 4

Results : **ISO Class 3**

Note : CETA CAG-002-2006 requires minimum cleanliness of ISO Class 5

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:
 ★ CETA CAG-002-2006 Section 2.09

8. Recovery Time Determination Test

Purpose : To determine the amount of time it takes the main chamber to recover to ISO 14644-1 Class 4 at 0.3 micron particle levels after an event such as a full window opening or large scale contamination generated by the compounding process.

Instrument : 1. Theatrical Smoke Generator and cylindrical diffuser for airflow visualization test
 2. Met One Laser Particle Counter Model A2400
 3. Stopwatch

Procedure : 1. Use same set-up from the previous Product Ingress and Egress Test.
 2. Put the isokinetic probe with mini tripod on the center of the work tray.
 3. Close the probe inlet air tight with tape so it will not damage the particle counter during smoke injection.
 4. Turn off the blower and fill the chamber with Dräger Sicherheitstechnik smoke generated from smoke tube.
 5. Turn on the blower and start timer.
 6. Wait until the smoke is visibly cleared (about 20-25 sec) to prevent damage on the particle counter
 7. Open the isokinetic probe cover at 25 sec after the blower is started
 8. Start the particle counter at 30 sec after the blower is started
 9. Total recovery time is considered from isolator blower turn-on time to the first ISO Class 4 particle count

Test #1	Test #2	Test #3
51 Seconds	51 Seconds	52 Seconds

Acceptance : Particle count of 0.3 micron shall not exceed 30 in less than 60-seconds.

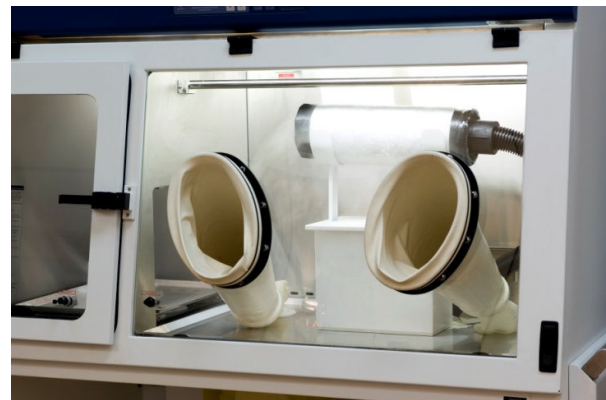
Result : **Pass**

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

★ CETA CAG-002-2006 Section 2.07



Smoke recovery visualization-first 5 second



Smoke recovery visualization-next 15 second

9. Smoke Pattern Test

Purpose : To determine that the airflow pattern inside the isolator is correct or not

Instrument : 1. Dräger Sicherheitstechnik smoke tube for airflow visualization test

Procedure : 1. Use same smoke tube as the Recovery Time Determination Test, but remove the isokinetic probe.
 2. Spray the smoke at 2.5 cm from all main chamber perimeters at middle of work zone height.
 3. Spray the smoke at the center of the work zone, from left to right, at middle of work zone height.
 3. Spray smoke at all penetrations: pass-through door, trash disposal caps, gloves, gauntlets.

Acceptance : 1. Near the perimeter, gauntlets, gloves, and at center, smoke shall smoothly and rapidly goes downward.
 2. The smoke shall smoothly and rapidly be removed through the air grilles with no reflux or billowing.
 3. At all penetrations, smoke shall not be blown into the work zone (no inward leaking).

Result : **Pass**

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

★ CETA CAG-002-2006 Section 2.08

10. Gauntlet Breach Air Velocity Test

Purpose : To ensure some level of operator protection in the event of significant glove or gauntlet integrity failure

Instrument used : Vane meter Model AV-2 & Vane Air Vel. Accuracy: 1% of reading or ± 1 digit ± 0.02 m/s

Procedure : 1. Remove one glove/sleeve from the view screen.
 2. Measure the velocity from the glove port plane at the center of the opening three times as below:

1 st Reading (m/s)	2 nd Reading (m/s)	3 rd Reading (m/s)	Average Reading (m/s)	Acceptance (m/s)	Pass ?
1.12	1.11	1.12	1.12	≥ 0.5 m/s (100 fpm)	Yes

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

- ★ CETA CAG-002-2006 Section 2.04
- ★ NSF / ANSI 49



11. Noise Level Test

With the cabinet running under regular parameters, a calibrated noise level meter was used to obtain a noise level of the cabinet during normal operation, at 30 cm in front of the drain pan lower edge and 38 cm above the recessed work surface area (not the front grill).

Cabinet noise level (dBA)	Ambient noise – blower off (dBA)	Corrected noise level (dBA)
60.4	48.3	60.4

Acceptance : Maximum corrected noise level of 67 dBA (Based on NSF 49:2002 standard).

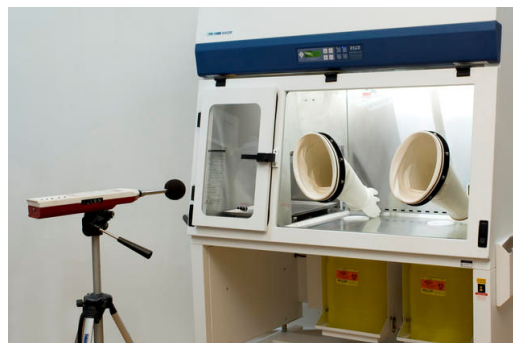
Instrument used : Quest Technologies (USA) Model 1100 Sound Level Meter and QC-20 Calibrator
 Accuracy: 0.5 dBA (sound meter), 0.3 dBA (calibrator)

Result : **Pass**

In the event of EN12469:2000 method is used, the noise reading is to be performed at 1 m in front of the center of the front aperture and 1 m above the ULPA exhaust filter, with the acceptance criteria of 65 dBA.

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

- ★ NSF Standard 49:2002 (Section 6.4 and Annex A Section 4)
- ★ EN12469:2000 (Annex A Section 3)



12. Lighting Intensity Test

A light intensity meter was used to obtain light intensity at the cabinet work surface. Zero the meter before taking the readings. Readings were taken along the front to back centerline within the interior work area:

Distance between measuring point to:

- Wall : 150 mm
- Another point : 282 mm

Cabinet ON	905	974	840
Cabinet OFF	0	0	0

Acceptance : Net light intensity shall average a minimum of 800 lux (74 ft-cd)

Instrument used : Extech Instruments (USA) Model 407026 with accuracy: $\pm 4\%$ of reading ± 2 digits

Result : **Pass**

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

- ★ NSF Standard 49:2002 (Section 6.5 and Annex A Section 5)
- ★ EN12469:2000 (Annex A Section 2)



13. Vibration Test

Actual vibration (cabinet on), averaged from 20 consecutive readings : 0.27×10^{-5} m RMS amplitude
 Background vibration (cabinet off), averaged from 20 consecutive readings : 0.12×10^{-5} m RMS amplitude
 Net vibration (actual vibration minus background vibration) : 0.15×10^{-5} m RMS amplitude

Acceptance : Maximum net vibration should not exceed 0.5×10^{-5} m (0.002 inch) RMS amplitude

Instrument used : Quest Technologies (USA) Model VI-100 Vibration Meter
 Accuracy: $\pm 5\%$ of reading

Disclaimer : Occasional transient background vibration may vary the result by $\pm 0.07 \times 10^{-5}$ m (2.75×10^{-5} inch)

Result : **Pass**

Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:

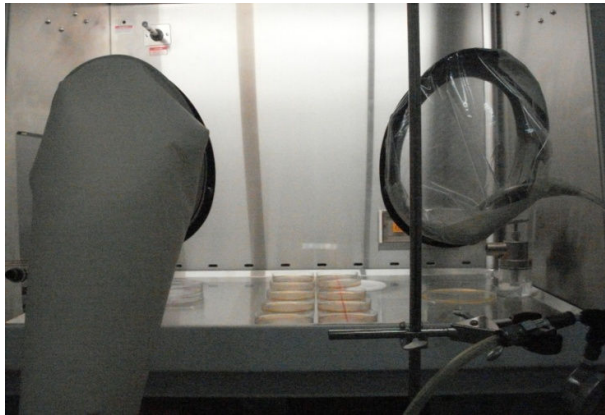
- ★ NSF Standard 49:2002 (Section 6.6 and Annex A Section 6)
- ★ EN12469:2000 (Annex A Section 4)

14. Cross Contamination at Work Tray Test

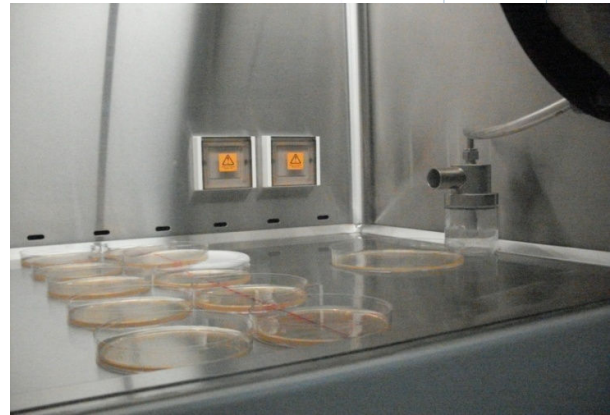
Purpose : to measure cross contamination protection of the isolator work tray, following the procedure adopted from NSF/ANSI 49:2002 standard for biosafety cabinet

Instrument : 1. Nebulizer containing 55 ml *Bacillus subtilis* spore suspension with $5-8 \times 10^4$ spore/ml
 2. Agar plates with trypticase soy medium
 3. Compressed air source and calibrated pressure gauge

Procedure : 1. Put the nebulizer right next to the right wall, discharging towards left wall
 2. Arrange two columns of agar plates. The first row of dishes are placed with a distance of 14 inches from the right wall (measured from the center of the dish). The second row is placed on the left side (behind) of the first row.
 3. Place one gar plate as control plate, right underneath the nebulizer nozzle
 4. Run the nebulizer for 5 minutes
 5. Do this test 3 times on the right and 3 times on the left wall
 6. Incubate the agar plates at 37°C (98°F) for 48 hours, then check the number of CFU



Front view, showing the overall setup



Close-up view of the nebulizer and agar plates

Test data : The number of CFUs after 48 hours incubation is as follows:

Tests	Left Side		Right Side	
	Run 1	Run 2	Run 1	Run 2
Control	>300	>300	>300	>300
Front Row (near nebulizer)	1.0	1.0	1.0	1.0
	2.0	2.0	2.0	2.0
	3.0	3.0	3.0	3.0
	4.0	4.0	4.0	4.0
	5.0	5.0	5.0	5.0
Back Row (far away from nebulizer)	1.0	1.0	1.0	1.0
	2.0	2.0	2.0	2.0
	3.1	3.0	3.0	3.0
	4.0	4.0	4.0	4.0
	5.0	5.0	5.0	5.0

Acceptance : The number of Colony Forming Units (CFU) in all plates for each run is ≤ 2

Result : **Pass**

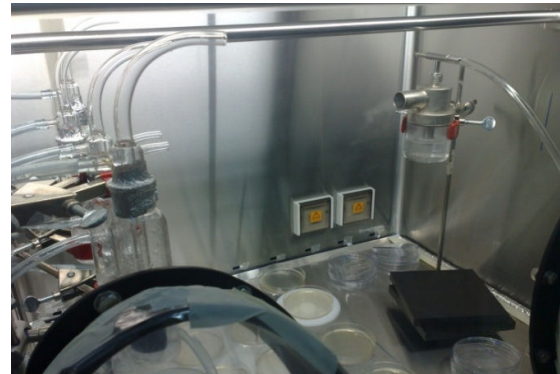
Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:
 ★ NSF / ANSI Standard 49:2002 (Section 6.7 and Annex A Section 7)

15. Cross contamination at underneath the IV bar (starting height of critical work zone)

Purpose : to measure cross contamination protection of the isolator work chamber, where the IV bags may be hanged on the IV bars, using the adapted cross contamination and operator protection procedure from NSF/ANSI 49:2002 standard for biosafety cabinets

- Instrument :
1. Nebulizer containing 55 ml *Bacillus subtilis* spore suspension with $5-8 \times 10^4$ spore/ml
 2. Agar plates with trypticase soy medium
 3. Compressed air source and calibrated pressure gauge
 4. Six AGI-30 impingers, filled with 20 ml distilled water
 5. Vacuum pump, tubes, and valves, set to give 12.5 l/m suction at each impinger
 6. Digital flow meter, to calibrate the valves
 7. Glass funnel and membrane papers to extract spores from impingers

- Procedure**
1. Ensure that the IV bar is installed on the work zone
 2. Set the nebulizer at 10 cm (4") below the IV bar, and 15 cm (6") from the centerline
 3. Put three columns of agar plates as control (5 plates each). One column at the centerline of the work zone. The other two columns are set exactly beside the center column.
 4. Put the 6 impingers in a different height (per step 5-7), three on each side of the IV bar. The impinger inlets shall be 150 mm (6") from the centerline.
 5. The 2 top impingers are 550mm (21½") above work tray and 160 mm (6¼") out from IV bar
 6. The 2 middle impingers are 530mm (21") above work tray and 75mm (3") out from IV bar
 7. The 2 bottom impingers are 420mm (16½") above work tray and 13mm (½") out from IV bar
 8. Start nebulizer for 1 min, turn on the samplers for 5 min, turn off nebulizer 30 sec after
 9. Do this test twice, with the nebulizer on the right side only
 10. Extract the possible spores from impingers using funnel and filter membrane papers
 11. Paste the paper on agar plate, and incubate the agar plates at 37°C (98°F) for 48 hours



Test data : The number of CFUs after 48 hours incubation is as follows:

Tests	Run 1	Run 2
Control	1. 0 6. 1 11. 2	1. 1 6. 0 11. 0
	2. 1 7. 6 12. 4	2. 1 7. 5 12. 5
	3. 5 8. >100 13. >300	3. 4 8. 82 13. >200
	4. 19 9. >300 14. >300	4. 56 9. >300 14. >300
	5. >100 10. >300 15. >300	5. >200 10. >300 15. >300
		closest to nebulizer and front of isolator
Impingers	1. 1	1. 0
	2. 0	2. 0
	3. 0	3. 0
	4. 0	4. 0
	5. 1	5. 0
	6. 0 Front of Isolator	6. 0 Front of Isolator
	Result: Pass	Result: Pass

Acceptance : The number of Colony Forming Units (CFU) in each impinger for each run is ≤ 2
 Acceptance criteria / testing procedures have been adopted in accordance with the requirements of the:
 ★ NSF / ANSI Standard 49:2002 (Section 6.7 and Annex A Section 7)



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Cleanroom Equipment Division

Worldwide Headquarters • Esco Micro Pte Ltd • 21 Changi South Street 1 • Singapore 486777
Phone +65 6542 0833 • Fax +65 6542 6920 • mail@escoglobal.com • www.escoglobal.com

ROC No. 198400165W

Conclusion

The extensive mechanical and microbiological test results performed above indicate that the Esco HPI-4P1 Positive Pressure Compounding Aseptic Isolator meets and exceeds the requirements of the CETA CAG-002-2006 and USP 797 for providing a safe and clean environment for compounding of non hazardous, sterile drug preparations.

The ULPA filters used on Esco HPI-4P1 isolators help to provide ISO Class 3 environment inside the work chamber, which is far cleaner than the ISO Class 5 required by USP 797, that is obtained using the HEPA filters typically obtained inside most isolators in the market.

The advanced airflow and filtration system featured in Esco HPI-4P1 isolators helps to maintain ISO Class 3 cleanliness inside work zone even during dynamic condition, such as opening the inner pass through door and transfer the material from the pass through to the work chamber. Additionally, this isolator features a fast recovery, not only to ISO Class 5, but to ISO Class 4 in less than 60 seconds, after a gross contamination inside the work zone.

Going beyond product safety dictated by CETA CAG-002-2006 and USP 797, Esco HPI-4P1 isolators also feature user comfort, by having sufficient light intensity that exceeds the NSF/ANSI 49 requirement, and having low noise and low vibration that are below the limit imposed by NSF/ANSI 49.

Finally, the microbiological tests indicates that Esco HPI-4P1 isolators can provide good cross contamination protection to the samples manipulated on the work tray and inside the critical work area underneath the IV bar, despite it is customary practice for the user to work on only one compounding drug at a time inside the work chamber.

By surpassing the requirements imposed by CETA CAG-002-2006 and USP 797, and some additional requirements adopted from NSF/ANSI 49, Esco HPI-4P1 isolators offer superior performance than the typical isolators sold in the market.

Literature References

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IEST-RP-CC002.2: Unidirectional Flow Clean-Air Devices, Institute of Environmental Sciences and Technology, 5005 Newport Drive, Rolling Meadows, IL 60008-3841, USA.

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NSF/ANSI 49-2002: Class II (laminar flow) Biosafety cabinetry, NSF International, P.O. Box 130140, Ann Arbor, MI 48113-0140, USA.

USP28-NF23: United States Pharmacopeial Convention, Inc., 12601 Twinbrook Parkway, Rockville, MD 20852.