SUMMARY

Date of Test: _____ Date of Prior Certification: _____

Test Report Number: _____ Certified by: _____

Re-certification Due Date: _____

Unit Description:

Make : _____

Model: _____

Serial Number: _____

Location: _____

Client Information:

Client: _____

Contact: _____

Address:

City, State: _____

Phone: _____

E-mail: _____

CERTIFIER INFORMATION

Name: _____

Company: _____

Phone: _____

Results

4.1 Particulate Test (non-viable) – ISO Class 5	Pass _____	Fail _____
4.2 First Air Test - ISO Class 5	Pass _____	Fail _____
4.3 Egress Test - ISO Class 5	Pass _____	Fail _____
4.4 Pressure Differential Test	Pass _____	Fail _____
4.5 HEPA Filter Integrity Test	Pass _____	Fail _____

5.0 Viable Samples Taken

	Airborne PEC	Airborne Area	Surface PEC	Finger Tip
Yes or No				

6.0 Unidirectional Airflow Smoke Test – CTG Certification Protocol Version 3.1 (2-5-2018)

Unidirectional Airflow		Yes	No

Signature below verifies that you have read and understand the protocols set forth by Containment Technologies Group, Inc. for certification of CTG products. The protocols are based on compliance to FDA guidelines and USP standards*. Questions are comments should be addressed hrahe@mic4.com

Protocol Approvals

Date: _____

Protocol Executed by _____

Protocol Prepared by:
Technical and Regulatory Consultant
Hank Rahe _____

***USP <797> contains tests that represents a potential health hazard if preform in a pharmacy environment. These tests is excluded from consideration when preparing this protocol**

1.0 Purpose

1.1 The purpose of the certification protocol is to verify that the isolator is operating as designed after installation. The design criteria for the isolator is to meet federal and state regulations and standards.

Verification of the internal environment is accomplished by specified testing procedures described in this document. After testing is complete the results of the test are documented on form Appendix A.

Note: It is acceptable to substitute different formats for certification given the information is required and referenced by regulatory agencies.

The current standards for air quality particulate measurement is the International Organization for Standardization (ISO). ISO Class 5 particulate air quality is required for aseptic manipulations in the critical preparation zone by both FDA and state boards of pharmacy.

The following ISO standards apply to the particulate air quality specifications, test methods and acceptance criteria.

1. ISO 14644-1:2015(E) –Cleanroom and associate controlled environments
2. ISO 14644-2: 2015 (E)-Specifications for testing and monitoring to prove continued compliance with ISO 14644-1:2015 (E)
3. ISO 14644-3:2005(E) – Test methods
4. ISO 14644-7:2004(E) – Separative devices (clean air hoods, gloveboxes, isolators and mini-environments

Note: The ISO documents are the basis for particulate air quality test described.

Other guidance and standards requirements utilized in the certification process are:

1. FDA Guidance for Industry - Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice; 2004
2. United States Pharmacopeia Standards*: USP <797> 2008; USP <800> 2018

1.2 Verification Approach

Verification will consist of testing isolators to verify that both particulate air quality, FDA guidance and required standards are met.

Critical parameters for the isolator are meeting ISO 5 conditions in the critical zone where compounding occurs, first air requirements, airflow design, and egress requirements per USP <797>.

The isolators are designed with HEPA filtration for both inlet and exhaust air.

Airflow design is based on regulatory requirements and falls into three categories:

1. Re-circulating
2. Once through
3. Once through exhausted

In the re-circulating system the air passes through two HEPA filters. In the once through the inlet air is HEPA but not the exhaust and the once through exhausted is HEPA filtered both inlet and exhaust.

The inlet HEPA filter is the critical filter for controlling particulate and this filter is tested per the HEPA filter integrity test. For facilities requiring once through exhaust the exhaust filter should also be tested.

Testing frequency for ISO 5 environments or when the chamber is moved or modified in such a way that the modification would impact the filter system. Test that involve particulate air quality are to be valuated against the ISO 14644-1:2015(E) standard.

1.3 Testing Conditions

ISO 14644-1:2015 (E) Cleanrooms and associated controlled environments – PART 1 Classification of air cleanliness by particulate concentration specifies a standard method of testing to determine particulate cleanliness. The test methods described in ISO 14644-3-2005(E) describes three "Occupancy states" or conditions under which testing is to take place.

1. As-built
2. At-rest
3. Operational

USP standards call for "dynamic testing" which is the same as to the operational testing conditions described in the ISO standard.

The specific air quality tests in this protocol to demonstrate compliance with both ISO standards, FDA, USP and state pharmacy board regulations are as follows:

1. Chamber particulate counts (Direct Compounding Area (DCA))
2. First air
3. Egress

The air quality results of each of these tests are to be ISO class 5 – not more than 3520 particle of 0.5 microns or larger per m^3.

The following sequence of compounding operations should be followed to create "dynamic compounding conditions"

1. Load materials for manipulations into trays
2. Place trays into airlock/ transition chamber
3. Spray decontaminating agent (hydrogen peroxide or sterile alcohol into chamber
4. Close door on chamber
5. Enter gloves/ sleeves
6. Open inter chamber door
7. Remove tray
8. Close door
9. Perform manipulations
10. Place finished compound into tray and place into airlock/transition chamber

2.0 System Overview

2.1 System Boundaries

The MIC / MIC/EDU isolator consist of the following components:

1. Main chamber
2. Airlock / transition chamber
3. Glove ports for personnel interaction
4. Air handling system
    a. Inlet HEPA filter
    b. Pressure control valve
    c. Blower
    d. Pressure control valve
    e. Outlet HEPA filter

The 797P consist of the following components

1. Main chamber
2. Airlock / transition chamber
3. Glove ports for personnel interaction
4. Air handling system
    a. Inlet HEPA filter
    b. Blower
    c. Pressure control plate

The 800N consist of the following components

1. Main chamber
2. Airlock / transition chamber
3. Glove ports for personnel interaction
4. Air handling system
    a. Inlet HEPA filter
    b. Pressure control plate
    c. Blower
    d. Outlet HEPA filter
    e. Gate Valve

3.0 References

3.1 Owner's Manual

3.2 Industry Guidance and Standards:

a. ISO 14644-1:2015 (E) Cleanrooms and associated controlled environments – PART 1 Classification of air cleanliness by particulate concentration
b. ISO 14644-2:2015 (E) Specifications for testing and monitoring to prove continued compliance with ISO 14644-1:2015 (E)
c. ISO 14644-3:2005(E) – Test methods
d. ISO 14644-7:2004(E) – Separative Devices (clean air hoods, gloveboxes, isolators and mini-environments
e. FDA Guidance for Industry - Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice; 2004
f. United States Pharmacopeia Standards: USP <797> 2008 *; USP <800> 2018
g. IEST-RP-CC034

4.0 Performance Test Procedures

4.1 Particulate Test – Non-viable

Item 4.1	Particulate Test
Purpose:	Determine compliance to ISO 14644-1:2015(E) Class 5 Particulate count less than 3520 particles per cubic meter 0.5 microns or greater
Regulatory Requirement	USP <797>*, USP <800>*, FDA guidance[1]
Acceptance Criteria:	Particulate count less than 3520 particles per cubic meter 0.5 microns or greater ISO class 5
Equipment required:	Calibrated Particulate Counter

[1]FDA Guidance for Industry - Sterile Drug Products Produced by Aseptic Processing — 2004

Test Instructions

1. Establish background air quality where the isolator is located. Take initial air samples with the zero filter in place (verifies the sample tubing is clean and free of leaks)
2. Place sample probe on top of the airlock, take two (2) samples and record results on Summary Requalification Report. If area background exceeds 18,500,000 particles contact CTG for additional instructions.

Sample 1	Sample 2	Average

3. Test will consist of three locations within the critical compounding zone which is defined as between the glove ports (outside from the center of the zone). Location A- Centerline of left gloveport and twelve inches from back wall; Location B Twenty inches from left wall and twelve inches from back wall is twelve inches from the back wall and Location C is twelve inches from the back wall and six inches from the left wall.
4. Place probe into the isolator through the airlock. The particle counter is external to the isolator chamber (Note when operating the particle counter will remove one CFM from the chamber causing the chamber to go negative). Balance the pressure valves to reduce the negative pressure as must as possible.
5. Connect the particle counter tubing by cutting off a glove finger and inserting the tubing through the hole in the glove. Tape the tubing to the glove making a gas tight seal.
6. Place the glove over the tube opening for the trash container. Check Pressure.
7. **Caution when moving probe do not slide**
8. Take a sample count clear tubing. Take three counts at each location. Record each count

Location	Sample 1	Sample 2	Sample 3	Average
Location A				
Location B				

4.0 Performance Test Procedures

4.2 Particulate Test – First Air

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Item 4.2	First Air Test
Purpose:	Verify air exiting the HEPA filter in a unidirectional air stream is essentially particle free.
Regulatory Requirement	USP <797>*, USP <800>*, FDA guidance[1]
Acceptance Criteria:	Particulate count less than 35 particles per cubic meter 0.5 microns or greater ISO class 5 Reference USP < 788.
Equipment required to perform this test:	Calibrated Particulate Counter

Test Instructions

1. Test will consist of one location
2. Place probe into the isolator through the airlock. The particle counter is external to the isolator chamber (Note when operating the particle counter will remove one CFM from the chamber causing the chamber to go negative). Balance the pressure valves to reduce the negative pressure as must as possible.
3. Connect the particle counter tubing by cutting off a glove finger and inserting the tubing through the hole in the glove. Tape the tubing to the glove making a gas tight seal.
4. Place the glove over the tube opening for the trash container.
5. Take a sample count at location one to assure any contamination is clear in the tubing.
6. Take two counts at approximately 6 to 12 inched below the center point of the inlet HEPA filter. Record each count and average at each location.

Location	Sample 1	Sample 2	Average
Center Inlet HEPA			

4.3 Particulate Test – Egress Test

Item 4.3	Egress Test
Purpose:	Verify during transfer of materials from airlock to main chamber particulate count will not exceed ISO 5. Particulate count less than 3520 particles per cubic meter 0.5 microns or greater
Regulatory Requirement	USP <797>*, USP <800>*
Acceptance Criteria:	Particulate count less than 3520 particles per cubic meter 0.5 microns or greater during transfer of materials
Equipment required to perform this test:	Calibrated Particulate Counter

Test Instructions

1. Prepare transfer tray materials for compounding (vial, syringe and piggy back)
2. Place particle counter probe fourteen inches from the center line of the inter airlock door with the probe facing toward the critical zone.
3. Load transfer tray into airlock by opening outside door and placing it into airlock. Spray down the transfer tray and airlock with decontaminating agent (3% hydrogen peroxide). Close the outside door and wait thirty seconds.
4. Enter the gloves and open the inside airlock door. Note: airlock is filled with decontamination aerosol wait sixty seconds for aerosol to clear before beginning counts.
5. Start particle counter.
6. Repeat test two times

Sample	1	2

4.0 Performance Test Procedures

4.4 Pressure Differential Test

Item 4.4	Pressure Differential Test
Purpose:	Verify the isolator is operating within the proper pressure range
Regulatory Requirement	USP <797>*, USP <800>*
Acceptance Criteria:	Greater than 0.02 inches of water column positive Less than 0.02 inches water column negative
Equipment required to perform this test:	Visual

Test Instructions

The differential pressure acts as a secondary containment barrier either protecting the product or personnel. It is important that this feature is operating correctly.

1. Before checking the differential pressure, verify that the Isolator has been sealed properly. Check for leaks around the trash ports, sharps ports and glove ports.

2. After ensuring there are no leaks in the Isolator, turn the isolator off and verify that the pressure gauge reads zero (it may take up to two minutes for the pressure to reach zero).

3. After the zero pressure reading has been verified, turn the Isolator on and allow three minutes for it to return to proper operating range. Ensure that the pressure differential gauge reads in the range of +/- 0.2 to 0.5 inches of water column.

Item	Yes	No
Pressure verified within range		

4.0 Performance Test Procedures

4.5 HEPA Filter Integrity Test

Item 4.5	HEPA Filter Integrity Test
Purpose:	This test verifies the integrity of the supply HEPA filter, filter housing and gel seals are in situ operating conditions.
Regulatory Requirement	USP <797>*, USP <800>*
Acceptance Criteria:	Leak rates greater than 0.01% (direct filter scan) of the up stream aerosol concentration are not acceptable. A leak rate greater than 0.01% is considered a leak (reference ISO 14644-3:2005, Annex B, B.6)
Equipment required to perform this test:	Aerosol generator and aerosol photometer

Note 1: Portions of the test methods have been adopted from IEST-RP-CC034.
Note 2: Some Isolators may be set up where access for a direct filter scan is not possible. In these cases, it is acceptable to probe the membrane that separates the chamber from the filter duct.

Test Instructions

Introduce the aerosol challenge:

1.The output of one Laskin nozzle operating at 20 PSI will be introduced into the blower inlet. Remove the plug adjacent to the pressure control HEPA (PURPLE) on the left side of the Blower. Note: this is a 3/8 inch opening.
2. PAO ug/l of air—13,500 / airflow volume cfm
3. Determine supply air volume
    A. Measure velocity 2-3 inches below diffuser (3x3 grid—nine locations—2” from edge)
    B. Q cfm = V fpm X A sq ft
        V fpm = Average of nine velocity readings
        A sq ft = (10” x 10”) / 144 sq in / sq ft

4.6 HEPA Filter Integrity Test Continued

3. Recommended Test Method – Full access for a direct scan of HEPA filter.

1. Make sure the Isolator is on. Gain access to inlet HEPA filter.
2. Using aerosol generator, add aerosol upstream of HEPA filter.

2. Setting the photometer gain:

1. Most digital aerosol photometers will only allow a maximum internal calibration of 100 ug of PAO/liter of air.
2. Set internal cal to 1/3 of challenge
3. You must now divide the leak reading size by 3

For example—a .03% photometer reading needs to be divided by 3 and therefore equals .01%

Note: Penetration is measured as a percent of the upstream aerosol challenge of cold poly dispersed PAO (Poly-alpha olefins). A forward light scattering aerosol photometer measures downstream penetration.

3. Scan 100% of the HEPA filter face or media.

Note: To assure a homogenous mixing of the aerosol to the supply airflow the PAO should be added upstream of the blower. The upstream aerosol concentrations should not vary more than +/- 15% from the average value. Upstream concentration should be verified. Consult IEST-RP-CC034 for additional information.

1. With a photometer sampling rate set at 2.5 cm (one inch) from filter face, scan the downstream filter face of the HEPA filter. The sampling rate is 1.0 CFM (1.7 meter cube per hour). Leak rate greater than 0.01% of the upstream aerosol concentration is considered a leak.
2. If applicable, repair any leaks. Record results.

5.0 Viable Sampling

Item 5.0	Identify Viable Samples Taken
Purpose:	Verify viable samples taken.

Sample Taken	Yes	No
Airborne PEC		
Airborne Area		
Surface PEC		
Finger Tip		

6.0 Smoke Test Protocol Reference

Unidirectional Airflow Smoke Test Protocol
CTG Certification Protocol --- Version 3.1 (2-5-2018)