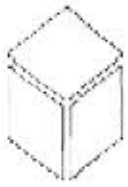

Containment Technologies Group, Inc.

Engineering Studies and Validation Protocol Summary Report:

Validation MIC – July 2014

Location: Indianapolis, Indiana

Date: August 19, 2014

Written By: Joe Robinson, QCxP, CPIP
Commissioning Agents, Inc.

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SUMMARY REPORT APPROVAL

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1. PURPOSE

1.1. The purpose of this Summary Report is to summarize the executed Engineering Studies and Validation protocol performed for the MIC family of Isolators manufactured by Containment Technologies Group in Indianapolis, Indiana. This summary report will be attached to the executed protocol.

2. REFERENCES

2.1. The documents listed below were used as references during the development and execution of the protocol.

Document Number	Title
N/A	FDA Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing 2004 Appendix 1: Aseptic Processing Isolators.

3. SYSTEM DESCRIPTION

3.1. The MIC family of isolators is designed to provide an aseptic environment in which aseptic operations can occur. The isolators are designed with a standard chamber configuration of 40" wide by 24" deep and 26" high for the single. The MIC dial has two chambers joined to provide two chambers on the same base. The MIC EDU configuration is 40" wide by 27" deep and 34" high. The MIC single and MIC dual use the same chamber configuration. They can be operated in either a positive or negative pressure environment inside the isolator.

4. EXECUTIVE SUMMARY

4.1. The Engineering Studies and Validation protocol was executed for the MIC family of Isolators manufactured by Containment Technologies Group in Indianapolis, Indiana. During the execution activities all aspects of each isolator were reviewed; including operation and documentation. No issues were noted with the actual performance of the isolators but there were two (2) items noted pertaining to chemical indicators during execution. In the first case a chemical indicator that was installed on the back wall of the isolator did not change color after being exposed to the VHP cycle in the MIC-EDU. The reason identified was incorrect installation of the chemical indicator, preventing the chemical indicator from being exposed to the VHP. Prior successful color change for that area as well as all others in the cycle substantiated the acceptance of the results. The second case was failure of a color change on all chemical indicators during the continuous VHP decontamination cycle on the MIC. The cycle was developed to achieve a four log reduction (kill) in a known population on the biological indicators (geobacillus stearothermopilis) that were used for the test. A color change on the chemical indicators is a visual indication only that there is hydrogen peroxide present in the chamber and not an actual requirement to show successful results from a scientific perspective. In light of the cycle achieving the required results for the biological indicators (a four log reduction in geobacillus stearothermopilis for all biological indicators) the results were accepted and noted as not achieving color change. Explanations for each occurrence are recorded in the appropriate tests in the protocol. There is no further testing required for the two tests.

4.2. All data collected during the execution of this protocol was evaluated and the overall conclusion is the acceptance criteria for the protocol were met.

4.3. The table below summarizes the Engineering Studies and Validation Protocol of the MIC family of Isolators.

Test Title	Acceptance Criteria for Test Met? Yes/No	Comments Provided for Test
Record of Test Equipment Used During Engineering and Validation Studies (Section 4.5)	Yes	Not Required
Glove and Sleeve Integrity Section (Section 5.5)	Yes	Not Required
Air Flow Design (Section 6.5)	Yes	Not Required
Materials of Construction (Section 7.5)	Yes	Not Required
Pressure Differential Verification (Section 8.5)	Yes	Not Required
Clean Air Classification as ISO Class 5 Verification, Dynamic Conditions (section 9.4.1.1)	Yes	Not Required
Clean Air Classification as ISO Class 5 Verification, Dynamic Conditions Room Environment (section 9.4.2)	Yes	Not Required
Chamber Pressure Verification (Section 10.5)	Yes	Not Required
Material Transfer from Decontamination Chamber to the Main Chamber, Manual Spray Chemical Indicator-Right Decontamination Chamber (Section 11.6.1)	Yes	Not Required
Material Transfer from Decontamination Chamber to the Main Chamber, Manual Spray Tri Log Indicator-Right Decontamination Chamber (Section 11.6.2)	Yes	Not Required
Material Transfer from Decontamination Chamber to the Main Chamber, Continuous VHP Decontamination-Right Chamber-Chemical Indicator (Section 11.7.3)	Yes	Minimal color change on chemical indicators in 11.7.3 (Continuous VHP)
Material Transfer from Decontamination Chamber to the Main Chamber, Continuous VHP Decontamination-Right Chamber-Tri Log Indicator (Section 11.7.4)	Yes	Not Required
Material Transfer from Decontamination Chamber to the Main Chamber, MIC-EDU-Chemical Indicator (Section 11.9.1)	Yes	1 chemical indicator failed to change color in 3rd run of 11.9.1.
Material Transfer from Decontamination Chamber to the Main Chamber, MIC-EDU-Tri Log Indicator (Section 11.9.2)	Yes	Not Required
Gas Tight Construction (Section 12.6)	Yes	Not Required

5. TESTING RESULTS

5.1. Record of Test Equipment Used During Engineering and Validation Studies

5.1.1. Objective: Critical testing and measurement equipment providing a measured value during execution shall be in a calibrated state at the time of use. The calibration must be traceable to NIST or an equivalent National Standard.

5.1.2. Results: A single instrument, a Climet CL-450t serial number 102723 was used for testing and had a current calibration that expires on March 31, 2015.

5.1.3. Conclusion: Acceptance criteria for this test were met.

5.2. Glove and Sleeve Integrity

5.2.1. Objective: To verify that gloves and sleeve are attached correctly and are not comprised by improper connection or holes in the gloves or sleeves.

5.2.2. Results: Both the right and left glove port and sleeves had no visual breach and both successfully passed an ammonia leak test.

5.2.3. Conclusion: Acceptance criteria for this test were met.

5.3. Air Flow Design

5.3.1. Objective: To verify that the air flow is moving in a single direction, in a robust and uniform manner, and at sufficient speed to reproducibly sweep particles away from the critical processing or compounding area. The airflow is from left to right when facing the isolator across the critical area. The critical area is defined as between the outer edge of the glove ports and three inches in from the front and back wall of the isolator.

5.3.2. Results: Air particulate testing showed removal of particles to less than the limits required for an ISO Class 5 environment. A smoke visualization in the form of a video were captured that show the air movement from left to right across the critical zone when facing the front of the MIC.

5.3.3. Conclusion: Acceptance criteria for this test were met.

5.4. Materials of Construction

5.4.1. Objective: Verify the materials od construction for the isolator product contact components.

5.4.2. Results: The product contact materials of the MIC isolator are 316L stainless steel as verified from material inspection certificate provided by the vendor of the material.

5.4.3. Conclusion: Acceptance criteria for this test were met.

5.5. Pressure Differential Verification

5.5.1. Objective: Verify that the MIC chamber will maintain a set level of pressure.

5.5.2. Results: The pressure was set at +0.2, +0.4, -0.2 and -0.4 inches of water column (WC) and held for five (5) minutes at each pressure. There were no fluxuations in pressure over the five minute period for each pressure.

5.5.3. Conclusion: Acceptance criteria for this test were met.

5.6. Clean Air Classification as ISO Class 5 Verification, Dynamic Conditions

5.6.1. Objective: Verify that the MIC chamber meets ISO Class 5 air quality during dynamitic operation.

5.6.2. Results: There were 2 data collection runs performed at each of three locations (probe six inches off the left wall of the isolator and 9" above the isolator floor with the probe opening facing toward the critical area, the three floor locations are: six inches, twelve inches and eighteen inches from back wall). Results obtained with the Climet particle counter are all less than the limit required for an ISO Class 5 environment and are recorded in the following table:

Test	Run 1 Count	Run 2 Count	Particle Counter Information. Name Model and Serial Number	Calibration Date
A	10	42	Climet, CL450t, SN 102723	31MAR14
B	2	7	Climet, CL450t, SN 102723	31MAR14
C	23	91	Climet, CL450t, SN 102723	31MAR14

5.6.3. Conclusion: Acceptance criteria for this test were met.

5.7. Clean Air Classification as ISO Class 5 Verification, Dynamic Conditions Room Environment

5.7.1. Objective: Verify the room environmental conditions surrounding the MIC isolator chamber where the isolator chamber is placed.

5.7.2. Results: Three separate data collection runs were performed in the room surrounding the MIC isolator chamber. These results are recorded in the table below:

Run Number	Count	Particle Counter Information. Name Model and Serial Number	Calibration Date
1	58140	Climet, CL450t, SN 102723	31MAR14
2	54127	Climet, CL450t, SN 102723	31MAR14
3	53264	Climet, CL450t, SN 102723	31MAR14

5.7.3. Conclusion: Acceptance criteria for this test were met.

5.8. Chamber Pressure Verification

5.8.1. Objective: To verify that a negative pressure is maintained in the chamber and that pressures can be varied between -0.20 inches of water column (WC) and - 0.40 inches of water column (WC). To verify that a positive pressure is maintained in the chamber and that pressures can be varied between + 0.20 inches of water column (WC) and + 0.40 inches of water column (WC).

5.8.2. Results: The results are the same as those recorded for the Pressure Differential Verification, the pressure was set at +0.2, +0.4, -0.2 and -0.4 inches of water column (WC) and held for five (5) minutes at each pressure. There were no fluxuations in pressure over the five minute period for each pressure. The table that contains the results can be viewed in section 5.6.2 above.

5.8.3. Conclusion: Acceptance criteria for this test were met.

5.9. Material Transfer from Decontamination Chamber to the Main Chamber, Manual Spray Chemical Indicator-Right Decontamination Chamber

5.9.1. Objective: To demonstrate that each level of the decontamination process performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.9.2. Results: There were three separate runs performed on the chamber using five chemical indicators in each run. All chemical indicators used changed color showing hydrogen peroxide present in the decontamination chamber.

5.9.3. Conclusion: Acceptance criteria for this test were met.

5.10. Material Transfer from Decontamination Chamber to the Main Chamber, Manual Spray Tri Log Indicator-Right Decontamination Chamber

5.10.1. Objective: To demonstrate that each level of the decontamination process performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.10.2. Results: There were three separate runs performed on the chamber using three biological indicators (tri logs containing a four log, five log and six log population of geobacillus stearothermopilis). All three runs were successful in killing the four log, five log and six log population of the geobacillus stearothermopilis. The requirement is to kill the four log population.

5.10.3. Conclusion: Acceptance criteria for this test were met.

5.11. Material Transfer from Decontamination Chamber to the Main Chamber, Continuous VHP Decontamination-Right Chamber-Chemical Indicator

5.11.1. Objective: To demonstrate that each level of the decontamination process performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.11.2. Results: There were three separate runs performed on the chamber using five chemical indicators in each run. All chemical indicators used had very little color change. The chemical indicators merely show there is a presence of hydrogen peroxide in the chamber. The fact that all four log populations of the biological indicators used (geobacillus stearothermopilis) validate the cycle is adequate. No further testing is requred..

5.11.3. Conclusion: Acceptance criteria for this test were met based on the kill of the four log population of the biological indicators (geobacillus stearothermopilis) used.

5.12. Material Transfer from Decontamination Chamber to the Main Chamber, Continuous VHP Decontamination-Right Chamber-Tri Log Indicator

5.12.1. Objective: To demonstrate that each level of the decontamination process performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.12.2. Results: There were three separate runs performed on the chamber using three biological indicators (tri logs containing a four log, five log and six log population of geobacillus stearothermopilis). All three runs were successful in killing 100% of the four log population of the geobacillus stearothermopilis. There was a 89% kill for the five log population on the first run then 100% on the following two runs. There was a 22% kill on the six log population on the first run, a 100% kill on the second run and a 78% kill on the third run.

5.12.3. Conclusion: Acceptance criteria for this test were met.

5.13. Material Transfer from Decontamination Chamber to the Main Chamber, MIC-EDU-Chemical Indicator

5.13.1. *Objective: To demonstrate that each level of the decontamination process* performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.13.2. Results: There were three separate runs performed on the chamber using six chemical indicators in each run. One chemical indicator was placed incorrectly on the back wall of the isolator on the third run causing there to be no color change. The chemical indicator was facing the wall of the isolator not allowing hydrogen peroxide to come in contact with the chemical indiicator. All other chemical indicators used during this test had color change. Prior successful color change for that area as well as all others in the cycle substantiated the acceptance of the results. No further testing is requred..

5.13.3. Conclusion: Acceptance criteria for this test were met.

5.14. Material Transfer from Decontamination Chamber to the Main Chamber, MIC-EDU-Tri Log Indicator

5.14.1. Objective: To demonstrate that each level of the decontamination process performed for use of the MIC reduces the bioburden of materials placed in the process chamber.

5.14.2. Results: There were three separate runs performed on the chamber using three biological indicators (tri logs containing a four log, five log and six log population of geobacillus stearothermopilis). All three runs were successful in killing the four log, five log and six log population of the geobacillus stearothermopilis. The requirement is to kill the four log population.

5.14.3. Conclusion: Acceptance criteria for this test were met.

5.15. Gas Tight Construction

5.15.1. Objective: The gas tight construction verification is to determine that the MIC is gas tight.

5.15.2. Results: An ammonia leak test with the isolator under positive pressure was performed. All areas checked during the testing (all door seals, panel seals, filter housing seals, blower housing, ductwork connection from blower to filter housing, window seals, glove ports and sharps/trash ports) were verified to have no leakage as noted with pH sensitive cloth. Results of the test are contained in the protocol and on a separate ammonia leak test form captured in attachment 14 to the protocol..

5.15.3. Conclusion: Acceptance criteria for this test were met.

6. COMMENTS

6.1. The following comments were recorded during the execution of the Engineering Studies and Validation protocol performed for the MIC family of Isolators.

Comment	Reference	Recommended Corrective Action	Initial/Date
1 chemical indicator failed to change color in 3rd run of 11.9.1.	N/A	None. Other chemical indicators support decision.	**
Minimal color change on chemical indicators in 11.7.3 (Continuous VHP)	N/A	Chemical indicators are indicators only. Actual 4 log reduction in section 11.7.4 supports this.	**

**Initials and date are recorded in the actual protocol.