Good Aseptic Behaviors in RABS and Isolators

Implementation of Barrier Systems – Where is the A Team?

Marsha Steed, CEO & Founder Steed MicroBio LLC www.steedmicrobio.com

INTRODUCTION

Companies are implementing barrier systems, RABS and isolators, to align with Annex 1 requirements. The implementation of a new filling line requires a cross-functional team of highly skilled staff to ensure success. Even more critical is the importance of having skilled aseptic processing operators to run the filling lines. Companies used to put in the "A team" staff when they implemented a new barrier system. In a post-covid world, the reality is that staffing in operations has been impacted and there are sometimes less "A team" operators to tackle these critical tasks. The importance of ensuring that the staff in place has adequate and thorough aseptic behaviors training is crucial for contamination control on the lines.

The FDA is issuing 483 observations related to poor aseptic behaviors. Don't be the next 483 or Warning Letter.
Ensure your manufacturing operators know the importance of proper aseptic behaviors.

ISOLATORS

GOOD ASEPTIC BEHAVIORS

FIRST AIR – Minimize Breaking First Air Over Critical Components and Sterile Isolator Parts
AVS – Have Air Visualization Studies (AVS) with good camera angles and adequate smoke coverage to visualize interventions and processing
Glove Management – Have the right sized gloves, made of the proper material for your needs. Do not over stretch to reach in the gloves
Glove Leak Testing – Perform Glove Leak Testing Pre and Post Use per Manufacturing Batch
VHP – Validate VHP Cycles with Biological Indicators. Determine Min and Max Loading Patterns for the Validations
Environmental Monitoring – Have an EM Risk Assessment (EMRA) in place for the rooms and the barrier.
Environmental Monitoring of Barrier Gloves – Monitor RABS and/or isolator gloves post processing and post critical interventions. Have a detailed SOP on proper glove sampling technique. Sample the fingertip by rolling the finger pad area on a media plate one finger at a time. Do not sample the tips.
EM Surface Samples – Ensure the proper contact plate sampling is used and ensure the media comes in contact with the gown and/or surface being sampled.
Interventions – Have an Intervention Risk Assessment (I-REM) in place to rank all interventions, including setup and EM. Involve the operators in the I-REM to ensure consistency and repeatability in how the interventions are performed. Train operators on the RA results.
Cleaning and Disinfection – Have Disinfectant Efficacy studies that match your current practice and contact times. Record contact times. Clean the isolator prior to VHP to ensure kill can be achieved.
Training – Have adequate aseptic behaviors training for new hires. Demonstrate competency before performing manipulations.
Aseptic Qualification –Operators need to perform critical tasks in Aseptic Processing Simulations (APS) prior to performing in production.
IPA – Allow 70% IPA to air dry on gloves prior to performing an intervention or touching anything with the gloves.
EM Trends – Trend data, review data, react to data in a timely manner. Identify trends. Have an Environmental Action Committee.
BFPC – Consider using Bioflourescent particle counters in your barrier system to detect and count airborne particles.
Sterile Tools – Use sterile tools and not gloved arms to breach first air (example over turntables or stopper bowls)

483 OBSERVATIONS

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established.
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the sterilization process.
Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.
Your firm failed to follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b))
Poor Aseptic Practices During the inspection of your facility, we observed poor practices and behaviors in ISO 5 areas during the manufacturing of sterile (b)(4) drug products. These poor practices included, but were not limited to: Operators blocked first air by placing their gloved hands directly over open sterilized bottles without clearing them from the aseptic filling line. Operators used their gloved hands instead of using appropriate sterile tools to remove jammed bottles. Operator movements in the critical areas were not always slow and deliberate.
Your smoke studies did not adequately demonstrate unidirectional air flow in the ISO 5 classified areas used for the aseptic filling of …

CONCLUSION

Invest in aseptic behaviors training. Have adequate risk assessments.
Validate interventions. Perform AVS. Train the trainers.
Run glass, run glass, run glass before initiating APS.

REFERENCES

MBV AG photo https://www.mbv.ch/en/microbial-air-samplers/mas-100-iso-mh/
MP Insiders Airflow Visualization Smoke Studies (AVS) in Cleanrooms photo https://gmpinsiders.com/airflow-visualization-smoke-studies-avs/
Isolator photo https://www.adcdirectory.com/products/skan-isolator-psi-l-37
www.fda.gov warning letters