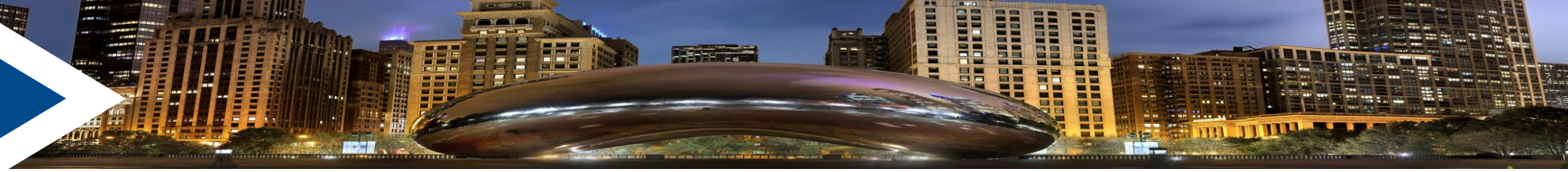

How to Design a Risk-Based EM Performance Qualification

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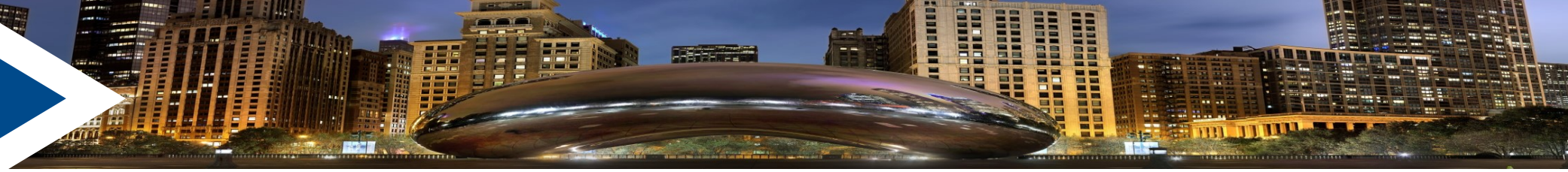
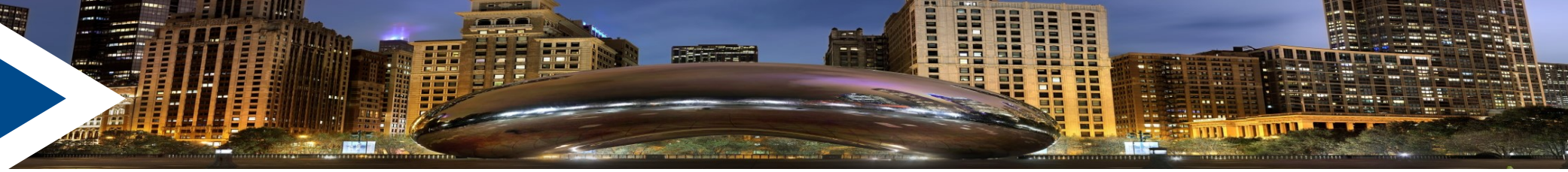


Agenda

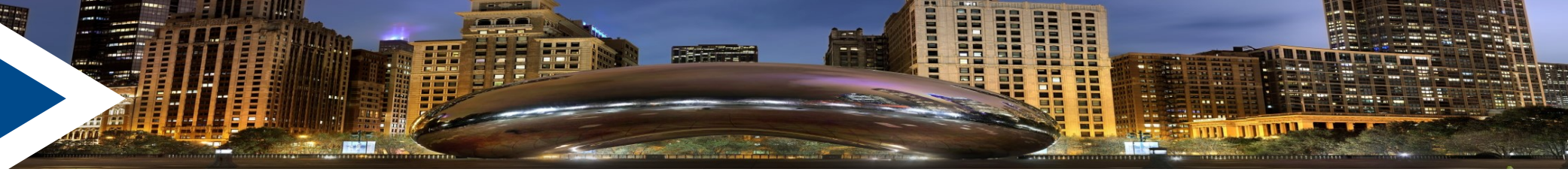
1. What is an EMPQ and why are they important?
2. When are EMPQs required?
3. General overview of the EMPQ process
4. How to gain an understanding of the cleanroom for your EMPQ
5. Introduction to performing EMPQ risk assessments
6. Overview of selecting sampling sites



What is an EMPQ?

Environmental Monitoring (EM) is the monitoring of a controlled environment to demonstrate that the area is in a state of control, to detect excursions and trends, to assess effectiveness of cleaning, and to monitor personnel. It is a critical part of a contamination control strategy.

An **EM Performance Qualification** (EMPQ) is based on Quality Risk Management principles and is used to qualify the cleanroom. It provides the risk-based justifications for the decisions made when designing your EM program and demonstrates that you're controlling contamination by monitoring the appropriate locations at the right frequency.



Why EMPQs Are Important

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

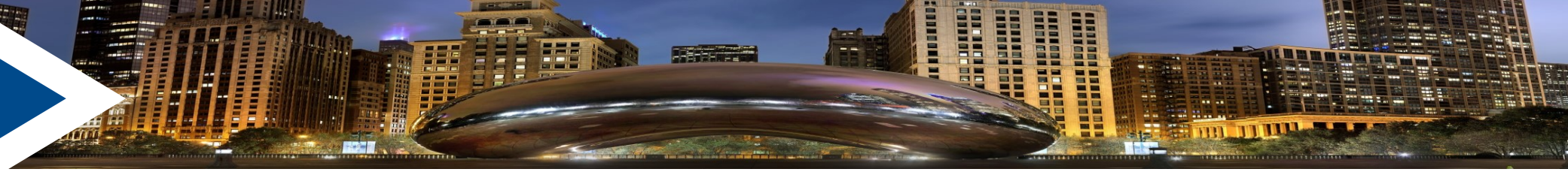
1. Environmental monitoring surface sampling conducted in the vial filling room (ISO-5) is not taken in the most critical areas where aseptic manipulations occur.

Your airborne particulate monitoring program for aseptic filling operations is not designed and conducted to provide meaningful data to support the quality of your drug products intended to be sterile. You do not monitor airborne particulates to ISO 5 air classifications in all critical locations; the frequency of airborne particulate monitoring is not adequately supported; and the orientation of particle counter probes is not directed into the flow of air in monitored locations.

Scientific justification for the position of the permanent non-viable monitors in the critical adjacent grade A areas was not provided.

(A) The firm does not routinely perform viable and nonviable environmental sampling in classified rooms or hoods during the production of drug products prepared pursuant to patient-specific prescriptions.

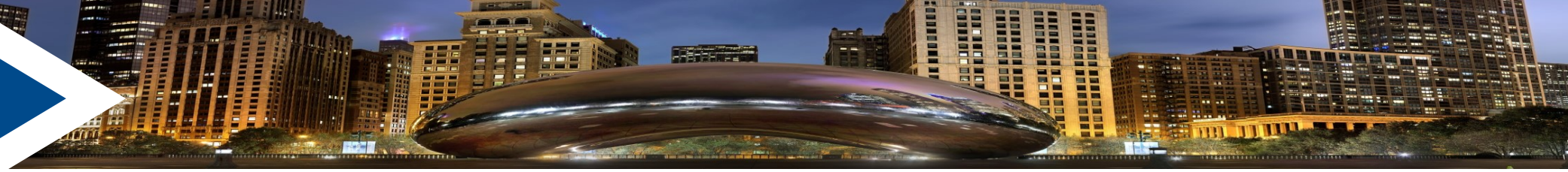
Additionally, the door handles of the cleanroom, the handles of the (b) (4) door, and the computer keyboards in the anteroom and (b) (4) room, which are frequently touched with gloved and ungloved hands during operations, are not included in the firm's environmental monitoring program without justification.



When are EMPQs Required?

EMPQs are required:

- Startup of a new facility/cleanroom suite.
- After planned/unplanned room shutdowns.
- Upcoming in Annex 1: Periodic requalification of cleanrooms.
- Requalification after modification of controlled classified areas.
  - Changes to room layout
  - Process flow changes
  - Change to room use
  - Changes in EM data trending

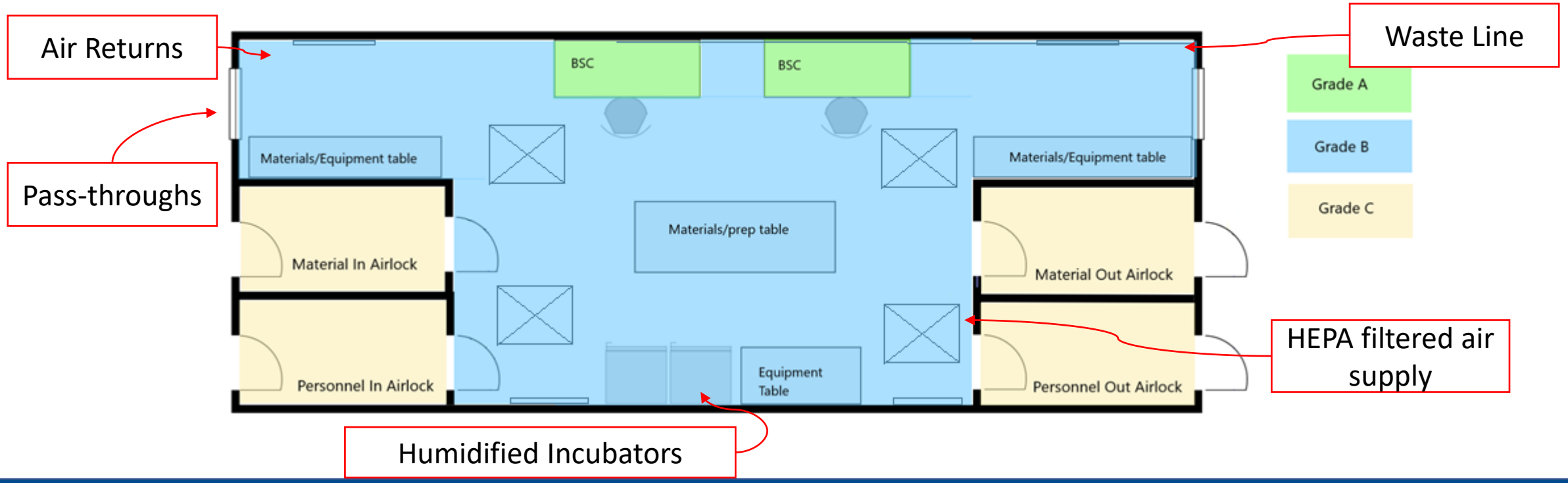


General Overview of EMPQ Process

1. Understand the Space
2. Risk assessments, sample site selections
3. Write EMPQ protocol
4. 3x cleaning, baseline sampling
5. EMPQ sampling
6. Evaluate results
7. Design routine EM program
8. Review on a regular basis

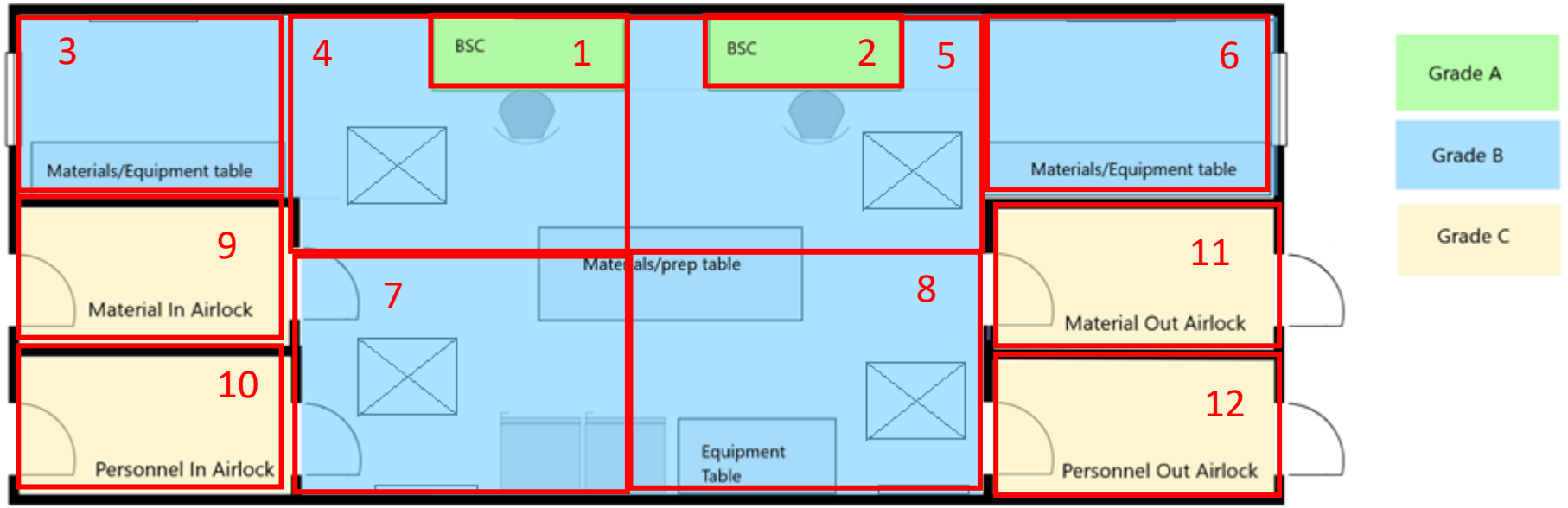
1. Gain an Understanding of the Space

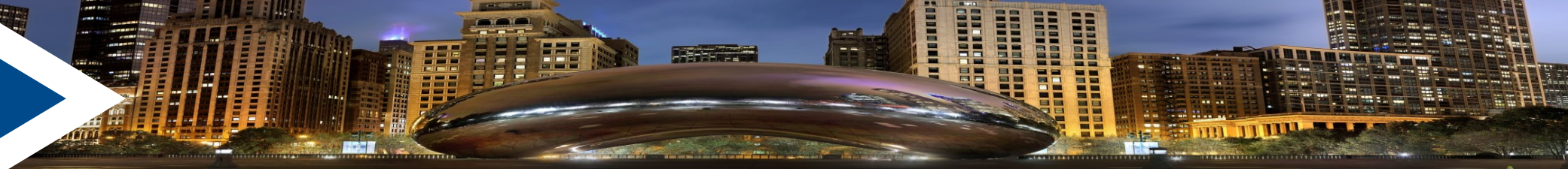
Create your risk assessment team consisting of folks from microbiology, sterility assurance, facilities and engineering, QA, manufacturing, and process engineering. You will also need a detailed map of the suite.



1. Gain an Understanding of the Space

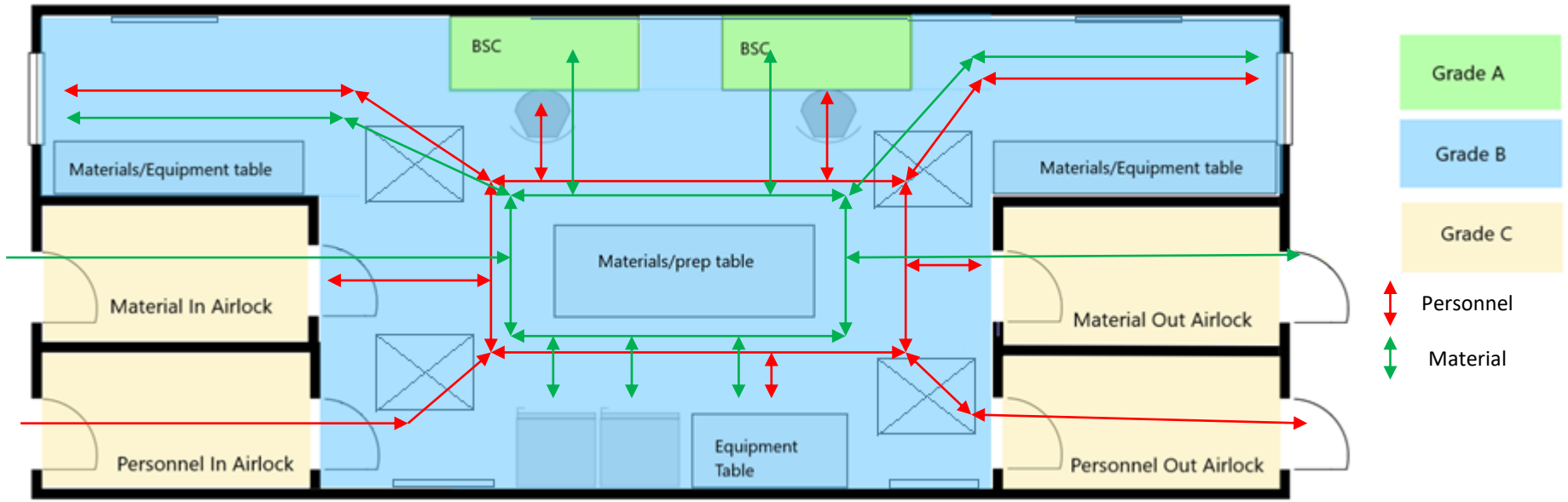
Divide the room into grids.



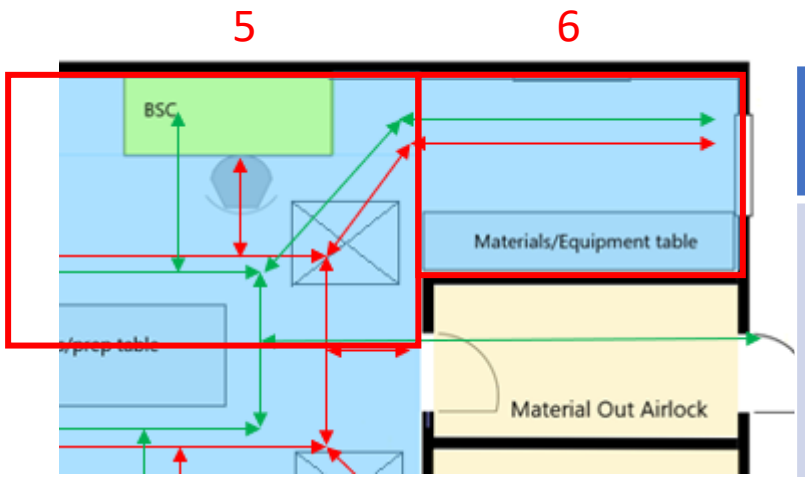


1. Gain an Understanding of the Space

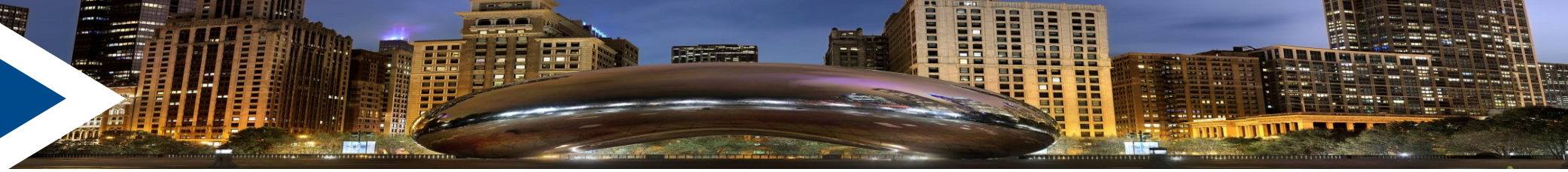
Walk the process with the team to understand personnel and material flow, what activities occur in each grid space, and what risks are in each grid space.



1. Gain an Understanding of the Space



Grid	Activities in this Grid	Potential Source of Contamination	Notes
5	Transport of materials in and out of BSC, background to Grade A BSC, within personnel and material flow, staging table	Waste line, chair wheels difficult to clean, heavy traffic / personnel presence, materials pending disinfection for BSC	HEPA unit in ceiling in this grid.
6	Transport of materials through pass-through, closed manufacturing processing, within personnel and material flow.	Waste line, personnel use of equipment, pass-through is not HEPA filtered or pressurized.	Air return in north wall.



2. Perform Your Risk Assessment(s)

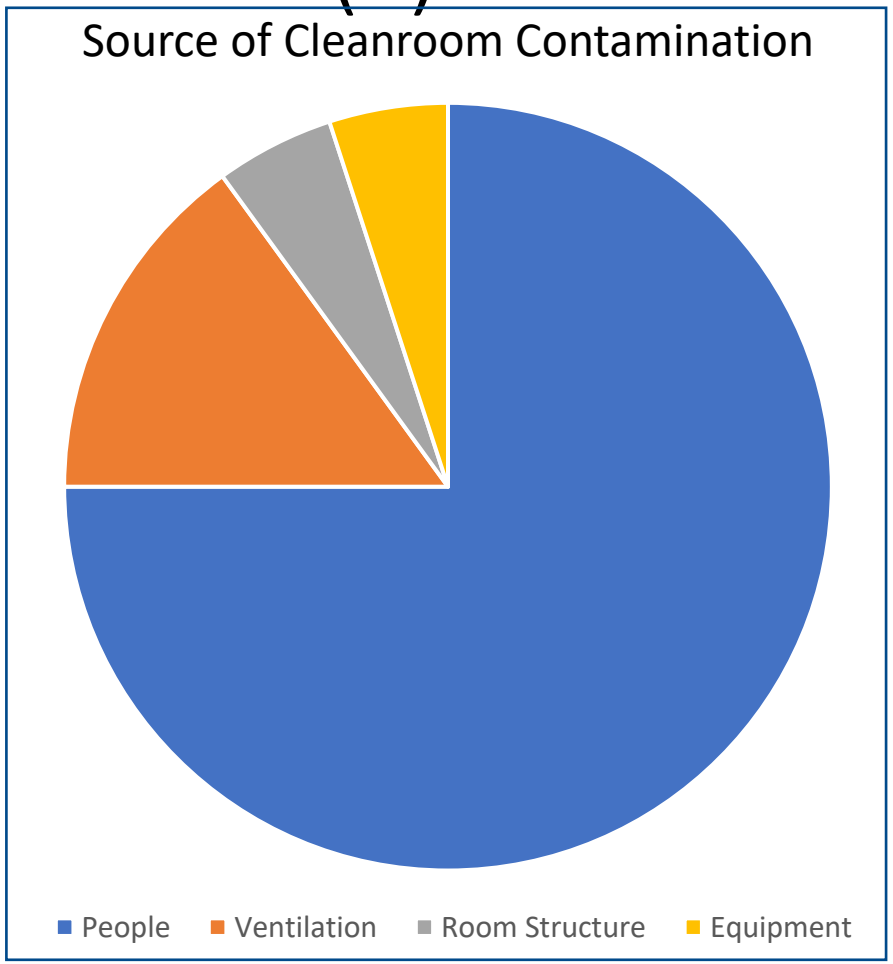
Choose your risk assessment tool. The most commonly used tools are the Failure Mode and Effects Analysis (FMEA) and the Hazard Analysis and Critical Control Points (HACCP).

FMEA	HACCP
Process-based: What within the process is vulnerable?	Hazard-based: What could impact the process from outside?
Quantitative, assigning numbers for Low/Medium/High risk and ranking the risks.	Qualitative, evaluates each risk individually.
Tool produces a list of risky grids with potentially artificial risk ratings.	Tool produces a list of risks and provides the prompt to control/mitigate the risks before monitoring each site.

2. Perform Your Risk Assessment(s)

No matter which tool you use, the recommendation is to risk-assess each grid based on these factors:

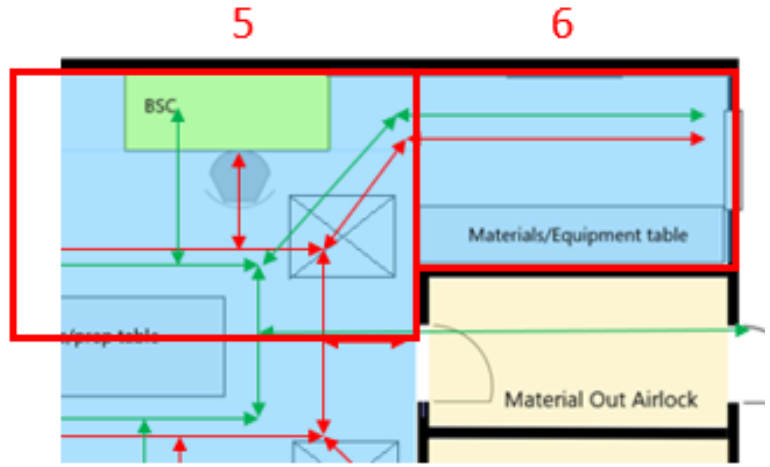
- Cleanability
- Personnel presence and flow
  - Look at need for and frequency of operations
- Material presence and flow
- Proximity to open product or open product-contact materials

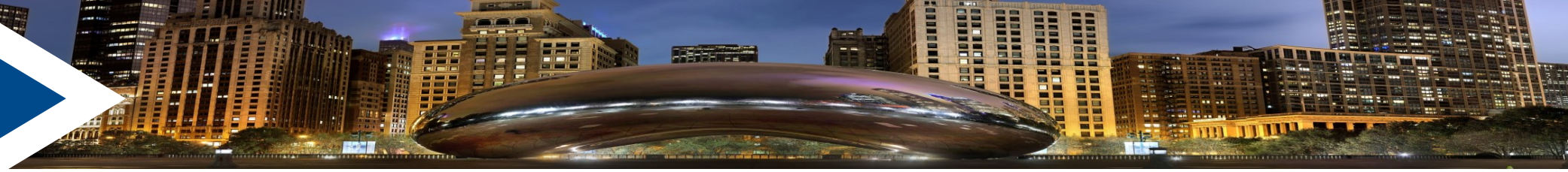


Sampling Site Selections

General Considerations

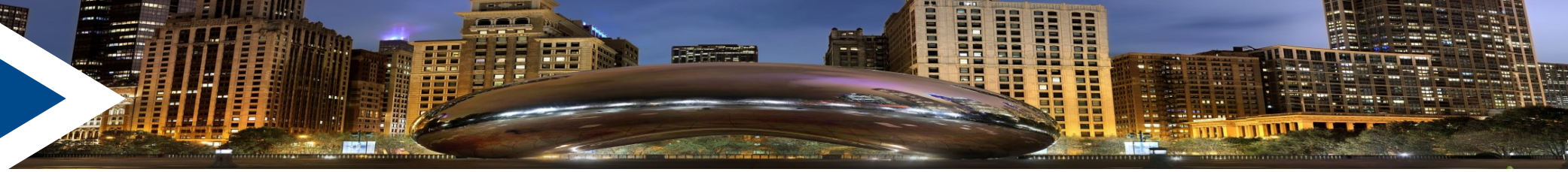
- Focus on higher-risk areas but include sites in all grids. Generally, there should be at least one sample set (viable air, total particulate, surface) within each grid.
- Focus on areas of personnel activity, areas that are difficult to disinfect, areas close to open processing.
- There are required sampling types and locations (ex. Within Grade A) in the regulations to consider.





In Conclusion…

- The entire EMPQ and subsequent design of your EM program must be risk-based, scientifically justified, and documented.
- Create a project team with knowledgeable members from all relevant departments (Microbiology, Manufacturing, Facilities, process engineering, etc)
- QA review and approval is required of both the EMPQ protocol and the final executed EMPQ.
- Don’t be scared. You are the experts on your process, and this activity provides a structured way to document what you already know.



Further References

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