Global Risk-Based Approach for Sample Location Selection in Personnel Monitoring

Hilary Chan
Global Sterility Assurance and Microbiology Lead
Takeda

Better Health, Brighter Future

Overview

- Regulatory Requirements & Expectations
- Why is Personnel Monitoring Important?
- What is the purpose of Personnel Monitoring?
- When is Personnel Monitoring Required?
- How to Determine Personnel Monitoring Sampling Locations Using Risk Assessments?
- Lifecycle Management
- Case Study

Regulatory Requirements & Expectation

EU Annex 1 Manufacture of Sterile Medicinal Products (2023)

- A **risk assessment** should evaluate the **locations, type and frequency of personnel monitoring** based on the activities performed and the proximity to critical zones.

FDA Guidance for Industry Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice (2004)

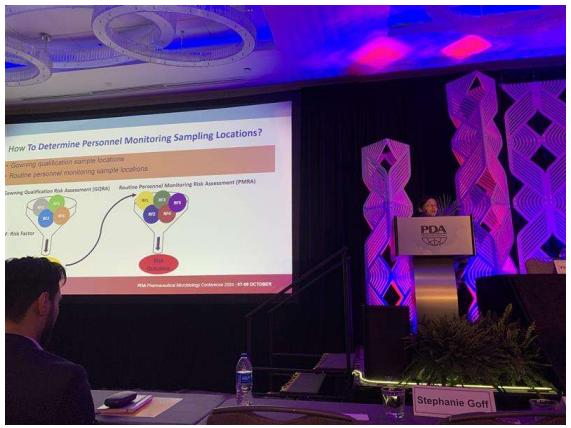
- Personnel can significantly affect the quality of the environment in which the sterile product is processed. A **vigilant and responsive personnel monitoring program** should be established.
- An aseptic gowning qualification program should assess the ability of a cleanroom operator to maintain the quality of the gown after performance of gowning procedures.

USP <1116> Microbiological Control and Monitoring of Aseptic Processing Environments

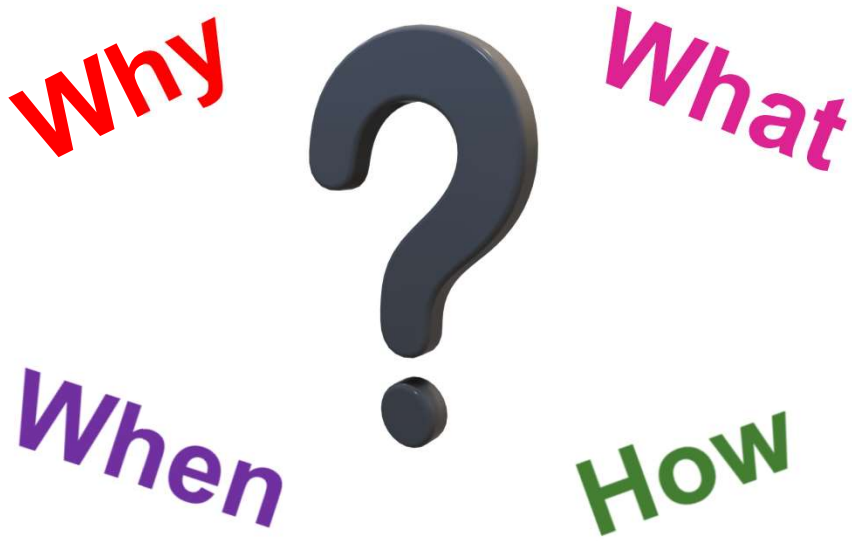
- The only significant **sources of microbial contamination** in aseptic environments are the **personnel**.
- **Good personnel performance** plays an essential role in the **control of contamination**, proper training and supervision are central to contamination control.

Using a Science- and Risk-Based Approach to Meet Regulatory Requirements

- Currently, there is no regulatory or industry guidance for determination of Personnel Monitoring and Gowning Qualification sample locations.
- Takeda has developed Personnel Monitoring/Gowning Qualification Risk Assessment (PMRA/GQRA) guidance to address this gap, which will be reviewed in this presentation.
- This approach was presented at the **2024 PDA Microbiology Conference,** during a **Biopharma Webinar**, at the **2025 Pharma Ed Aseptic Processing Summit**, all of which received positive feedback.
- We presented Takeda's approach for consideration as an industry best practice at **BioPhorum Focus Group Discussion.**



Personnel Monitoring Program



Why Is Personnel Monitoring Important?

- Personnel are the biggest source of contamination
- Personnel are the source and vector of contamination
- A robust personnel monitoring program allows us to detect contamination on the personnel


1


3


2

1. https://www.vecteezy.com/vector-art/92363-dirty-and-clean-hand-vectors
2. https://www.pharmout.net/basic-cleanroom-requirements/
3. https://covid.ri.gov/prevent/clean-air

What and When Is Personnel Monitoring Required?

- Verifies performance of personnel based on predefined parameters for microbial limits

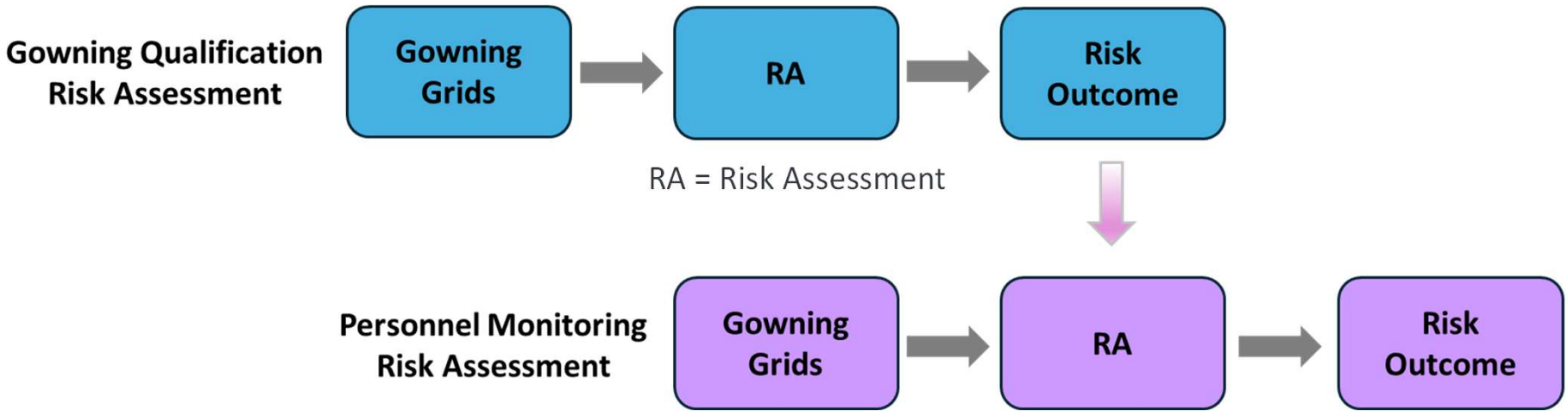
Gowning qualification

Routine operation

1. https://www.terrauniversal.com/blog/cleanroom-gowning-procedures-steps-in-order-with-instructions
2. https://www.kellertechnology.com/blog/aseptic-system-production/

Gowning Qualification and Routine Personnel Monitoring Are Separate Processes But Sequential in Operation

Gowning qualification evaluates effectiveness of personnel gowning technique



Routine personnel monitoring evaluates effectiveness of personnel aseptic behaviors during operations

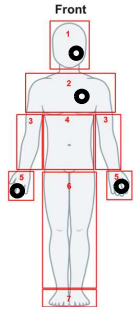
Perform the gowning qualification risk assessment first to inform subsequent routine personnel monitoring risk assessment.

Risk-Based Approach Adaptable to Low Bioburden Operations

Aseptic Operations

Gowning Grids → RA → Risk Outcome

Gowning Qualification Risk Assessment



Determination of Gowning Qualification Sample Locations

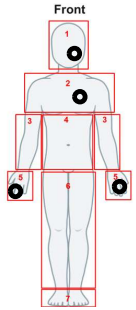
Low Bioburden Operations

Risk Outcome ← RA ← Gowning Grids

Gowning Process Risk Assessment

Gowning Grids → RA → Risk Outcome

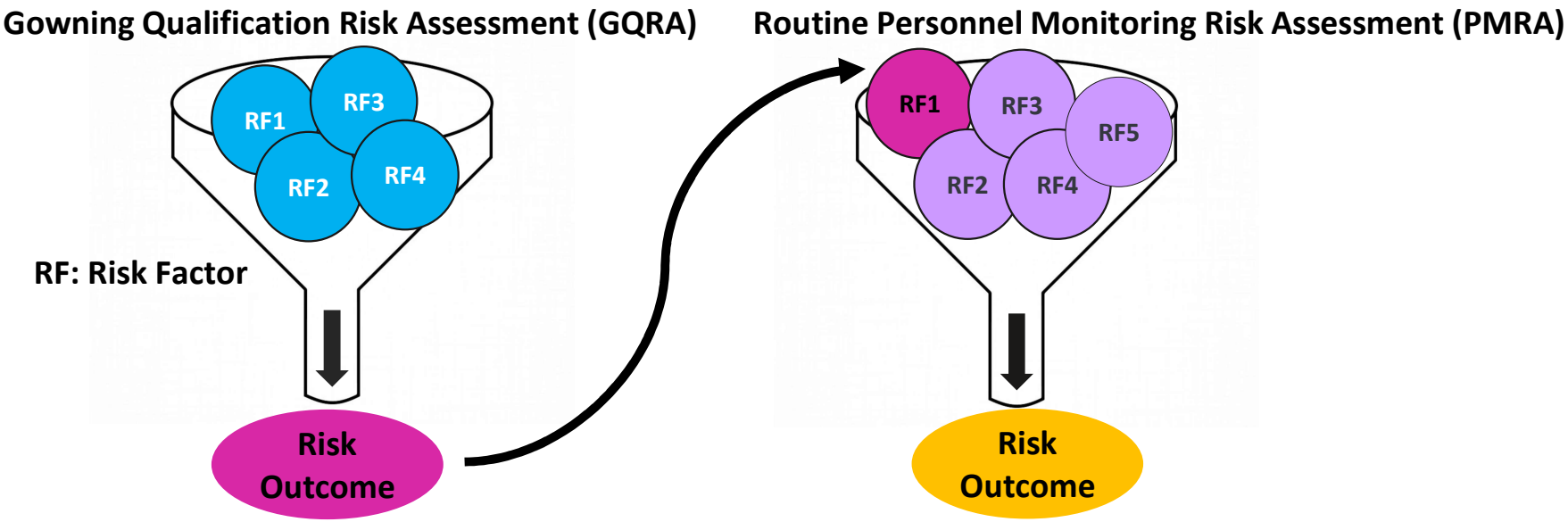
Personnel Monitoring Risk Assessment



Determination of Personnel Monitoring Sample Locations

How To Determine Personnel Monitoring Sample Locations?

- Gowning qualification sample locations
- Routine personnel monitoring sample locations



Personnel Monitoring Sample Locations – Risk-Based Approach

process

Map out the grids of a person

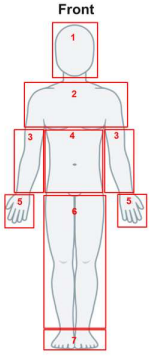
Walk through the gowning/ manufacturing process

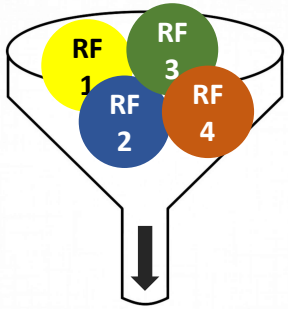
Assess each grid against risk factors

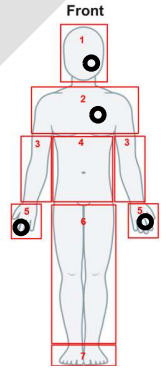
Evaluate the results and determine the sampling grids based on the overall risks

Evaluate the exact sample location for the sampling grids

Implementing sampling locations for gowning qualification and routine personnel monitoring

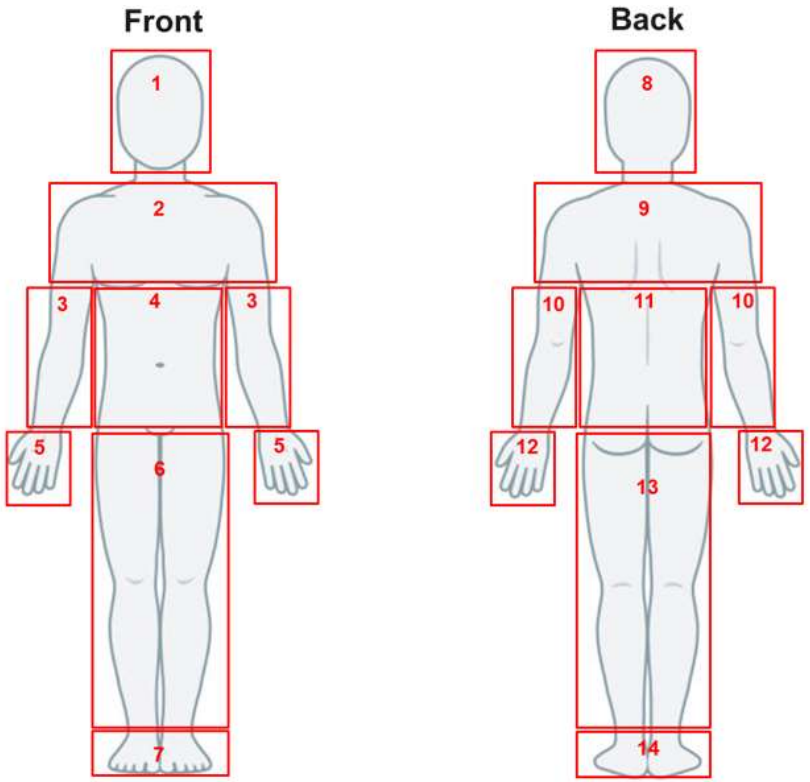






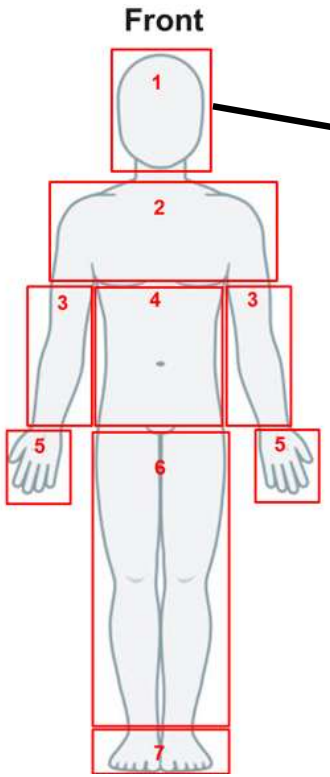
Risk Assessment Recommended Gridding

Map out the grids of a person



Risk Assessment Process Understanding

Walk through the gowning/ manufacturing process



EXAMPLE

Gowning Process Description:
Grid 1: In this grid, a sterile **hood** is donned followed by a sterile **mask overlapping** the sterile hood. The mask is **manipulated** to ensure it fully covers nose and mouth areas. Once the mask is secured, a sterile **goggle** is donned .

Gowning Qualification Risk Assessment (GQRA)

Rating	RF1 Contact with cleanroom and material surfaces (e.g., bench, gowning packaging, and door)	RF2 Frequency of direct handling of the gown within a grid	RF3 Proximity to mouth and nose areas where emission of particles can occur due to breathing and talking	RF4 Status of gown junction where two gown articles meet	Overall Risk Score
Low	1	1	1	1	1
Medium	2	2	2	2	16
High	4	4	4	4	256

RF1 x RF2 x RF3 x RF4 = Overall Risk Score

Gowning Qualification Risk Assessment (GQRA)

RF1

Rating	Contact with cleanroom and material surfaces (e.g., bench, gowning packaging, and door)
Low 1	Does not contact cleanroom or material surfaces.
Medium 2	Can make contact with cleanroom or material surfaces inadvertently.
High 4	Directly contact cleanroom or material surfaces during gowning process.


1


2

1. https://www.dupontdenemours.fr/content/dam/dupont/amer/us/en/personal-protection/public/documents/fr/EMEA-DuPont-E-Guide-Tyvek(r)_Pharma_FR_Final.pdf
2. https://www.terrauniversal.com/free-standing-clean-room-gowning-benches.html

Gowning Qualification Risk Assessment (GQRA)

RF2

Rating	Frequency of direct handling of the gown within a grid
Low 1	No direct handling
Medium 2	1 - 2 occurrences of direct handling
High 4	>2 occurrences of direct handling


1


2


3


4

1. https://www.ncbionetwork.org/course-catalog/cleanroom-gowning-concepts
2. https://x.com/AramarkUniforms/status/1444000913073573888
3. https://healthcare.contecinc.com/blog/5-best-practices-for-nonhazardous-garbing
4. https://midposi.com/how-is-proper-gowning-for-class-b-area/

Gowning Qualification Risk Assessment (GQRA)

RF3

Rating	Proximity to mouth and nose areas where emission of particles can occur due to breathing and talking.
Low 1	>60 cm (24 in) from the mouth/nose areas OR Located on the Back and does not change proximity to mouth/nose area
Medium 2	30 cm (12 in) - 60 cm (24 in) from the mouth/nose areas OR Moves to between 30 cm (12 in) - 60cm (24 in) from the mouth/nose areas
High 4	<30 cm (12 in) from the mouth/nose areas OR Moves to within < 30 cm (12 in) from the mouth/nose areas

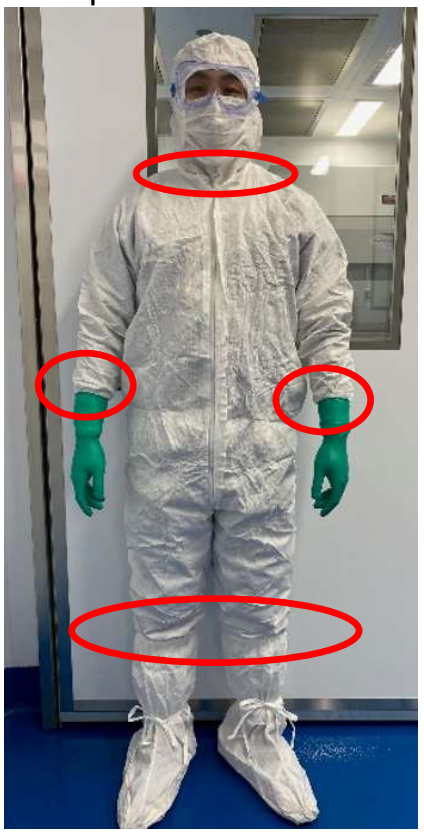
Example

Gowning Qualification Risk Assessment (GQRA)

RF4

Rating	Status of gown junction where two gown articles meet
Low 1	No junction present in the grid
Medium 2	High Overlap – boot and gown
High 4	Little overlap at the junction or no overlap - mask

Example



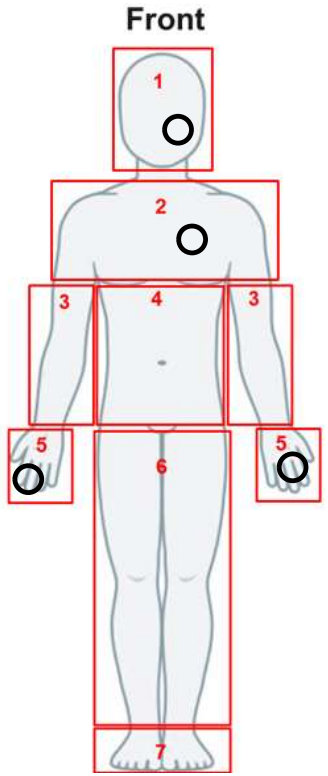
Gowning Qualification Risk Assessment – Overall Risk Scoring Evaluation

Risk Category	Possible Risk Score	Sampling Requirement
Low	1	Sampling is not required.
	2	
	4	
Medium	8	Sampling is optional.*
	16	
	32	
High	64	Sampling is required.
	128	
	256	

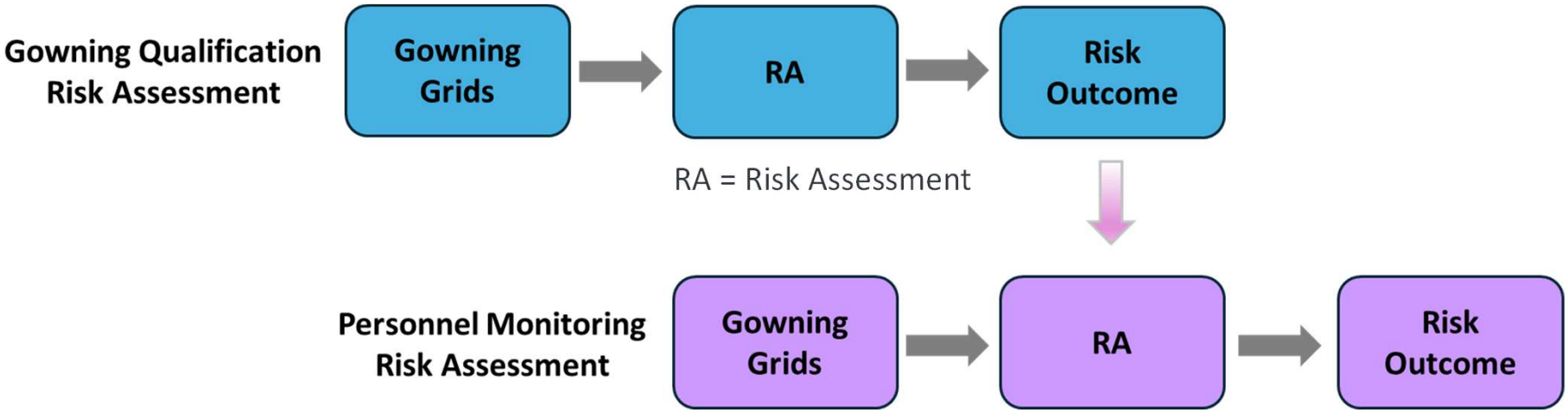
*Sampling is optional and based on process understanding and historical data, if available (e.g., existing monitoring and recoveries in that grid) and sound judgement. Samples can be collected to generate data to inform/support decision for collecting sample point.

Gowning Qualification Risk Assessment – Determining Sample Location

- Identify the specific points on the gown that are:
  - touched by the operator
  - touch cleanroom surfaces
  - closest to the mouth/nose area



Gowning Qualification and Routine Personnel Monitoring Are Separate Processes But Sequential in Operation



Routine Personnel Monitoring Risk Assessment (PMRA)

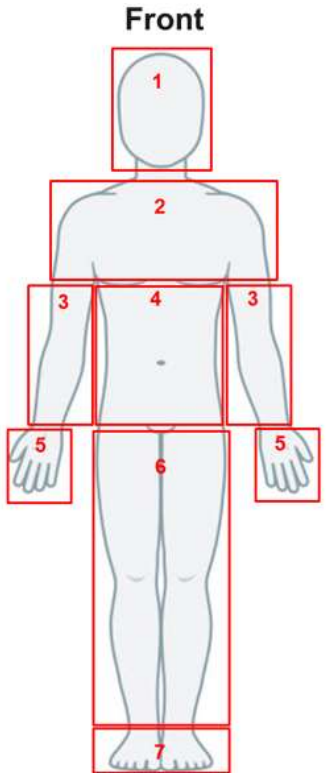
Rating	RF1 GQRA Outcome	RF2 Product / Process Proximity	RF3 Disinfection, replacement, or additional gowning can be performed as required per operational activities.	RF4 The grid is associated with direct handling of the gown while donning of new/additional gown article.	RF5 Interaction with surfaces (e.g., clean room surfaces, equipment, and material surfaces)	Overall Risk Score
Low	1	1	1	1	1	1
Medium	2	4	N/A	N/A	2	16
High	4	8	4	4	4	2084

RF1 x RF2 x RF3 x RF4 x RF5 = Overall Risk Score

Routine Personnel Monitoring Risk Assessment (PMRA)

RF1

Rating	GQRA Outcome
Low 1	Low risk
Medium 2	Medium risk
High 4	High risk



Routine Personnel Monitoring Risk Assessment (PMRA)

RF2

Rating	Product/Process Proximity
Low 1	>60 cm (24 in) OR No potential exposure to product/direct product contact material (e.g., RABS glove)
Medium 4	30 cm (12 in) - 60 cm (24 in)
High 8	<30 cm (12 in)


1


2


3

1. https://www.syntegon.com/solutions/pharma/filling-systems/
2. https://www.biopharminternational.com/view/best-practices-restricted-access-barrier-systems
3. https://www.ipsdb.com/expertise/industries/aseptic

Routine Personnel Monitoring Risk Assessment (PMRA)

RF3

Rating	Disinfection, replacement, or additional gowning can be performed as required per operational activities
Low 1	Can be disinfected, and disinfection is performed at some frequency OR Can be replaced as necessary (e.g., gloves). OR New/additional gowning article is donned prior to critical activity (e.g., sterile sleeves).
Medium 2	N/A
High 4	Cannot be disinfected or replaced (e.g., coverall). No new/additional gowning article is donned prior to critical activities.


1


2

1. https://www.sterislifesciences.ie/cleanroom-sleeves-and-armcovers
2. https://www.cleanroomsupplies.com/p/kimberly-clark-kimtech-g3-sterile-nitrile-gloves/

Routine Personnel Monitoring Risk Assessment (PMRA)

RF4

Rating	The grid is associated with direct handling of the gown while donning of new/additional gown article.
Low 1	No direct handling of the gown article occurs in this grid.
Medium 2	N/A
High 4	directly handled during donning of new/additional gown articles

1. https://www.sterislifesciences.ie/cleanroom-sleeves-and-armcovers
2. https://www.cleanroomsupplies.com/p/kimberly-clark-kimtech-g3-sterile-nitrile-gloves/

Routine Personnel Monitoring Risk Assessment (PMRA)

RF5

Rating	Interaction with surfaces (e.g., clean room surfaces, equipment, and material surfaces)
Low 1	Does not contact equipment or material (e.g., mask)
Medium 2	May make contact with equipment and/or material on occasion (e.g., forearm)
High 4	Directly contact equipment and/or material (e.g., gloves directly contacts equipment or material during handling)

1. https://www.syntegon.com/solutions/pharma/filling-systems/
2. https://www.biopharminternational.com/view/best-practices-restricted-access-barrier-systems
3. https://www.ipsdb.com/expertise/industries/aseptic

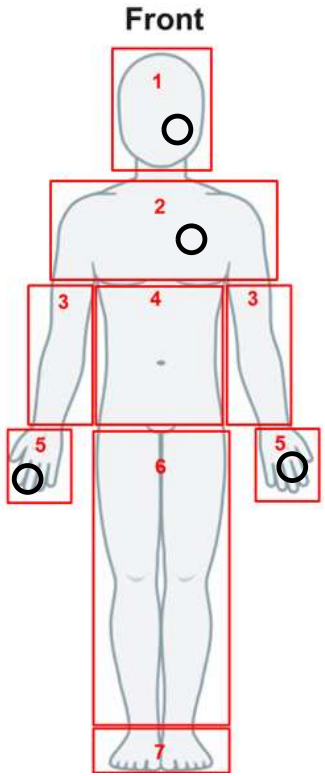
Routine Personnel Monitoring Risk Assessment – Overall Risk Scoring Evaluation

Risk Category	Possible Risk Scores		Sampling Requirement
Low	1	2	Sampling is not required.
	4	8	
Medium	16	32	Sampling is optional.*
	64	128	
High	256	512	Sampling is required.
	1024	2048	

*Sampling is optional and based on process understanding and historical data, if available (e.g., existing monitoring and recoveries in that grid) and sound judgement. Samples can be collected to generate data to inform/support decision for collecting sample point.

Routine Personnel Monitoring Risk Assessment – Determining Sample Locations

- Identify the specific point(s) within the grid that:
  - Contact surfaces
  - Are closest to the product/product contact surfaces
- Task specific considerations
  - Grade A operations – review of airflow visualization study
  - Grade B operations – sample points that are used to touch/transfer materials that support Grade A operations



Lifecycle Management

Periodic Review	Change Driven Re-Assessment
• Minimally at least every 3 years	• New or additional gowning garments • Changes to the gowning airlocks or process • Changes to the cleanroom/equipment or manufacturing process

Case Study: Gowning Qualification and Routine Personnel Monitoring Risk Assessment in Cell Therapy Manufacturing Facility

Manufacturing Facility for clinical phase allogeneic cell therapy products

Open aseptic process conducted in a Grade A Biosafety Cabinet with a Grade B background

Pre-existing gowning qualification and routine personnel monitoring program. Assessment performed to meet Annex I requirement.

Case Study: Points to Consider

Case Study: Gowning Qualification Risk Assessment

Grid #	Sample Description	Contact with cleanroom and material surfaces	Frequency of direct handling of	Proximity to mouth and nose areas	Status of gown junction where two gown articles meet	Overall Risk Score	GQ Sampling Grid
1	Front Head Area	1	4	4	4	64	s
2	Chest Area	1	4	4	4	64	s
3	Front Forearm Area	1	2	4	2	16	s
4	Abdomen Area	1	4	2	1	8	
5	Front Hand Area	4	4	4	1	64	s
6	Front Leg Area	1	2	4	2	16	s
7	Front Foot Area	2	2	1	1	4	
8	Back Head Area	1	4	2	4	32	s
9	Upper Back Area	1	2	1	4	8	
10	Back Forearm Area	1	2	2	2	8	
11	Lower Back Area	1	1	1	1	1	
12	Back Hand Area	1	1	2	1	2	
13	Back Leg Area	1	1	1	2	2	
14	Back Foot Area	2	1	1	1	2	

S = Sample

Example

Case Study: Routine Personnel Monitoring Risk Assessment – Grade A Operator

Grid #	Sample Description	GQRA Outcome	Product/ Process Proximity	Operational disinfection, replacement, or additional gowning	Interaction with surfaces	Direct handling of the gown while donning of new/additional gown article	Overall Risk Score	Routine Sampling Grid
1	Front Head Area	4	1	4	1	1	16	
2	Chest Area	4	1	4	1	1	16	
3	Front Forearm Area	2	8	1	4	4	256	S
4	Abdomen Area	2	1	4	1	1	8	
5	Front Hand Area	4	8	1	4	4	512	S
6	Front Leg Area	2	1	4	1	1	8	
7	Front Foot Area	1	1	4	1	1	4	
8	Back Head Area	2	1	4	1	1	8	
9	Upper Back Area	2	1	4	1	1	8	
10	Back Forearm Area	2	8	1	2	4	128	
11	Lower Back Area	1	1	4	1	1	4	
12	Back Hand Area	1	8	1	2	4	64	
13	Back Leg Area	1	1	4	1	1	4	
14	Back Foot Area	1	1	4	1	1	4	

Example

*not shown - additional sterile sleeve and gloves

Case Study: Routine Personnel Monitoring Risk Assessment – Grade B Operator

Grid #	Sample Description	GQRA Outcome	Product/ Process Proximity	Operational disinfection, replacement, or additional gowning	Interaction with surfaces	Direct handling of the gown while donning of new/additional gown article	Overall Risk Score	Routine Sampling Grid
1	Front Head Area	4	1	4	1	1	16	
2	Chest Area	4	1	4	1	1	16	
3	Front Forearm Area	2	4	1	4	4	128	S
4	Abdomen Area	2	1	4	2	1	16	
5	Front Hand Area	4	4	1	4	4	256	S
6	Front Leg Area	2	1	4	1	1	8	
7	Front Foot Area	1	1	4	1	1	4	
8	Back Head Area	2	1	4	1	1	8	
9	Upper Back Area	2	1	4	1	1	8	
10	Back Forearm Area	2	4	1	2	4	64	
11	Lower Back Area	1	1	4	1	1	4	
12	Back Hand Area	1	4	1	2	4	32	
13	Back Leg Area	1	1	4	1	1	4	
14	Back Foot Area	1	1	4	1	1	4	

Example

Acknowledgement

- **Takeda Global Sterility Assurance and Microbiology (GSAM)**
  - Christina Oberhuber
  - Alberto Gonzales
  - **Anna Campanella**
  - Christine Sherman
  - Liz Brockson
  - **Luyen Nguyen**
- **Takeda Pilot Site**
  - Anusuya Hazarika
  - Crystal Blake

Thank You!

Questions?

Better Health, Brighter Future

©2025 Takeda Pharmaceutical Company Limited. All right reserved.