Session 7:

Updated EU GMP Annex 1 Guidelines: Current Expectations

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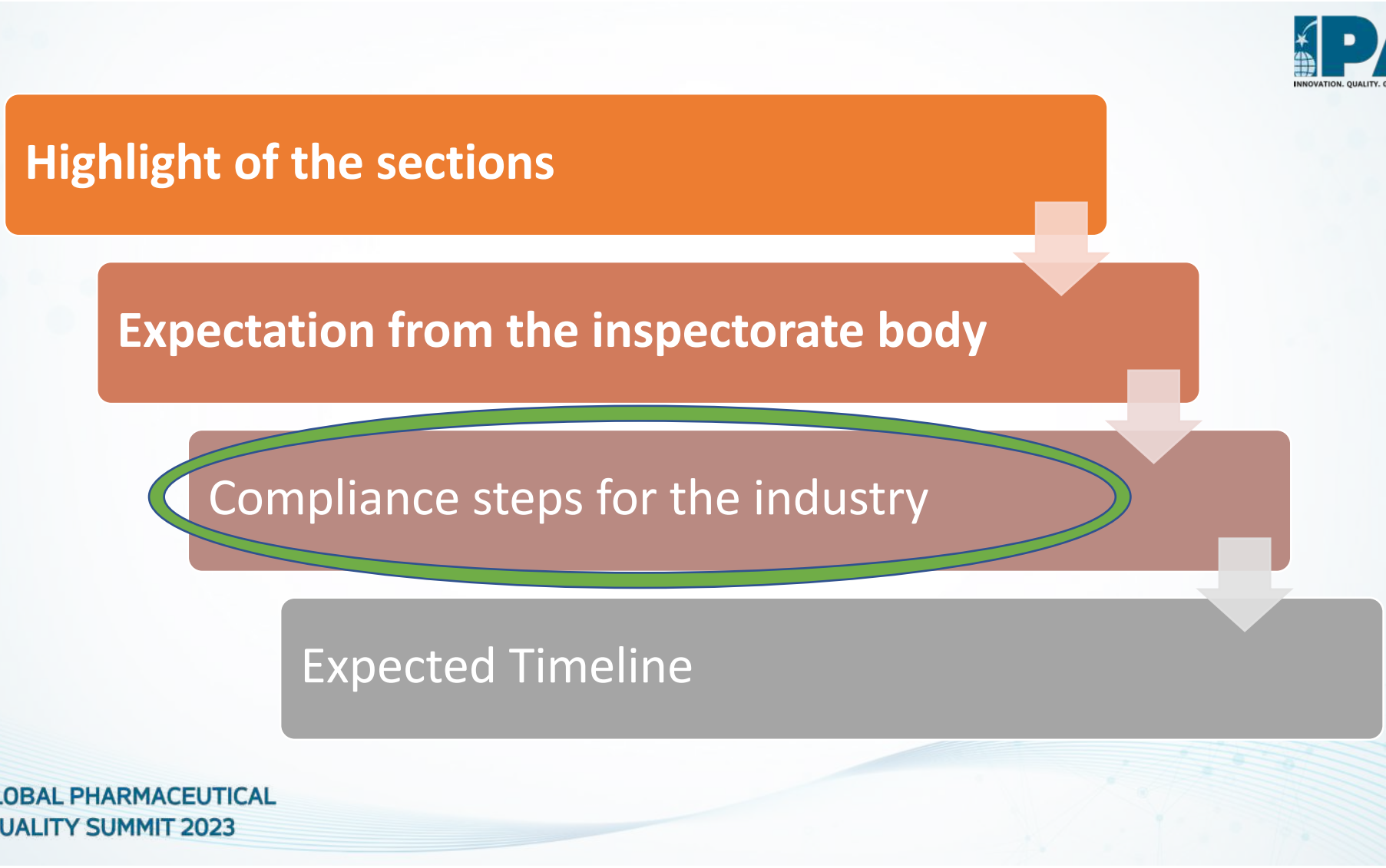
Annex 1

Select Shop-floor activities

(The Expectations from the Inspectorate Authorities)

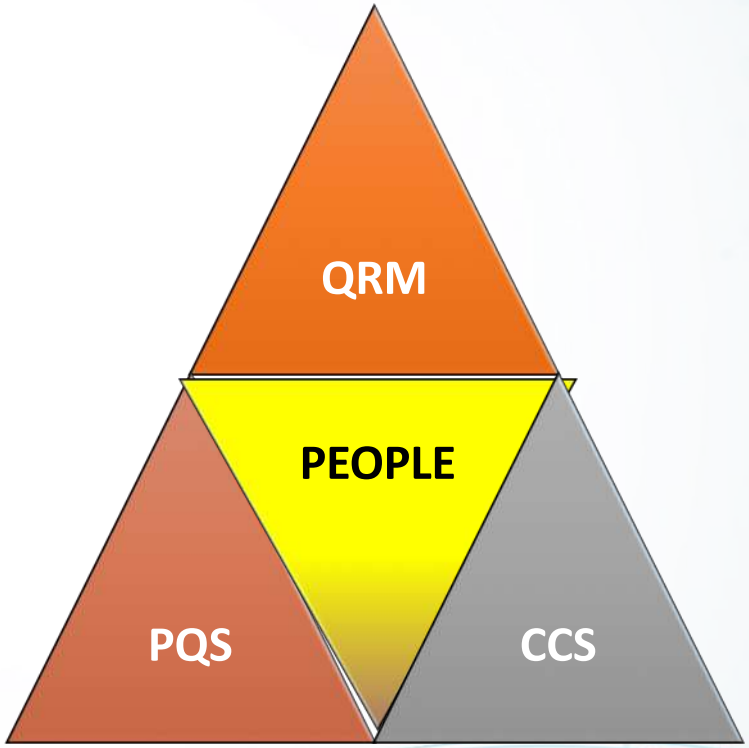
The Options/Opportunities for the practicing professionals


Highlight of the sections
Expectation from the inspectorate body
Compliance steps for the industry
Expected Timeline

The Central SUBJECT

EU Annex 1 – 2008	
Contamination	32
Control	11
Strategy	0
Contamination Control Strategy	0

EU Annex 1 – 2022	
Contamination	115
Control	111
Strategy	5
Contamination Control Strategy	54



From PDA Tech Report 90

Examples of Metrics to be assessed during periodic review

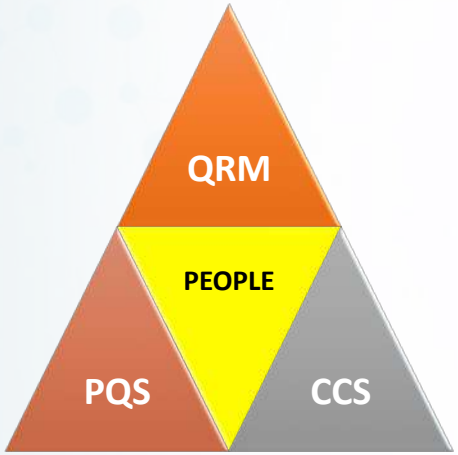
Predictive Metrics	Reactive Metrics
KPI's related to Quality Culture	Facility nonconformance related to controls within CCS (e.g., EM deviations)
Capital reinvestment focused contamination control including new control and measurement technologies	Process nonconformance related to controls within the CCS (e.g., DS or raw material pyrogen/endotoxin levels)
Mitigation of contamination control risks uncovered through QRM activities	Product nonconformance related to controls within the CCS (e.g., Sterility test failure)
CAPA effectiveness and on-time implementation	Process capability and machine performance
Conformance to schedule for planned contamination control qualifications and validations	EM trending across the site and deviations', root causes analysis, risk assessments and mitigations in response to adverse trends
Conformance to schedule for planned contamination control risk assessments	Other deviations associated with contamination control including but not limited to control failures, training gaps, faulty knowledge transfer
Conformance to schedule for maintenance activities related to the CCS	Unplanned/corrective maintenance

CCS: Personnel (From Dr. Thomas Hecker's presentation)

CCS: Personnel (From TR 90)

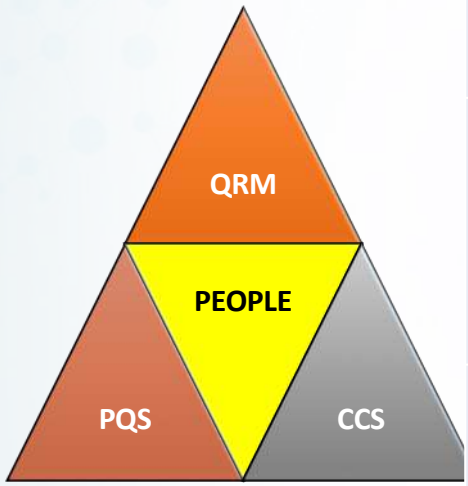
Personnel Roles & Responsibilities related to CCS
Leadership Roles
Makes contamination prevention a priority
Advocates and practices non-blaming culture
Assigns personnel with appropriate knowledge and mindset
Understands the benefit of contamination prevention
Expert Role Sterility Assurance/Contamination Control (Governance)
Oversees the performance of contamination controls
Escalates contamination hazards
Provides technical leadership to continuously improve
Shop floor Operators/Technician Role
Performs contamination control and acts as guardians
Escalates contamination hazards
Provides technical expertise on individual CCS elements

Personnel
& THE CENTRAL DOGMA



Personnel and references	
Section	Details
2.1(ii)	Personnel should have **adequate qualifications** and **experience**, **training** and **behaviour** with a specific focus on the **principles** involved in the **protection** of sterile product during the **manufacturing, packaging and distribution** processes.
2.1(iii)	Processes and monitoring systems for sterile product manufacture should be **designed, commissioned, qualified, monitored and regularly reviewed** by personnel with appropriate **process, engineering and microbiological** knowledge.
5.3	As far as practicable, equipment, fittings and services should be designed and installed so that operations, maintenance, and repairs can be performed outside the cleanroom. If maintenance has to be performed in the cleanroom, and the required standards of cleanliness and/or asepsis **cannot** be maintained, then precautions such as restricting access to the work area to **specified personnel**, generation of clearly defined work protocols and maintenance procedures should be considered. Additional cleaning, disinfection and environmental monitoring should also be considered. If sterilisation of equipment is required, it should be carried out, wherever possible, after complete reassembly.

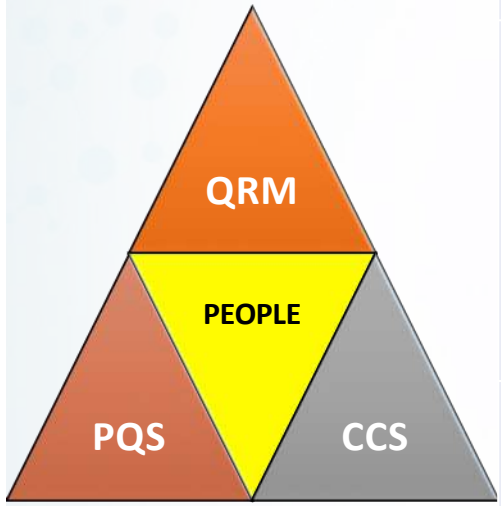
Personnel
& THE CENTRAL dogma



Personnel and references

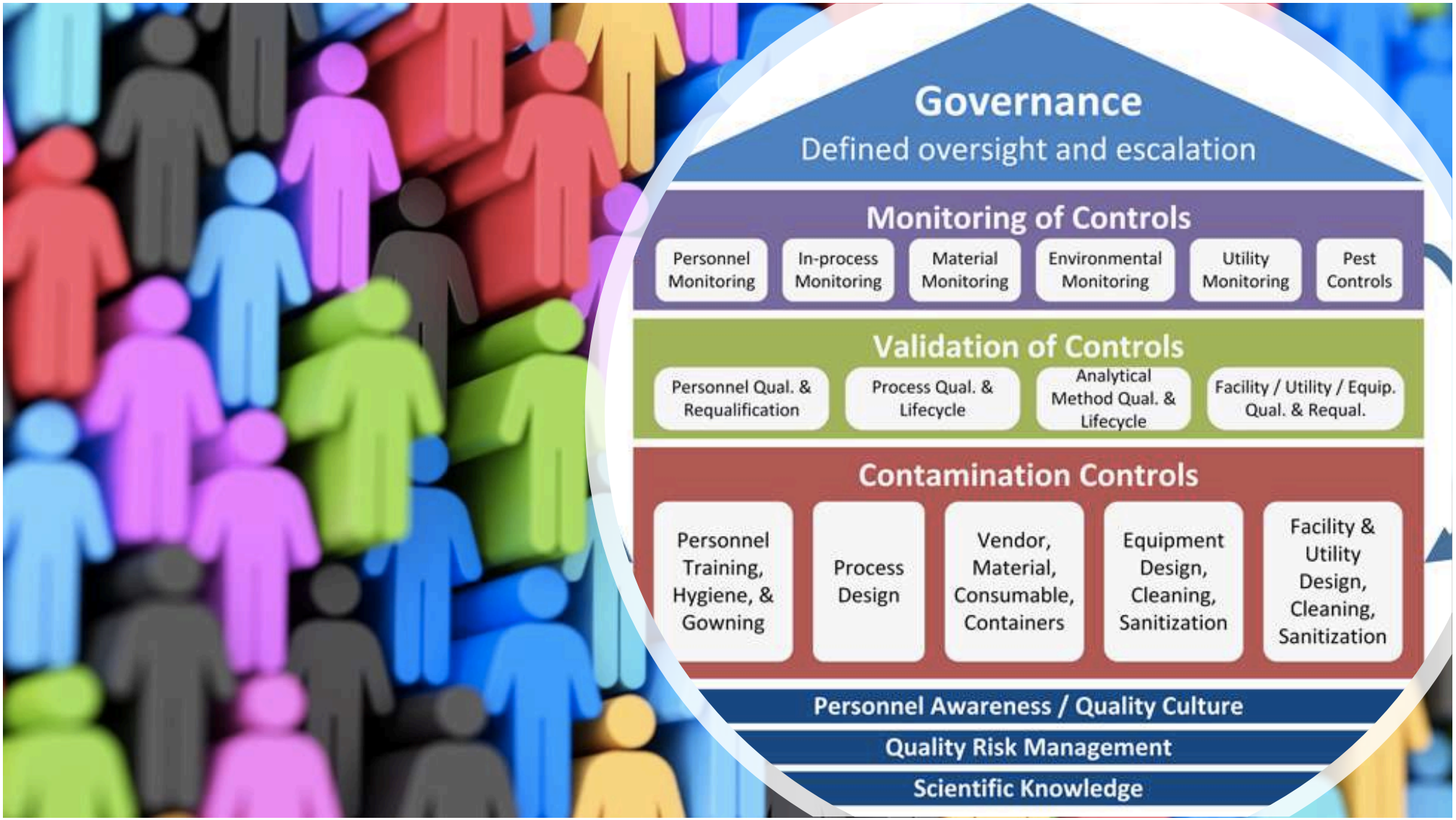
Section	Details
	Section 7: Exclusive - Personnel
7.1	The manufacturer should ensure that there are **sufficient appropriate personnel**, suitably **qualified, trained** and **experienced** in the **manufacture and testing** of sterile products, and any of the specific manufacturing technologies used in the site's manufacturing operations, to ensure compliance with GMP applicable to the **manufacture and handling** of sterile products.
7.3	All personnel including those performing cleaning, maintenance, monitoring and those that access cleanrooms should receive **regular training**, gowning qualification and assessment in disciplines relevant to the correct manufacture of sterile products. This training should include the basic elements of microbiology and hygiene, with a specific focus on cleanroom practices, contamination control, aseptic techniques and the protection of sterile products (for those operators entering the grade B cleanrooms and/or intervening into grade A) and the potential safety implications to the patient if the product is not sterile. The **level of training** should be based on the **criticality of the function** and area in which the personnel are working.
7.4	The personnel accessing grade A and B areas should be trained for aseptic gowning and aseptic behaviours. **Compliance with aseptic gowning procedures** should be confirmed by assessment and periodic reassessment at least annually, and should involve both visual and microbial assessment (using monitoring locations such as gloved fingers, forearms, chest and hood (facemask / forehead). The unsupervised access to the grade A and grade B areas where aseptic operations are or will be conducted should be restricted to **appropriately qualified personnel**, who have passed the gowning assessment and have participated in a successful APS.
7.7	High standards of personal hygiene and cleanliness are essential to prevent excessive shedding or increased risk of introduction of microbial contamination. Personnel involved in the manufacture of sterile products should be instructed to report any specific health conditions or ailments that may cause the shedding of abnormal numbers or types of contaminants and therefore preclude cleanroom access. Health conditions and actions to be taken with regard to personnel who could be introducing an undue microbial hazard should be provided by the **designated competent person and described in procedures**.

Personnel
& THE CENTRAL dogma



Personnel and references

Section	Details
8.19	Aseptic operations (including APS) should be **observed** on a regular basis by **personnel** with **specific expertise** in aseptic processing to **verify** the correct performance of operations including **operator behaviour** in the cleanroom and address **inappropriate** practices if detected.
10.1	There should be **personnel** available with **appropriate training** and **experience** in **microbiology, sterility assurance** and **knowledge** of the processes to support the **design** of the manufacturing activities, **environmental monitoring regime** and any **investigation assessing** the **impact** of **microbiologically linked** events to the safety of the sterile product.


Governance
Defined oversight and escalation
Monitoring of Controls
Personnel Monitoring
In-process Monitoring
Material Monitoring
Environmental Monitoring
Utility Monitoring
Pest Controls
Validation of Controls
Personnel Qual. & Requalification
Process Qual. & Lifecycle
Analytical Method Qual. & Lifecycle
Facility / Utility / Equip. Qual. & Requal.
Contamination Controls
Personnel Training, Hygiene, & Gowning
Process Design
Vendor, Material, Consumable, Containers
Equipment Design, Cleaning, Sanitization
Facility & Utility Design, Cleaning, Sanitization
Personnel Awareness / Quality Culture
Quality Risk Management
Scientific Knowledge

Contamination control strategy:

- An **integrated** set of controls, planned actions, and conditions that are designed to limit product contamination to defined criteria. The strategy is designed to **assure process performance** and **product quality**.

The **UNTOLD** need for Altering **K&S** of **PEOPLE** manning activities - Sterile

Contamination Control Strategy Development in Pharmaceutical Manufacturing

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