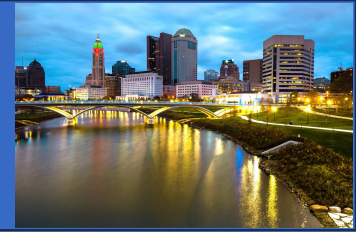
2024 Ohio Event –
Essentials of Contamination Control Strategies



Essentials of Contamination Control Strategies in ATMPs

Frederic B. Ayers
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ValSource, Inc.
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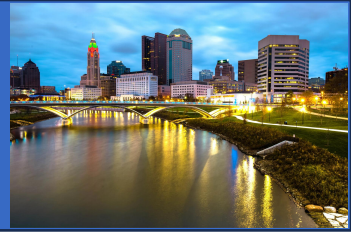


Agenda

PDA Technical Report No. 90

Build It

Foundation

Contamination Controls

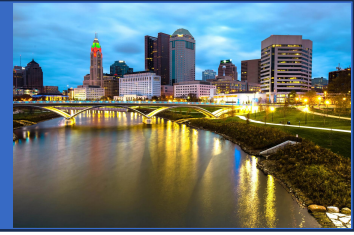
Validation Controls

Monitoring Controls

Governance

Feedback Loops

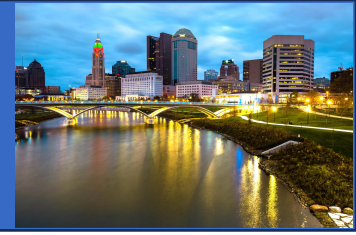
ATMP Specifics

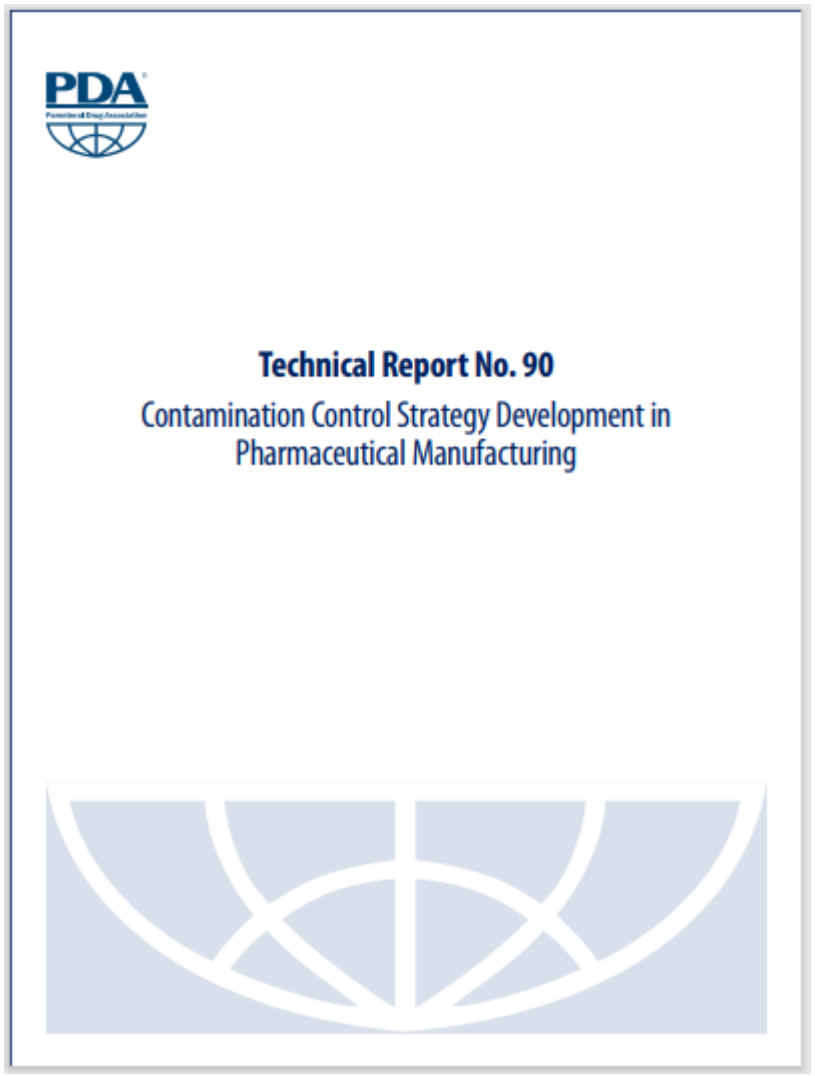


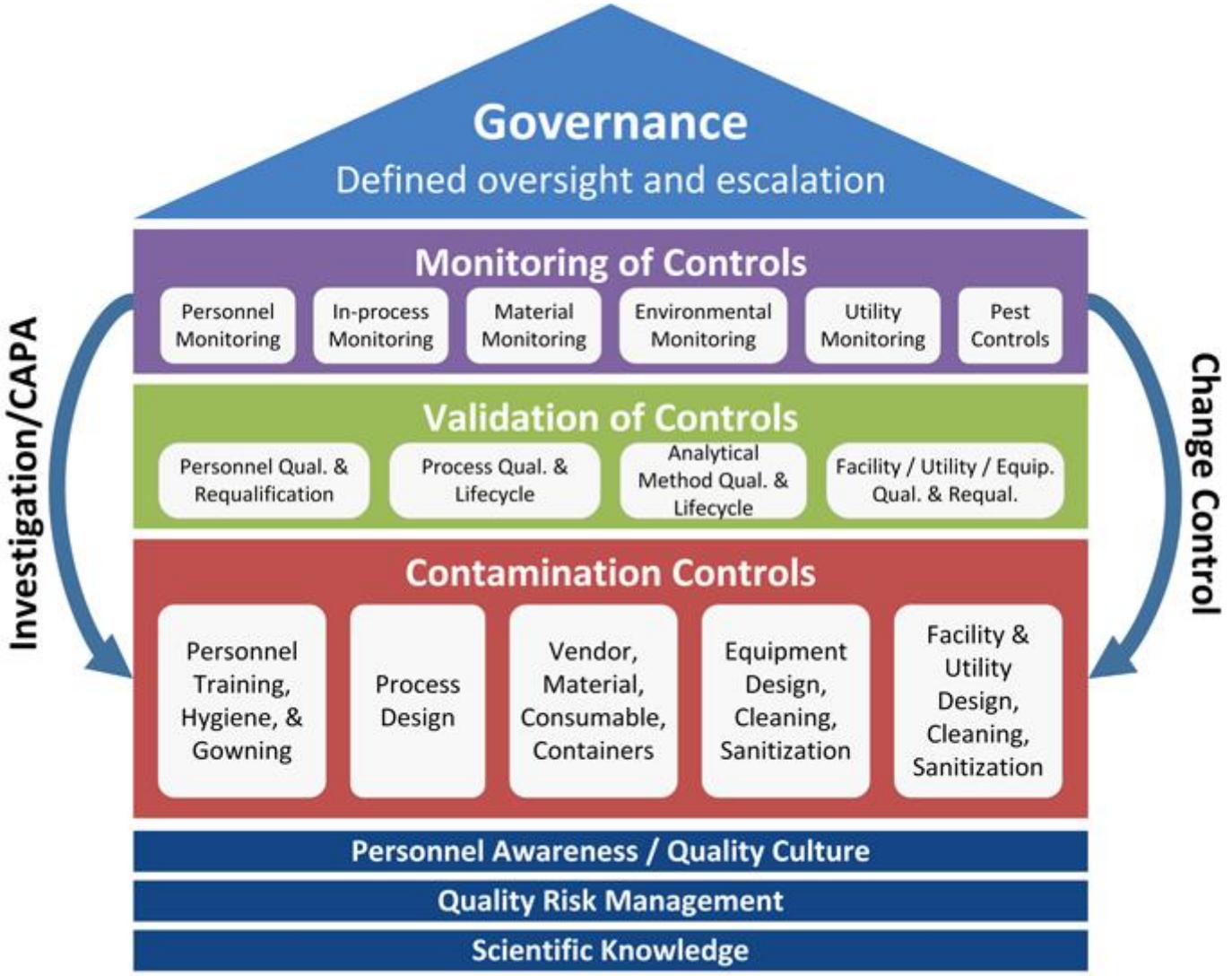
Contamination Control Strategy – PDA Technical Report No. 90

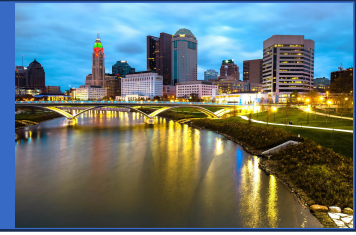
2024 Ohio Event – Essentials of Contamination Control Strategies

September 18th

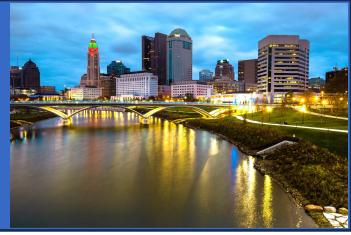








- Holistic vs. Non-holistic examples (throughout)
- List of process & technical information needed to inform CCS (section 3.0)
- Current expectations for in-process monitoring limits of biologics (section 4.0)
- Table of Container Closure Integrity considerations (section 10.0)
- Roadmap to relevant Industry Guidance Docs (section 14.0)



Contamination Control Strategy – Build It

Build an interdisciplinary Team

Identify a CCS Lead

Must be truly cross-functional

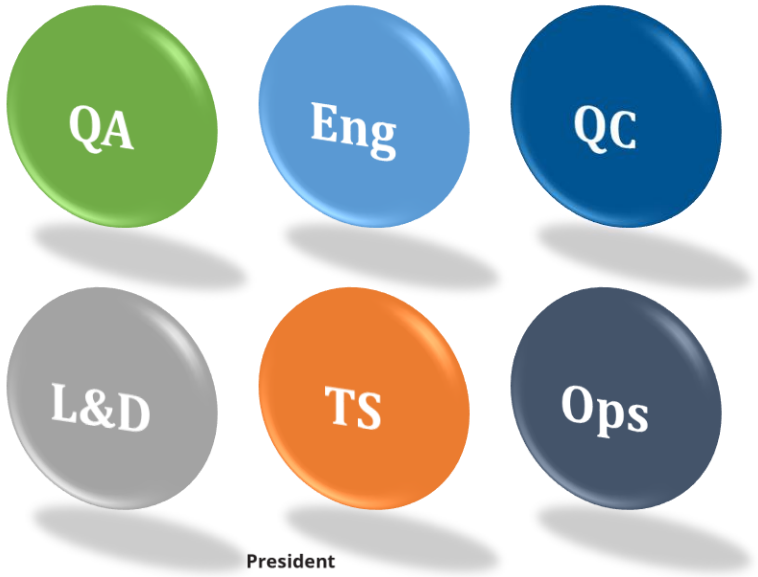
Multiple levels of the organization

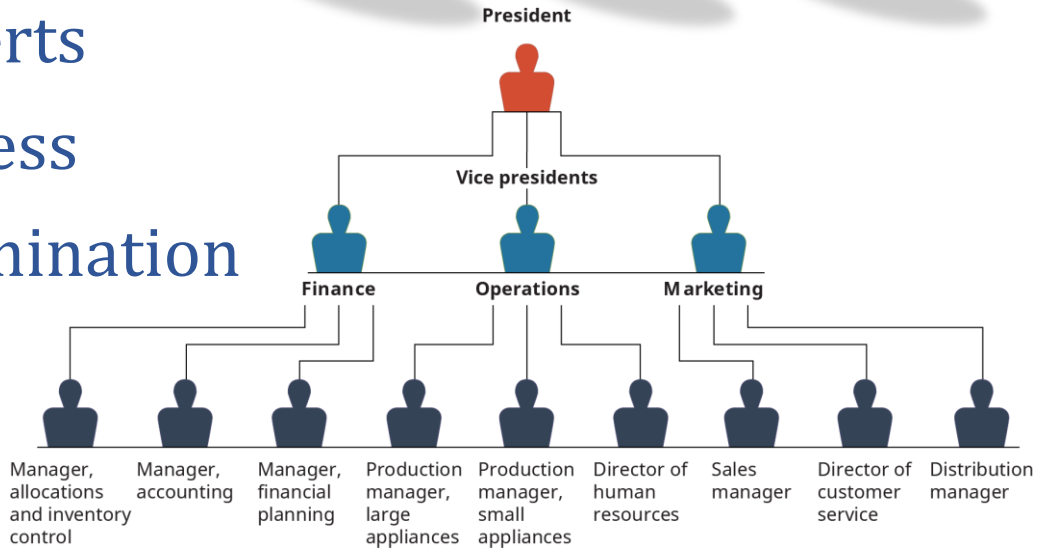
CCS Lead coordinates efforts

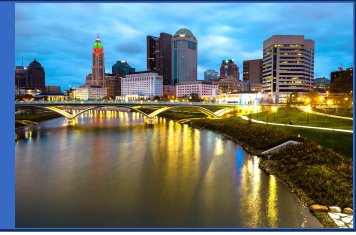
CCS Lead ensures input from functional area experts

Create Knowledge Management around CCS Process

Culture Change that focuses on preventing contamination







Execute a gap assessment to regulatory requirements

Create a formal CAPA plan to mitigate documented gaps

Ensure the *BLINDERS* are off

Identify current assessments

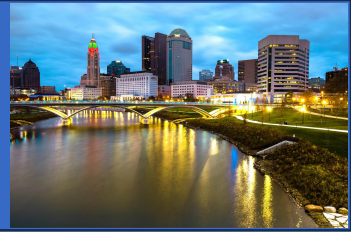
Identify needed assessments and fill the QRM gaps

Write CCS doc(s)…

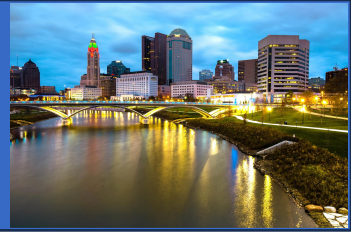
More gaps may be identified (additional CAPA to close)

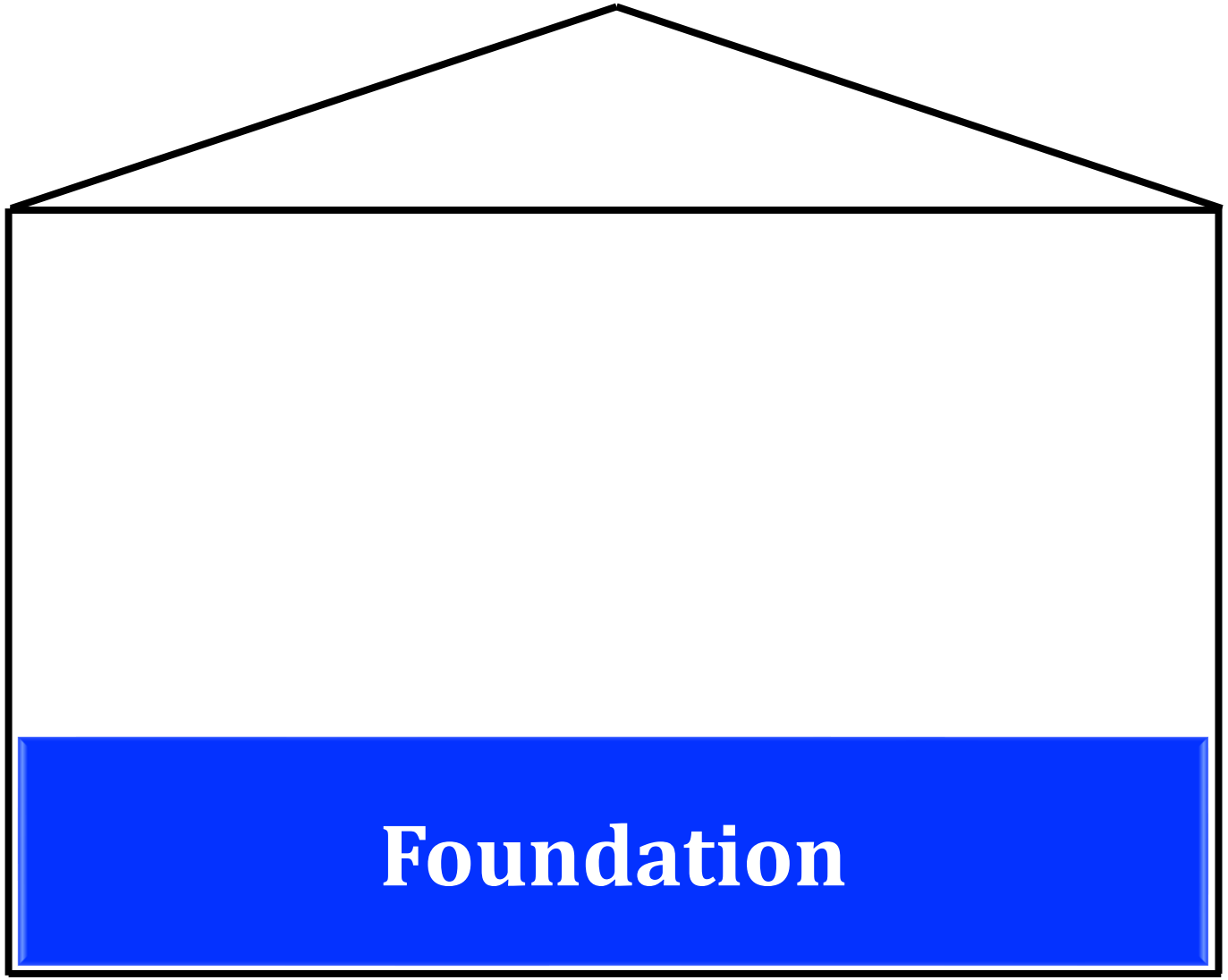
Establish periodic review of CCS

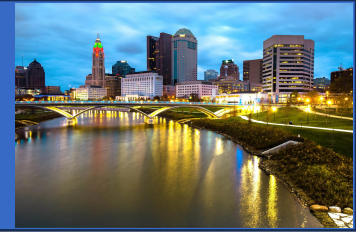
Require CCS impact assessment as part of QMS



Contamination Control Strategy – Foundation




Foundation



Scientific Knowledge

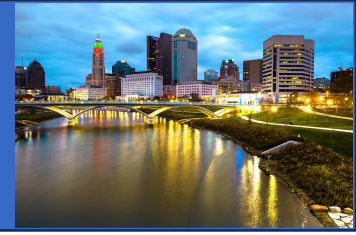
Process / Technical Knowledge

Quality Risk Management

Personal Awareness & Quality Culture

2024 Ohio Event – Essentials of Contamination Control Strategies

September 18th



Science and Evidence based risk assessments

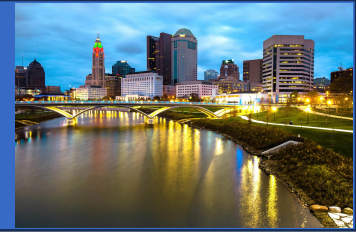
Recognizing uncertainty

Multi-dimensional approach to decision making

Well-defined scope/objective and risk question

Risk-based decision making (RBDM)

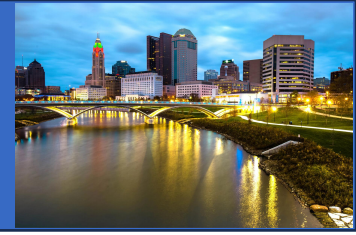
Selecting the correct tool for the job



The control strategy is the protective layer your organization builds to protect product quality and a patient safety.

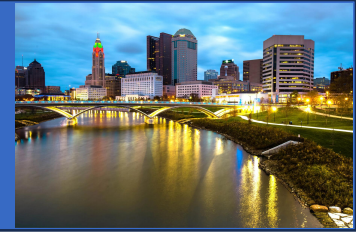
Risk Assessment and Scientific Rationale are the foundation of your control strategy .

The foundation of your strategy needs continuous care to ensure relevance.

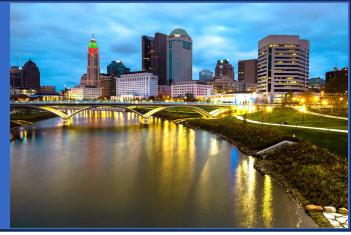


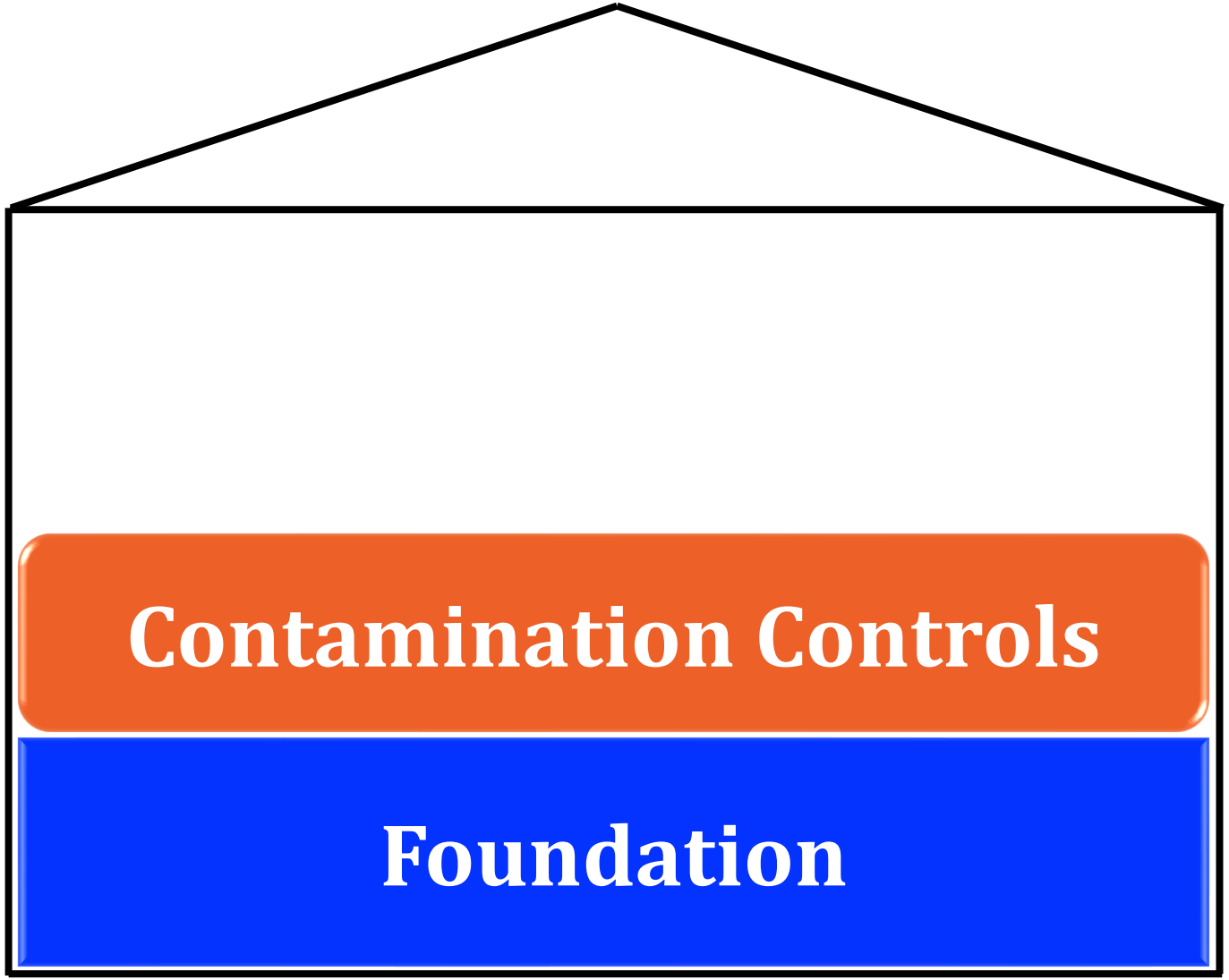
The House of CCS

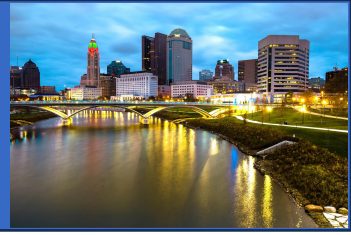
the **Foundations**



Contamination Control Strategy – Contamination Controls




Contamination Controls
Foundation



Eliminate

Prevent

Reduce

Detect

2024 Ohio Event – Essentials of Contamination Control Strategies

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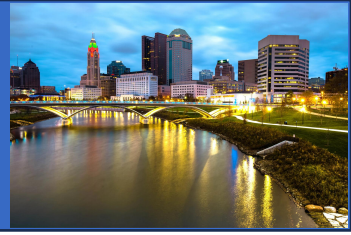
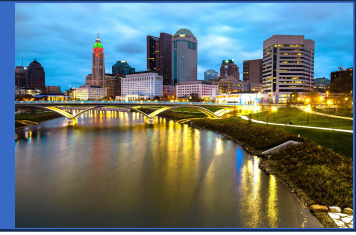


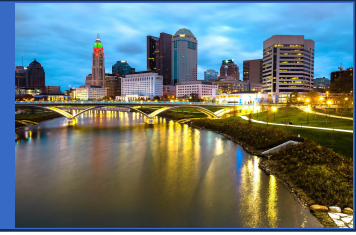
- Facility & Utilities
- Material & Waste
- Personnel Flow
- Personnel Hygiene & Gowning
- Raw Materials



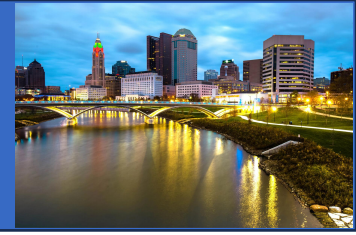
The House of CCS

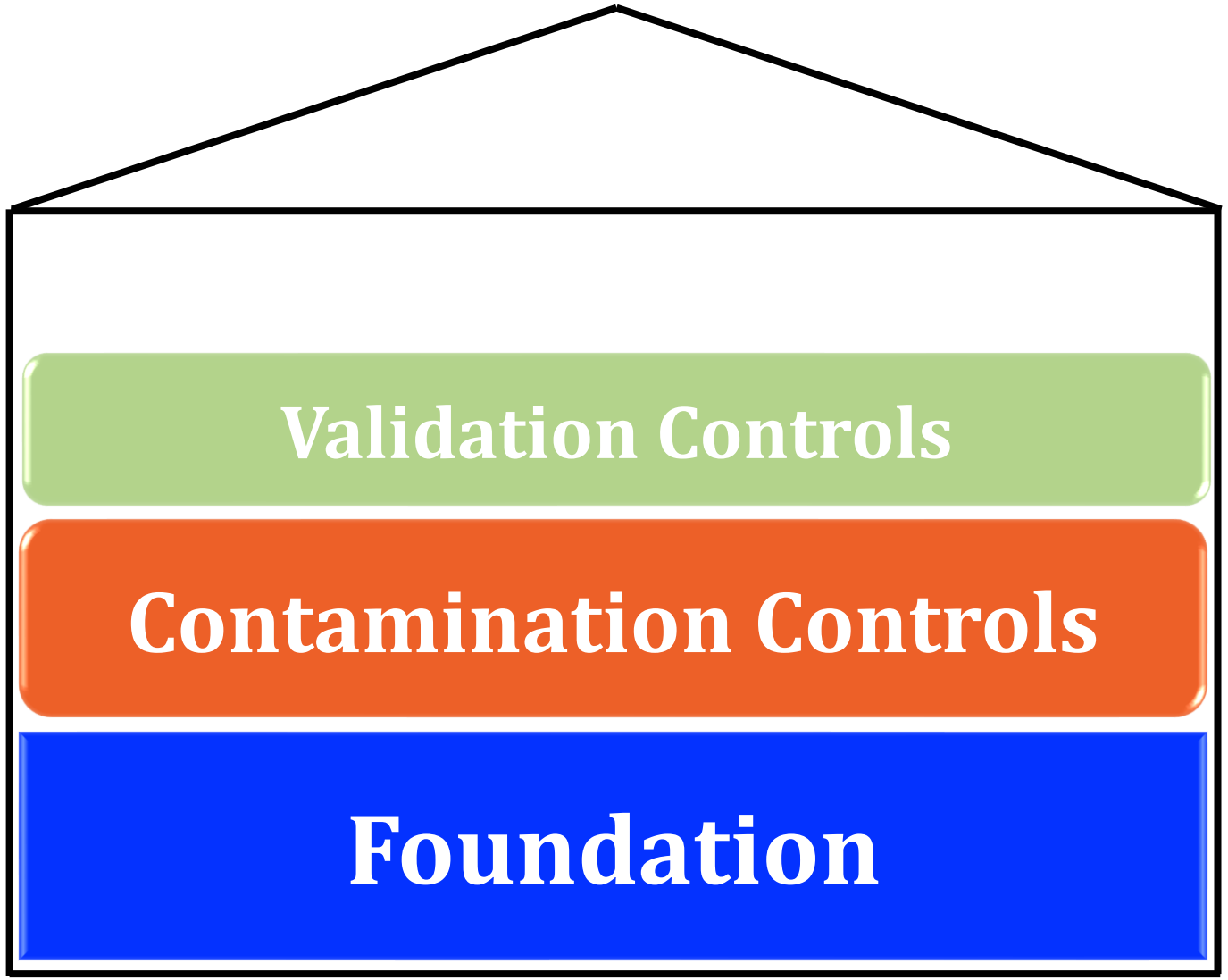
the **Pillars** of Control

the **Foundations**



Contamination Control Strategy – Validation Controls




Validation Controls
Contamination Controls
Foundation

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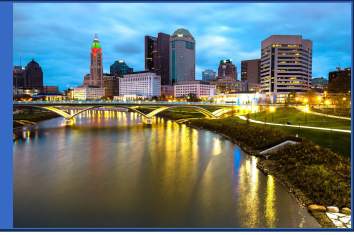
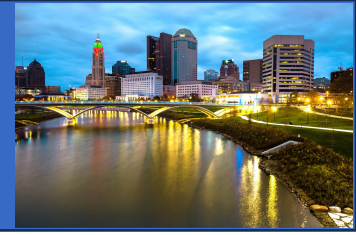
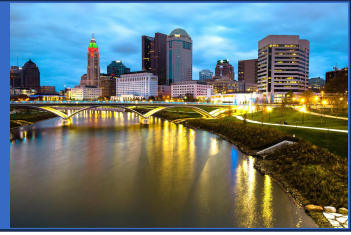


- Analytical Method
- Equipment
- Facility
- Personnel
- Process
- Utilities



- Not simply reading – training implies that there has been a transfer of knowledge

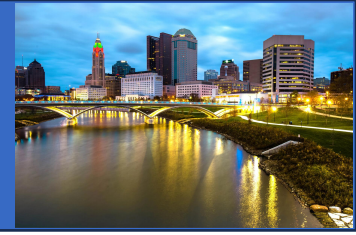
- Several training modalities:
  - Reading
  - Computer Based
  - Instructor led
  - On the job



How?

When?

Redo?



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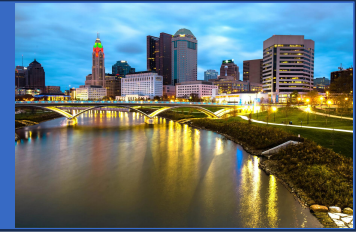
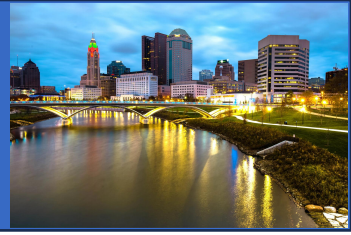
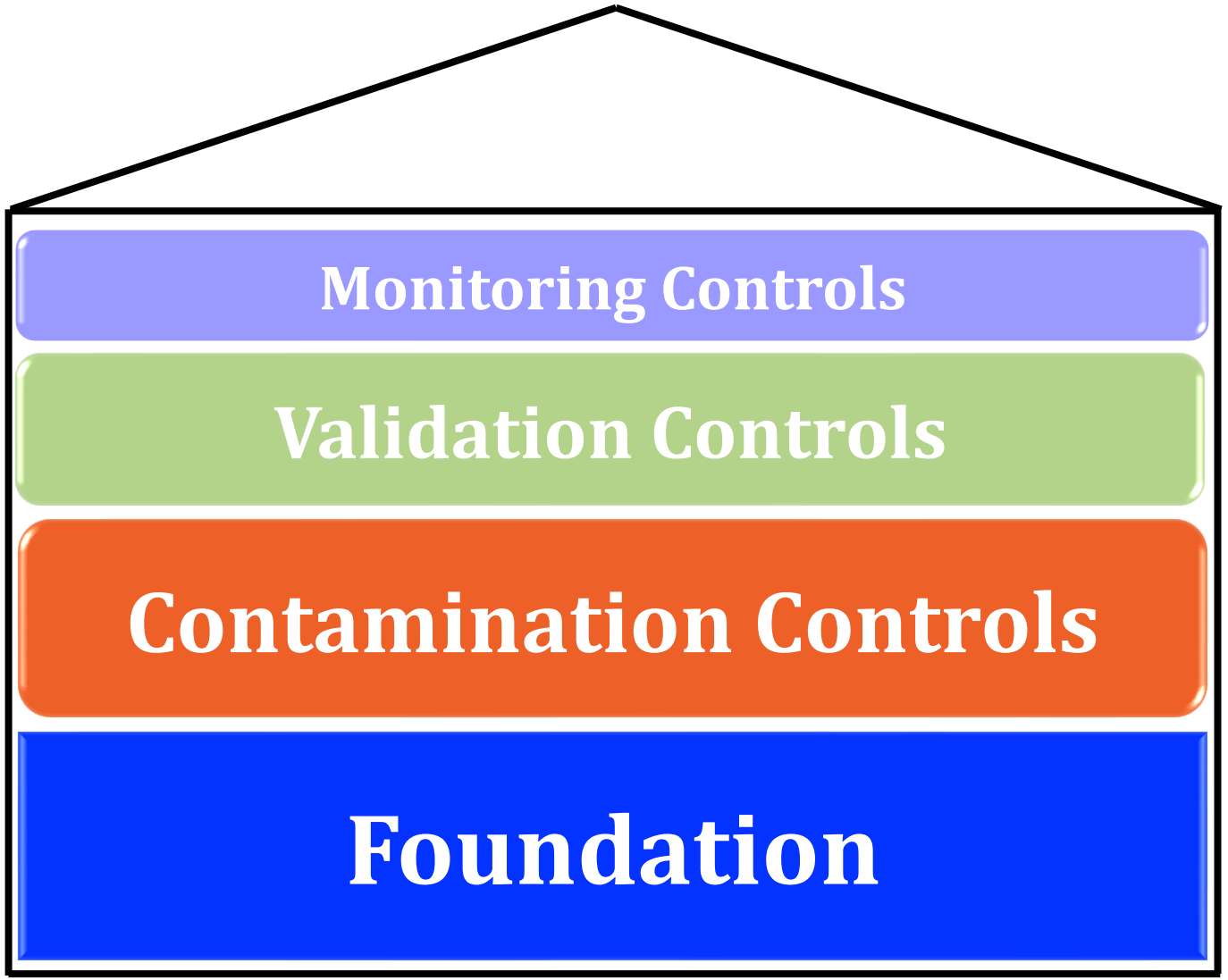
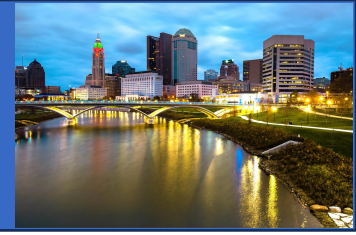


Contamination Control Strategy – Monitoring Controls




Monitoring Controls
Validation Controls
Contamination Controls
Foundation



4.1 The manufacture of sterile products should be carried out in appropriate cleanrooms, entry to which should be through change rooms that act as airlocks for personnel and airlocks for equipment and materials. Cleanrooms and change rooms should be maintained to an appropriate cleanliness standard and supplied with air that has passed through filters of an appropriate efficiency. Controls and monitoring should be scientifically justified and should effectively evaluate the state of environmental conditions of cleanrooms, airlocks and pass-through hatches.

5.2 Equipment monitoring requirements should be defined in "user requirements specifications" during early stages of development, and confirmed during qualification. Process and equipment alarm events should be acknowledged and evaluated for trends. The frequency at which alarms are assessed should be based on their criticality (with critical alarms reviewed immediately).

5.6 All equipment such as sterilisers, air handling systems (including air filtration) and water systems should be subject to qualification, monitoring and planned maintenance. Upon completion of maintenance, their return to use should be approved.

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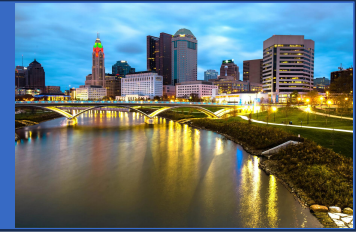
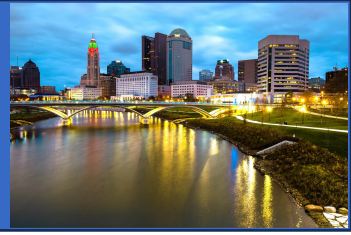


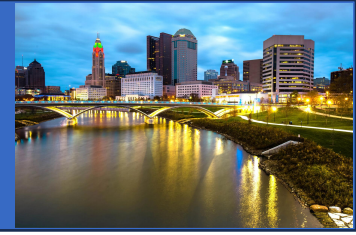
- Environmental
- In-Process
- Material
- Personnel
- Pest
- Utility



What?

Meaning?

React?



The House of CCS

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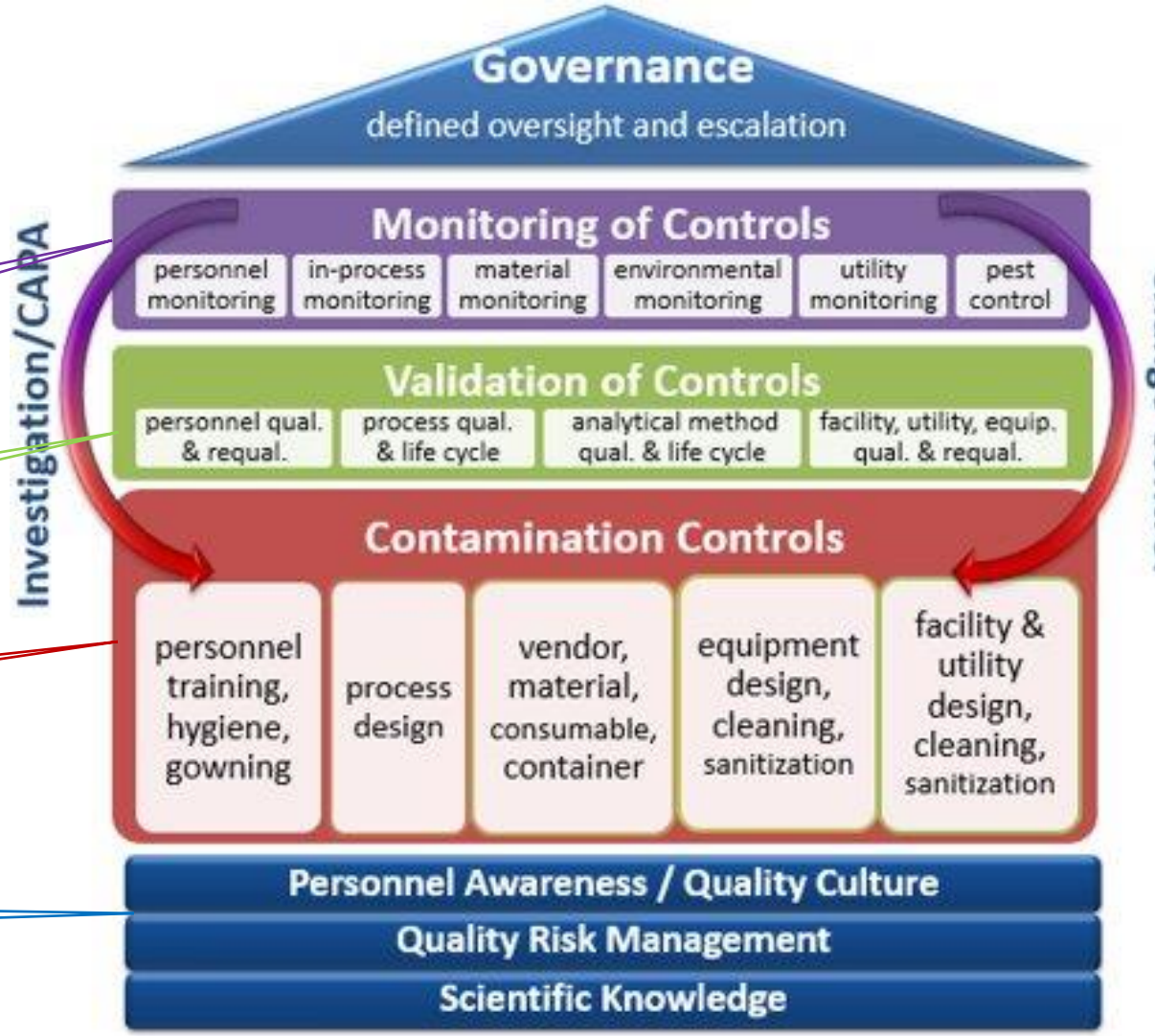
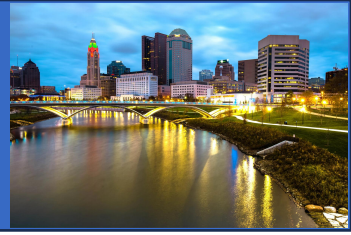
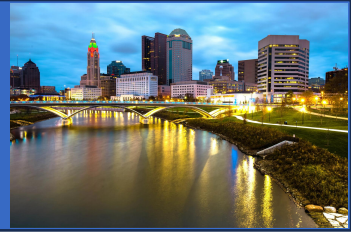
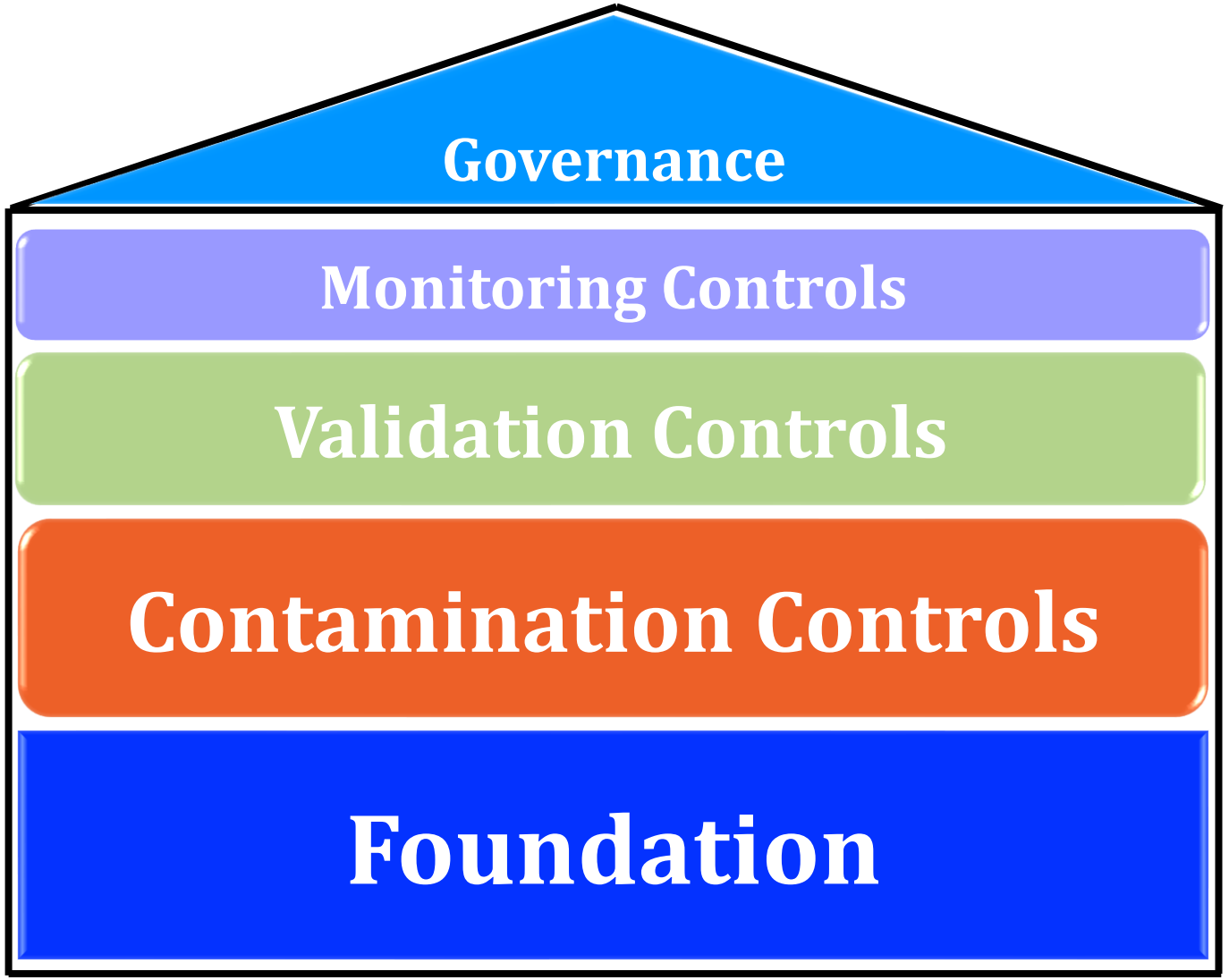
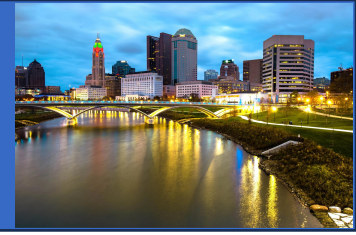




Contamination Control Strategy – Governance

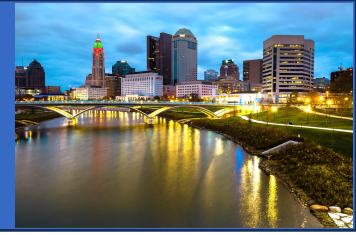



Governance
Monitoring Controls
Validation Controls
Contamination Controls
Foundation



Escalation

Oversight



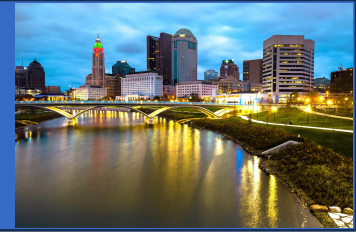
CCS Lead

SME Team Members:

- Quality Risk Management
- Manufacturing Operations / Process Experts
- Contamination Control / Sterility Assurance
- Engineering / Facilities / Utilities
- Equipment
- Validation
- Raw Materials / Vendor Oversight
- Quality Control
- Quality Assurance

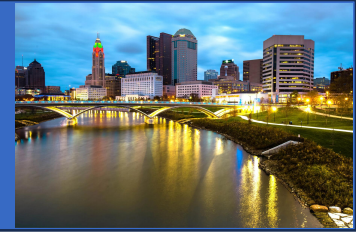
Program Owner / Steward:

- Empowered System Owner
- Collaboration with various functional groups
- Linkage to other aspects of the Quality Management System
- Movement through all the elements of the CCS
- Always asks the question ”is there impact to the CCS?”

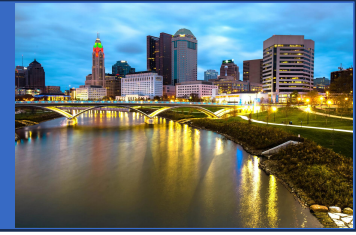


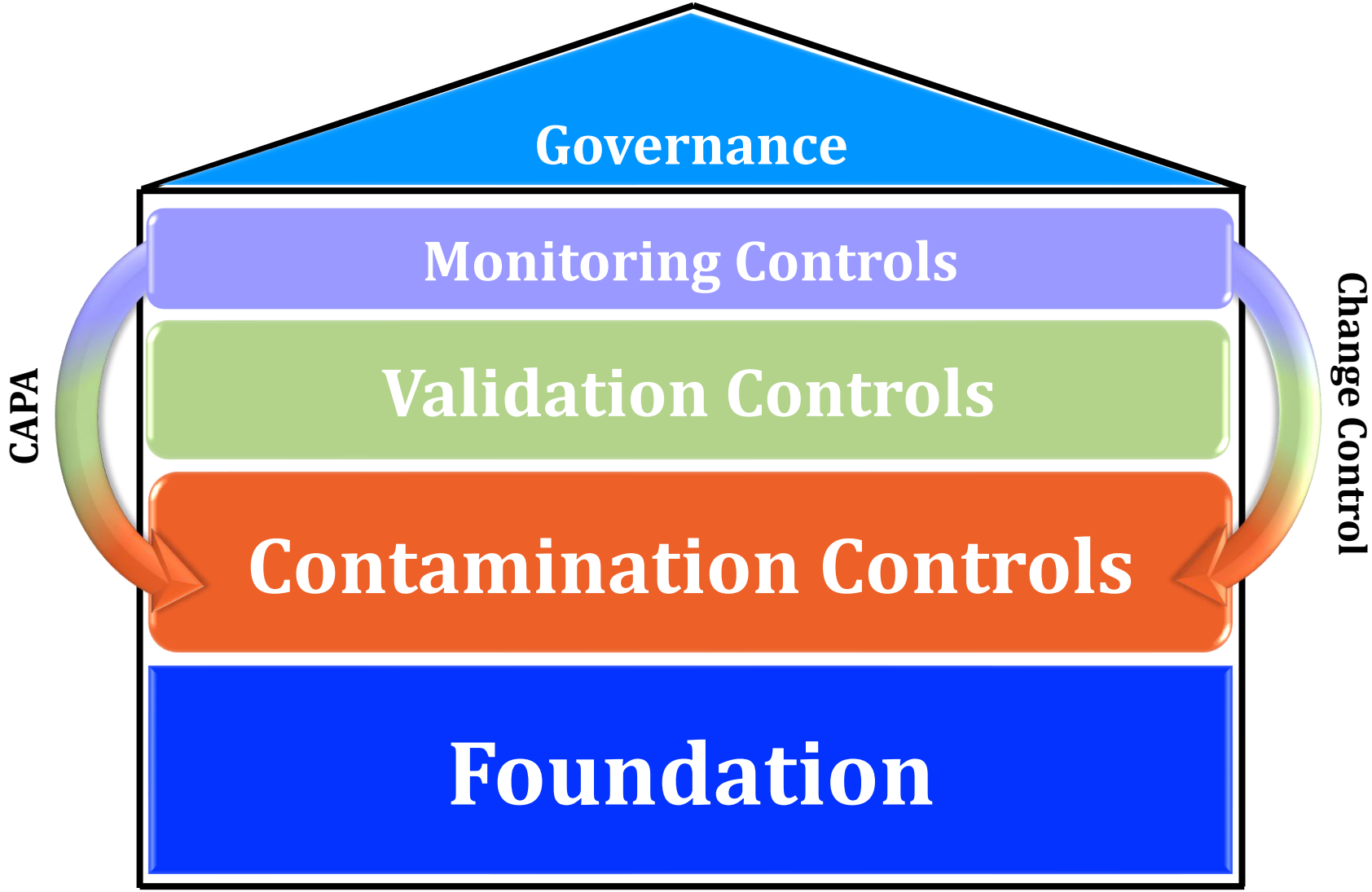
The House of CCS

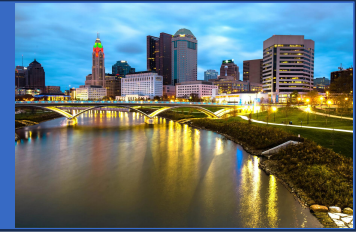
- the **Oversight**
- the **On-going Monitoring** of Control
- the **Confidence** in Controls
- the **Pillars** of Control
- the **Foundations**



Contamination Control Strategy – Feedback Loops




Governance
Monitoring Controls
Validation Controls
Contamination Controls
Foundation
CAPA
Change Control



Key Process Indicators

- Reactive
- Proactive

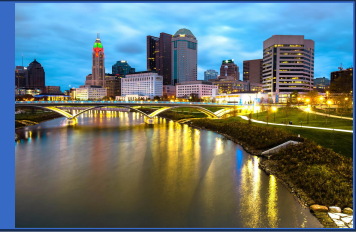
Capital Investment / Re-Investment

Quality Risk Management activities

CAPA Effectiveness

Conformance to CCS Program

- Qualification / Validation / Verification
- Risk Assessment
- Maintenance



The House of CCS

the **Oversight**

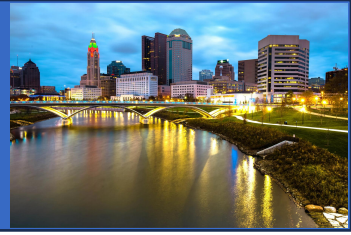
the **Continuous Improvement** loops

the **On-going Monitoring** of Control

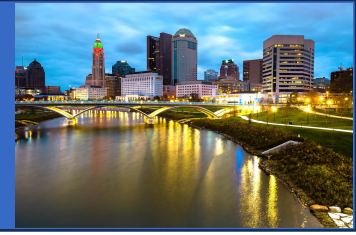
the **Confidence** in Controls

the **Pillars** of Control

the **Foundations**



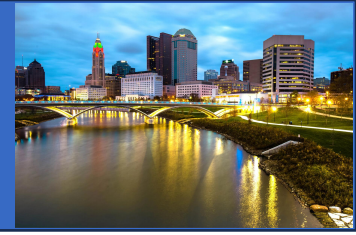
Contamination Control Strategy – ATMP Specifics



Facilities & Utilities	Special design considerations for multi-product and multi-patient operations with multiple suites and/or multiple workstations for segregation purposes
	Many of the recently designed facilities have VHP capabilities for manufacturing areas and transfer of materials / components entering the cleanrooms, which requires full isolation of these areas (especially for those processes using multiple viral vectors for gene modification)
Equipment	Newer process equipment are designed to be automated (or semi-auto), “closed” systems for aseptic unit operations (cell growth / harvesting / activation / etc…)
	A risk-based approach is thus key in evaluating the entirety of the system, the processing steps, and the environment in order to determine appropriate levels of controls and monitoring.

2024 Ohio Event – Essentials of Contamination Control Strategies

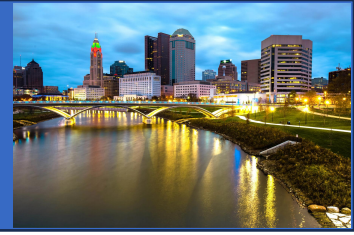
September 18th



Personnel	Highly manual and aseptic thus aseptic practices are incredibly important so there should be a focus on training, qualification, and quality / design of procedures.
	Operator fatigue is common and can be overlooked for personnel working within the cleanrooms increasing contamination related risks.
Materials	Ancillary materials of biological origin (human- and animal-derived) are used in cell therapy processes thus controls for reducing introduction of adventitious viruses and other contaminants are essential, as well as traceability of materials to origin
	Manufacturers need to work with the suppliers to ensure the overall CCS is robust.

2024 Ohio Event – Essentials of Contamination Control Strategies

September 18th



Vendors / Suppliers

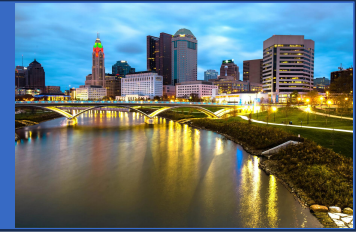
Many materials and components are unique and custom, there may be only a single supplier (or very limited number) offering 'research-grade' only quality and these materials may not be manufactured to GMPs.

Supplier selection, auditing, and additional testing / controls are important to assess (e.g., sterilization filtration of solutions prior to use in the cell therapy process by a process that is validated may be needed).

Containers / Closures

Many cell therapy products and intermediates need to be stored at cryo-temperatures where the materials of construction for bags / containers (typically constructed with FEP) and their components are fragile.

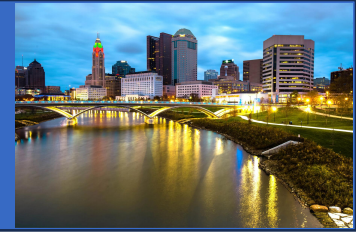
Materials need to be handled and stored, appropriately, based upon the hazards associated with the shipping / transport of these finished products.

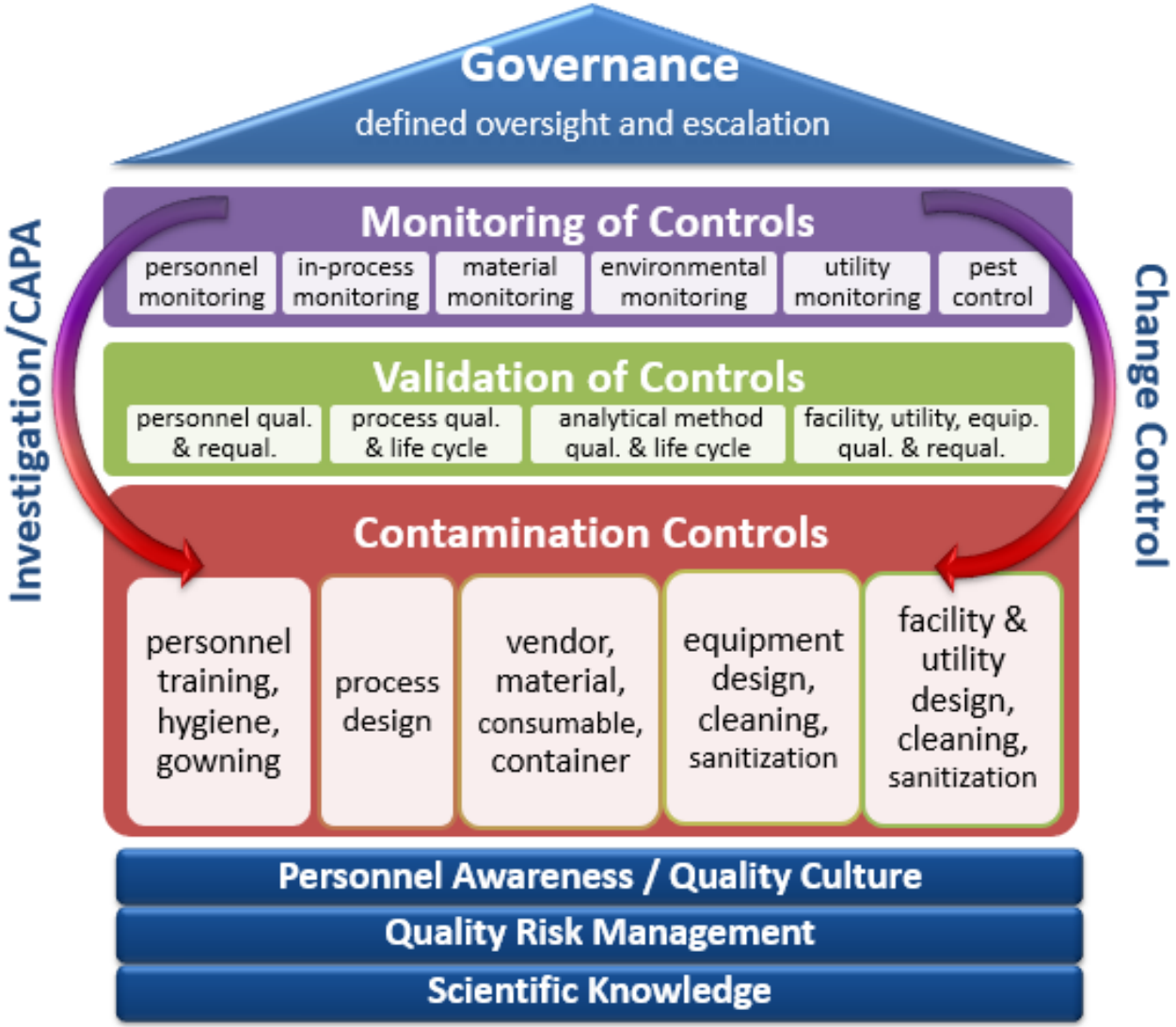


Process Validation

Cell therapy products cannot be terminally sterilized, most of the production steps are aseptic.

Design of APS can be complex and difficult to manage, as well as difficult to determine root cause if a contamination / failure is observed




Governance
defined oversight and escalation
Monitoring of Controls
personnel monitoring
in-process monitoring
material monitoring
environmental monitoring
utility monitoring
pest control
Validation of Controls
personnel qual. & requal.
process qual. & life cycle
analytical method qual. & life cycle
facility, utility, equip. qual. & requal.
Contamination Controls
personnel training, hygiene, gowning
process design
vendor, material, consumable, container
equipment design, cleaning, sanitization
facility & utility design, cleaning, sanitization
Personnel Awareness / Quality Culture
Quality Risk Management
Scientific Knowledge
Investigation/CAPA
Change Control


thank you
danke
謝謝
ngiyabonga
شكراً جزيلاً
рахмат
teşekkür ederim
gracias
спасибо
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