Microbial Contamination and Control Conference

Micro Lab General Contamination Control and Personnel Training

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Introductions

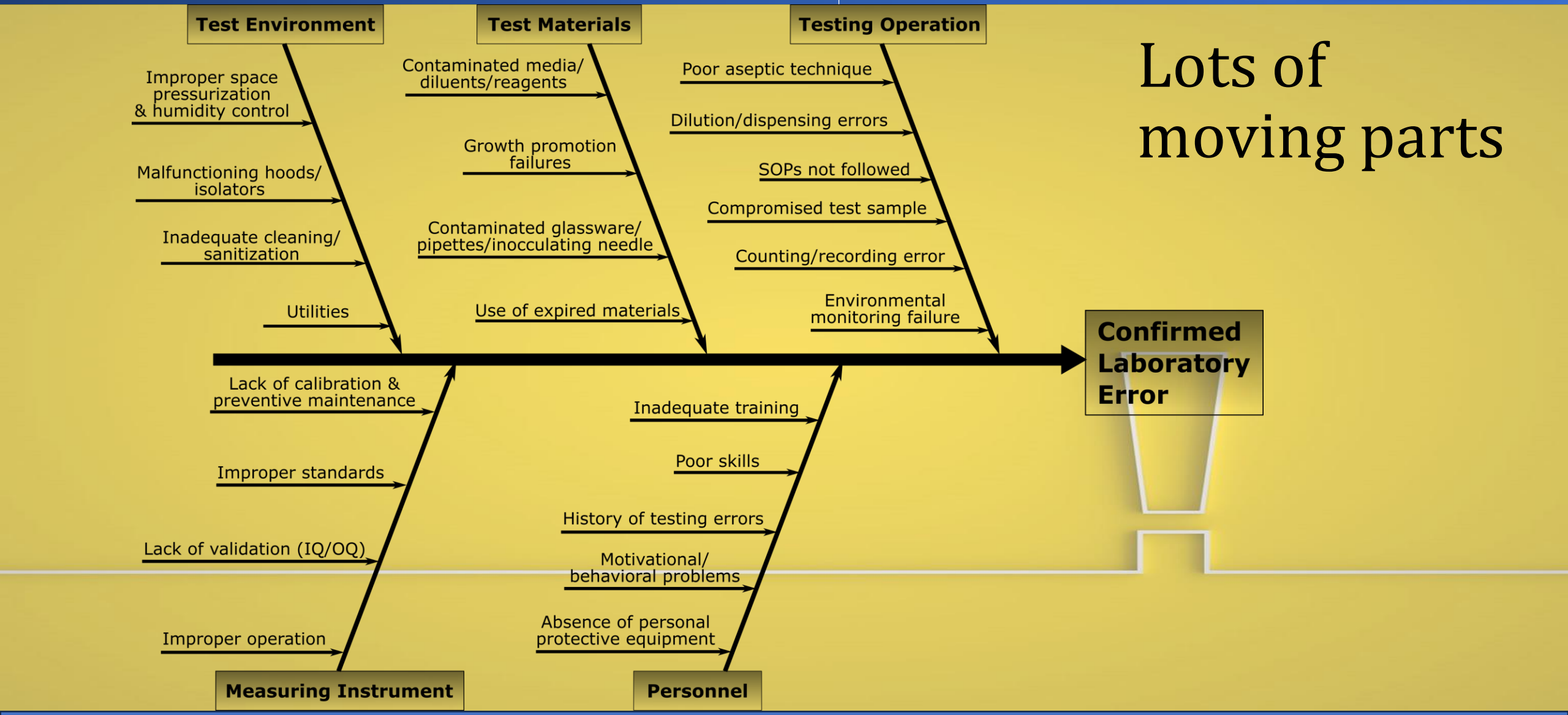
- MS in Biotechnology from Georgetown University
- Background in protein chemistry and separation science
  - Made drug discovery and research reagents
- First job was researching *Pseudomonas aeruginosa*
- S&RA department in PDA is the conduit for all:
  - Technical Reports
  - Points to Consider
  - Standards
  - Interest Groups
  - Technical Advisory Boards

On the Docket

- Contamination Control Considerations
- Training Requirements and Strategies
- PDA and Industry Resources

What do Micro Labs do?

- Sterility testing
- Detection, isolation, enumeration and identification of microorganisms (bacteria, yeast and molds) and testing for bacterial endotoxins in different materials (e.g., starting materials, water), products, surfaces, garments and the environment
- Assay using microorganisms as part of the test system



Lots of moving parts

How to get it done:

Contamination Control Strategy/ Policies

Trained Operators/ Analysts

Micro Lab Operations

The Contamination Control Strategy (CSS)

- Why?
- What's it about?
- How does it happen?

Holistic CCS

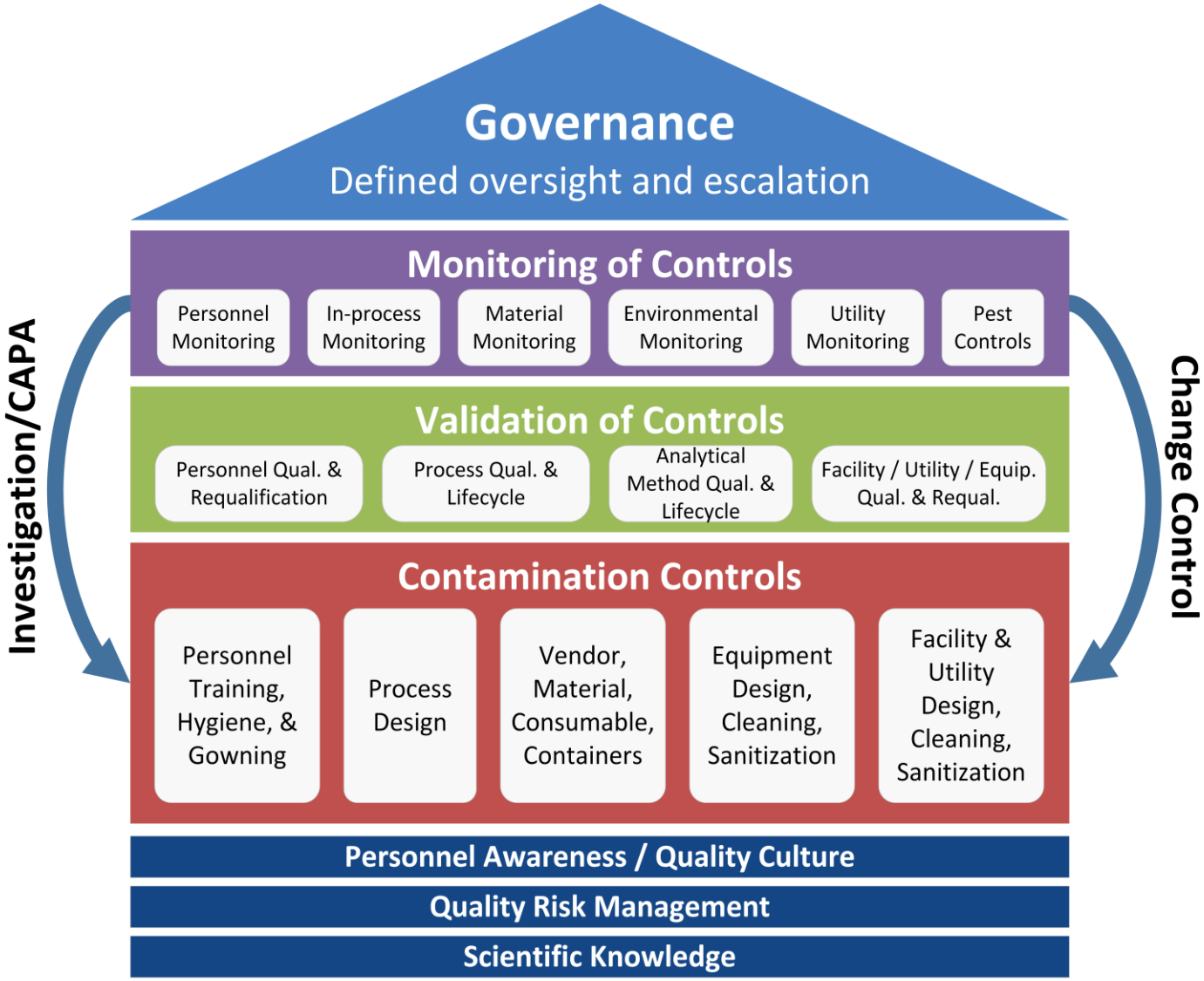
Holistic CCS is a major principle of the EU Annex 1 revision

"2.4 Contamination control and steps taken to minimize the risk of contamination from microbial, endotoxin/pyrogen and particle sources includes a series of interrelated events and measures.

These are typically assessed, controlled and monitored individually but their collective effectiveness should be considered together."

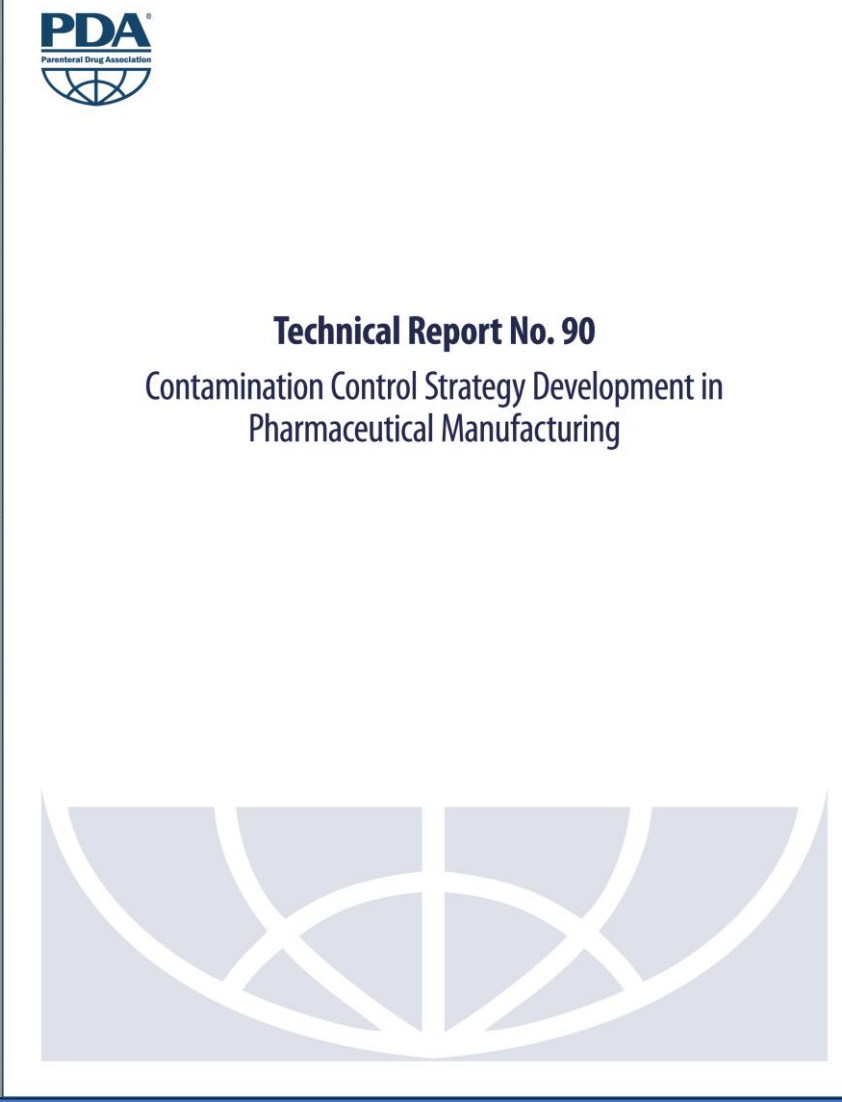
- 2022 EMA Annex 1

Building the CSS Structure



CCS Overview

- Holistic CCS
- Practical Considerations
- Case Study
- Template for CCS



Practical Considerations for CCS

Laboratory Facility

- Storage of Materials and Equipment
- Materials, Equipment, or Waste
- Movement and Gowning of Personnel

Maintenance

- Training of Maintenance Personnel
- Protection of Environment and Equipment during Maintenance
- Cleanup and Return to Service

Raw Materials/ Consumables

- Adventitious agents
- Vendor defects

Practical Considerations for CCS

Personnel

- Microbiological Awareness
- Training and Qualification
- Attitude and Mindset

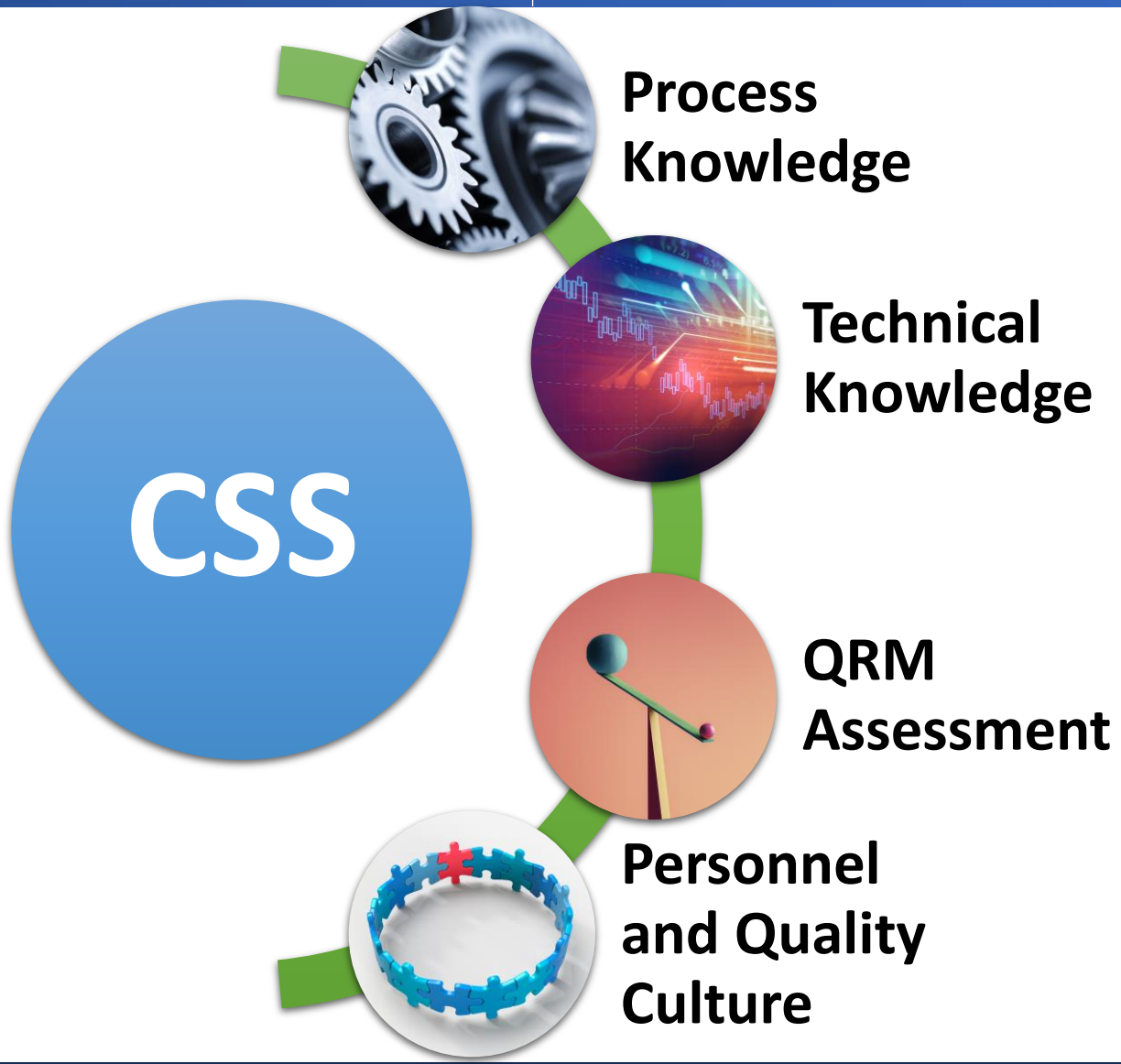
Monitoring of Controls

- Measuring performance of CCS
- Trending as proactive control
- Setting appropriate levels

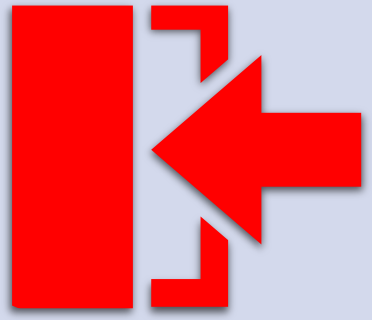
Testing and Limits

- Setting limits
- Trending

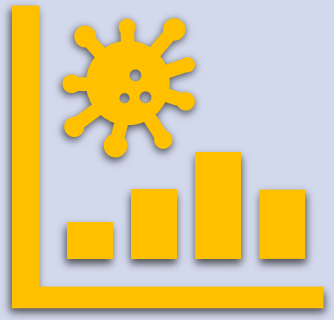
Constructing the CCS



Process Knowledge



Potential contaminant ingress points



Potential microbial / viral proliferation points

Microbial / viral growth potential

Removal or reduction of potential contaminants

History-of-contamination events

Technical Knowledge

Understanding how to prevent contamination

Microbial behavior and biofilm development	Equipment design principles
Aseptic processing	Cleaning, disinfection, decontamination, sanitization, sterilization principles
Viral behavior and host infection	Raw material quality
Process design principles	Quality Risk Management principles
Facility and utility design principles	

Use available knowledge – Don't reinvent the wheel!

PDA *Technical Report No. 41 (rev. 2008): Virus Filtration, Technical Report No. 42: Process Validation of Protein Manufacturing, Technical Report No. 44: Quality Risk Management for Aseptic Processes, Technical Report No. 45: Filtration of Liquids Using Cellulose-Based Depth Filters, Technical Report No. 60: Process Validation: A Lifecycle Approach, Technical Report No. 81: Cell-Based Therapy Control Strategy*

ICH *Quality Guideline Q7A: Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*

PDA *Points to Consider 1 Aseptic Processing*

Technical Report No. 83: Virus Contamination in nufacturing: Risk Mitigation, Preparedness and Response

Biotechnology Manufacturing Operations, ICH *Quality Guideline Q9: Quality Risk Management*

PDA Technical Report No. 26 (Rev. 2008): Sterilizing Filtration of Liquids, for Clea

ISPE *Baseline Guide: Volume 3 – Sterile Product Manufacturing Facilities*, PDA *Points to Consider for Aging Facilities*

ms: Design, Commissioning, Operation, nd Maintenance, Technical Report No. 49: Points Biotechnology Cleaning Validation, Technical Steam In Place, Technical Report No. 70: of Cleaning and Disinfection Programs for Aseptic Manufacturing Facilities,

PDA *Technical Report No. 34: Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products*, PDA *Points to Consider for the Aseptic Processing of Pharmaceutical Products in Isolators*

Quality Risk Management Assessment

- Is the lab designed properly?
- Where are the manual and the automated steps?
- Can standardized practices from other parts of the organization be applied?
- Are new contamination control technologies and procedures being implemented?

The CCS should be designed with redundant individual control elements so that **no single failure** in one element **will result in contamination**.

Personnel Awareness and Quality Culture

Contamination control should be a priority reflected in the goals of the firm

- A dedicated champion or team should oversee the CCS performance

Ongoing campaign to promote contamination control awareness

- One-time or annual training does not ensure ongoing awareness

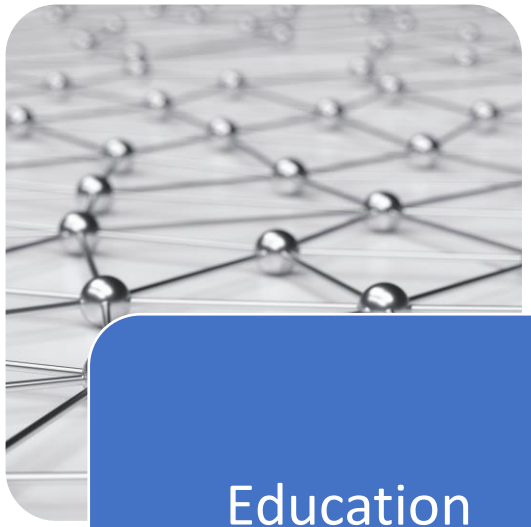
Personnel Awareness and Quality Culture

Hallmarks of a robust quality culture that promotes contamination control:	Focus on prevention
	Willingness to improve
	Strong response to contamination events
	Management support and recognition
	Strong, supportive communities of practice
	Employees who feel ownership over product quality
	Employees who understand their responsibilities
	Non-blaming culture

Personnel Awareness and Quality Culture

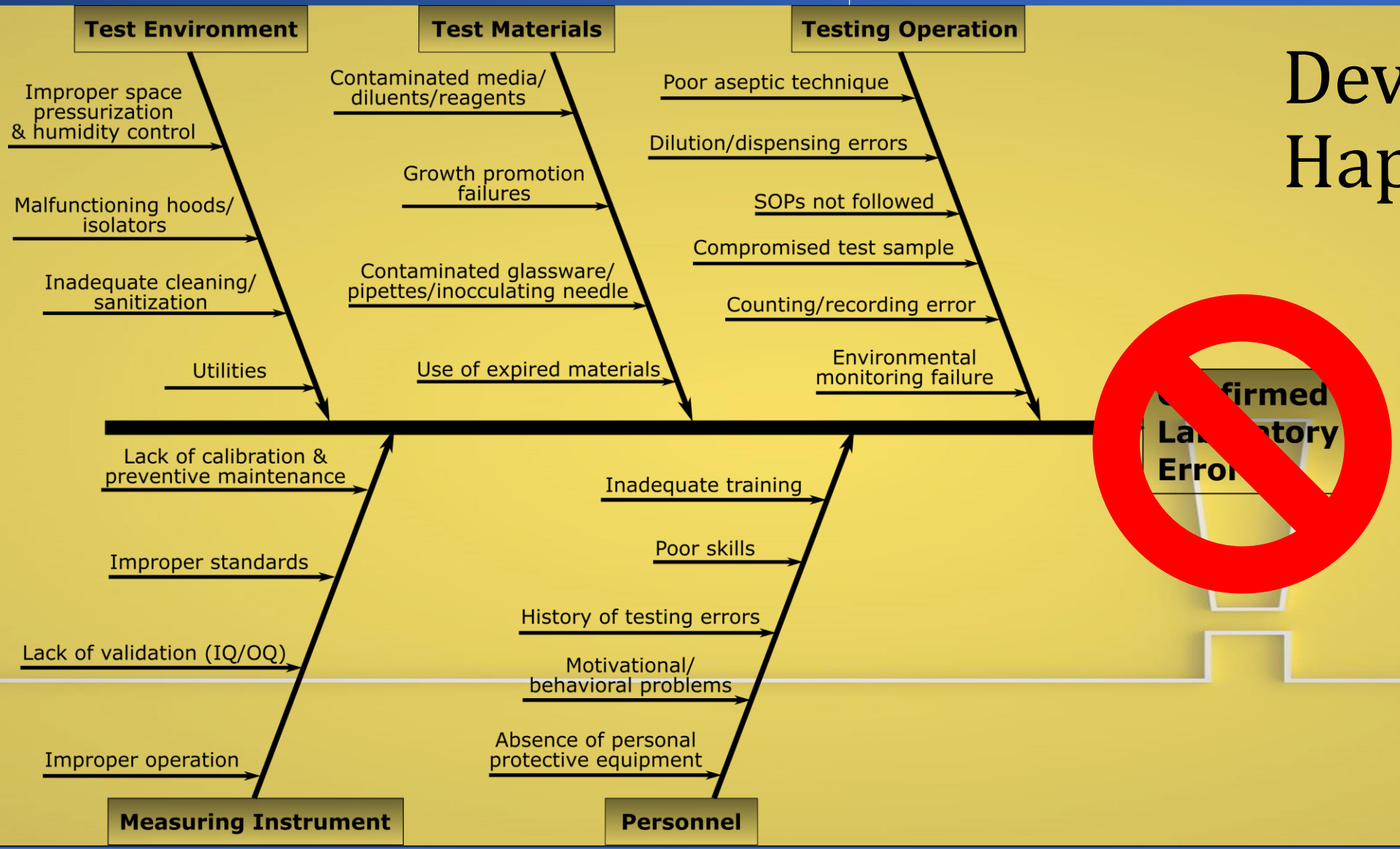
Personnel awareness is achieved through training, education, and ongoing diligence

Training addresses what a task is and how it is done



Education addresses why it is done

Deviations Happen



Training Expectations

- "Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with current Good Manufacturing Practices (GMP) requirements applicable to them." (CFR 21:211)
- "Microbiological test results represent one of the most difficult areas for the evaluation and interpretation of data. These evaluations require extensive training and experience in microbiology." (FDA, 1993)
- "Good manufacturing proactive regulations require an active training program and the documented evaluation of the training of analysts."(FDA, 1993)

Where to start?

Micro Team: Assemble

Laboratory Management

Microbiology SMEs

Microbiology Trainers

Micro Team: Assemble

Laboratory Management

- Selects the team
- Approves the program
- Reviews audits and operations

Micro Team: Assemble

Microbiology SMEs

- Provides deep knowledge
- Leads development of training/ assessments program
- Oversight/ monitoring of training program

Micro Team: Assemble

Microbiology Trainers

- Experienced operators/analysts
- Command/understanding of the material
- Passion/knack for training
- Effective communicator
- Personable

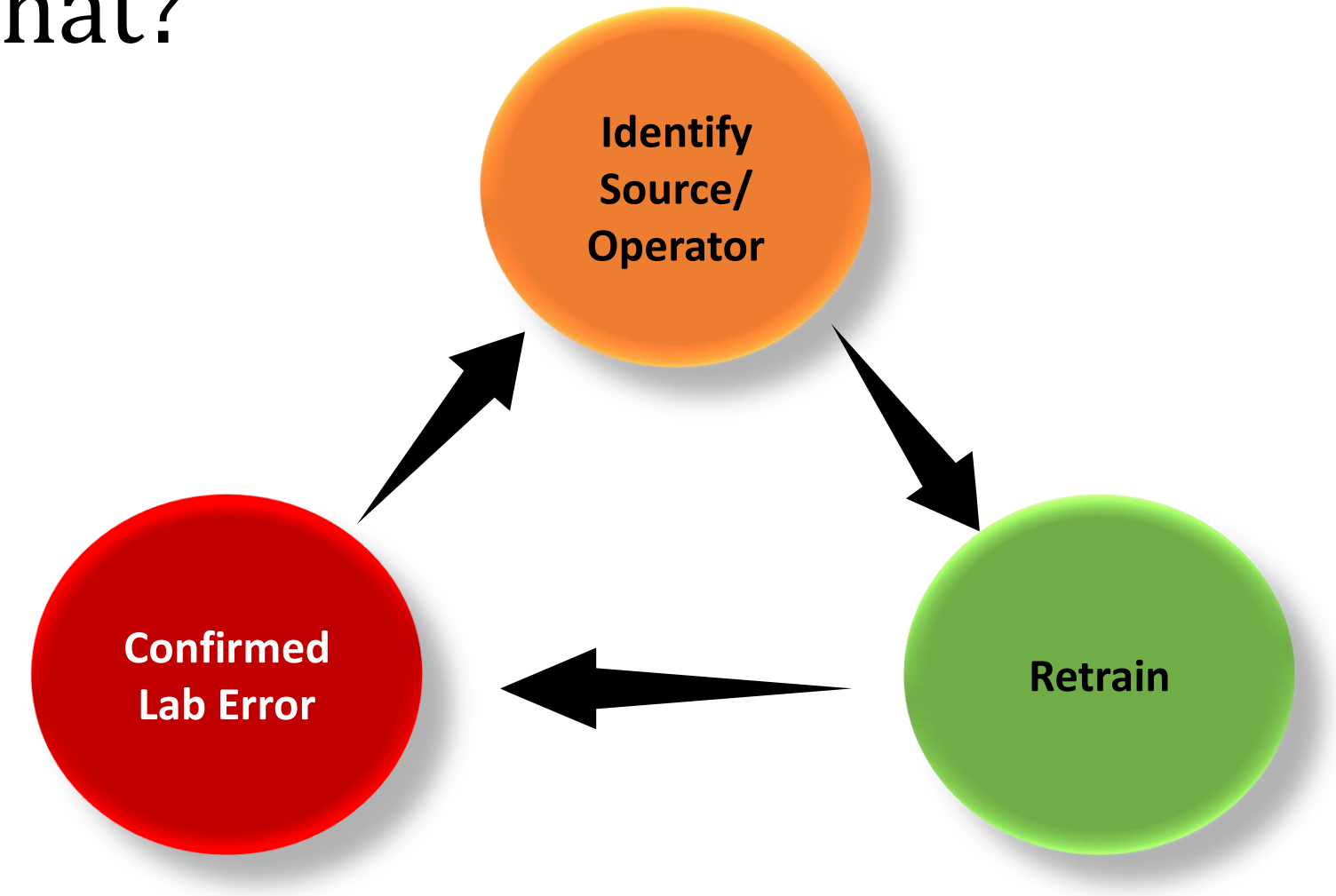
Micro Team in Action

- Results are in line with specs
- Operators are efficient and proficient
- Everything is on track

Micro Team Inaction

Until it isn't

Now what?



Training More vs Training Right

Insanity:

Doing the same thing over and over and expecting different results

Training Right

- Be specific
- Assume nothing
- Teach your method/process in detail
- Explain the what **AND** the why
- Use a variety of training methods
- Involve the learner
- Confirm comprehension

PDA Resources and References

- **TR 13** Fundamentals of an Environmental Monitoring Program
- **TR 13-2** Fundamentals of an Environmental Monitoring Program Annex 1: Environmental Monitoring of Facilities Manufacturing Low Bioburden Products
- **TR 33** Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods
- **TR 54 Series** on Quality Risk Management
- **TR 82** Low Endotoxin Recovery
- **TR 88** Microbial Data Deviation Investigations in the Pharmaceutical Industry

PDA Training Opportunities

- PDA 100 Aseptic Processing
- PDA 102.3 Technical Report No. 13: Fundamentals of an Environmental Monitoring Program
- PDA 247 Fundamentals of Contamination Control, Cleaning and Disinfection Programs for Aseptic Manufacturing Facilities
- PDA 612 Analysis of Environmental Monitoring Data with Respect to cGMP and Data Integrity Guidelines
- PDA 620 Technical Report No. 88 Microbial Data Deviation Investigations in the Pharmaceutical Industry

Industry Resources and References

- USP <1117> Microbiological Laboratory Best Practices
- USP <1116> Microbiological Control and Monitoring of Aseptic Processing Environments
- USP <1113> Microbiological Characterization, Identification, and Strain Typing
- WHO TRS 961 – Annex 2: Good Practices for Pharmaceutical Microbiology Laboratories

Take home messages

- Use your team
- Take advantage of existing resources
- Be critical of your existing processes and procedures
- Change things that aren't working

Thank you!

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