Introduction to Contamination Control Strategy for Cleaning Disinfection and Decontamination

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AGENDA

Understanding how cleaning, disinfection and bio-decontamination align with a contamination control strategy

1

WHAT IS A CONTAMINATION CONTROL STRATEGY?

2

THE CONTAMINATION SOURCES AND FOCUS AREAS

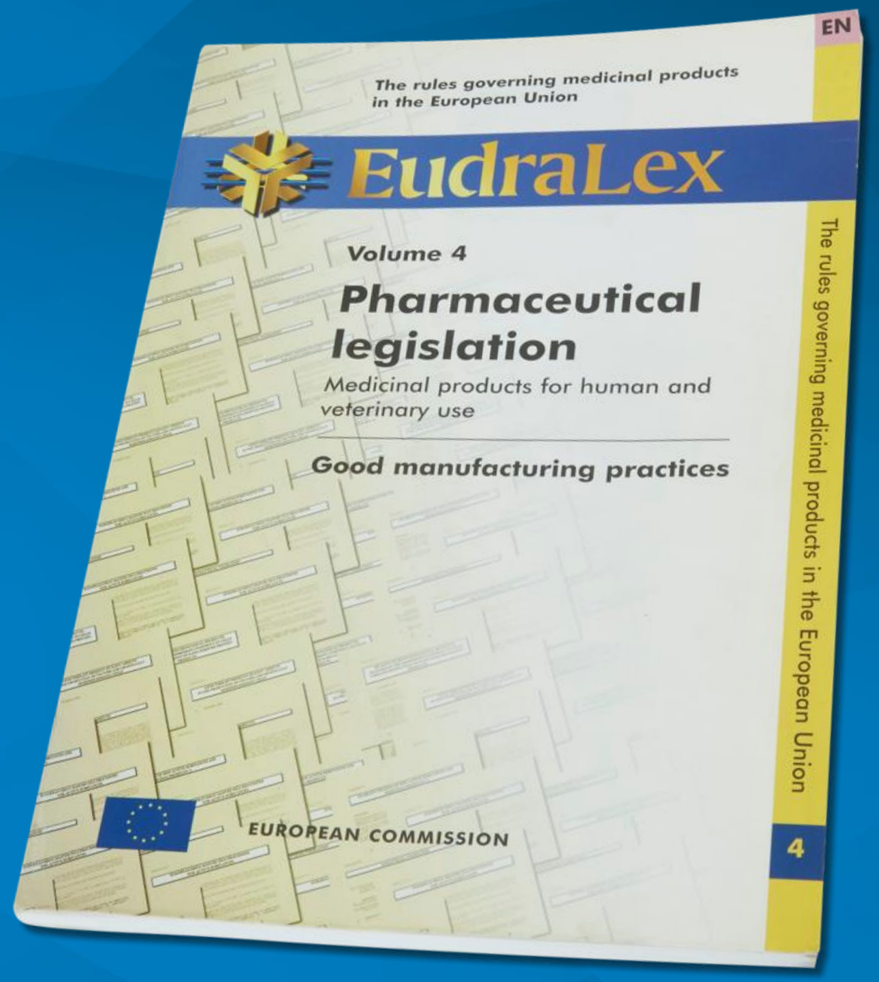
3

CASE STUDY FOCUS:
Material Transfer
Residue Management

CONTAMINATION CONTROL STRATEGY AND ANNEX 1

A new addition to Annex 1

Alignment with ICH Q9 & Q10 (QRM and PQS)



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Why is an update to Annex 1 important?

Global Impact

Provides the rules governing manufacture of medicinal products in the EU

Countries that wish to sell products into the EU must also abide by these rules

Annex 1 is common to member states of the EU, and participating authorities of Pharmaceutical Inspection Co-operation Scheme (PIC/S)

As of January 2022, 54 countries around the globe have participant authorities of PIC/S

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Why has CCS been added to Annex 1?

Criticality

- Recent recalls/citations show the contamination of products is a real and current problem
- Humans arguably learn best from trial and error. Unfortunately, this way of learning, when working with pharmaceutical products is far from safe

"Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established…"
FDA citation

"The control systems necessary to prevent contamination or mix-ups are deficient…"
FDA citation

"Non-microbial contamination was observed in your production area. Specifically, thick white powder residues were observed on the ceiling intake vent and on top of the hood…"
FDA citation

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What is the Contamination Control Strategy?

Definition

Glossary– Annex 1 AUGUST 2023

“Contamination Control Strategy (CCS) – A planned set of controls for microorganisms, endotoxin/pyrogens and particulates, derived from current product and process understanding that assures process performance and product quality. The controls can include parameters and attributes related to active substance, excipient and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control.”

Any clearer?

WHAT IS THE CONTAMINATION CONTROL STRATEGY?

A system that considers all the integral elements of pharmaceutical product manufacturing

Quality risk management principles and supporting risk assessments for contamination control and monitoring (detectability of contamination event)

ELEMENTS

Microbial contamination

Particle contamination (visible and sub-visible)

Sterility Assurance

Viral Control

Facility Design

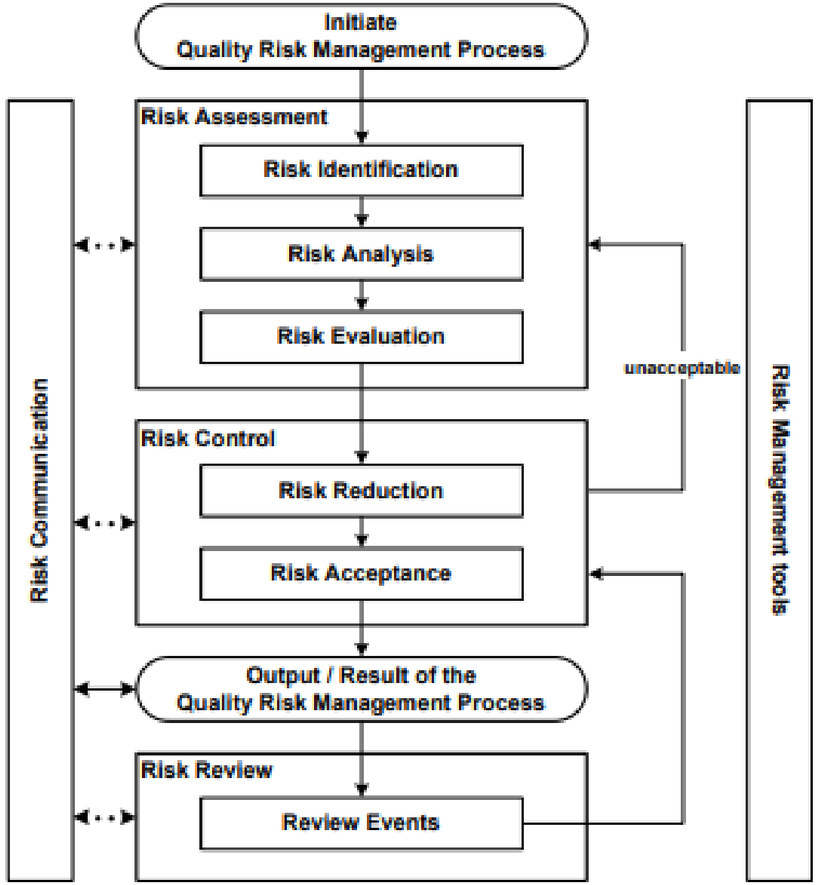
Mix-ups

Chemical Contamination

Primary and secondary packaging

What is the Contamination Control Strategy?

Quality Risk Management



- Essentially the CCS is bringing the principles of ICH Q9 to contamination
- Part of your Pharmaceutical Quality System
- Be proactive
- Identify your contamination risks
- Put a plan in place to control them
- Not a one off exercise, continuous feedback on control

ICH guideline Q9 on quality risk management EMA/CHMP/ICH/24235/2006

CONTAMINATION CONTROL STRATEGY PRINCIPLES

Quality By Design	Organizational Control Measures
Technical control measures, applied based on science and knowledge of process and risks	The organization of operations, as defined in the Pharmaceutical Quality System, procedural control, and human factors

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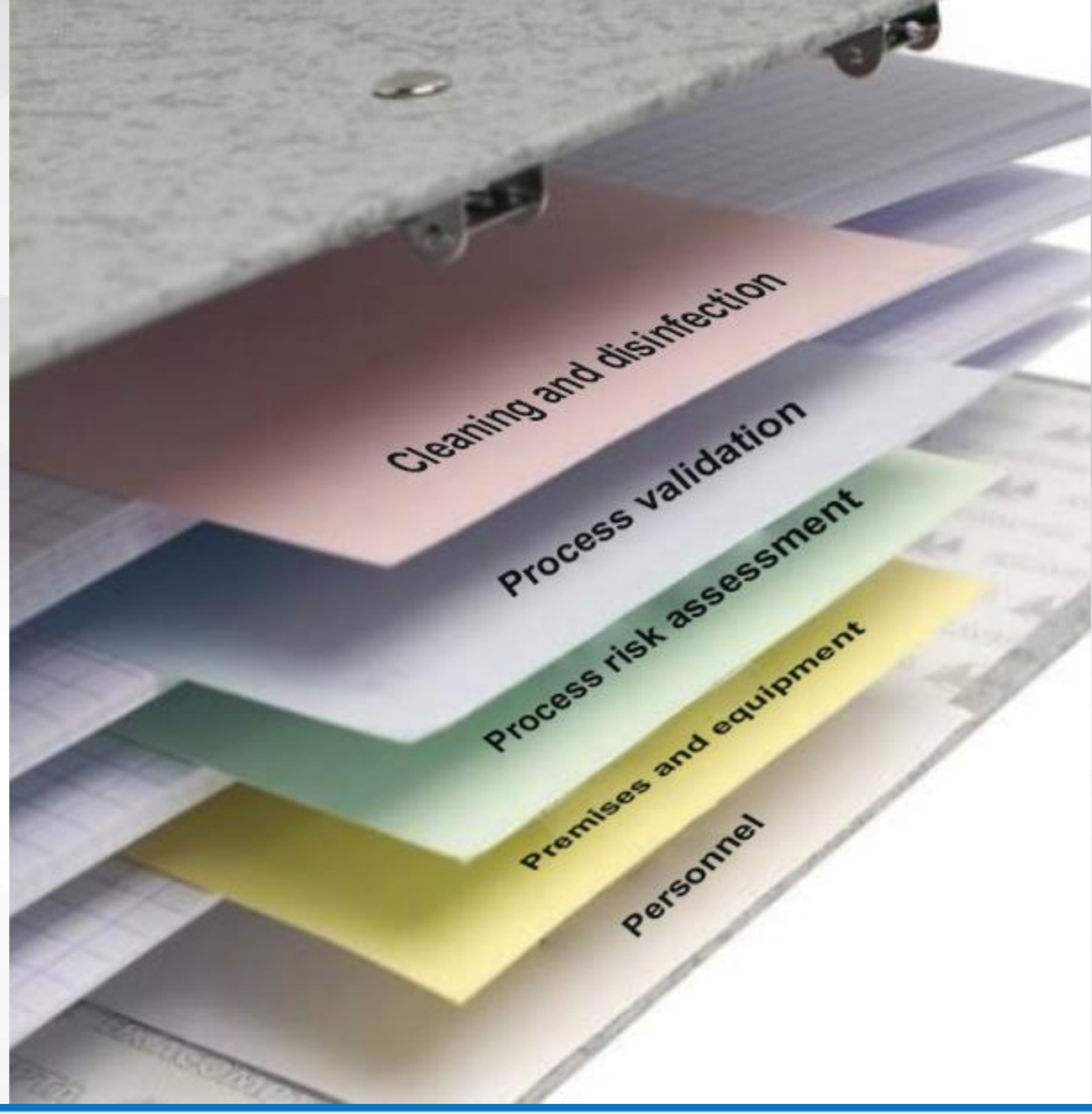
KEY ELEMENTS TO BE ASSESSED

Process flows should be outlined for the entire manufacturing process including:

- Manufacturing Plant
- Processes
- Premises
- Personnel
- Utilities
- Raw materials
- Product containers
- Process Validation
- **Cleaning and disinfection**



CONTROL YOUR RISKS – CLEANING & DISINFECTION

Control Measures

Can’t eliminate all the contamination coming in

Control it proactively with Cleaning and Disinfection regime

Identify contamination risks to develop the regime

BUILDING A CCS FOR CLEANING & DISINFECTION

Contamination Risks

Cleaning

Addressing Physical / Chemical Contamination

BUILDING A CCS FOR CLEANING & DISINFECTION

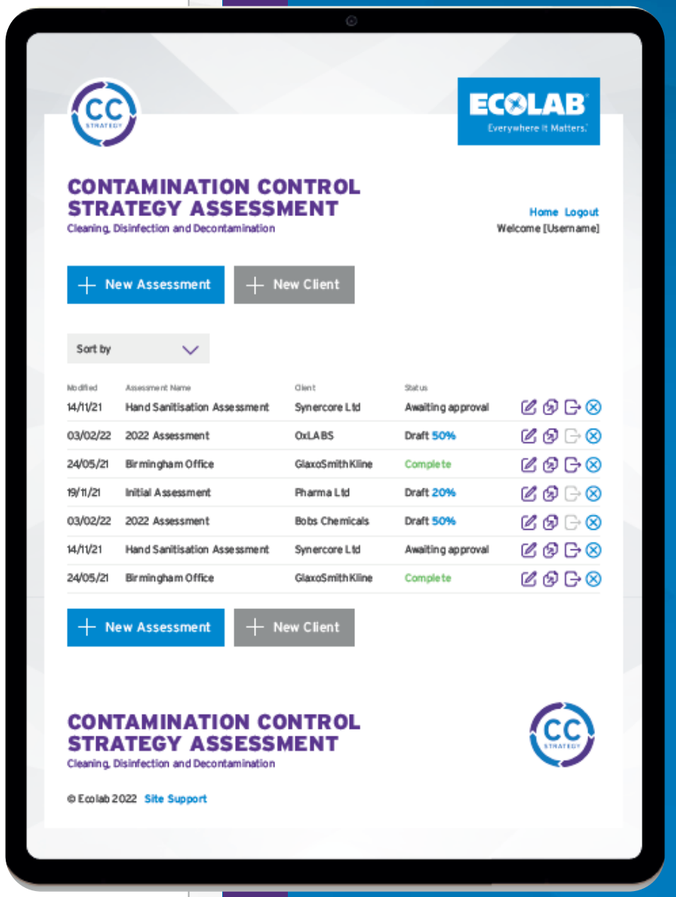
Contamination Risks

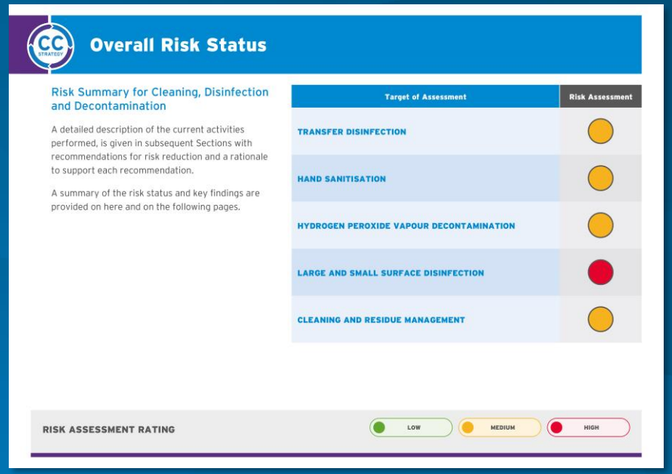
Disinfection

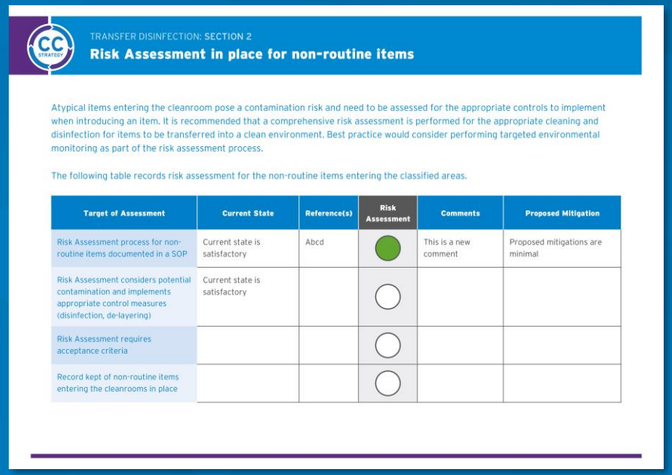
Addressing Microbiological Contamination

ECOLAB'S CCS ASSESSMENT TOOL

- Reviews current state against regulatory requirements and best practices
  - Aligned to global regulations
  - Digital tool for efficient recording
- Risk score the current state
- Where gaps are identified – mitigate risks







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CCS CASE STUDY

BIO PRODUCTS LABORATORY

- Sterile pharma manufacturer, based in Eastern England
- 215 cleanrooms, Grades A to D
- Complex manual manufacturing processes
- Good contamination control history

Two areas reviewed with Ecolab's CCS assessment process

- Residue Management
- Material Transfer

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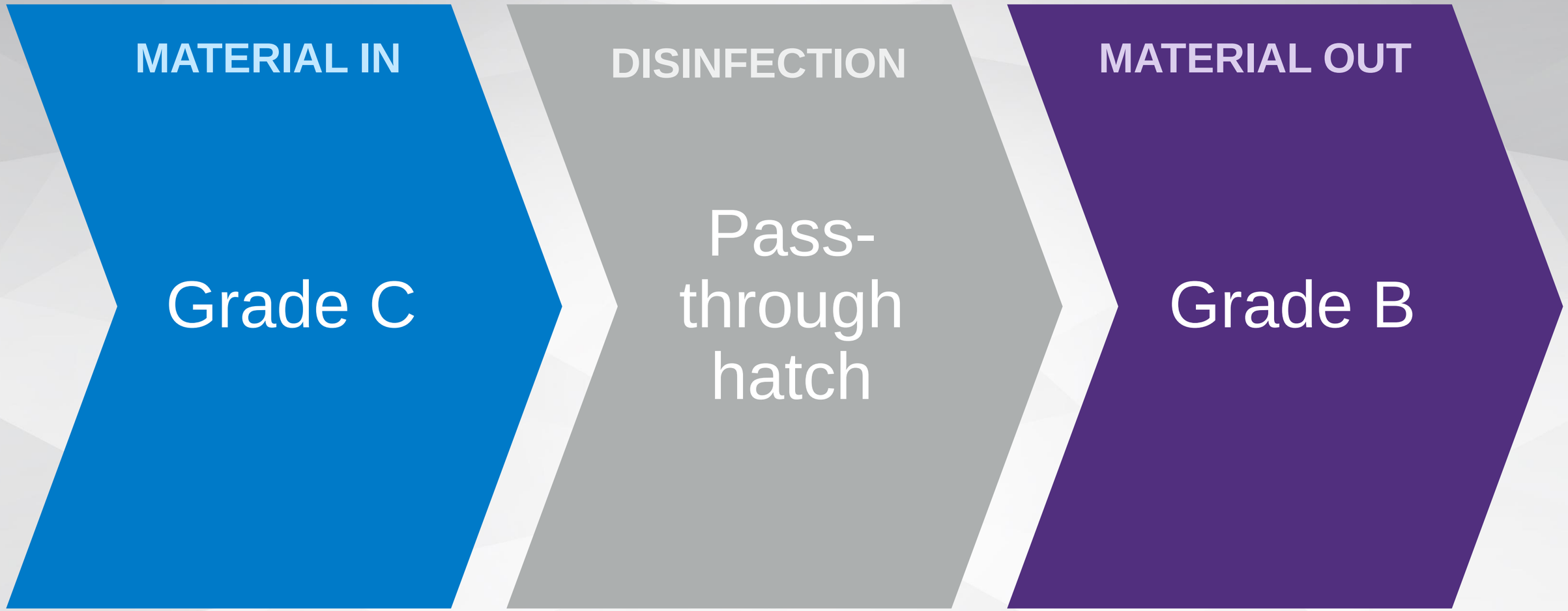
FOCUS ON MATERIAL TRANSFER

Protecting the Product

Bacterial spores in the Grade A environment present a significant risk of contamination in aseptically prepared products and potential patient harm.

KEY PROTECTIVE MEASURE IS TRANSFER INTO THE ASEPTIC CORE



MATERIAL TRANSFER METHODS

Protecting the Product

- Autoclaving / depyrogenaton tunnels
- Automated cycle decontamination chambers
- ‘Dynamic’ pass-through hatches with HEPA filtered air supply
- ‘Static’ pass through chambers with no air supply
- Personnel transferring items (e.g., via changing rooms)

CASE STUDY MATERIAL TRANSFER

- Packaging
- Environmental Monitoring
- Validated disinfectants
- Non-routine item risk assessment
- Methodology

RISK ASSESSMENT

MATERIAL TRANSFER

Current state

The first stage of transfer from warehouse to CNC is not part of the transfer disinfection process

Risks

Fungal and Bacterial Spores present on packaging materials enter the classified areas

Assessment

High risk of contamination - Sporicidal disinfectant is not used until transfer from Grade C to Grade B

Mitigation

Introduce validated sporicidal disinfectant to early stages of transfer Update and train out procedure for amended process

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RISK ASSESSMENT

MATERIAL TRANSFER

Current state

Wet contact time is not monitored in practice

Risks

Disinfection is not effective, contaminants remain on items being transferred

Assessment

High risk of contamination - Wet contact time is critical for effective disinfection. If the validated time is not being achieved, contamination may persist on the surface of the items

Mitigation

Introduce a process to ensure the validated contact time is being achieved in practice – by procedural controls or equipment controls on transfer hatches

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RISK ASSESSMENT

MATERIAL TRANSFER

Current state

No ongoing monitoring of bioburden associated with incoming items

Risks

Changes in contamination risks not detected and addressed

Assessment

Medium risk of contamination - No feedback on the effectiveness of the contamination controls

Mitigation

Consider periodic bioburden assessments of high risk items. Amend EM strategy to align to transfer of high risk items

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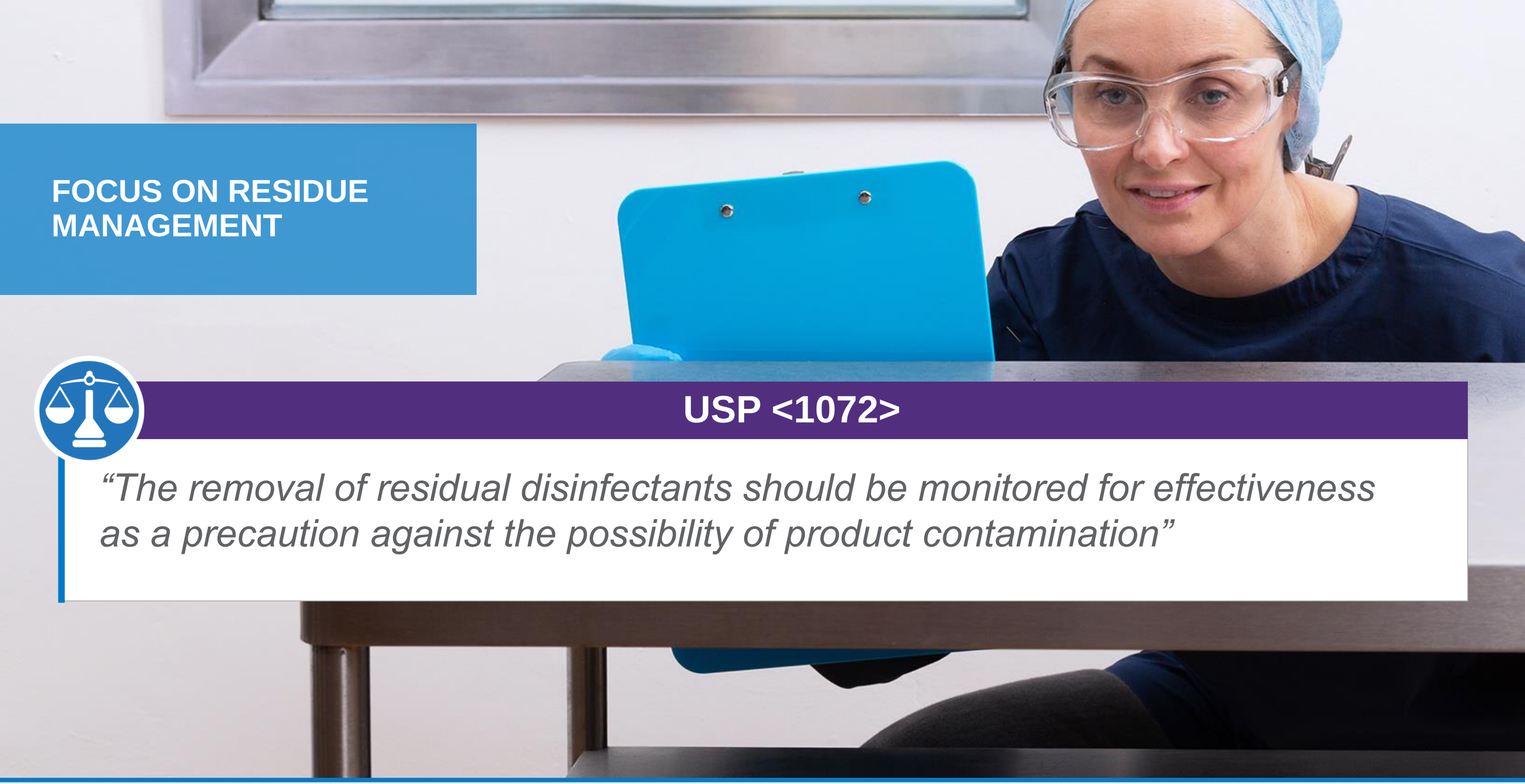
FOCUS ON RESIDUE MANAGEMENT



USP <1072>

“The removal of residual disinfectants should be monitored for effectiveness as a precaution against the possibility of product contamination”

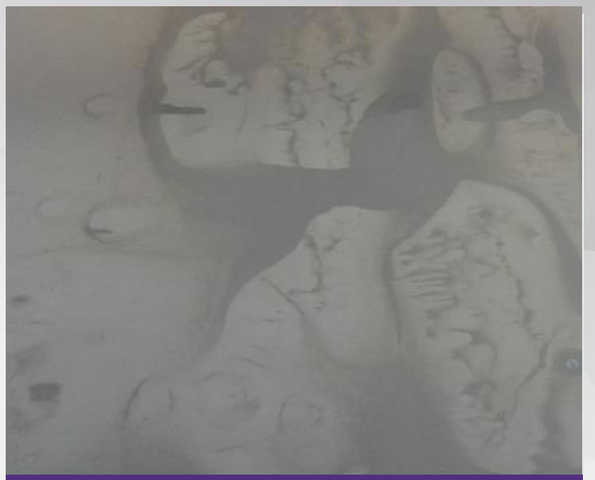
RESIDUES

Not all residues are white spots...

White Flaky Smears

Oily Layer or Smears

White Crystalline Powder



Sticky Coating

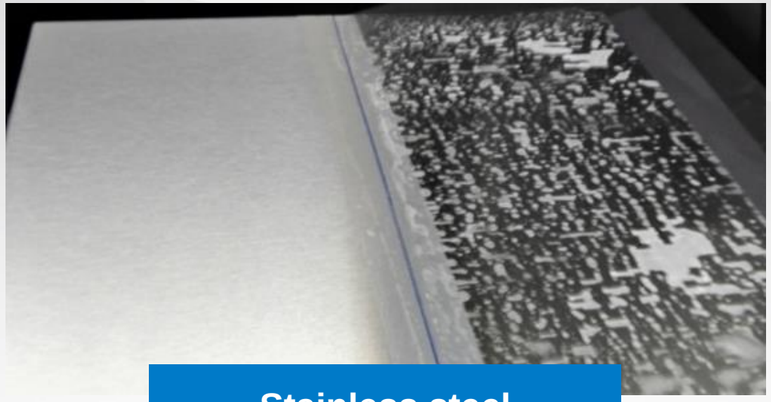
Residues can result in contamination risks – sticky surfaces / disinfectant inactiviation

Residues can result in safety risks – slippages / chemical interactions

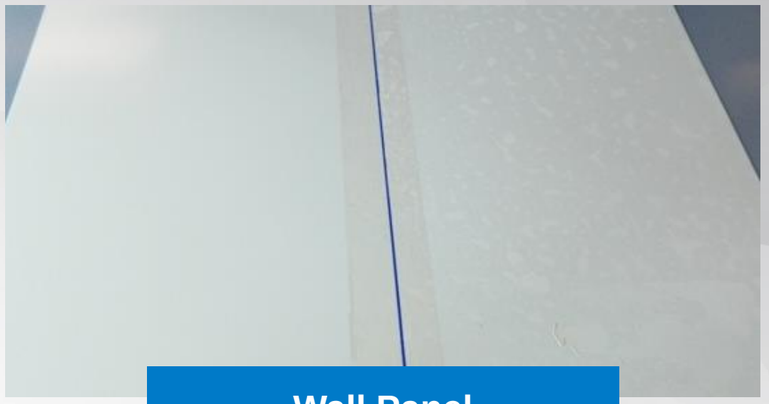
DISINFECTANT RESIDUES – VISUAL ASSESSMENT

Detectability depends on surface material

Glass



Stainless steel

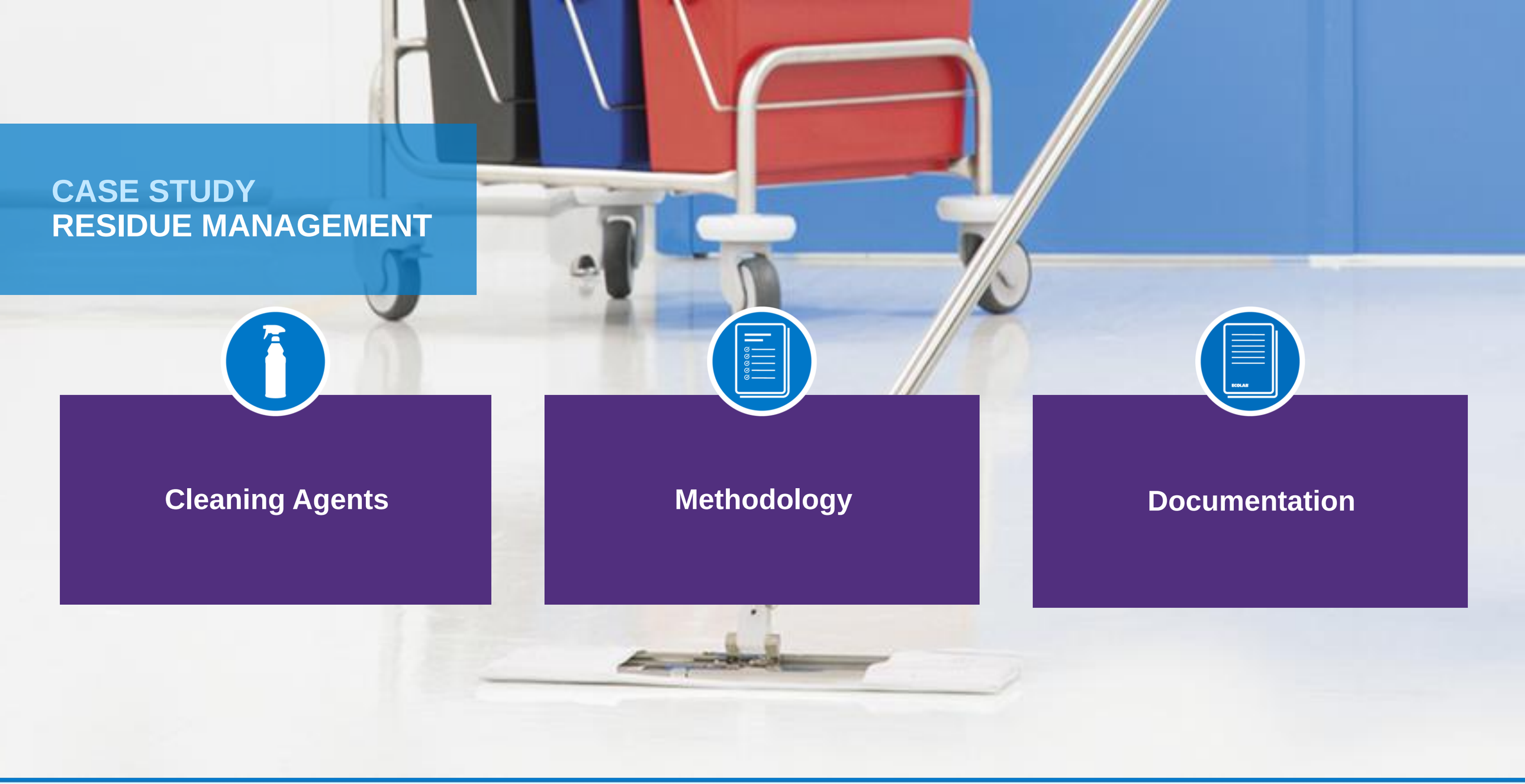


Wall Panel

PVC

Terrazzo

CASE STUDY
RESIDUE MANAGEMENT



Cleaning Agents

Methodology

Documentation

RISK ASSESSMENT

RESIDUE MANAGEMENT

Current state

Residues are not removed between cleaning agent (detergent) and disinfection rotations

Risks

Ineffective disinfection resulting in contamination on surfaces

Assessment

High risk of contamination - Interaction of chemicals results in disinfectant inactivation. Additional safety risk of chemical interactions

Mitigation

Implement rinsing between different chemistries using appropriate solvent

SUMMARY

The CCS is a key feature of the revision to EU GMP Annex 1 to proactively manage contamination

Systemically identify the contamination risks in your process

e.g., Ecolab's CCS assessment tool

Implement the appropriate strategy “planned set of controls” to manage the risks


Thank you and
any questions?