Contamination Control Strategy (CCS)

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The views expressed in this presentation are my own personal views and is not intended to represent the views of Emergent BioSolutions. References made within this presentation reflect the latest EMA Annex 1 draft available (v.13) as of May 5th, 2022.
Agenda

• Key Requirements
• Developing a Contamination Control Strategy
  • Getting Started
  • Opportunities
  • Challenges
• Practical Example
What is CCS

• Not an entire new concept
• First time there is a single document requirement
• Plays a significant role within the new Annex 1
• Explicit in requirements
• Explicit in the role of the microbiologist
• Holistic, beginning to end overview
Scope

The intent of the Annex is to provide guidance for the manufacture of sterile products. However, some of the principles and guidance, such as contamination control strategy, design of premises, cleanroom classification, qualification, validation, monitoring and personnel gowning, may be used to support the manufacture of other products that are not intended to be sterile such as certain liquids, creams, ointments and low bioburden biological intermediates but where the control and reduction of microbial, particulate and endotoxin/pyrogen contamination is considered important. Where a manufacturer elects to apply guidance herein to non-sterile products, the manufacturer should clearly document which principles have been applied and acknowledge that compliance with those principles should be demonstrated.
Annex 1 Draft - Principles

2.3 A Contamination Control Strategy (CCS) should be implemented across the facility in order to define all critical control points and assess the effectiveness of all the controls (design, procedural, technical and organisational) and monitoring measures employed to manage risks associated with contamination. The CCS should be actively updated and should drive continual improvement of the manufacturing and control methods. Its effectiveness should form part of the periodic management review. Where existing control systems are in place and are appropriately managed, these may not require replacement but should be referenced in the CCS and the associated interactions between systems should be understood.

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.
Annex 1 Draft - Principles

2.6 The CCS should consider all aspects of contamination control with ongoing and periodic review resulting in updates within the quality system as appropriate. Changes to the systems in place should be assessed for any impact on the CCS before and after implementation.

2.7 The manufacturer should take all steps and precautions necessary to assure the sterility of the products manufactured within its facilities. Sole reliance for sterility or other quality aspects should not be placed on any terminal process or finished product test.
House of CCS

2.5 The development of the CCS requires detailed technical and process knowledge. Potential sources of contamination are attributable to microbial and cellular debris (e.g. pyrogen, endotoxin) as well as particulate (e.g. glass and other visible and sub-visible particles). Elements to be considered within a CCS should include (but are not limited to):

- Design of both the plant and processes including the associated documentation.
- Premises and equipment.
- Personnel.
- Utilities.
- Raw material controls – including in-process controls.
- Product containers and closures.
- Vendor approval – such as key component suppliers, sterilisation of components and single use systems (SUS), and services.
- Management of outsourced services and availability/transfer of critical information between parties, e.g. contract sterilisation services.
- Process risk management.
- Process validation.
- Validation of sterilisation processes.
- Preventative maintenance – maintaining equipment, utilities and premises (planned and unplanned maintenance) to a standard that will ensure there is no additional risk of contamination.
- Cleaning and disinfection.
- Monitoring systems - including an assessment of the feasibility of the introduction of scientifically sound, alternative methods that optimize the detection of environmental contamination.
- Prevention mechanisms – trend analysis, detailed investigation, root cause determination, corrective and preventive actions (CAPA) and the need for comprehensive investigational tools.
- Continuous improvement based on information derived from the above.
Which came first?

Risk Assessment

CCS
Successful CCS
Define Strategy

- Audience
- Process focus
- Product focus
- Level of Specificity
Observe process from beginning to end

High level process flow for phases selected

Walk down the product path

Leverage existing SOP’s

Determine applicable technical documents
Add Controls

- **Equipment Controls**
  - Cycle Parameters
  - Mixing times
  - Agitation
  - Process Holds

- **Facilities Controls**
  - Temperature
  - Humidity
  - Differential Pressure

- **Product testing**
  - In Process
  - Visual Inspection
  - Batch Release

- **Procedural controls**
  - Temporal
  - Spatial
Identify gaps

- Compare and contrast between risk assessment and CCS
- Check for handover between process stages
- Check for alternative paths that can bypass control points
- Check against the Annex requirements
Challenges

• Requires cross functional team
• Will undoubtedly identify gaps – which will need to be addressed (CAPA)
• Needs to be integrated into the deviation / change control processes to ensure it is kept current
• Resources to develop and to maintain
• Need to have an assigned owner (and bandwidth or develop and maintain)
Opportunities

• Great internal resource (knowledge sharing)
• Great external resource (regulators, clients)
• Single template outline can be leveraged across products / lines / sites reducing the effort
• Leverage external resources
• Culture shift from reactive to proactive
• Increased process knowledge
Remember

- Avoid duplication
- Write for your audience – not for yourself
- Describe the what and the why
- Cliff’s Notes – not War & Peace
- Cross-reference with care
- Check for redundancy
### Practical Example

1. **Incoming Materials**
2. **Weigh & Dispense**
3. **Formulation**
4. **Fill**
5. **Heat Treatment**
6. **Visual Inspection**
7. **Assembly**