Contamination Control Strategy – An Overview

Presented by Ashley Isbel, 7 August 2018

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Draft Annex 1 New Key Concept

Draft Annex 1 introduces the concept of "Contamination Control Strategy".

This is a new and specific documentation requirement for Annex 1.

Contamination Control Strategy (CCS)

> Quality Assurance is particularly important, and manufacture of sterile products must strictly follow carefully established and validated methods of manufacture and control. A contamination control strategy should be implemented across the facility in order to assess the effectiveness of all the control and monitoring measures employed. This assessment should lead to corrective and preventative actions being taken as necessary.

CCS is mentioned 16 times in the update, and it is defined within the principle.

The CCS is defined as a multi-element, formally documented strategy, which is implemented site-wide.

Most organisations will already have many of the elements of a CCS, but may not be collated through a single source, as to be appears the intent of this requirement.

What is it?

Contamination Control Strategy	An holistic, systematic set of control mechanisms which act together to provide a high degree of assurance of elimination of contamination in finished product
Contamination	*"The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto raw material, intermediate, or API during production, sampling, packaging or re-packaging, storage or transport "*
Annex 1 Relevance	For the purpose of annex 1, we are primarily interested in microbiological contamination

Contamination Control Strategy (CCS)

The Annex requires organisations to understand the sources and control mechanisms for contaminants, which are defined as microbiological and cellular debris, as well as particulate matter.

- The key purpose of a CCS is allow assessment of the strategies implemented.
  - Not just collation of risk assessments, validations, procedures and other information
  - Requires ongoing effectiveness evaluation and correction.

CCS and Annex 1

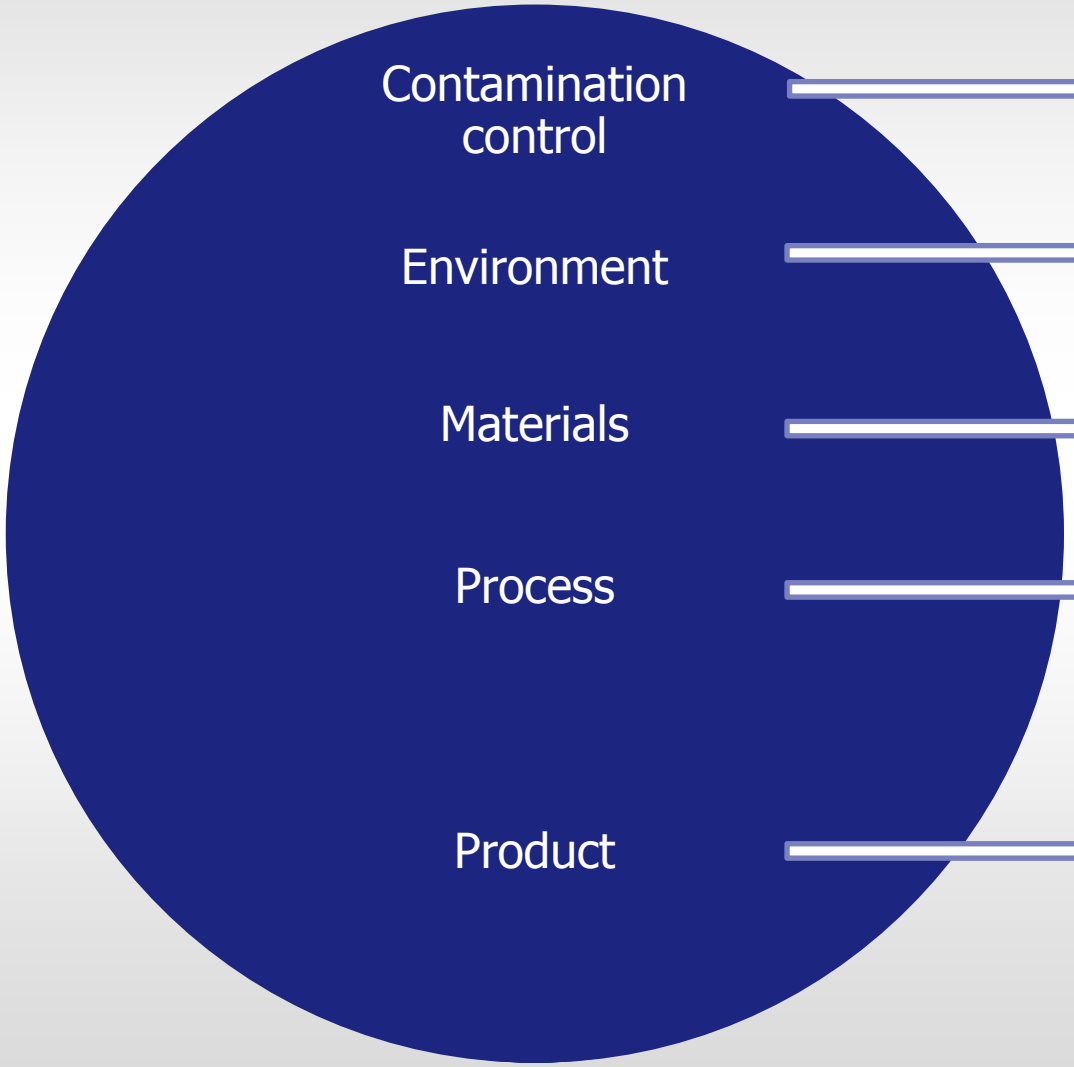
Adrew Hopkins at PHSS seminar

- CCS introduced as one of four key reasons for new Annex 1
  - (the others were clarity, new tech and addition of QRM)
- Concept linked to GMP clauses 3.6, 5.20 & 5.21
- Strategies driven by understanding of facilities, equipment & process
- Requires a feedback loop for regular update

A new requirement?

- Regulators would say no …
- Just a formalisation and consolidation of existing requirements

What's involved?



The overall strategy, procedures & risk based decisions which tie together the individual elements of contamination control

Personnel, facilities, utilities, HVAC

Raw materials, media/buffers, testing materials

Process controls, equipment & technology, cleaning, training, monitoring & trending

Product testing

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What does it look like?

Limited references available

- PHSS White Paper (member only)
- Some presenters beginning to give their thoughts

Intended to be a formal, documented strategy

Could be a stand-alone document, like a validation policy

May form part of a high level document – e.g. SMF, QM

To avoid bloat – likely to reference other parts of engineering and quality systems

No clear guidance yet available on content requirements

Components of CCS

Examples of Strategies
Process risk assessment
Process validation
Preventative maintenance
Cleaning and disinfection
Monitoring systems
Modern monitoring tools
Investigation, correction and prevention tools
Vendor approval
Continuous improvement

Examples of CCS topics
Number of operators in critical areas
Transfer of materials into Grade A/B areas
Isolator disinfection
Aseptic processing controls
Minimization microbiological, pyrogen and particulate contamination
BFS machine design and operational controls
Control of lyophilization processes
Environmental and process monitoring programs
Approach to managing hazardous materials.
Risk based requirements for identification of organisms
Strategy for starting materials
Monitoring requirements for CNC areas

Elements of a Good CCS

General Requirements

Site philosophy

Responsibilities

And for each key aspect of the CCS:

- Special features or enhancements
- Justification for differences from standard practices
- Details of supporting work – risk assessments, validations, studies, etc.

Key Aspects of a Good CCS

Good facility design

- Clean, GMP compliant physical design
- Materials of construction
- GMP Compliant HVAC regime

Good Process Design

- Aseptic considerations, pre-sterilisation handling
- Robust, validated sterilisation processes
- Validated depyrogenation processes

Key Aspects of a Good CCS

Effective supporting procedures

- Gowning
- Aseptic technique and handling
- Cleanroom behaviours
- Parametric release

Personnel Training

- Aseptic technique qualification
- Gowning qualification
- Effective production task training

Key Aspects of a Good CCS

Technology/Equipment

- Single use product contact equipment
- Barrier systems/isolators
- Automation, including CIP/SIP

Environmental Monitoring

- Robust, pro-active program
- Effective data analysis and appropriate alerts
- Acquired knowledge/understanding of facility risks

Key Aspects of a Good CCS

Cleaning & Disinfection

- Agents used, rotations, activity
- Types of clean and relevant frequencies
- Validation, both for disinfection and cleaning

Media Fills

- Appropriate for all product types
- Well defined interventions
- Data analysis and frequency of events

Example ToC

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Contents

At each section, consideration and reference to relevant risk assessment, validations, procedures, studies, etc. should be made as appropriate.

This will be a large document, and will be supported by procedure(s) around data collection and evaluation

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Common TGA Findings – Contamination Control

Lack of risk assessment to support risk-based decisions

- e.g. campaign length, cleaning frequency

Inadequate cleaning or disinfection validation

- e.g. single product focus, or lack of consideration of new products, lack of micro focus
- No validation of manual disinfection

Poor facility design

- Inappropriate air flow or pressure regimes
- Poor segregation

Inadequate periodic review

- Lack of critical assessment during review
- Lack of consideration of the effect of change

Questions?

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