Specialist Pharmacy Service

NHS

# Contamination Control Strategy (CCS)

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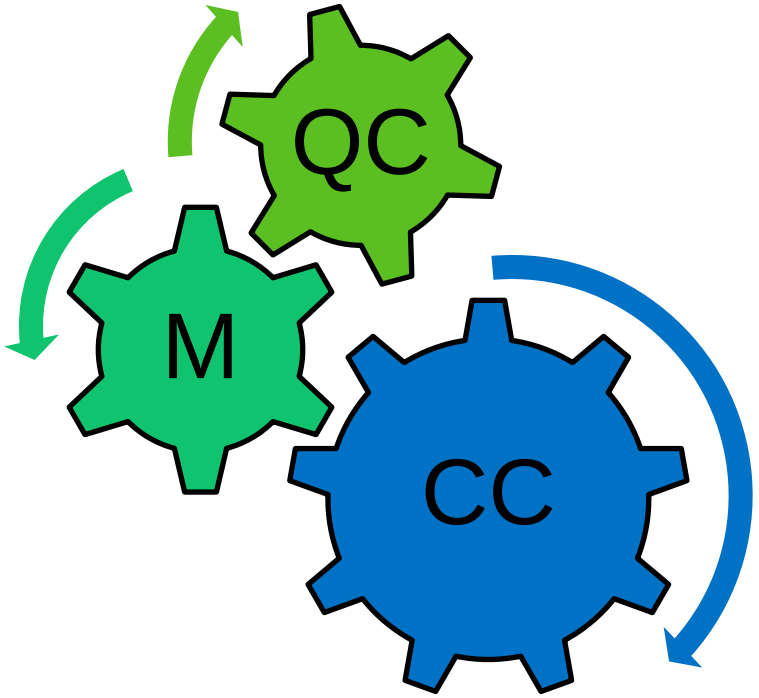
# Contamination Control Strategy – Introduction

## Background to CCS –
## Annex 1 Revision August 2022

## The importance of a CCS



A Contamination Control Strategy (CCS) should be implemented across the facility in order to define all critical control points and to assess the effectiveness of all the controls (design, procedural, technical and organisational) and monitoring measures employed to manage risks to medicinal product quality and safety.

The combined strategy of the CCS should establish robust assurance of contamination prevention.

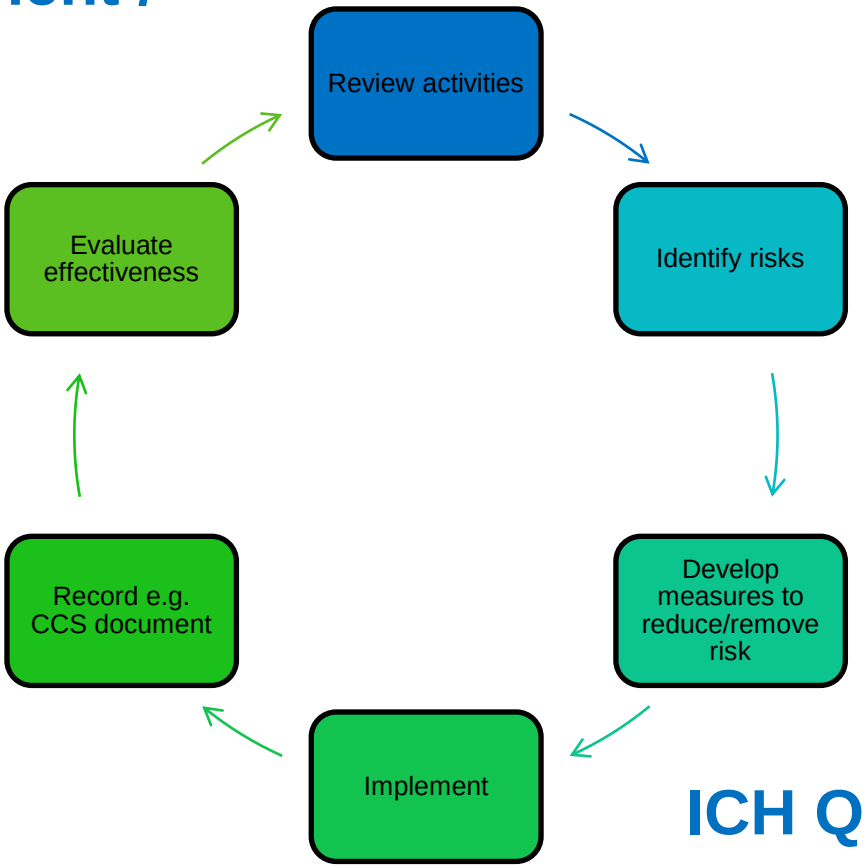
*(EU, 2022, Annex 1 para 2.3)*

The CCS is based on Quality Risk Management (QRM) principles. Within Annex 1, 2022, the reference to QRM is more extensive, utilising risk assessment development and review to augment quality improvement.

The CCS should consider all integral elements of sterile product manufacturing/ aseptic preparation, including QRM principles and supporting risk assessments of Contamination Control and monitoring (detectability of contamination event).

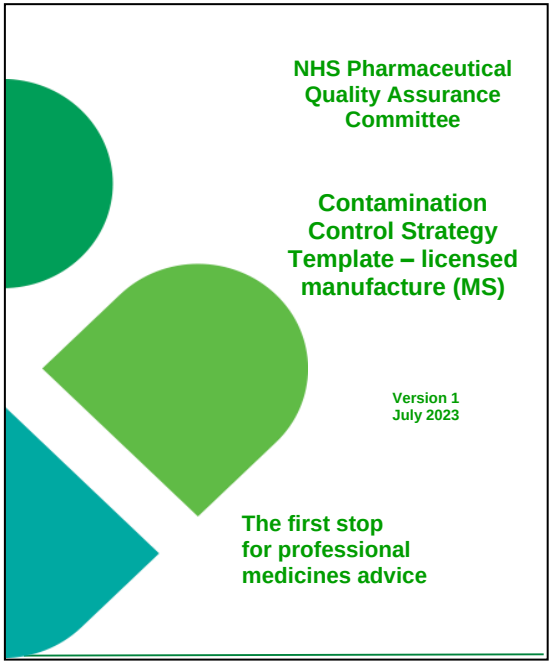
It should describe all control measures required to prevent / reduce risk of microbiological, non-viable particulate and endotoxin /pyrogenic contamination.

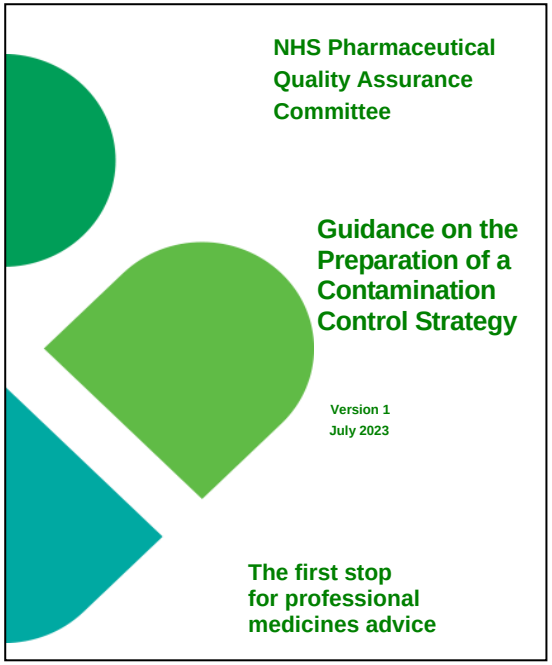
# CCS Development / Review




## ICH Q9 Quality Risk Management

# CCS Template development




## CCS Template format

Introduction

Definitions

Purpose

Scope

Responsibilities

Site overview

CCS – Technical and organisational elements – **16**

Appendices

# CCS – Technical and Organisational Elements

| Contamination Control Strategy – technical and organisational elements | |
|---|---|
| i. | Design of plant and process (including associated documentation) |
| ii. | Premises and equipment |
| iii. | Personnel |
| iv. | Utilities |
| v. | Raw Materials Controls (including in-process controls) |
| vi. | Product Containers and Closures |
| vii | Vendor approval – key component suppliers, sterilisation of components and single use systems (SUS) and critical service providers |
| viii | Management of outsourced activities and availability / transfer of critical information between parties |
| ix. | Process Risk Assessment |
| x. | Process Validation |
| xi. | Validation of sterilisation processes |
| xii. | Preventative Maintenance – maintaining equipment utilities and premises (planned and unplanned maintenance) to a standard that will ensure no additional risk of contamination |
| xiii. | Cleaning and disinfection |
| xiv. | Monitoring systems – including an assessment of the feasibility of the introduction of scientifically sound, alternative methods that optimise the detection of environmental contamination |
| xv. | Prevention mechanisms – trend analysis, detailed investigation, root cause determination, corrective and preventative actions (CAPA)and the need for comprehensive investigational tools |
| xvi. | Continuous improvement based on information derived from the above |

# CCS – Technical and Organisational Elements

Each element is referenced utilising the same nomenclature as in Annex 1.

Each element is set out as below :-

- Element title
- Suggested introductory text (in italics)
- Suggested Content – controls to be considered
- Examples of relevant reference documentation (listed in a table at the end of each element section)

There is a degree of duplication within the organisational and technical elements listed in Annex 1. Controls could be described under multiple element headings and be equally acceptable. The templates recognise this and offer potential options for inclusion.

The CCS “living” or dynamic document which will require updating in response to quality improvement, CAPA and audit.

The CCS document should be prepared, approved, implemented and reviewed in accordance with local documentation control systems.

## Example 1- process risk assessment (element ix)

Introductory text – suggested wording

*The manufacturing process is clearly defined and described e.g. via a process map. Each activity is risk assessed and mitigations put in place. Contamination control is designed into each stage of the preparation process (describe design parameters).*

Explanatory note: Units must establish an appropriate mechanism to assess the risk of each process using QRM principles (e.g. FMEA etc). Due to the range of processes in place for MS/Section 10 facilities, a matrix approach is advised. Describe the way in which this is executed here, including how required mitigation is applied and how often residual risks are reviewed. Flow charts may be a useful way of presenting this information. If this is contained in other documentation already part of the PQS, simply reference this information and provide a summary.

# Process risk assessment

- Define the Process
- List the Process Steps
- Risk Assess Steps
- Evaluate Process Risks
- Generate Action Plan
- Review

## Example of Risk Assessment tool

| Reference documentation | |
|---|---|
| Ref | Process maps |
| | Associated risk assessments |
| | Method SOPs |
| | Worksheets |

## Example 2 - environmental monitoring (element xiv)

Introductory text – suggested wording

*An environmental monitoring programme, which provides assurance of compliance with regulatory requirements is established. This programme also is designed to detect excursions from environmental limits triggering investigation and assessment of risk to product quality (annex 1, 2022). The environmental programme covers both viable and non-viable particles. All component parts of the environmental and process monitoring system are considered in combination to provide assurance of the integrity of the CCS. (refer to section 9, Annex 1, 2022)*

Explanatory note :- Environmental monitoring should be targeted at critical points of operator and material transfer and key interactions in the preparation process. In addition, results should be considered in conjunction with air changes, air flow patterns and pressure cascades. The microbiological contamination control strategy covers CAPA associated with repeated results above alerts levels or results reported above regulatory action levels.

## Example 2 - environmental monitoring (element xiv)

Controls to be considered within this element of the CCS – viable particles :-

Use of risk assessments to determine :-

Sampling/ test locations – during operations and at rest – risk based

Frequency of monitoring – include continuous monitoring for non-viable particles and pressures

Monitoring methods (including an assessment of the feasibility of the introduction of scientifically sound, modern methods that optimise the environmental detection of environmental contamination, and do not pose a risk of contamination to the product – Rapid Micro Methods (RMM)

At rest and operational monitoring

Acceptance criteria

Requirements for risk assessment review and frequency should be defined.

## Example 2 - environmental monitoring (element xiv)

Identification of potential sources/routes of microbiological contamination

Risk assessment - mitigation and controls

A description of the environmental and process monitoring programme

Media used – provide a description and refer to product specifications for settle plates etc

Refer to alert and action limits noted in (ii) Premises and equipment

Alert and action limits.  For Grade A – no growth i.e. every recovery requires investigation.

OOS investigation, root cause analysis and CAPA

Trending, setting alert and actions levels, data patterns

Media growth promotion – reference micro-organisms used / representation of facility flora

| Reference documentation | |
|---|---|
| **Ref** | Environmental monitoring programme |
| | Media growth promotion |
| | Validation reports |
| | Alert and action limits |
| | OOS / OOT action |
| | Trend analysis |

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# Questions ?

**What is your experience of CCS review and document development ?**

**What challenges have you encountered?**

**Good ideas to share?**