Contamination control strategy (CCS)

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Agenda

• Background
• Why
• When
• How
• Summary
Background

Draft Annex 1
• Refers to CCS 19 times
• So is it a new concept?
• Quality Risk Management (QRM) Q9 (2008)
• But also:
Background

Annex 1 (draft)
Processes, equipment, facilities and manufacturing activities should be managed in accordance with QRM principles that provide a proactive means of identifying, scientifically evaluating and controlling potential risks to quality. Risk assessments should be used to justify alternative approaches to those specified in this Annex only if these alternative approaches meet or surpass the intent of this Annex.

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.

The strategy should consider all aspects of contamination control and its life cycle with ongoing and periodic review and update of the strategy as appropriate.
Chapter 3 EU GMP Vol IV

“3.6 Cross-contamination should be prevented for all products by appropriate design and operation of manufacturing facilities. The measures to prevent cross-contamination should be commensurate with the risks. **Quality Risk Management** principles should be used to assess and control the risks. Depending of the level of risk, it may be necessary to dedicate premises and equipment for manufacturing and/or packaging operations to control the risk presented by some medicinal products.”
Chapter 5 EU GMP Vol IV

“5.20 A Quality Risk Management process, which includes a potency and toxicological evaluation, should be used to assess and control the cross-contamination risks presented by the products manufactured. Factors including; facility/equipment design and use, personnel and material flow, *microbiological controls*, physico-chemical characteristics of the active substance, process characteristics, cleaning processes and analytical capabilities relative to the relevant limits established from the evaluation of the products should also be taken into account. The outcome of the *Quality Risk Management process* should be the basis for determining the necessity for and extent to which premises and equipment should be dedicated to a particular product or product family. This may include dedicating specific product contact parts or dedication of the entire manufacturing facility. It may be acceptable to confine manufacturing activities to a segregated, self contained production area within a multiproduct facility, where justified. “
Chapter 5 EU GMP Vol IV

“5.21 The outcome of the Quality Risk Management process should be the basis for determining the extent of technical and organisational measures required to control risks for cross-contamination. These could include, but are not limited to, the following:”
ICH Q9

3. PRINCIPLES OF QUALITY RISK MANAGEMENT

Two primary principles of quality risk management are:

• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and

• The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.”
ICH Q9

4. GENERAL QUALITY RISK MANAGEMENT PROCESS

“Quality risk management is a **systematic** process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. A model for quality risk management is outlined in the diagram (Figure 1). Other models could be used. The emphasis on each component of the framework might differ from case to case but a robust process will incorporate consideration of all the elements at a level of detail that is commensurate with the specific risk.”
ICH Q9
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Why?

- Regulations require it
- Makes good business sense
- Protects patients
CCS

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When

• For existing facilities:
  • Should already exist! So as soon as possible if not already in place

• For new facilities:
  • As early as possible
  • Ideally should be part of the design process (URS/DQ)

• Rewind and start again!
  • Review information from the systems feedback
  • Change control, deviations and other feedback
  • Review of changes in technologies
CCS

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How

Assess

Design

Assess

Procedures

Assess

Monitoring
How

Firstly and primarily design:

• Facilities
• Equipment
• Process
Facilities

• Using appropriate current technologies

• Logical flows
  • Sterilisation of equipment (wherever possible)
  • People
  • Materials

• Appropriate classification of support and filling rooms
  • Isolators grade D? (or may be higher)
  • RABS Grade B
  • Closed systems Grade D/C/B?
  • Filling of products for Terminal sterilisation Grade C or Grade A

• Sufficient space
  • Changing rooms
  • Processing rooms
  • Support areas
Equipment

• Using appropriate current technologies
  • Isolators
  • Restricted Access Barrier Systems
  • Not open processing areas
  • Not curtains?

• Closed filling systems
  • But understand the risks

• Disposable technology
• No post filtration aseptic connections
CCS

Process

• Using appropriate current technologies
• Terminal sterilisation (if possible)
• Aseptic if you must
• Hybrid?
  • Not a fully lethal treatment but then performed in a higher classification
• Gowning
• Disinfection regime
Procedures (after design)

• Assess, review and identify residual risk

• Then mitigate with development of procedures e.g.:
  • Running the process
  • Line assembly
  • Intervention
  • Cleaning and disinfection
CCS

Monitoring (Then, and only then)

- Identify, assess and review residual risk
- Then understand with development of monitoring strategy

- Monitoring
  - Locations (Viable and no viable)
    - Based on process understanding
    - Smoke studies
Monitoring (Then, and only then)

- Types of monitor
  - Non viable particle samplers?
  - Swabs/Contacts/settle plates/air samplers?
  - Rapid Microbiological methods/automated systems (data governance)
- Frequencies
- Incubation strategy
Monitoring

- Aseptic process simulations:
  - Aerobic or anaerobic
  - Number of units filled
  - Duration of the simulation
  - Types and numbers of interventions
  - Incubation strategy
Monitoring

• Sterility test!!!?
  • Sampling plan (not just Beginning, Middle and End)
  • When – all interventions/critical interventions
  • Why – risk to product
How

But to do all of this **must** have the right personnel with the correct education, experience and technical knowledge available. Training and the correct attitude and culture are essential.
How

So how is it documented?
• Is it one document?
• Or multiple separate documents?
• Well it really just depends
How is it documented?

- If the documents already exist:
  - Then could take the Product Specification File approach. For example, an overview summary document that links all of the different elements and draws conclusions based on the entirety.
- Or:
  - Could be a single document:
    - Possibly easier to "control".
    - But likely to be a bit of a "monster".
How

So how is it documented?

But what ever you choose, it must be a “living” “document”
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- Not really a new requirement (Q9, Chapter 5 etc.)
- Required for regulatory/business and protection of the patient
- Based on good design
- Not used to justify poor design and bad practices
- Documented as one document or multiple that are linked
- Must be living/evolving document
- Updated based on feedback from the system, but also external feedback such as new technologies
Thank you for your time
Any questions?