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Navigating Annex 1

Frequently Asked Questions

Annex 1 introduces the concept of contamination control strategy (CCS) to ensure process performance and product quality by preventing microorganisms, pyrogens and particulate contamination. To comply with Annex 1, pharmaceutical manufacturers are required to identify, review and update critical controls to ensure holistic confidence in the measures implemented for contamination prevention.

We have answered a list of frequently asked questions related to implementation and evaluation of a CCS for Annex 1 compliance.

What is a Contamination Control Strategy (CCS)?

A CCS is "a planned set of controls for microorganisms, endotoxin/pyrogens and particles 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" (European Commission, 2022).

How Can We Implement a CCS at Our Facility?

Implementing a CCS involves three key steps:

Step 1: Develop – Identify contamination risks and the measures (procedures, control methods, etc.) that will be taken to minimize contamination.

Step 2: Document – Record the measures identified in Step 1 to provide evidence of proper CCS implementation as defined by Annex 1.

Step 3: Evaluate – Confirm all measures are effectively preventing contamination through periodic review and refinement.

What Existing Documentation/Other Elements Can We Use When Developing Our CCS?

Below is a non-exhaustive list of documents, measures and controls you can cross-reference when developing your CCS.

Documentation

- ☐ Manufacturing process flow map
- ☐ Product descriptions and specifications
- ☐ Module 3 of the Electronic Common Technical Document or product specification file
- ☐ Site master file

Risk Assessment Elements

- ☐ Aseptic intervention
- ☐ Sterility assurance
- ☐ Cleaning and disinfection
- ☐ Cross-contamination
- ☐ Environmental monitoring
- ☐ Microbial, endotoxin or viral contamination
- ☐ Personnel contamination
- ☐ Product contamination
- ☐ Qualification

Measures

- ☐ Cleaning and disinfection program
- ☐ Sterilization validation program
- ☐ Decontamination program
- ☐ Equipment design and use
- ☐ Facility layout
- ☐ Personnel and material flows
- ☐ Gowning programs per area
- ☐ Incoming material test program
- ☐ Monitoring strategy
- ☐ Product control strategy
- ☐ Rationale for monitoring strategy
- ☐ Room classifications and differential pressures
- ☐ Viral risk mitigation strategy

Controls

- ☐ Environmental monitoring data
- ☐ Preventative maintenance for equipment and utilities
- ☐ Procedure qualification records and specifications
- ☐ Aseptic process simulation data
- ☐ Change Control Committee

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How Can We Determine if Our Current Processes Meet Annex 1 Requirements?

We recommend conducting a gap analysis to compare your current processes to Annex 1 requirements for a CCS. A gap analysis is conducted via a three-step process.

Step 1: Verify the elements of your current process that are aligned with Annex 1 requirements for a CCS.

Step 2: Identify the elements of your current process that do not align with Annex 1 requirements for a CCS.

Step 3: Update your current process to include any missing elements you identified and finalize a CCS for your facility as required by Annex 1.

How Robust Must Our CCS Be to Comply with Annex 1?

At a minimum, a CCS should summarize:

- All critical points derived from your quality risk management (QRM) program
- Justification of residual risk acceptance
- Control and monitoring measures
- Trending and improvement measures
- How your facility will maintain holistic contamination prevention

How Do We Ensure Continuous Compliance of Our CCS?

A CCS should "consider all aspects of contamination control and its life cycle with ongoing periodic review resulting in updates within the pharmaceutical quality system as appropriate" (European Commission, 2022).

To ensure you are continuously improving your CCS, you need to identify the elements and controls needed to achieve a holistic approach, focus on comparing performance over a specified period and identify correlations between the data. The use of modern software is encouraged.

Additional Questions?

The STERIS Life Sciences team is here to help you navigate Annex 1. If you have any additional questions about Annex 1, contact a member of our team today.

References:

1. European Commission. (2022). EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines, Annex 1 – Manufacture of Sterile Medicinal Products.
2. ECA Foundation. (2022). CCS Task Force issues new Guideline.
3. El Azab, W. (2021). Contamination Control Strategy: Implementation Roadmap. PDA Journal of Pharmaceutical Science and Technology.