Decontamination and Sterilization of Indirect Product Contact Surfaces

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- Key changes in Annex 1
- Impact by technology
  - Traditional aseptic
  - RABS
  - Isolators (open / closed)
- Isolator and Filling Line Approaches
  - Process & Material Transfers
  - Design of the Filling Line with Material Transfers

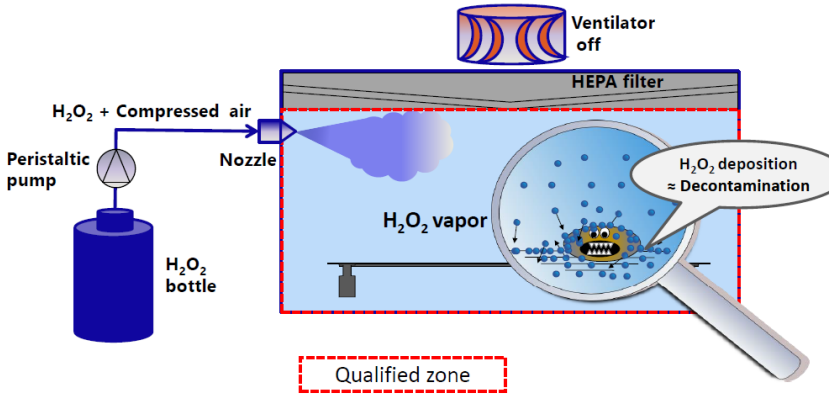
PDA Comment to Annex 1

"As currently written the section (5.5) can be interpreted as limiting sterilization to traditional methods that are not well suited for transfer indirect product contact parts into Barriers"

Isolators provide a validated surface decontamination.

Vaporized or nebulized Hydrogen Peroxide is seen as Surface Decontamination and not Sterilization.

Contamination Control Strategy



The Rules Governing Medicinal Products in the European Union
Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

Annex 1

Manufacture of Sterile Medicinal Products

For Isolators!

4.22 Decontamination methods (cleaning and bio-decontamination, and where applicable inactivation for biological materials) should be appropriately defined and controlled. The cleaning process prior to the bio-decontamination step is essential; any residues that remain may inhibit the effectiveness of the decontamination process. Evidence should also be available to demonstrate that the cleaning and bio-decontamination agents used do not have adverse impact on the product produced within the RABS or isolator.

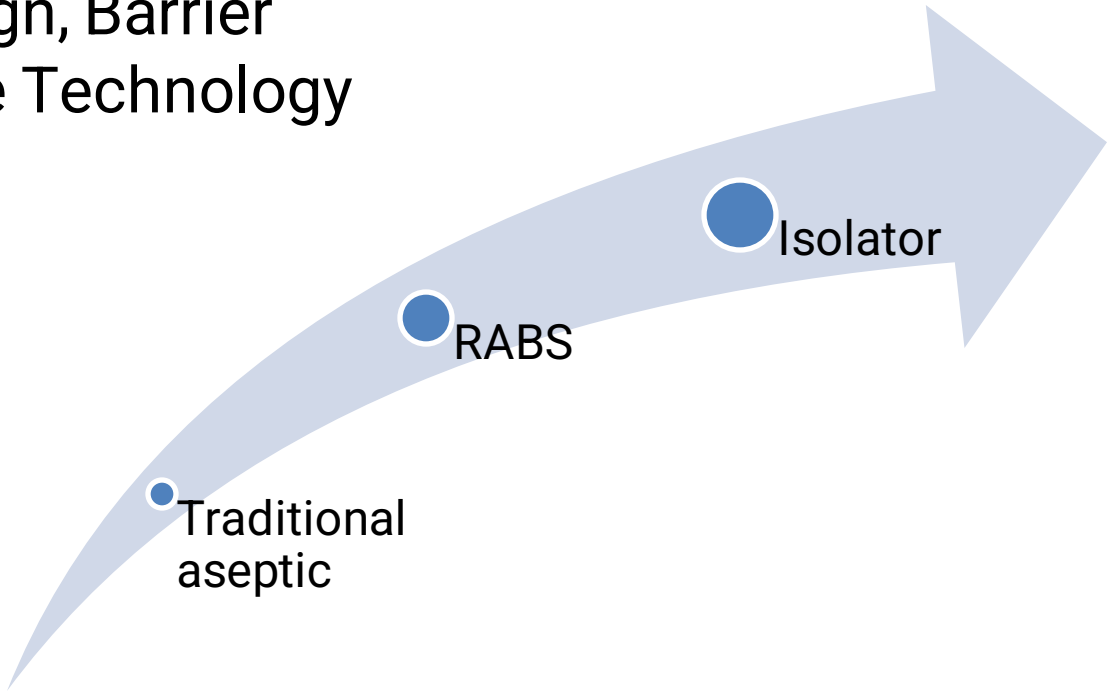
i. For isolators

The bio-decontamination process of the interior should be automated, validated and controlled within defined cycle parameters and should include a sporicidal agent in a suitable form (e.g. gaseous or vaporized form). Gloves should be appropriately extended with fingers separated to ensure contact with the agent. Methods used (cleaning and sporicidal bio-decontamination) should render the interior surfaces and critical zone of the isolator free from viable microorganisms.

For Cleanrooms!

4.36 Where fumigation or vapour disinfection (e.g. Vapour-phase Hydrogen Peroxide) of cleanrooms and associated surfaces are used, the effectiveness of any fumigation agent and dispersion system should be understood and validated.

Impact is Design, Barrier and Filling Line Technology dependent



Contamination Control Strategy for stopper transfers

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5.5 For aseptic processes, direct and indirect product contact parts should be sterilised. Direct product contact parts are those that the product passes through, such as filling needles or pumps. Indirect product contact parts are equipment parts that do not contact the product, but may come into contact with other sterilised surfaces, the sterility of which is critical to the overall product sterility (e.g. sterilised items such as stopper bowls and guides, and sterilised components).

What are the concerns and what is important to Consider for the stopper transfer in current installations.

- Stopper Bowl and Stopper transfer concerns and important to consider:
  - Evaluate the risk of your current technology e.g.,
  - How does the design of your stopper bowl and transfer looks like. It is easy to clean? Does the vaporized or sprayed hydrogen Peroxide reach all surfaces?
  - Does the assembly of the stopper transfer parts support aseptic assembly and reduce the risk of contamination?

What are the concerns and what is important to Consider for the stopper transfer.

- What are the reasons for stopping the line based on the stopper transfer and how often does this happen?
- May interventions be done without disturbing the first air and what can be done to reach this?
- Talk to your filling line and Barrier supplier to discuss solutions.

What is important to Consider for the stopper transfer in new installations.

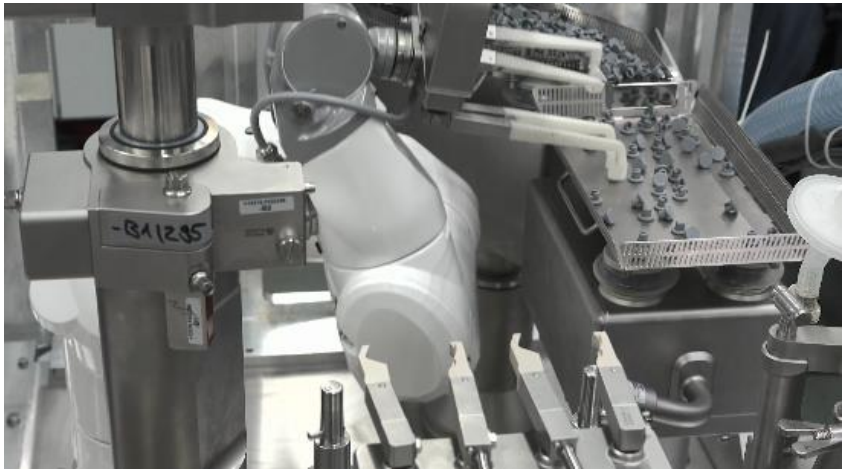
Stopper Bowl and Stopper transfer Design to meet Annex 1 requirements

- The design shall provide a first air protection in critical zones und unidirectional airflow that sweeps over and away from exposed products during processing
- The design shall allow to install all components without touching critical surfaces and avoid working above critical surfaces

What is important to Consider for the stopper transfer in new installations.

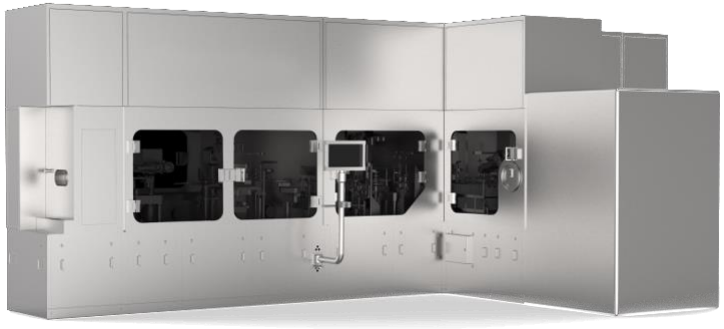
Evolution for Stopper Transfers from traditional to new installtions.

Left side: Traditional stopper sorting



Right side: Robotic based stopper sorting

Comparable with the evolution of conventional filling lines to fully automated gloveless robotic filling lines.



Source: Groninger RoboCell

Points to Consider for the Aseptic Processing of Sterile Pharmaceutical Products in Isolators

Q6-1: How should indirect product contact surfaces be sterilized or decontaminated?

Recommendation

PDA PtC for the Aseptic Processing of Sterile Pharmaceutical Products in Isolators Q6.1

1. Sterilize and transfer into decontaminated isolator through a transfer isolator or RTP
2. Sterilize, transfer into open isolator, unwrap, assemble and then close / decontaminate
3. Sterilize, transfer to open isolator, close, decontaminate and then unwrap and assemble
4. Equipment remains in place, in situ cleaning and decontamination

Process

- ❑ Equipment may or may not be wrapped
- ❑ Transfer Isolator attached to the Autoclave or RTP canister
- ❑ Unwrap and assemble

Concern

- ❑ Design choice can add complexity
- ❑ Isolator design to accommodate large ports

Process

- ❑ Cleaned, wrapped and sterilized
- ❑ Transfer through open doors
- ❑ Unwrap and assemble open (prior to decontamination)

Concern

- ❑ Minimize introduction of background air and operator impact
- ❑ Preservation of sterile surfaces

7.13 A description of typical clothing required for each cleanliness grade is given below:

iv. Additional gowning including gloves and facemask may be required in grade C and D areas when performing activities considered to be a contamination risk as defined by the CCS.

Process

- ❑ Cleaned, wrapped and sterilized
- ❑ Transfer through open doors
- ❑ Unwrap and assemble closed (after decontamination)

Concern

- ❑ Ensure removal of oily residues
- ❑ Loss of dexterity, higher stress on gloves, limited bo positioning, risk of contamination

7.13 A description of typical clothing required for each cleanliness grade is given below:

iv. Additional gowning including gloves and facemask may be required in grade C and D areas when performing activities considered to be a contamination risk as defined by the CCS.

Process

- ❑ Equipment remains in place
- ❑ No prior sterilization (but should consider periodic sterilization)
- ❑ Decontamination

Concern

- ❑ Validation of cleaning and justification of decontamination frequency
- ❑ Bioburden control at all stages

7.13 A description of typical clothing required for each cleanliness grade is given below:

iv. Additional gowning including gloves and facemask may be required in grade C and D areas when performing activities considered to be a contamination risk as defined by the CCS.

For the Breakout Session

- What is your contamination control strategy for the assembly of the stopper transfers and what would you improve?

Thank You

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