Steam Sterilization and Transfer of Parts into the Isolator / RABS

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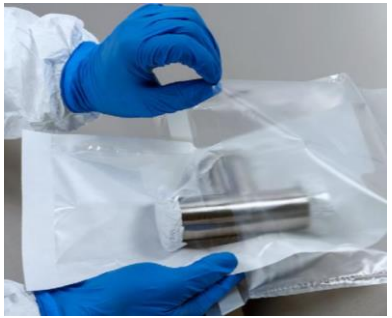
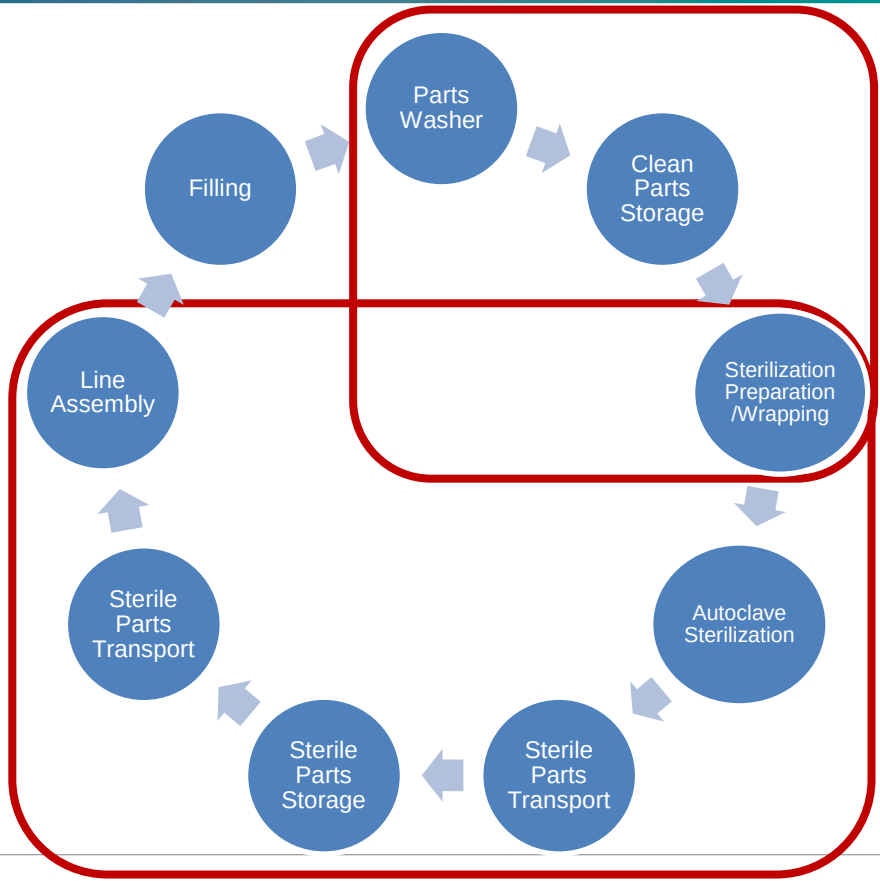
Agenda

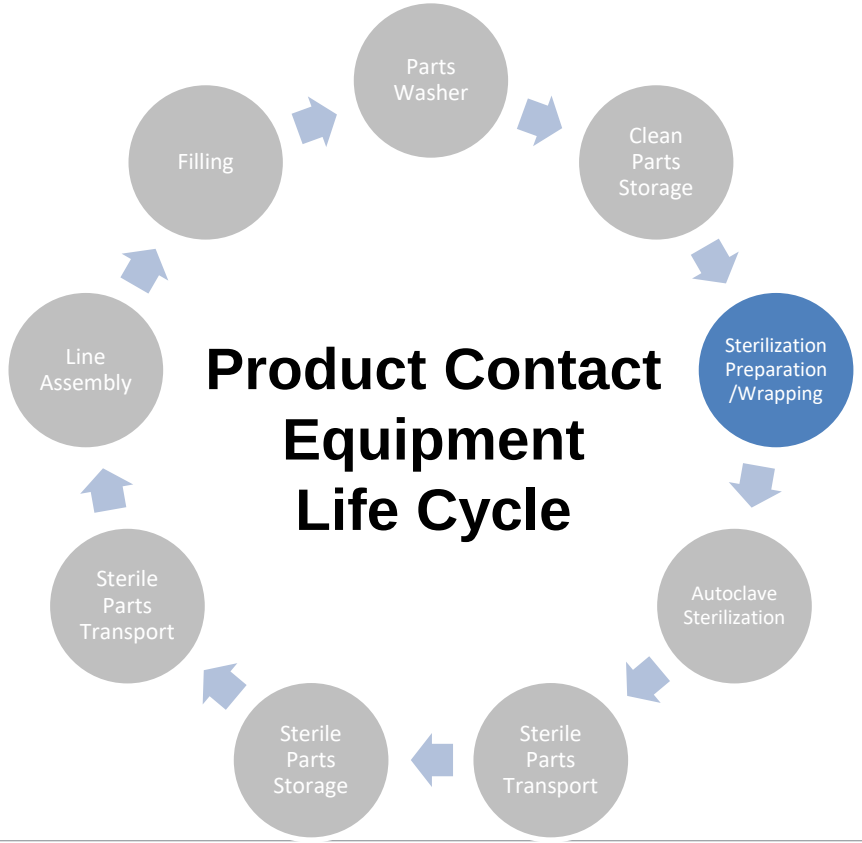
- Contamination Control Strategy Life Cycle
- Sterilization Wrapping
- Sterilization / Validation
- Transport and Line Assembly
- Q & A



Contamination Control Strategy (CCS)

A planned set of controls for microorganisms, endotoxin/pyrogen 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.





STOPPER BOWL COVERS

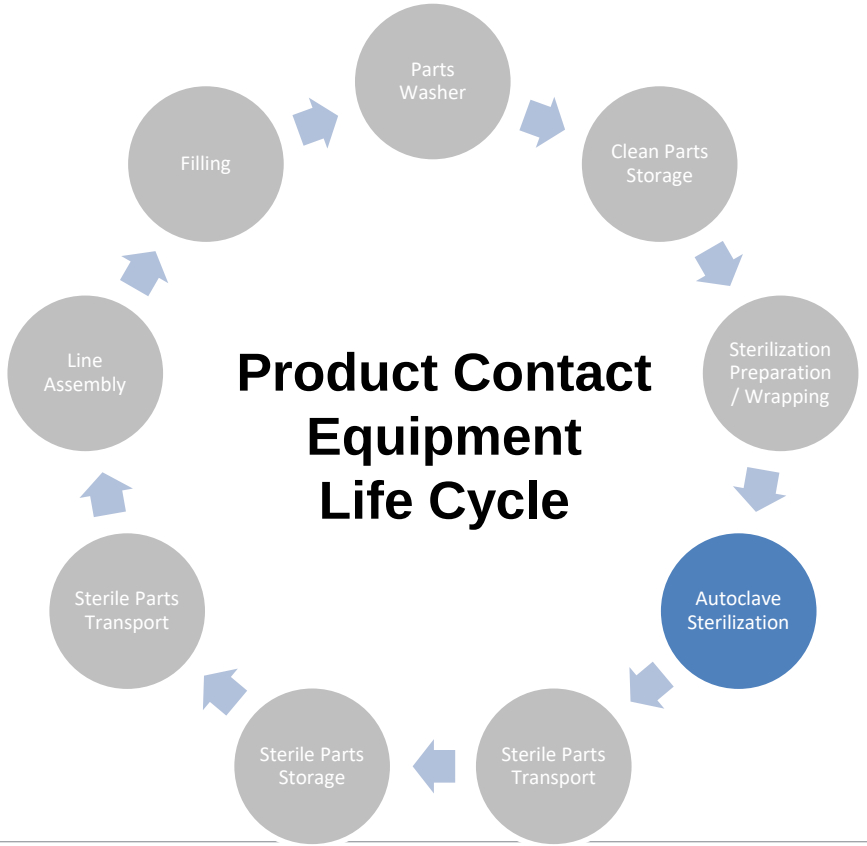
Primary and secondary covers for product contact surfaces

What is the Purpose of Sterilization Wrapping?

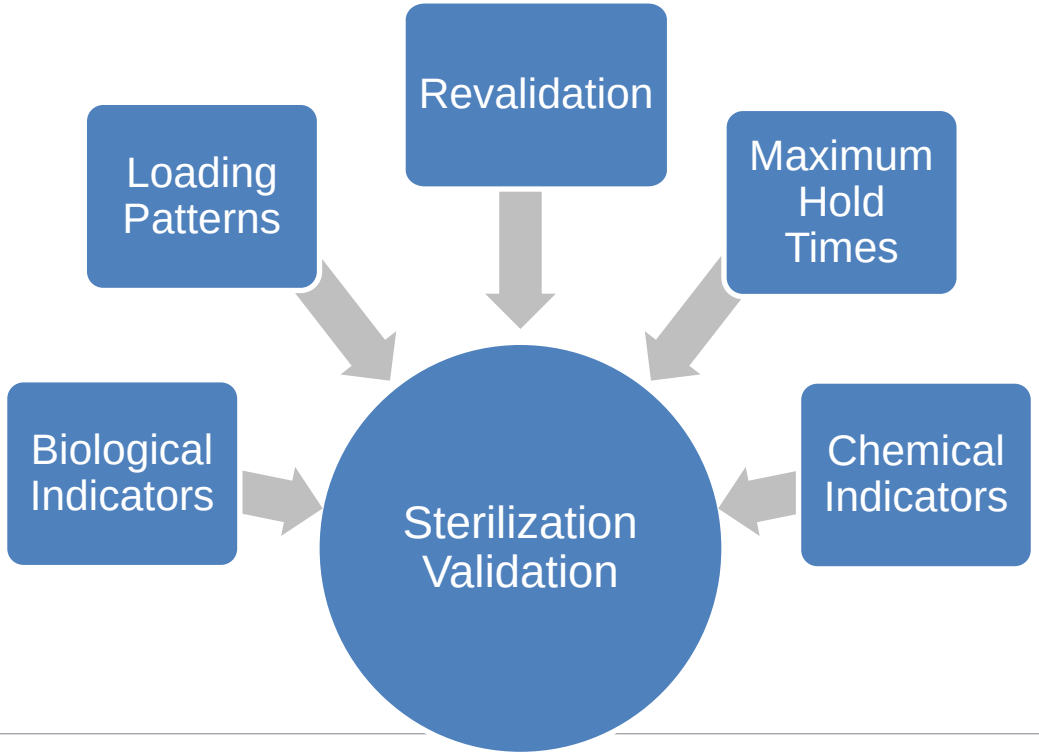
EU Annex 1, Section 8.48

"Where materials, equipment, components and ancillary items are sterilised in sealed packaging or containers, the packaging should be qualified for minimizing the risk of particulate, microbial, endotoxin/pyrogen or chemical contamination, and for compatibility with the selected sterilisation method. The packaging sealing process should be validated. The validation should consider the integrity of the sterile protective barrier system, the maximum hold time before sterilisation and the maximum shelf life assigned to the sterilised items. The integrity of the sterile protective barrier system for each of the sterilised items should be checked prior to use."

Manufacturers of ***aseptically filled*** drug product need to ***protect product contact surfaces*** through sterilization, until time of use on the filling line.



Autoclave Sterilization



Autoclave Sterilization Validation

EU Annex 1, Section 8.36

> All sterilisation processes should be validated. Validation studies should take into account the product composition, storage conditions and maximum time between the start of the preparation of a product or material to be sterilized and its sterilisation. Before any sterilisation process is adopted, its suitability for the product and equipment, and its efficacy in consistently achieving the desired sterilizing conditions in all parts of each type of load to be processed should be validated notably by physical measurements and where appropriate by Biological Indicators (BI). For effective sterilisation, the whole of the product, and surfaces of equipment and components should be subject to the required treatment and the process should be designed to ensure that this is achieved.

Product
- Composition
- Storage conditions
- Hold times

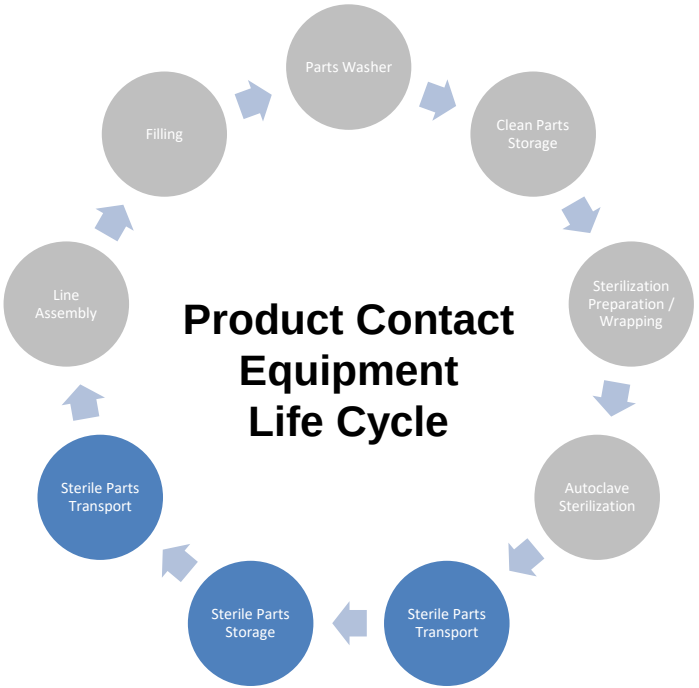
Sterilization method
- Suitability
- Efficacy

Validation
- Physical measurements
- Biological indicators
- All equipment surfaces

Transport and Assembly of Sterilized Equipment

EU Annex 1, Section 8.47

"Where materials, equipment, components and ancillary items are sterilised in sealed packaging and then transferred into grade A, this should be done using appropriate validated methods (for example, airlocks or pass-through hatches) with accompanying disinfection of the exterior of the sealed packaging. The use of rapid transfer port technology should also be considered. These methods should be demonstrated to effectively control the potential risk of contamination of the grade A and grade B areas and, likewise, the disinfection procedure should be demonstrated to be effective in reducing any contamination on the packaging to acceptable levels for entry of the item into the grade B and grade A areas."

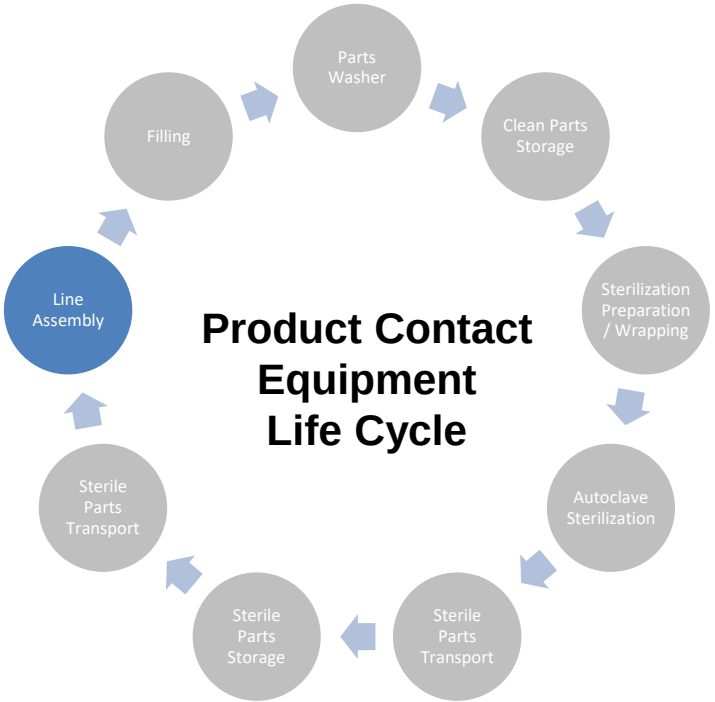


Line Assembly – RABS / Isolator

EU Annex 1, Section 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)."

Do not rely on environmental decontamination of the RABS/isolator using VHP® for sterilization of sterile processing stream.



Line Assembly – RABS / Isolator

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Autoclave Sterilization

Sterile Parts Transport

Line Assembly – RABS / Isolator

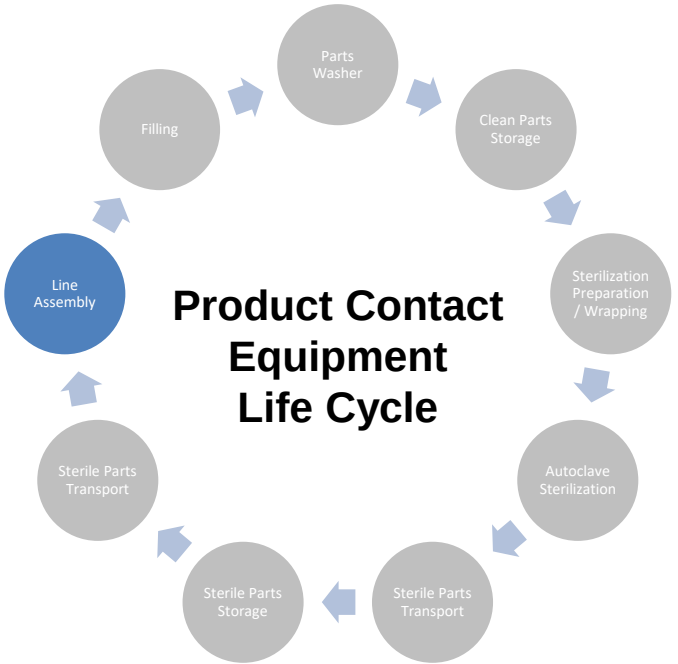
- 4.18 Isolators or RABS, which are different technologies, and the associated processes, should be designed to provide protection through separation of the grade A environment from the environment of the surrounding room. The hazards introduced from entry or removal of items during processing should be minimized and supported by high capability transfer technologies or validated systems that robustly prevent contamination and are appropriate for the respective technology.

- 8.12 The unwrapping, assembly and preparation of sterilised equipment, components and ancillary items with direct or indirect product contact should be treated as an aseptic process and performed in grade A with a grade B background. The filling line set-up and filling of the sterile product should be treated as an aseptic process and performed in grade A with a grade B background. Where an isolator is used, the background should be in accordance with paragraph 4.20.

Line Assembly – RABS / Isolator

Best Practice Recommendation

Stage wrapped/covered parts in RABS/isolator prior to environmental decontamination process (VHP®), unwrap/uncover sterilized parts through glove ports following decontamination aeration.



Thank You

What if we cannot remove our indirect product contacting parts?

Why would we leave the covers on the stopper bowl during the environmental decontamination cycle?

What is the best way to transfer parts if your sterilizer does not open into the room with the isolator?