

Single-Use Technology Used for Aseptic Processing and Final Fill Applications

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Agenda

Definitions

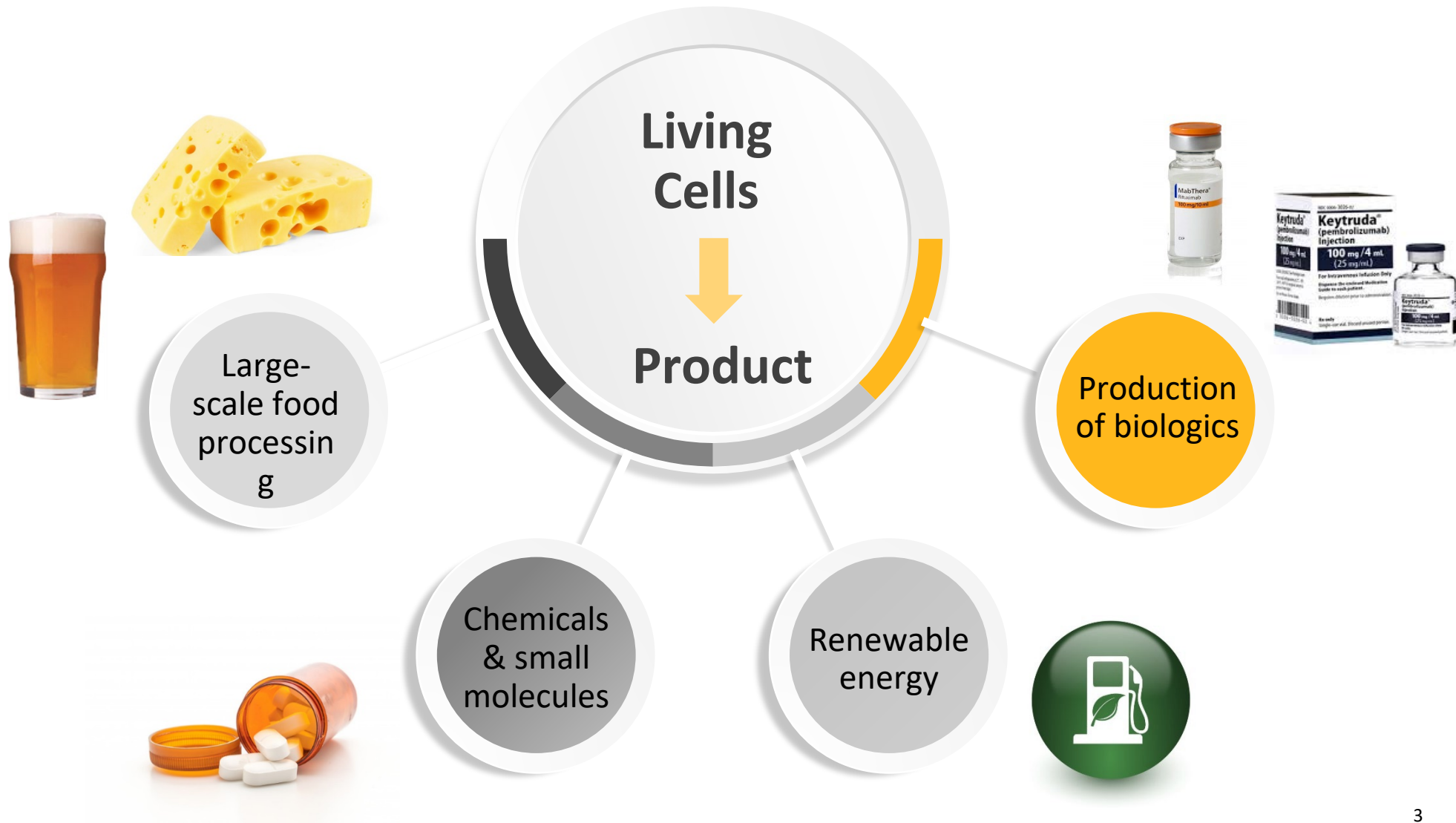
Single-Use Market and Concerns

Single-Use Solutions





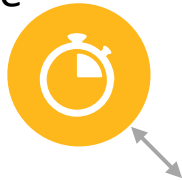
What is Bioprocessing?





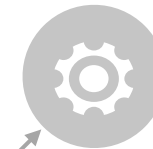
What is Single-Use?

Quick Set-Up /
Change-Over time



Single-use assemblies replacing

Reduction in capital
investment



Elimination of
cleaning validation
costs



Decreased time to
market – qualification/
validation



Reduced risk of
operator exposure



Eliminate risk of
cross contamination



Single-Use Market Dynamics

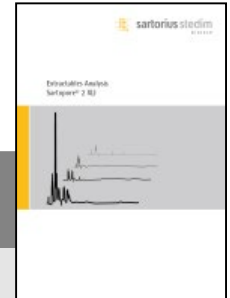
New Challenges

- Quality assurance:
Leaks -> Product Loss
- Integrity testing: at
supplier & point of use
- Extractables: transparency
on reports and testing
- Assurance of supply &
change control



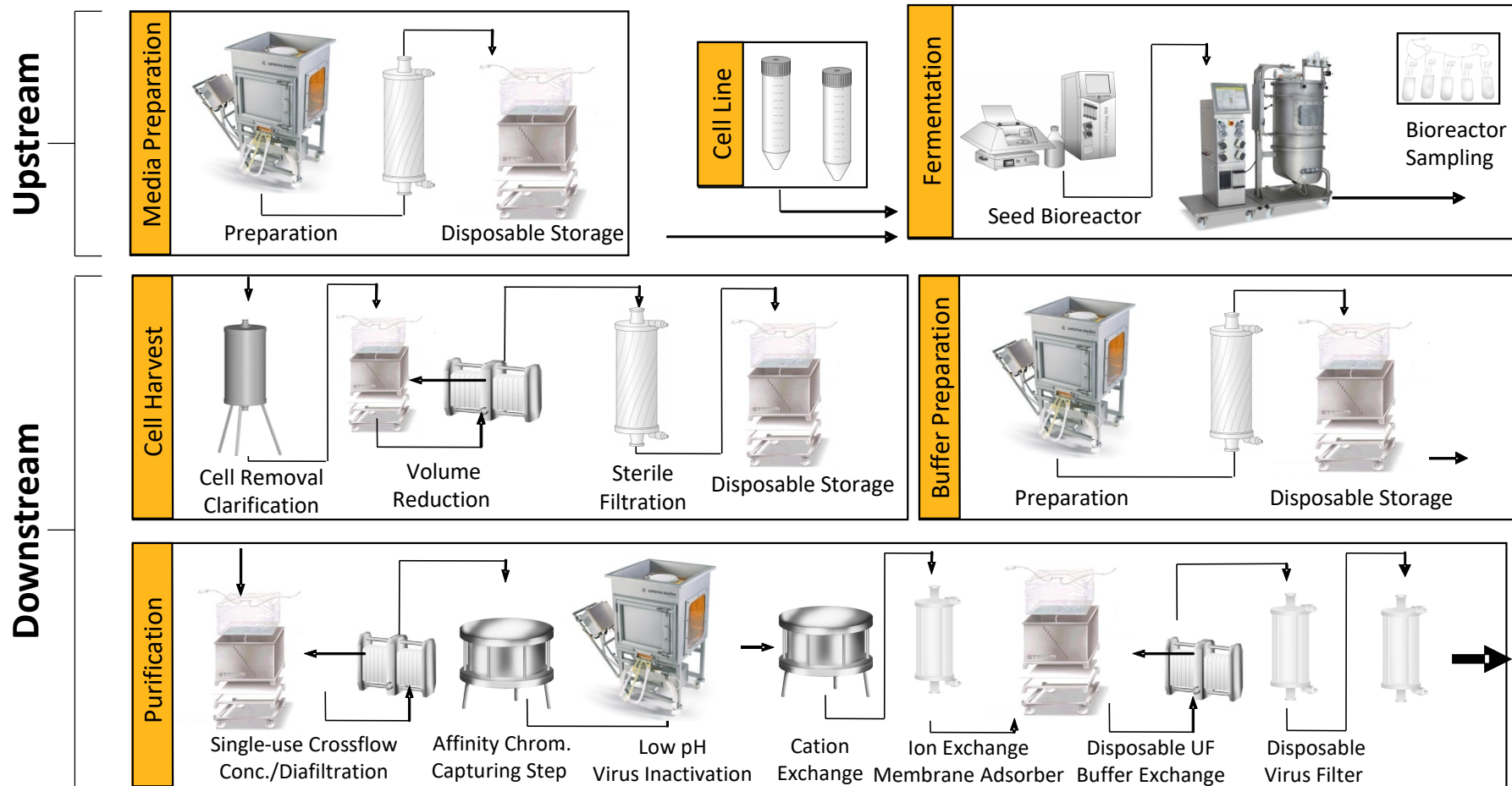
Key Needs

- Superior product
performance & ease of use
- Documentation, validation,
training support
- Standardization: materials,
connectors &
configurations
- Assurance of supply:
business continuity &
consistent quality



Application Areas for Single-Use Components in Bioprocessing

mAb Process





Bioreactors





Bioreactors





Filters





Filters



Chromatography

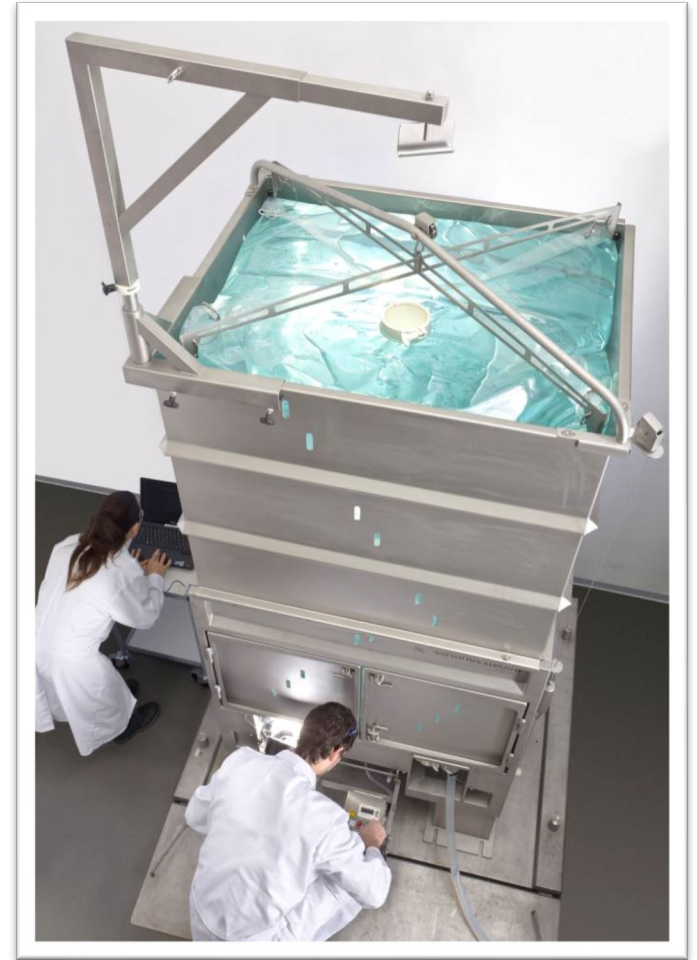




Chromatography



Mixing Systems

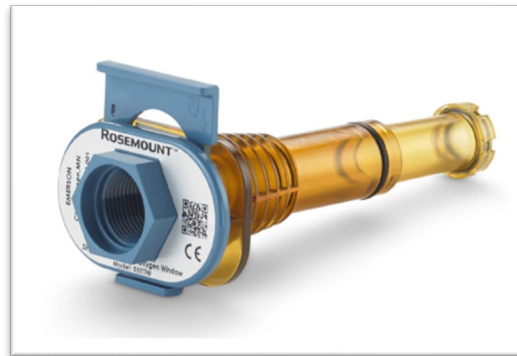
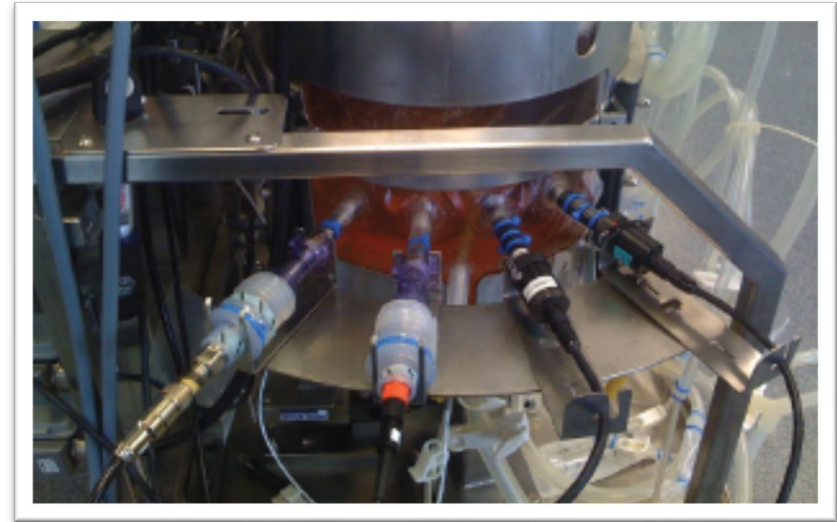
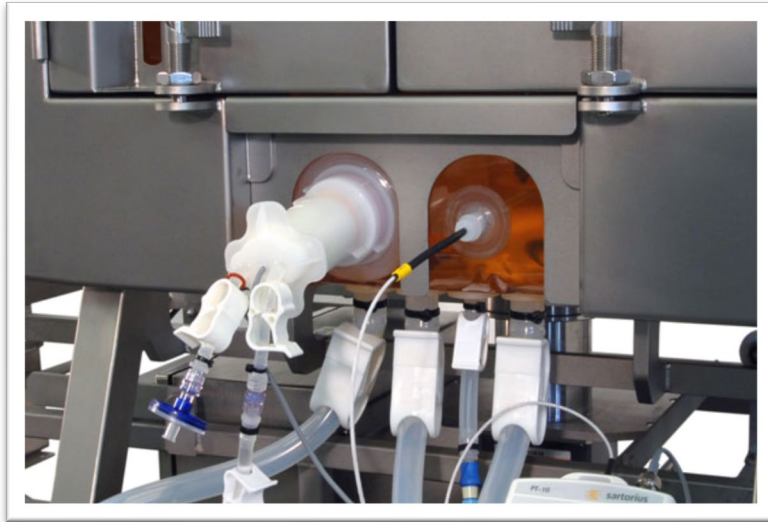




Mixing Systems



Single-Use Sensors



Storage Bags



2D Pillow Bags <50L
Small Volume
Storage & Transport Bags

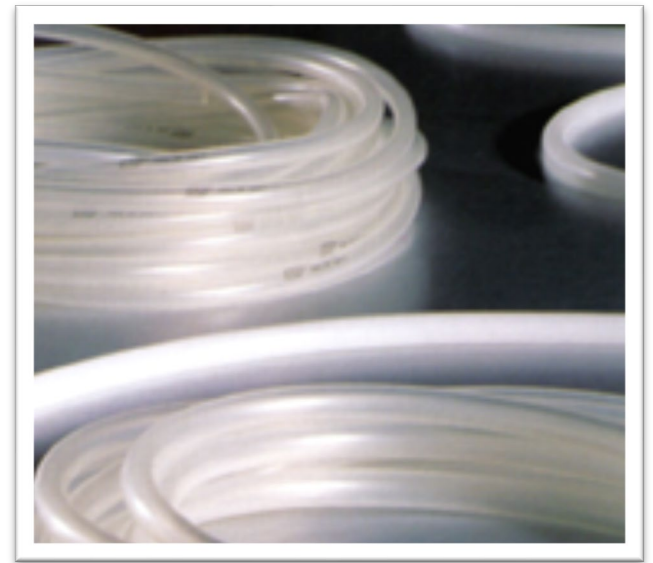


3D Bags 50L – 3000L
Large Volume
Storage & Transport Bags

Self-Deploying
Large Volume



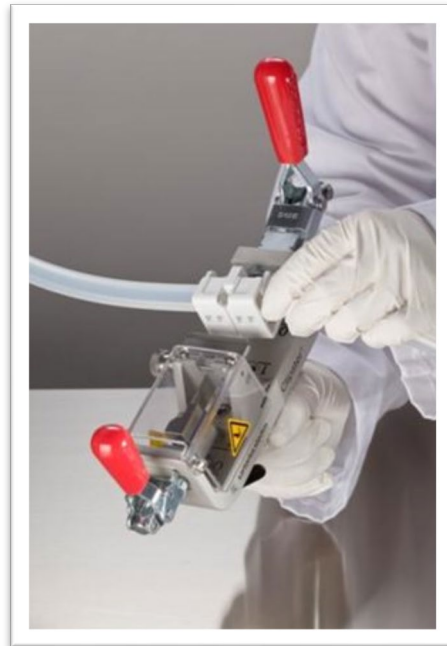
Tubing



Aseptic Connectors



Aseptic Disconnectors



Clipster Disconnecter

Sterile Connections & Disconnections



BioWelder TC



Frozen Storage & Transportation

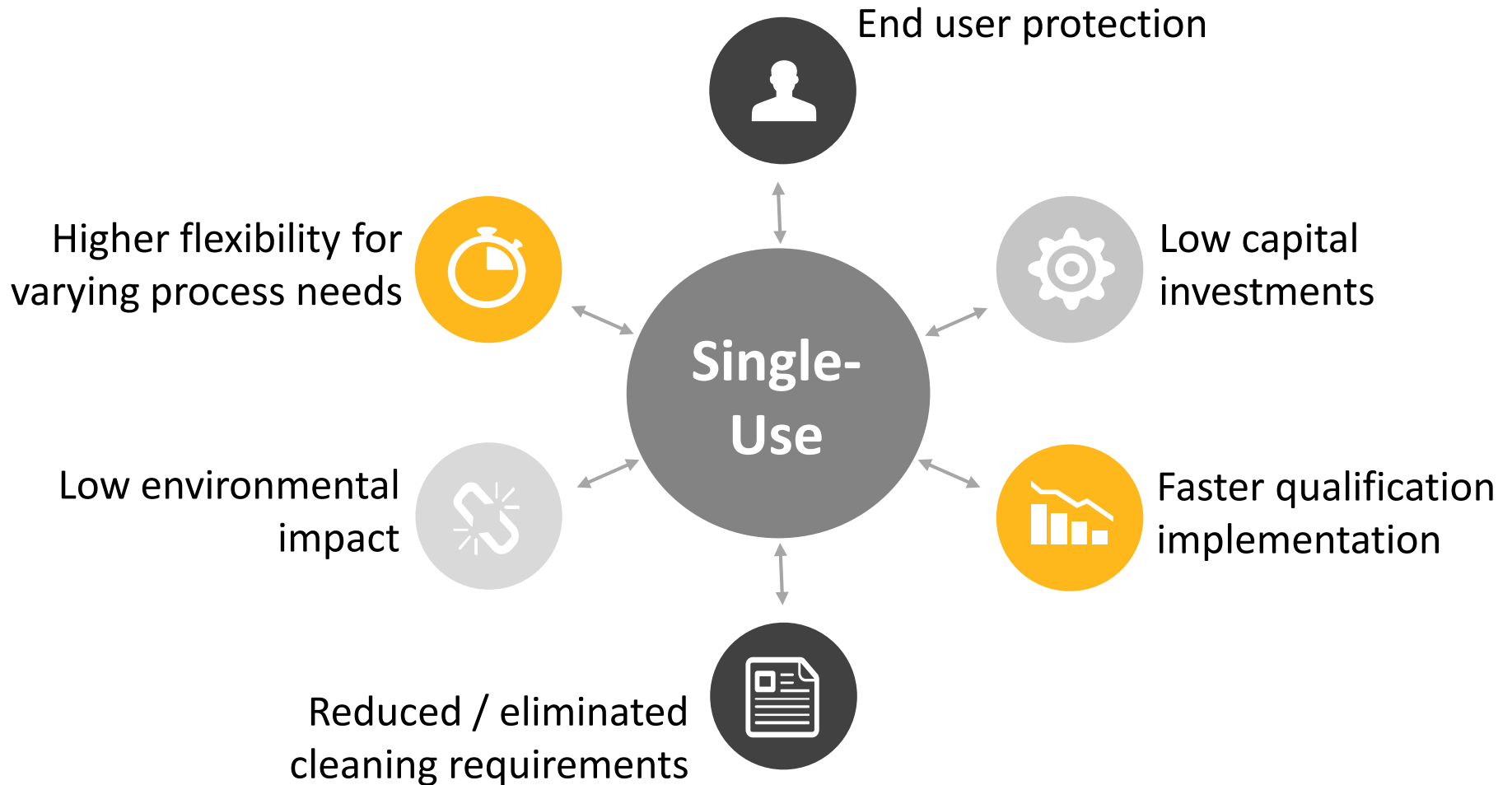




Frozen Storage & Transportation



Summary



Single-Use Technology Used for Aseptic Processing and Final Fill Applications

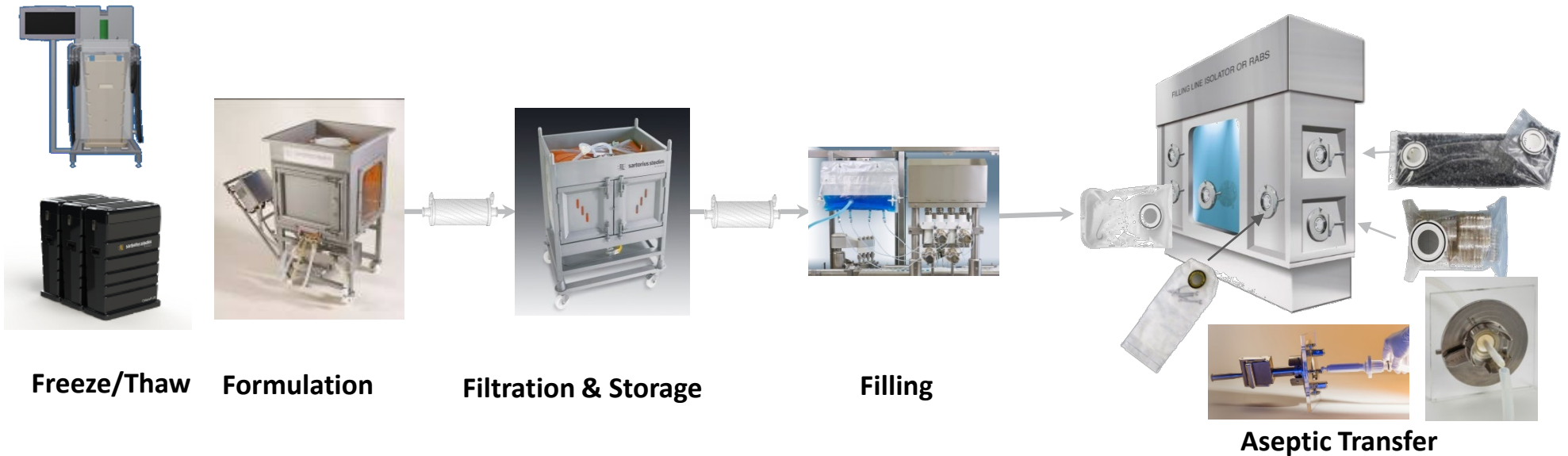
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Aseptic Transfer and Single-Use in Fill/Finish





Single-Use Final Filling Systems

Fully customized configuration

- Sterile connectors
- Filters
- Tubing
- Filling Needles

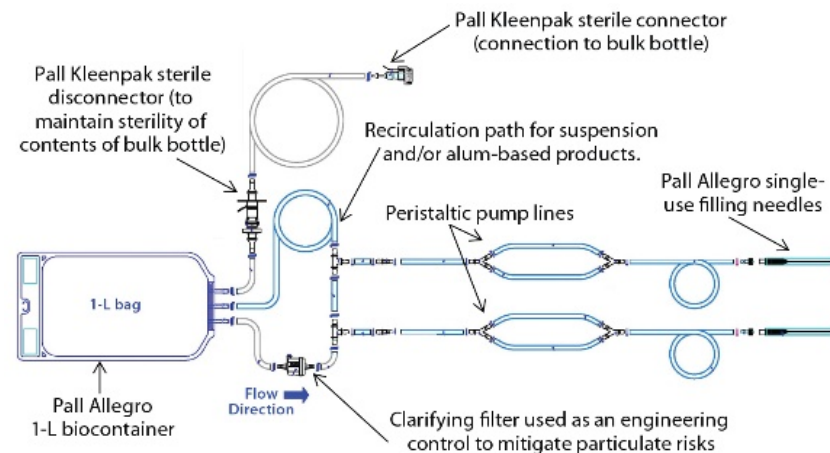
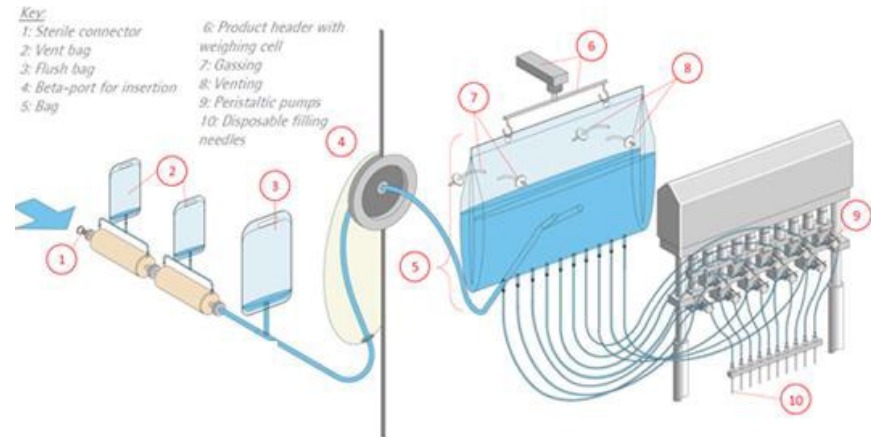
■ Ready-to-Use:

- Gamma Irradiated
- Double/Triple Bagged

■ Lot Release testing

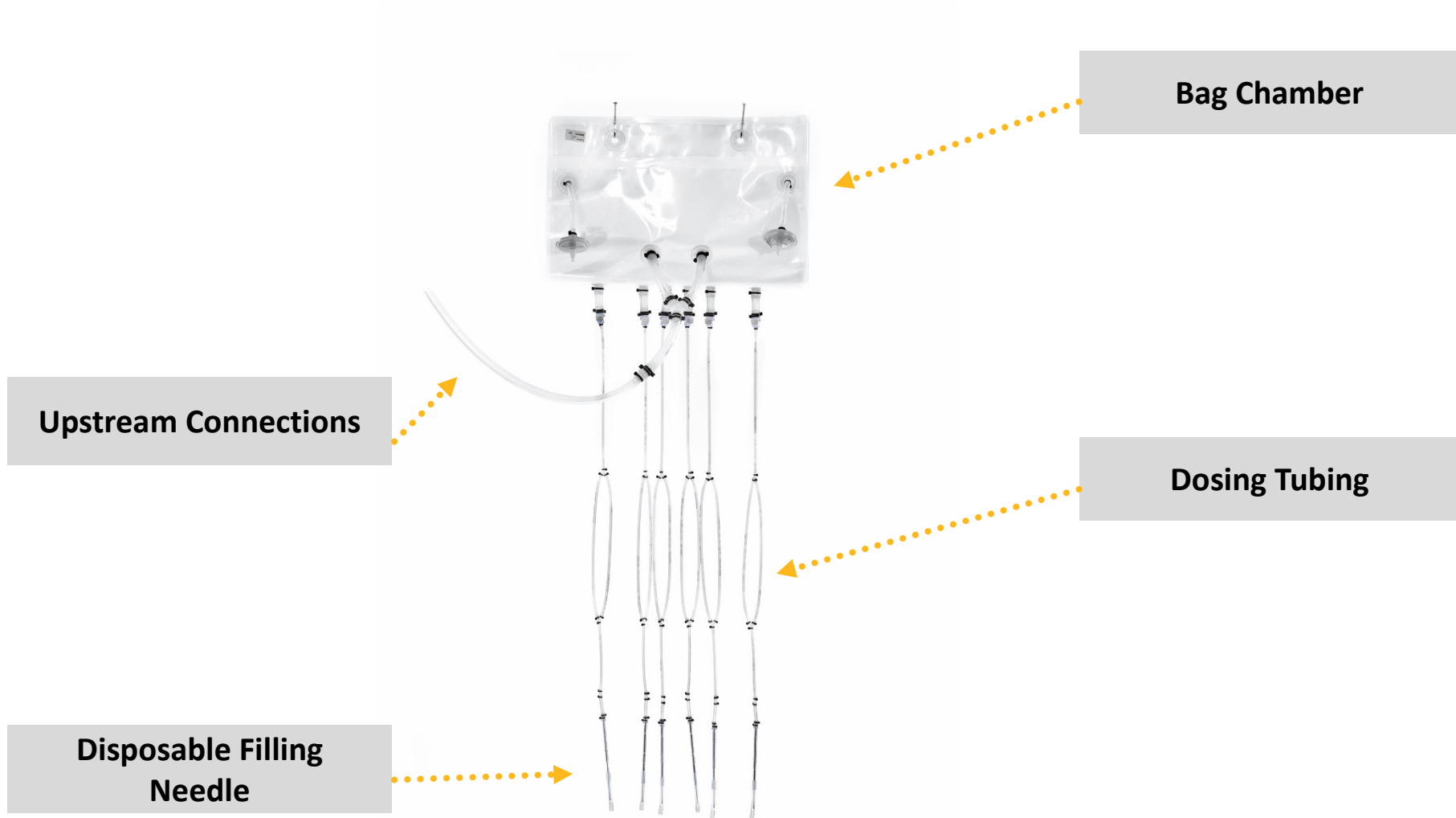
- Particulates
- Endotoxins
- Bioburden

Application Example for System Setup in Isolator





Single-Use Final Filling Systems



Single-Use Final Filling Systems



Connection to the Formulation tank/bag

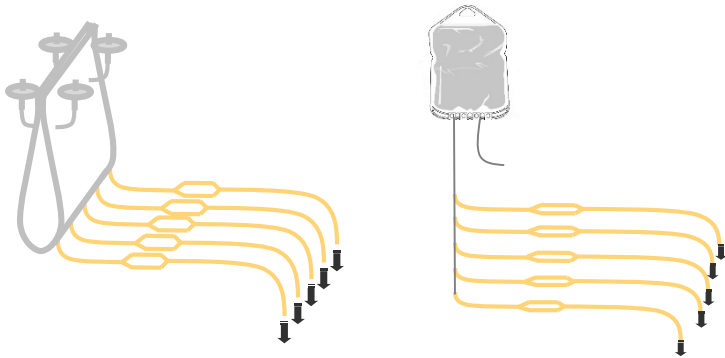
- Fully customized configuration = choice of sterile connectors, approved tubing material, length, diameter, etc...



Final Filtration

- Optional Sterilizing grade filters can be pre-assembled onto the system
- Single, Redundant & PUSIT configurations available
- Flush Bag &/or waste bags can also be incorporated into the assembly

Single-Use Final Filling Systems



Intermediate/Surge Bag

- Individual / Manifold type
- Inside / Outside of Grade A



Vent Filters

- Allows the bag to “breathe” during the filling process
- Allows N₂ neutralization/overlay for oxygen sensitive products

Single-Use Final Filling Systems



Peristaltic Dosing Tubing

- Platinum cured silicone / TPE
- Consider Pump type and tubing durometer

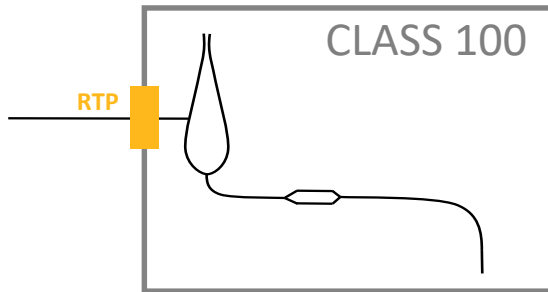
Single-Use Filling Needles

- 3 major suppliers
- Product contact is 316L stainless steel or Peek
- Compatible with all filling machines



Single-Use Final Filling Systems

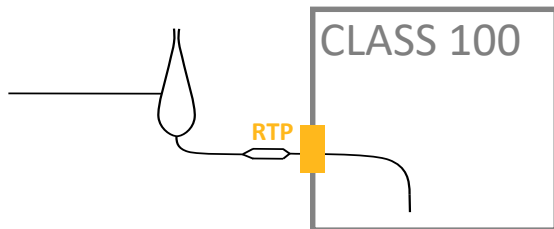
Bag Inside Configuration



Intermediate bag + dosing lines Transferred Through RTP into Class A

- RTP is used with a Liquid transfer bag to transfer the intermediate bag/filling lines into Grade A/Class 100 filling space

Bag Outside Configuration



Tubing lines transferred Through RTP into Class A

- RTP is used with a liquid transfer bag to transfer the tube lines after peristaltic pump loop into Grade A/Class 100 filling space

Single-Use Final Filling Systems



Manual Transfer into the Filling Line

- Entire package can be decontaminated with H_2O_2 .
 - Concentration of H_2O_2 inside the internal packaging during the decontamination cycle below 0.5 ppm
- Once decontaminated and installed, can be used in combination with another RTP for Liquid Transfer

Turn Around Times

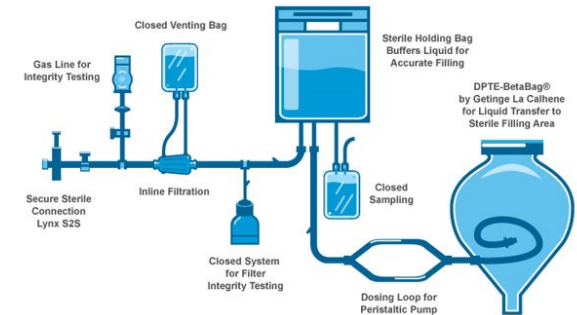
- Variable:
 - Number of fill lines
 - Transfer strategy
 - Average of 15 minutes



Single-Use Final Filling Systems

Points to consider

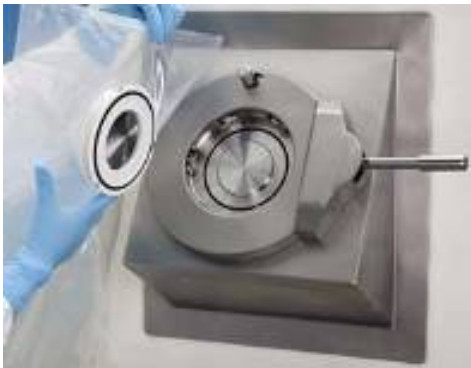
- Isolator/RABS
- Dosing System
- System Validation
- Mock-up / FAT / SAT / Commissioning / Qualification
- Intermediate Bag
- Drainability



Aseptic Transfer Systems

Standard uses for Aseptic Transfer Ports:

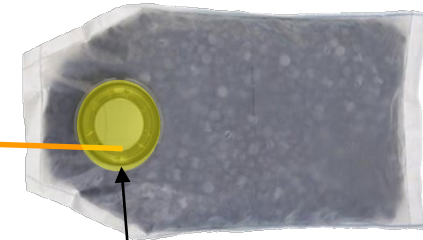
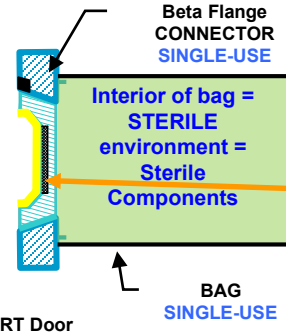
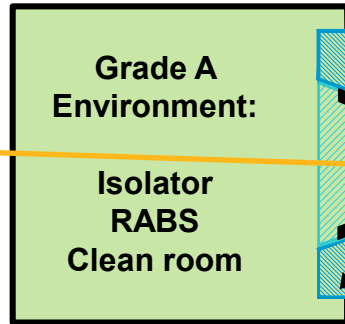
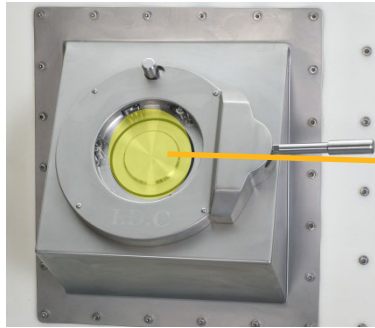
1. Stopper/plunger/cap transfer into Isolator/RABS filling lines
2. Single-Use Filling Manifold Transfer into Isolator/RABS filling lines
3. Liquid transfer (into Isolator/RABS filling lines or from room-to-room)
4. Entrance of Environmental Monitoring equipment into Isolator/RABS filling lines
5. Entrance of tools into Isolator/RABS filling lines
6. Contained transfer into/out of protected areas (BSL 1,2, +)
7. Waste Removal from Isolator/RABS



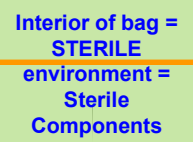
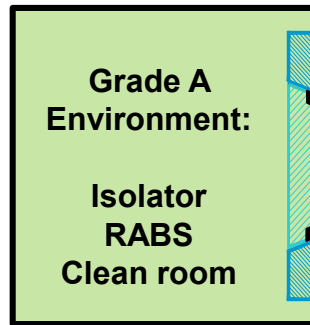
Aseptic Transfer Port



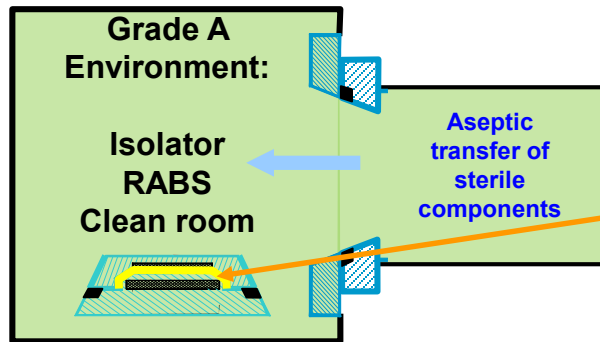
The surfaces highlighted in yellow are the surfaces that have been exposed to the Grade B/C/D area and are considered "dirty"



Beta Flange of the BAG SINGLE-USE



Magnetic connection between the surface of the port door and the surface of the beta flange of the bag



The surfaces highlighted in yellow contained by the magnetic connection between the surface of the port door and the surface of the beta flange of the bag

* All ports are referred to as "Rapid Transfer Ports" (RTPs) and/or "Alpha/Beta Ports"

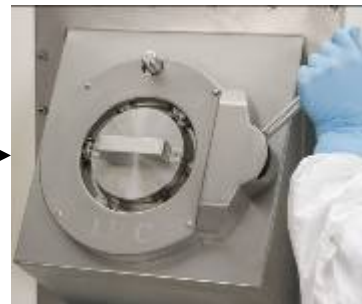
Aseptic Transfer Systems



Internal opening

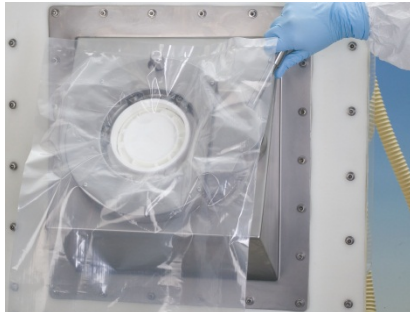
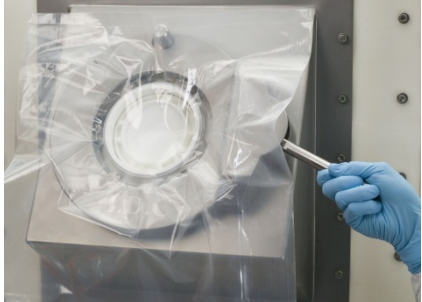
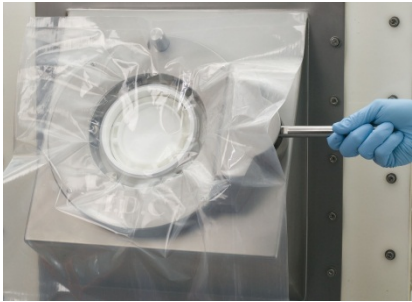


External opening

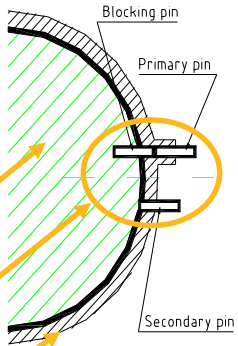




Aseptic Transfer

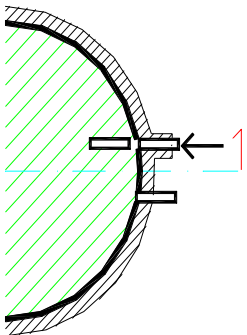


Before use

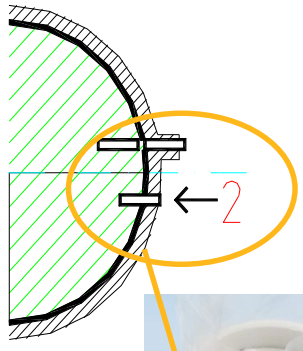


Before use

Handles to 'Open' position



Handles to 'Close' position



After use

Steam Sterilizable (Autoclavable) RTP® Bags (RTS – Ready to Sterilize)

Used for aseptic entry of:

- Stoppers (prefilled syringe, vial, cartridges)
- Caps
- Tools
- Environmental Monitoring equipment

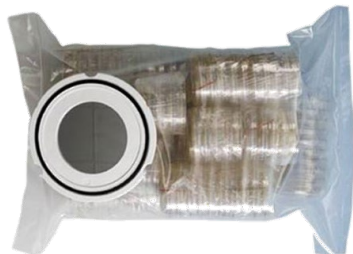


Options:

- RTP bags delivered open and filled on-site by end-user prior to autoclave (steam) sterilization
- RTP bags prefilled by component manufacturer and delivered ready-to-sterilize by components suppliers for the entry of stoppers.
- RTP bags prefilled by component manufacturer, steam sterilized and delivered ready-to-use by component suppliers for the entry of stoppers.



Gamma Irradiatable & Irradiated Bags: RTU (Ready-to-Use)



Used for the aseptic entry of:

- Pre-Sterilized Stoppers
- Liquids (RAFT/Final Filling)
- Environmental Monitoring plates

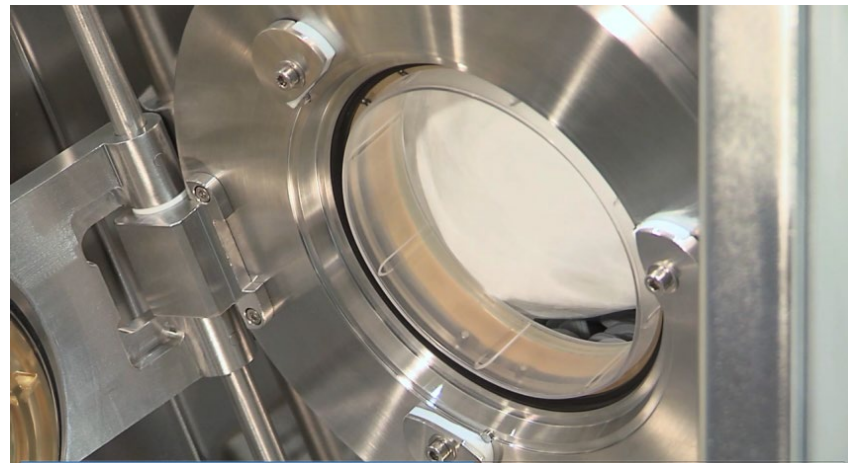
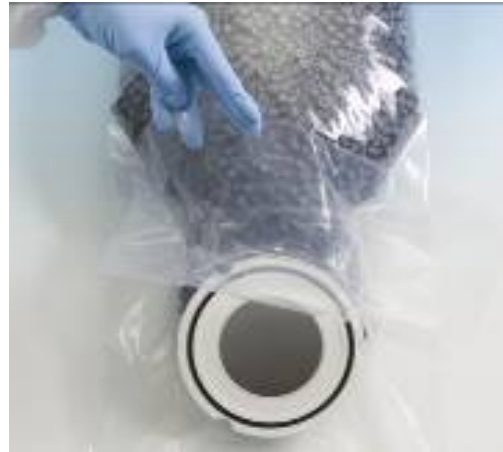
Used for the removal of:

- Waste
- Tools
- QC test devices

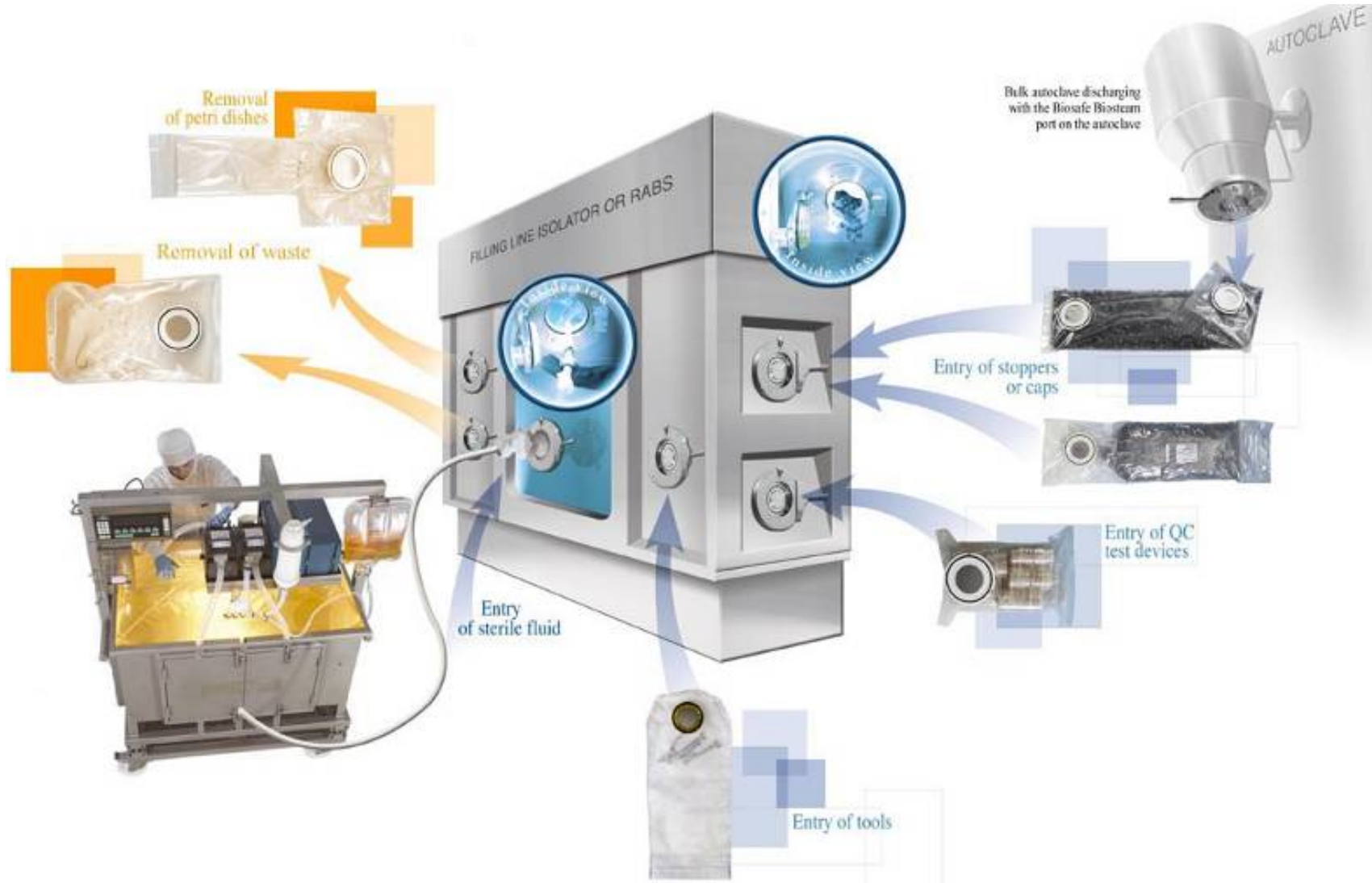
Options:

- RTP bags prefilled by component suppliers and delivered Gamma sterilized, ready-to-use, to the end-user
- RTP bags are empty, sealed and delivered Gamma sterilized directly to the end-user for transfer of materials out of the aseptic area

Aseptic Transfer Systems



Aseptic Transfer Systems





Thank You

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