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?

- Large-scale food processing
- Chemicals & small molecules
- Renewable energy
- Production of biologics
What is Single-Use?

Quick Set-Up / Change-Over time

Reduction in capital investment

Single-use assemblies replacing

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

**Upstream**
- Media Preparation
- Cell Line
- Fermentation
- Bioreactor Sampling

**Downstream**
- Cell Harvest
- Volume Reduction
- Sterile Filtration
- Disposable Storage
- Preparation
- Disposable Storage

**Purification**
- Single-use Crossflow
- Affinity Chrom. Capturing Step
- Low pH Virus Inactivation
- Cation Exchange
- Ion Exchange
- Membrane Adsorber
- Disposable UF
- Buffer Exchange
- Disposable Virus Filter
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
Tubing
Aseptic Connectors

Opta Connector
Aseptic Disconnectors
Sterile Connections & Disconnections

Biowelder TC
Frozen Storage & Transportation
Frozen Storage & Transportation
Summary

Single-Use

- End user protection
- Higher flexibility for varying process needs
- Low environmental impact
- Faster qualification implementation
- Reduced / eliminated cleaning requirements
- Low capital investments
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Aseptic Transfer and Single-Use in Fill/Finish

Freeze/Thaw  Formulation  Filtration & Storage  Filling  Aseptic Transfer
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
Single-Use Final Filling Systems

- Bag Chamber
- Dosing Tubing
- Upstream Connections
- Disposable Filling Needle
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 $N_2$ 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

**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

**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$_2$O$_2$.
  - Concentration of H$_2$O$_2$ 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

* 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

Handles to ‘Open’ position

Handles to ‘Close’ position

Before use

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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