Single-Use Final Fill: Benefits and Considerations

TENDÊNCIAS DE TECNOLOGIAS DE FABRICAÇÃO E ASSÉPTICA DE MEDICAMENTOS

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Agenda

1. **Benefits of single-use**
2. Single-use final fill overview
3. Considerations for implementation
4. Questions

What is a Single-Use Assembly?

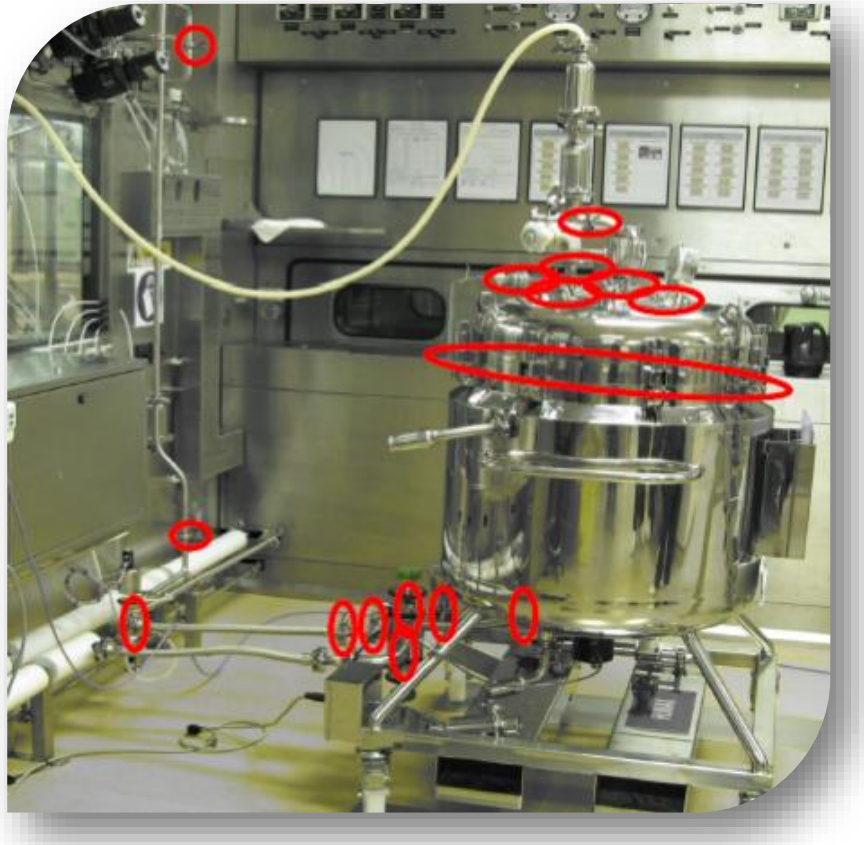
Prequalified, preassembled, pre-sterilized and ready-to-use

- Self-contained and preassembled plastic fluid path
- Combination of pre-qualified components:
  - Bags, tubing, connectors, filters, mixers, fittings, sampling containers rapid transfer ports, pumps, and filling needles
- Gamma irradiated & ready-to-use

Customized to meet defined user requirements

Stainless Steel Carry's Challenges in Today’s Market

- Large capital investment and long implementation timeline
- CIP and SIP required
- Significant set-up & break-down time
- Limited product changeover flexibility
- Multiple connections and potential leak points
- Complex operations



Restricted Access Barrier (RAB) with stainless steel hard piping

Single-Use Technology Benefits

Flexibility

- Ease of use, reduced change-over for multi-product and small batches
- Benefit for clinical phase (many different products, only a few that will go in commercial production)
- Production optimized with a flexible facility layout

Economics

- No CIP/SIP necessary, no cleaning validation
- Reduced utilities
- Reduced time-to-market = reduced time to patient
- Reduced downtimes = more batches

Safety

- Operator protection from: cleaning chemicals, steam, high potent drugs
- Minimized risk of cross contamination

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Single-Use Vs. Multi-Use?

Time and cost calculation of cleaning and steaming

BioProcess International 12(4)s April 2014

Pharmaceutical Technology Bioprocessing & sterile Manufacturing 2014

Customer data	Multi-Use	Single-Use
Equipment cost	$500,000	--
Equipment set-up	2 hours	45 min
CIP & SIP cycles	40 + 75 min	-- (ready to use)
SIP cool down cycle	75 min	-- (ready to go)
Equipment break down	1 hour	15 min
Post-use CIP	40 min	-- (throw it away)
Summary	**≈ 7 hours and $500,000**	**1 hour and cost of assembly**

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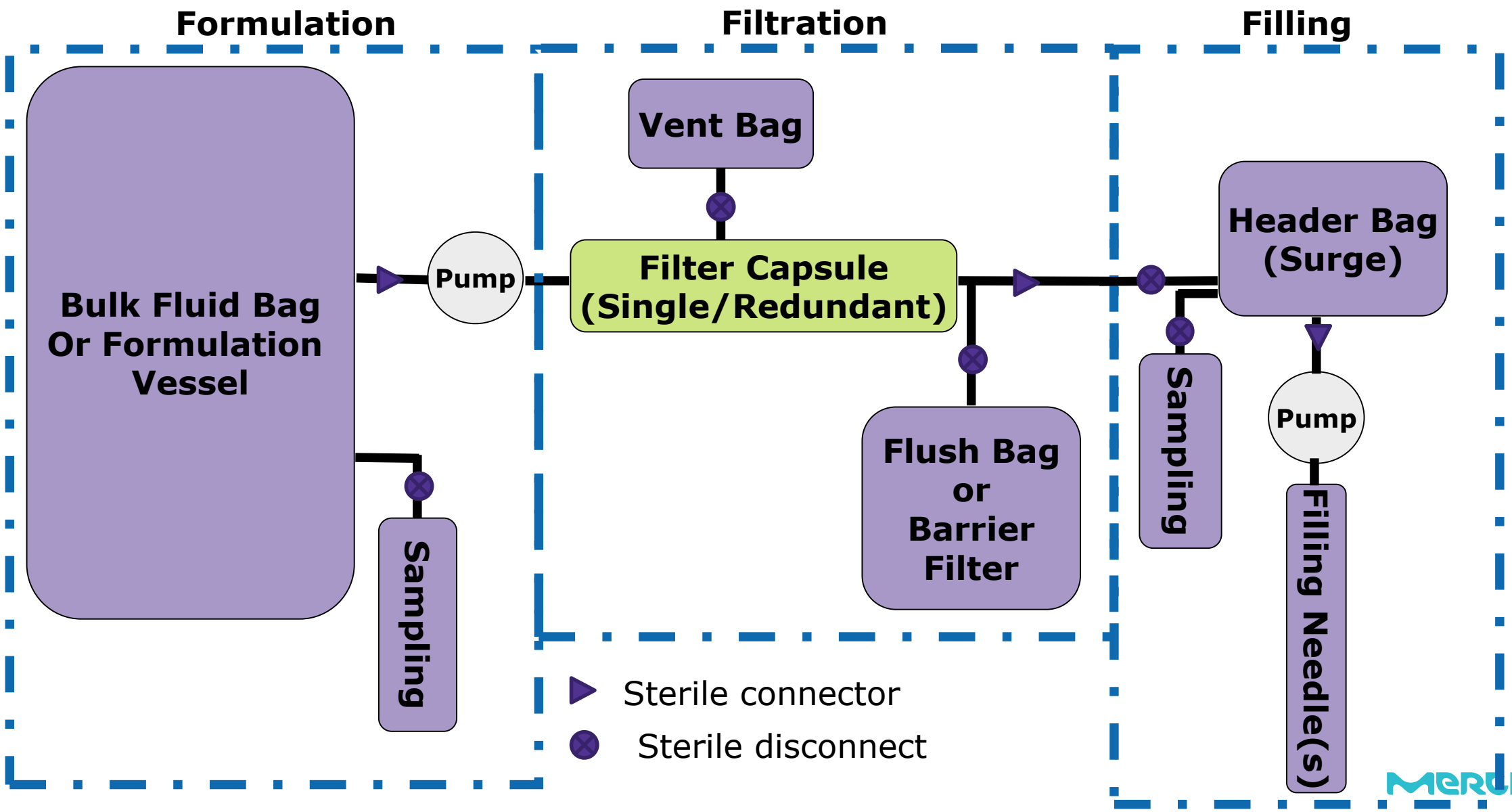
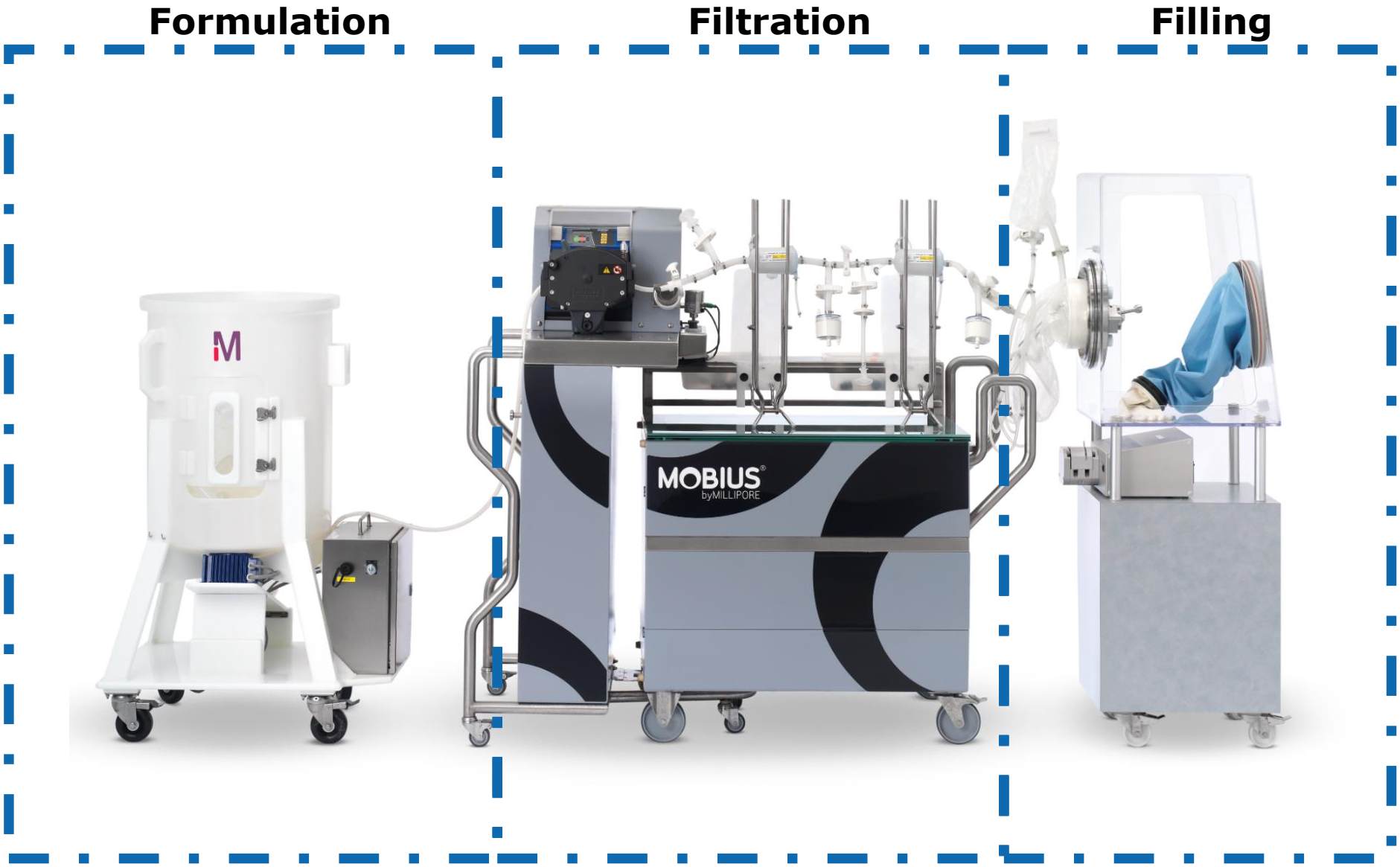
What does the process look like?

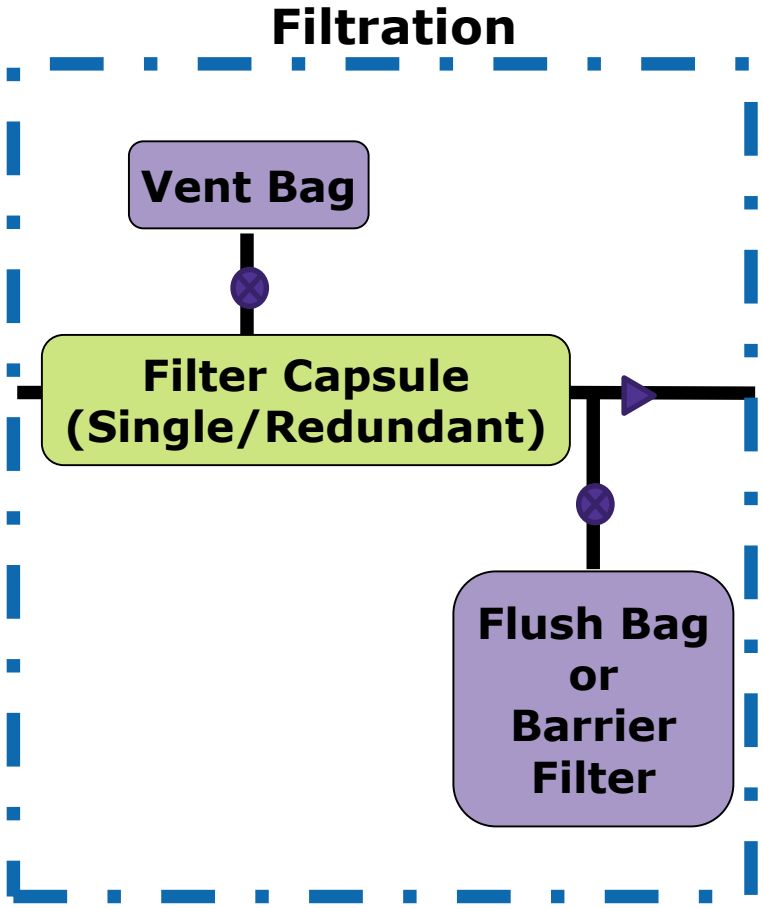


What does the single-use final fill process look like?



Design Considerations
Single-Use Filtration Assemblies

- **Flushing** → flush bag or filter
- **Filter integrity testing** → pre-use testing
- **Number of filters in system** → single, dual, redundant
- **Product recovery** → downstream blow down
- **Filters in or out of isolator**

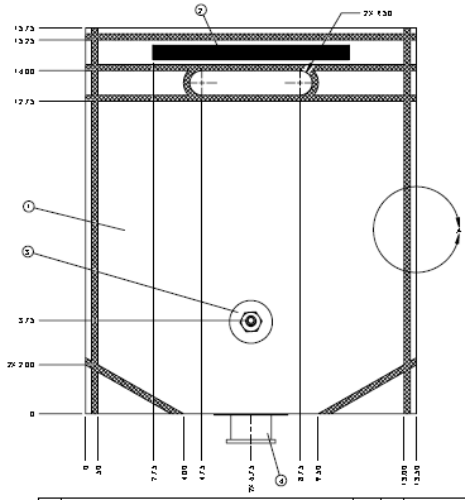


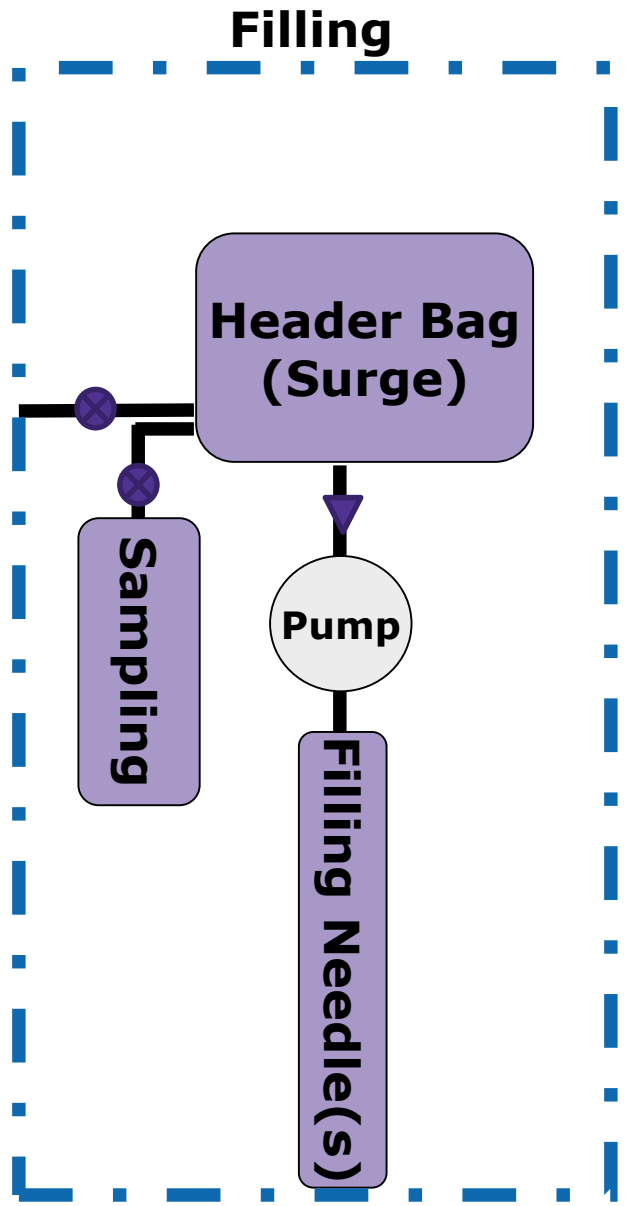
Final Filling
Header Bag

2-D and 3-D bag options

Alternative designs to enable:

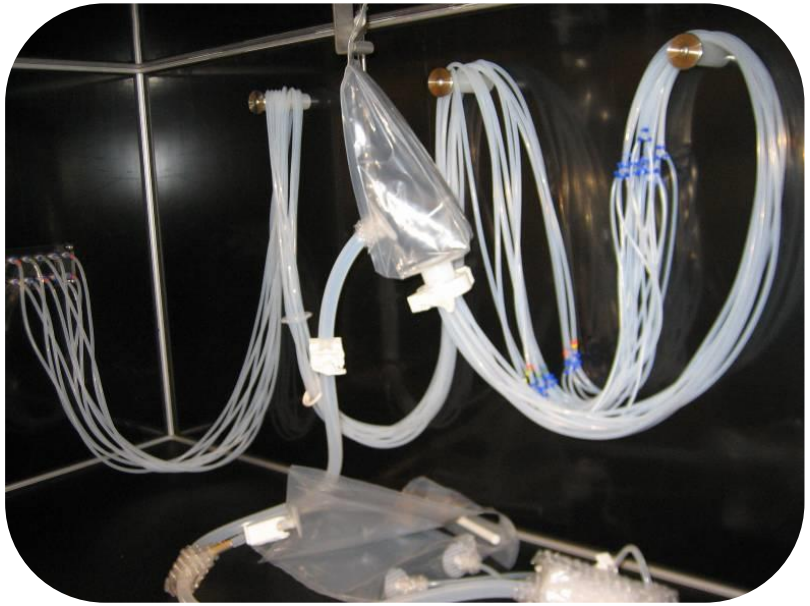
- Better drainage and/or higher product recovery without manipulation
- Recirculation for suspension products
- Batch vs. continuous processing
- Number of filling needles

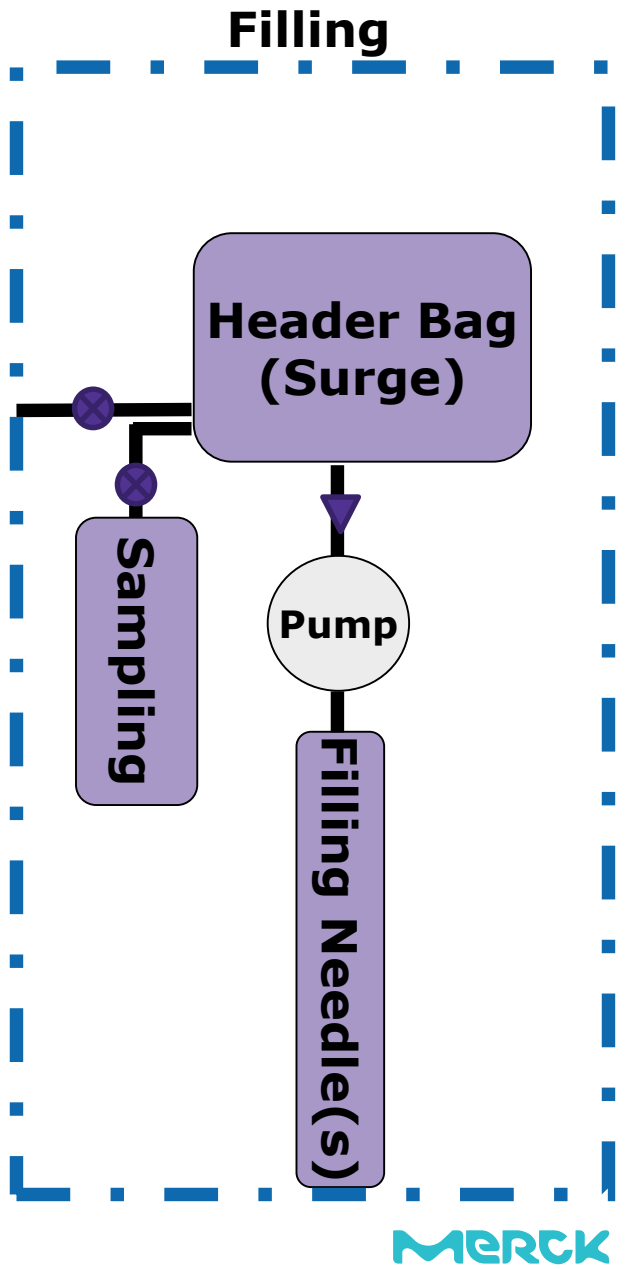




Final Filling
Tubing Manifold

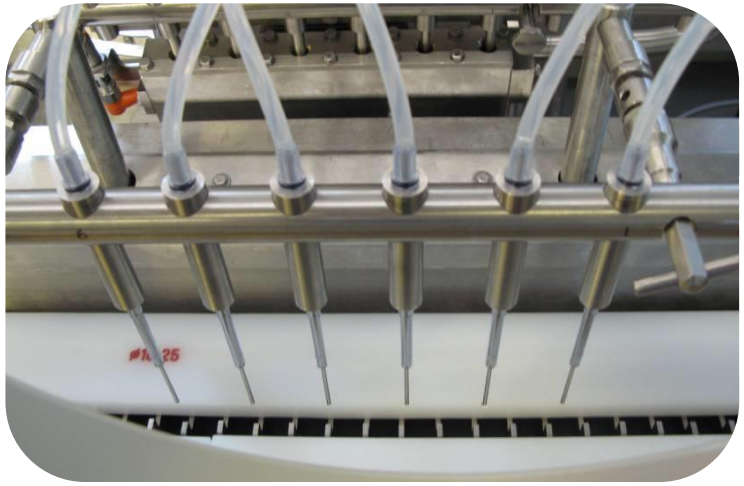
- Overmolded technology
  - Minimizes tubing/fitting connections
  - Decreases air entrainment in lines
  - Provides uniform flow distribution to all filling needles for fill volume accuracy and repeatability
- Available in a range of tubing sizes (ID/OD), lengths and durometers
- Improved product recovery from header bag

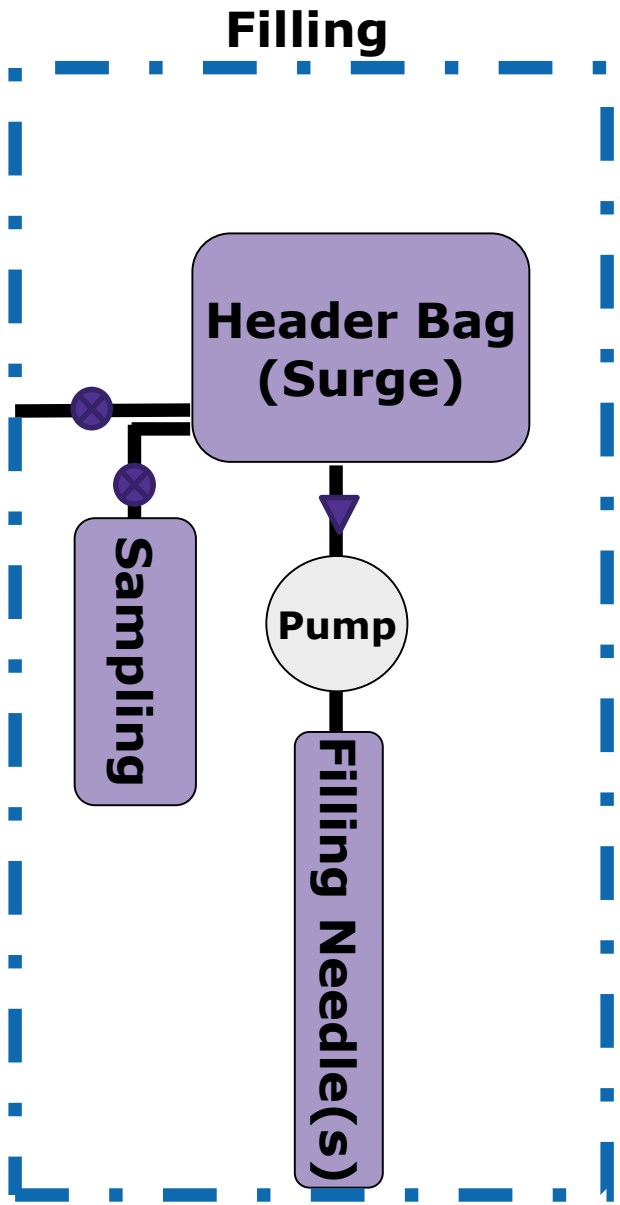




Final Filling
Tubing Manifold

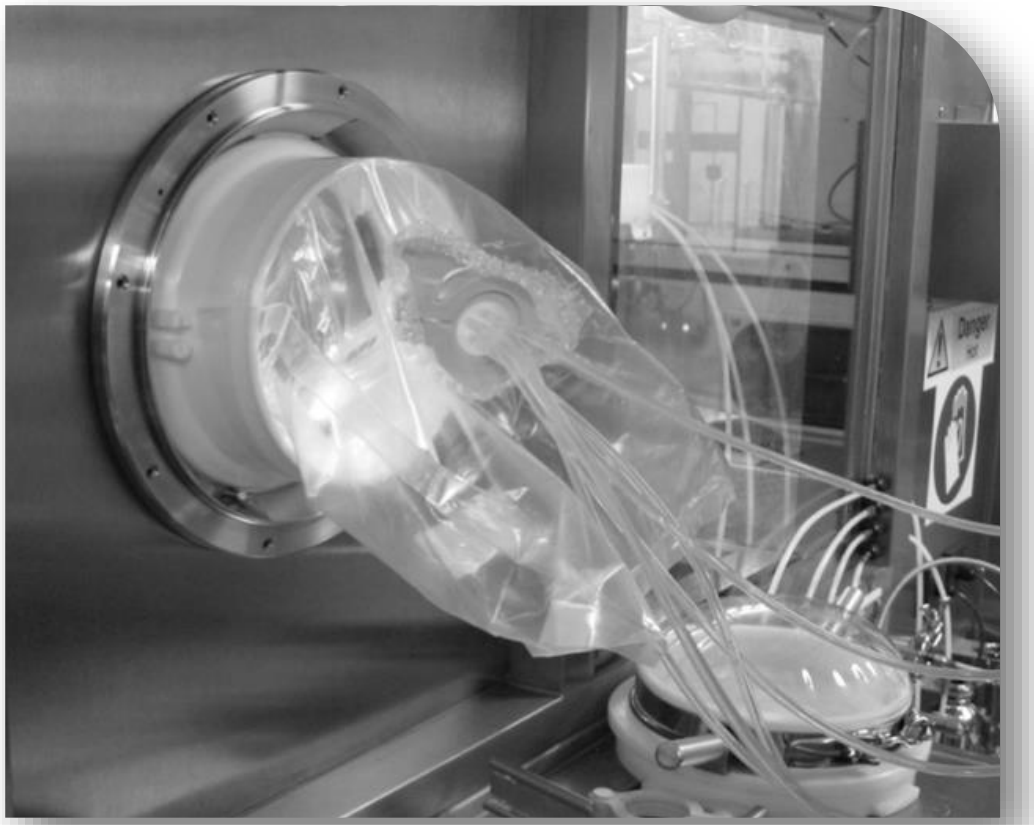
- Dosing accuracy is a function of tubing and needle type
- Filling needles options are available to meet the equipment manufacturer's requirements
- SU filling needles available in different formats



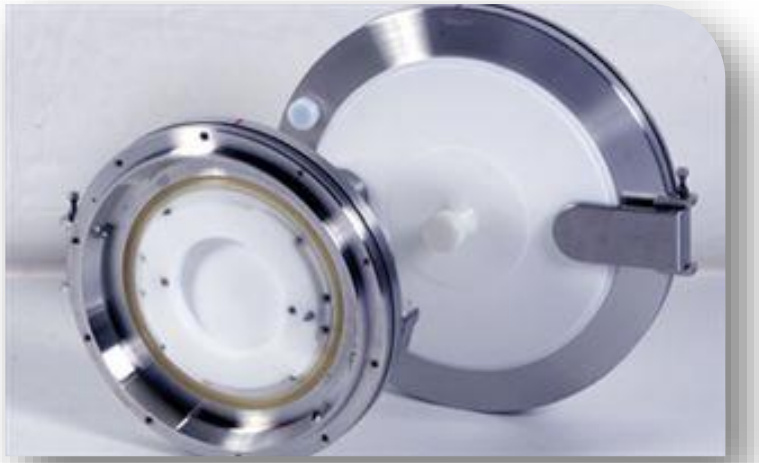


Ability to interface with an isolator while maintaining sterility

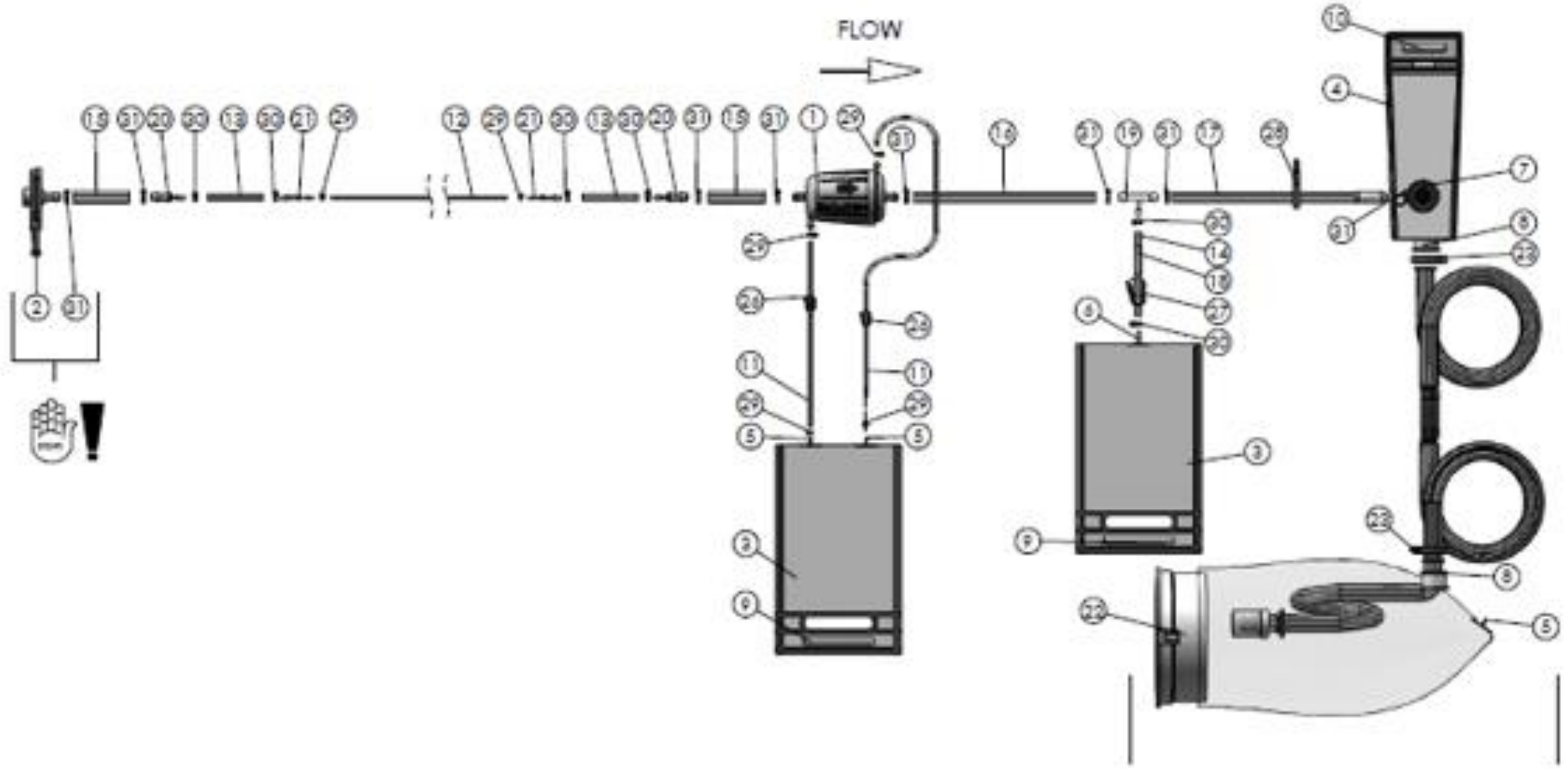
Isolator Interface with Getinge DPTE® Beta Bag



- Sterile transfer of fill lines and needles
- Sterility validation
- Integrity tested



Typical Final Fill Assembly



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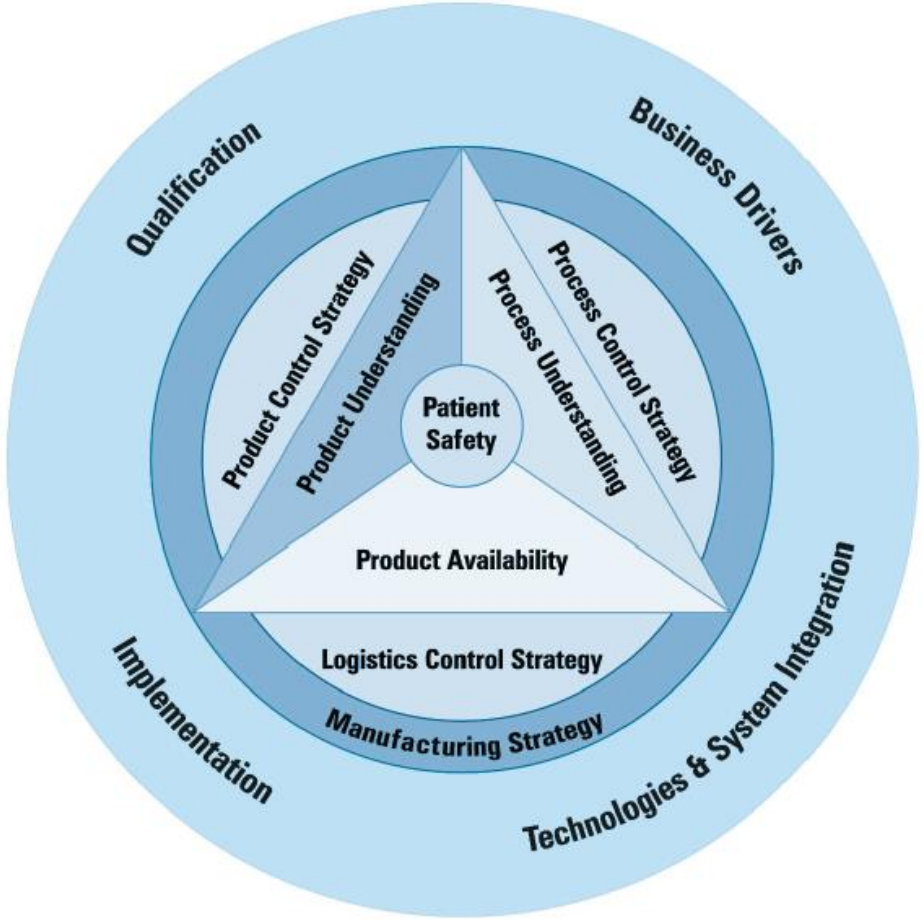
Single-Use Implementation Considerations & Best Practices

Considerations

- Assembly design
- Product compatibility
- Extractables, leachables and toxicity
- Particulates
- System integrity
- System sterility
- Packaging

How do you mitigate the risk?

- Supplier / End-user partnership



Key decision areas for a SUS manufacturing strategy

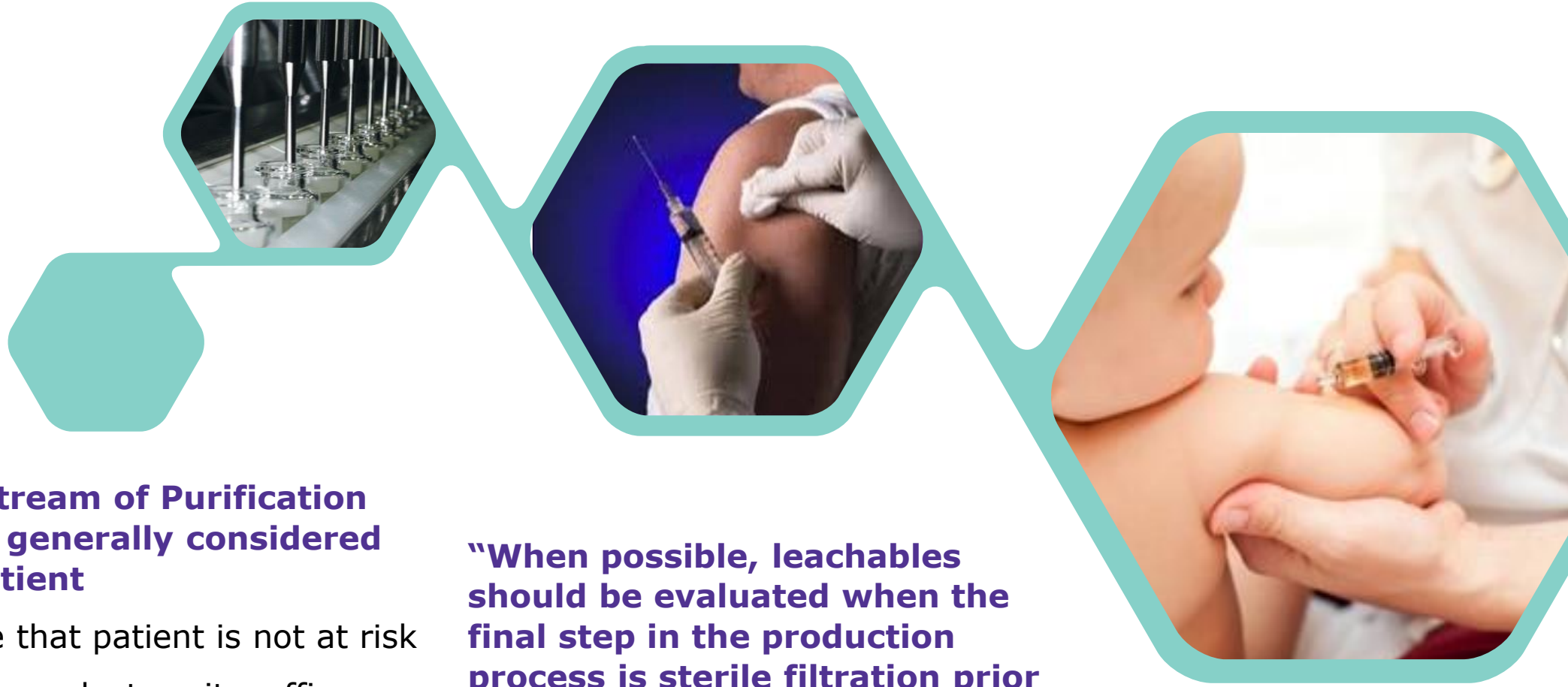
PDA Technical Report 66: Application of SUS in Pharmaceutical Manufacturing

« Adopter accepts to **transfer critical control parameters like sterility or cleanliness** to a third party… »

« The **V&Q Control strategy followed by the end user will then shift to a process of building partnership with the supplier** to gain assurance and set measurable performances…. »

Extractables and leachables

Requirements for Final Filling Operations



Operations downstream of Purification and Final Filling is generally considered greatest risk to patient

- Must demonstrate that patient is not at risk
- Must demonstrate product purity, efficacy, stability

“When possible, leachables should be evaluated when the final step in the production process is sterile filtration prior to filling.”

PDA® Technical report N°26, 2008

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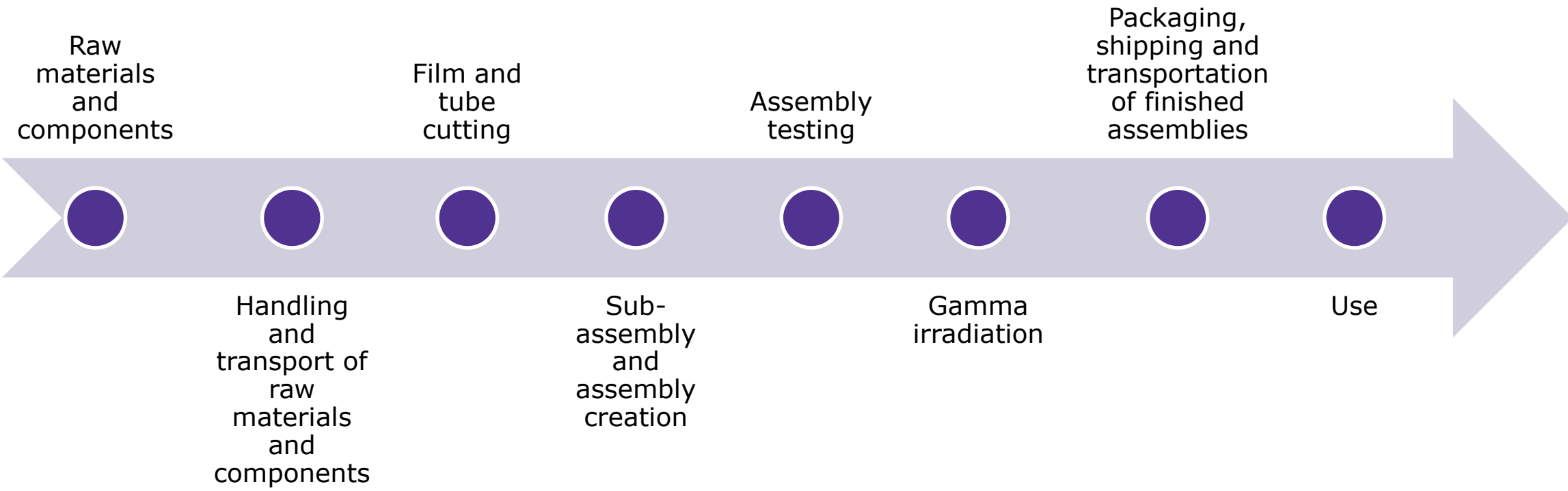
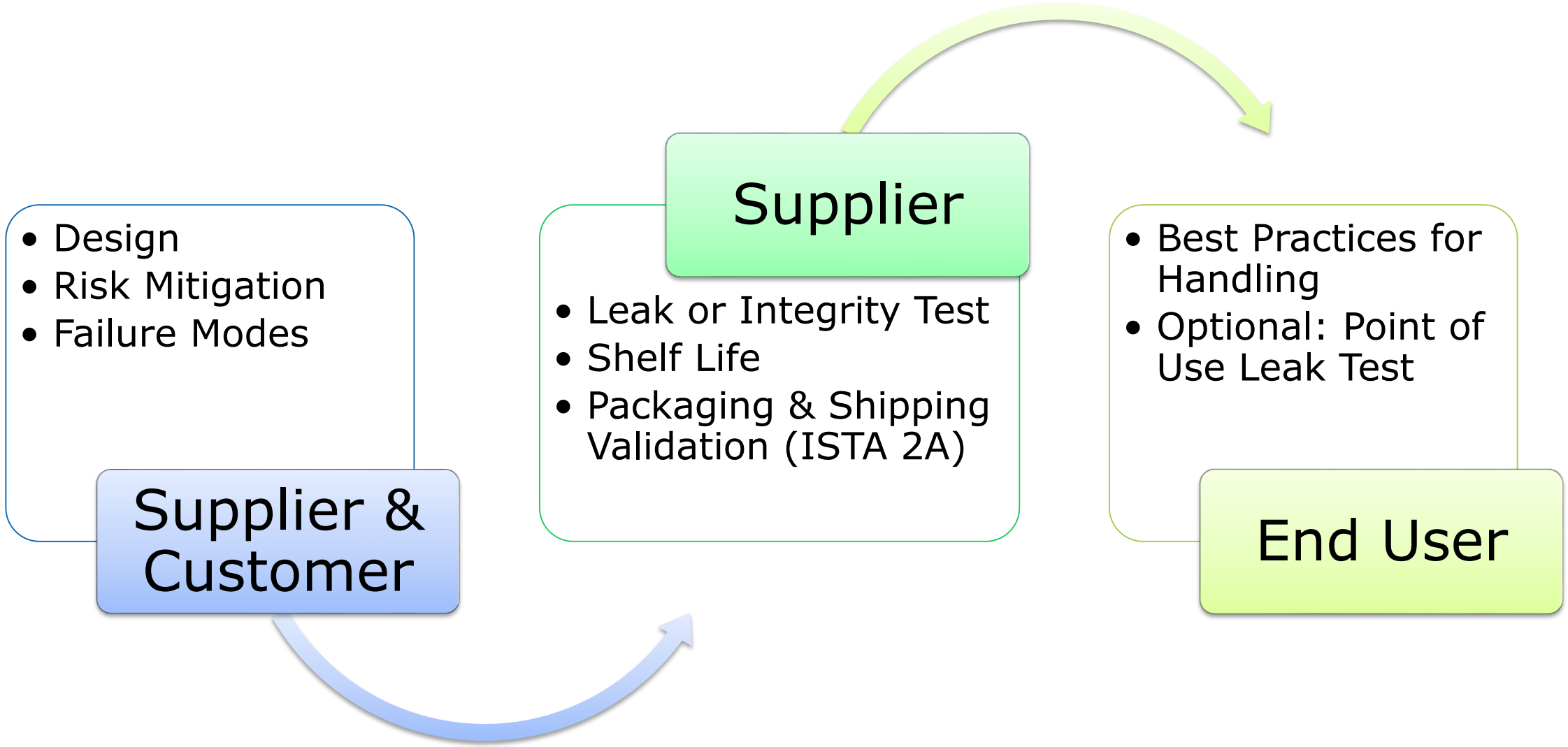
Risk-Based Approach to Particulates



Risk Assessment – All stages of assembly manufacture and use including raw materials, sub-assemblies, assemblies, and final product.

Integrity Assurance

Collaboration Between Supplier and End-User



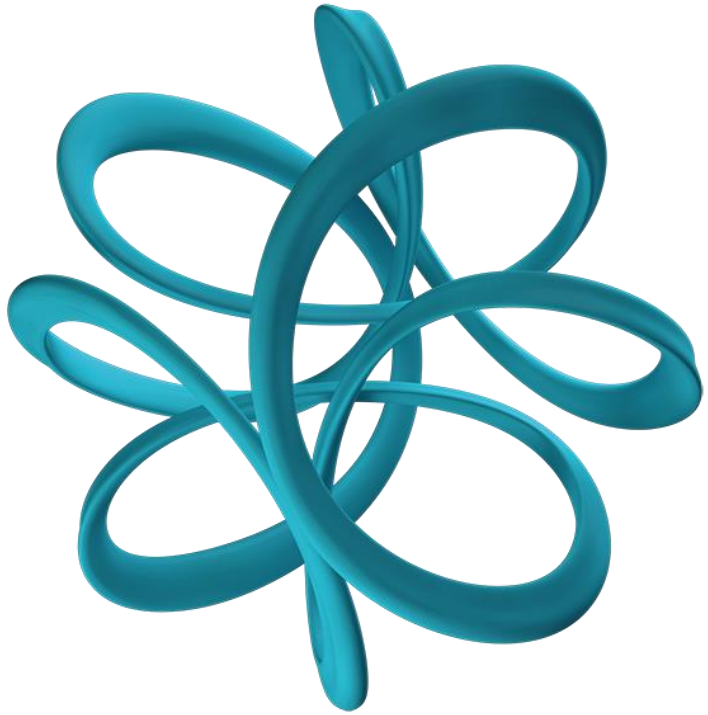
Bringing it all together

Do your homework

- Assess product compatibility
- Define user requirements and process specifications

Find the right partner

- Strong single-use technical support, knowledge and capabilities
- Quality systems are adequate and able to meet requirements



Testing

- ✓ Collaboration between end-user, filling manufacturer and single-use supplier
- ✓ Fit testing, factory acceptance testing (FAT), wet testing, engineering runs and validation

Training

- ✓ SOPs, standard work documents in place
- ✓ Operators receiving, unpackaging, handling and installing assemblies are properly trained

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Questions?

Thank you!