

# Design and Deployment Strategy for Single Use Components and Assemblies

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# Key Company Facts

**WHO WE ARE** Known as **Merck** in the United States and Canada, and **MSD** elsewhere

**RICH HISTORY** Operating since 1851

**BUSINESSES** Pharmaceuticals, Vaccines, Biologics, Consumer Care and Animal Health

**2012 REVENUES** \$47.3 billion; 57% of sales come from outside the United States

**2012 R&D EXPENSE** \$7.9 billion; 20 products in late-stage development; key areas: CV, diabetes, respiratory & immunology, neurology, infectious disease and vaccines

**EXTERNAL LICENSING** 61 significant licensing and business deals in 2012

**HEADQUARTERS** Whitehouse Station, New Jersey, U.S.A.

**EMPLOYEES** Approximately 82,000 worldwide (as of 3/31/13)

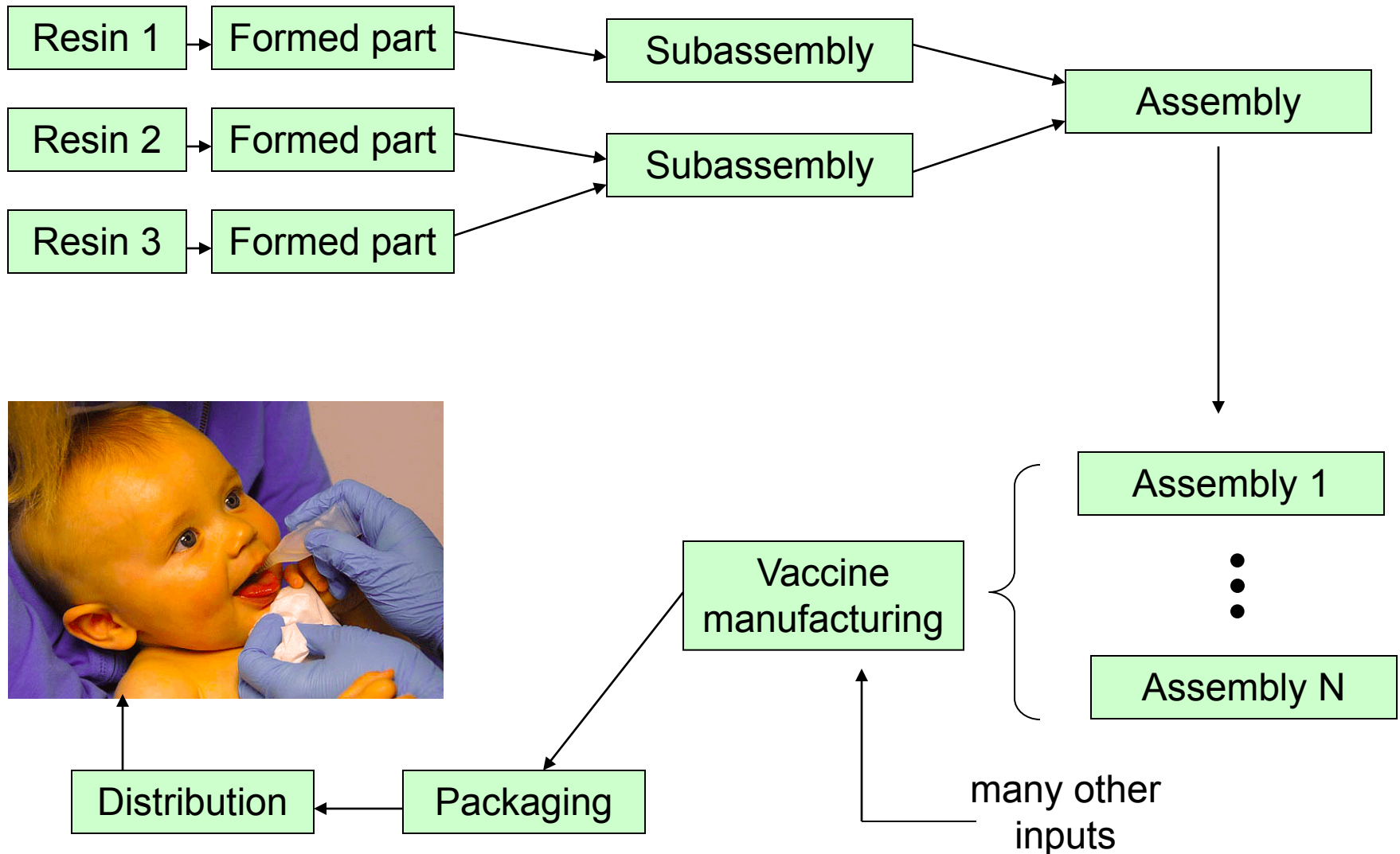
# Single Use Technologies offer many benefits

- Lower capital investment
  - Reduce infrastructure, automation, clean/sterilize
  - Facility set-up time reduced
  - Economies of scale become less important
- Ease of distributed manufacturing
- Faster tech transfer
- Closed-system operation
- Reduced risk for cross contamination
- Sterile, pyrogen free components
- Reduced equipment operation problems

# Obstacles make implementation challenging

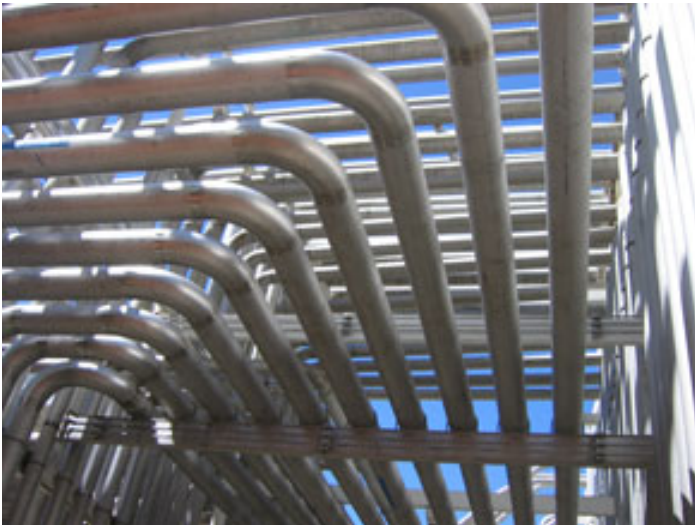
<b>Potential benefit</b>	<b>Experienced obstacles</b>
Contamination reduction	Leaks, particles, E&L
Closed systems	Leaks, integrity testing and design qualification approaches are not standard
Sterile, pyrogen-free	Irradiation validation practices vary – despite standards
Tech transfer is easier	Custom design-to-deployment takes too long (12-24 months, typ.)
Processes are flexible	Hardware from different suppliers cannot be exchanged; custom designs rarely work together
Reliable and reproducible	Integrity, particles, delivery problems, frequent changes

# “End Users” depend on “Suppliers”



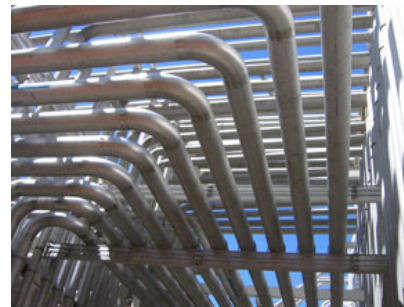
# “End Users” relinquish control as supply chains lengthen

- Cleaning
- Sterilization
- Equipment availability (= supply chain reliability)
- Configuration control (= change management)



# How can you tell a “supplier” from an “end user”?

- New roles have been inserted in the design process and supply chain
  - Component Engineers
  - Procurement
  - Inventory managers
  - Single use technician
- Internal suppliers must be prepared to accept shifting responsibilities



# Supply chain management is critical to single use success

- Sourcing
- Change Management
- Release procedures
- Inventory management
- Supplier Value Management
- Materials movement (empty and full and waste)
- Lean thinking is needed (5S: Sort, Set in Order, Shine, Standardize, Sustain)



# What can we do today to overcome the obstacles?

- Develop the roles needed to master the single use supply chain
- Recognize that new engineering approaches are needed to be successful in the SU manufacturing world
- Work with suppliers to make information readily available to support sourcing decisions
- Work with suppliers to limit changes in existing product lines, and to maintain availability of selected items

# Component Engineering is a critical supply chain function

- “It's in the engineer's best interest to select components that provide reliable, quality performance and that can withstand any required rigors of environment.” – *NMB Technologies website*

<http://www.nmbtc.com/nmb-component-applications/medical/device-engineer/>

- Component Engineers provide options that meet process design requirements. They must....
  - Simplify
  - Standardize
  - Communicate in both directions in the supply chain
- Component Engineers must define good engineering practices for single use technology

## We need internal standards

- Single use technology engineering standards will provide options that are qualified, supportable, and likely to match process and operator requirements.
- Engineering standards will also provide design principles and qualification methods to address those rare situations where new designs are required.

# Consistent information is needed to guide single use equipment selection

- Biocompatibility
- Mechanical Properties
- Gas/Vapor Transmission
- Compendial Physicochemical Properties
- TSE-BSE
- TOC Analysis
- pH/Conductivity
- Extractables and Leachables
- Chemical Compatibility
- Protein Adsorption Studies
- Endotoxin Testing
- Sterilization Validation
- Container Closure Integrity (CCI)
- Particulates (USP <788>, EP 2.9.19, visible)
- Calibration of Embedded Instrumentation

# Good engineering practices for single use technology design and support

- Start with user requirements
- Provide credible specifications for all components
- Use a readily accessible knowledge repository for all components, technologies, and suppliers
- Encourage selectivity in the component list: too many synonymous parts adds to supply complexity and adds to support costs
- Match user requirements with intelligent component sourcing and management strategy.
- Configuration Management: change evaluations, technical updates, response to user feedback and evolving requirements

# Components: The lowest form of single-use technology

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- Tubing
  - Connectors
  - Fasteners
  - Filters
  - Bottles
- 

Standard will define:

- Preferred materials of construction and selection guide
- Dimensions (e.g. tubing lengths, diameters)
- Allowed junction “compositions” (tubing/fitting/fastener)
- Connectivity parameters (filter inlet/outlet, bottle necks, ....)
- Qualified components list (“catalog”)

# Assemblies: Collections of Components

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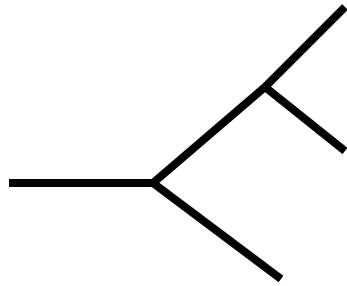
- Buy connections or make connections?
- Buy vs. make from scratch vs. “cake mix”
- If make, then how? What are the design principles?
- Need a strategy: standard modules is one idea

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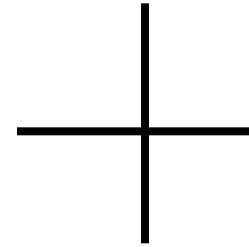
Standard will define:

- Standard multi-component building blocks
- Selection principles for make vs. buy
- Qualified components list (“catalog”)

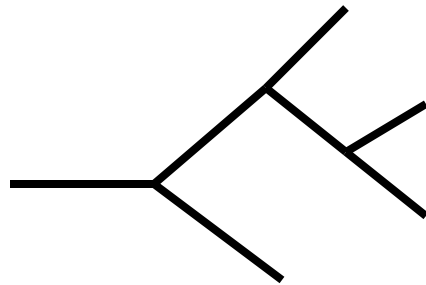
# Developing design principles for fluid transport networks



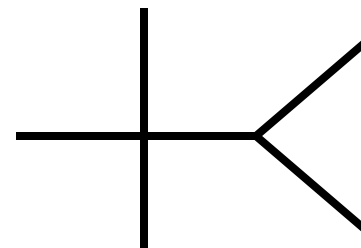
6 fasteners required, or  
2 molded junctions



4 fasteners required, or  
1 molded junction



9 fasteners required, or  
3 molded junctions

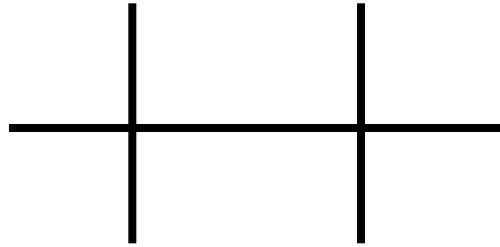


7 fasteners required, or  
2 molded junctions

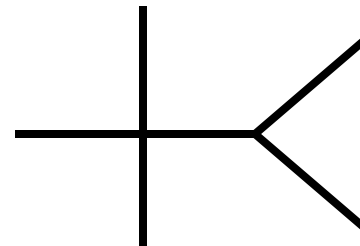
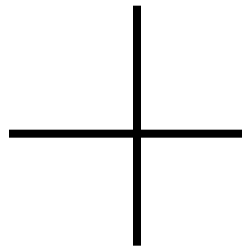
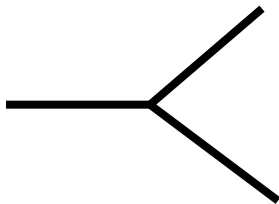


# “Simple and Standard” may look different than custom design

Could this:



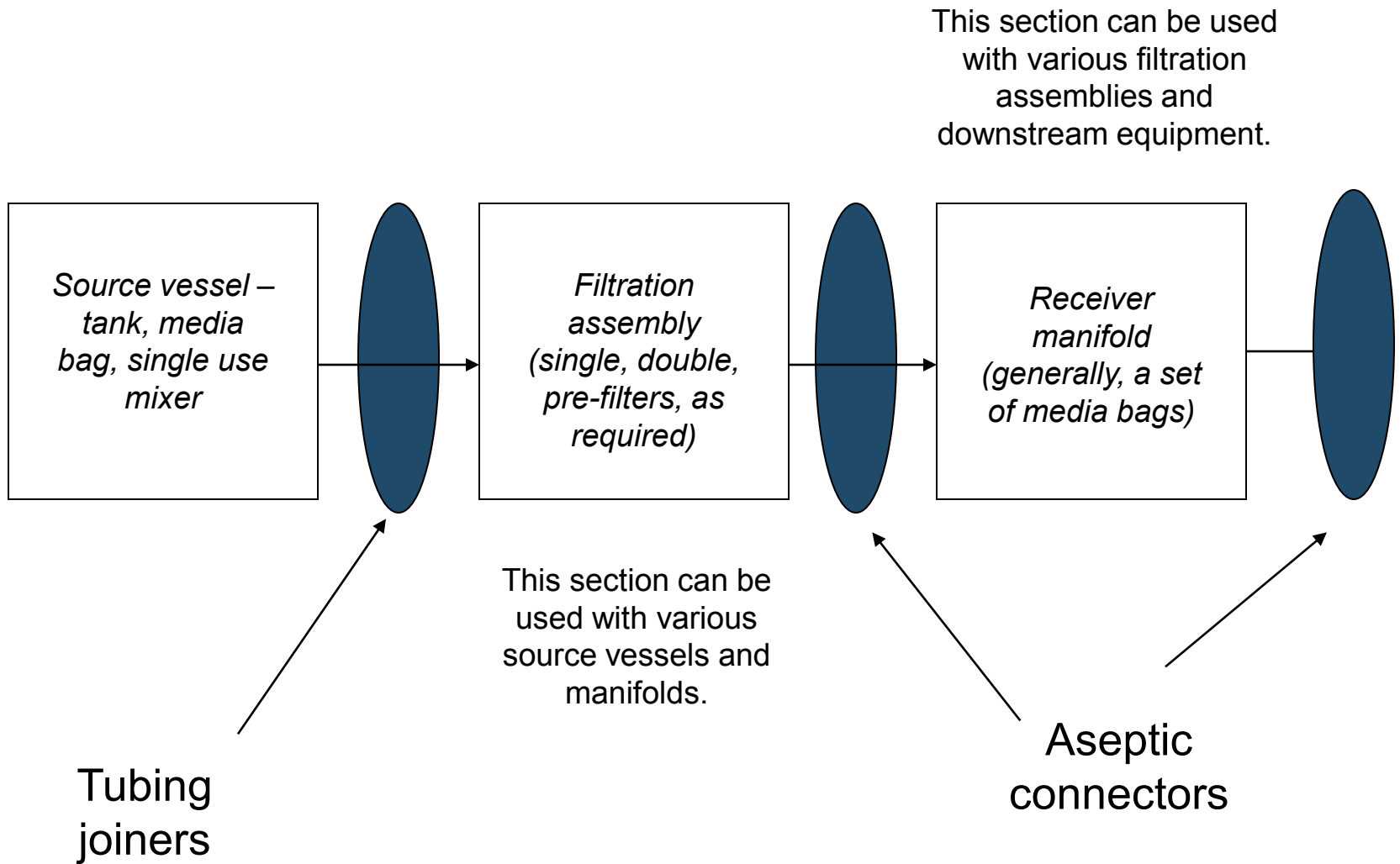
Replace all of these?:



# Analysis leads to assembly design principles

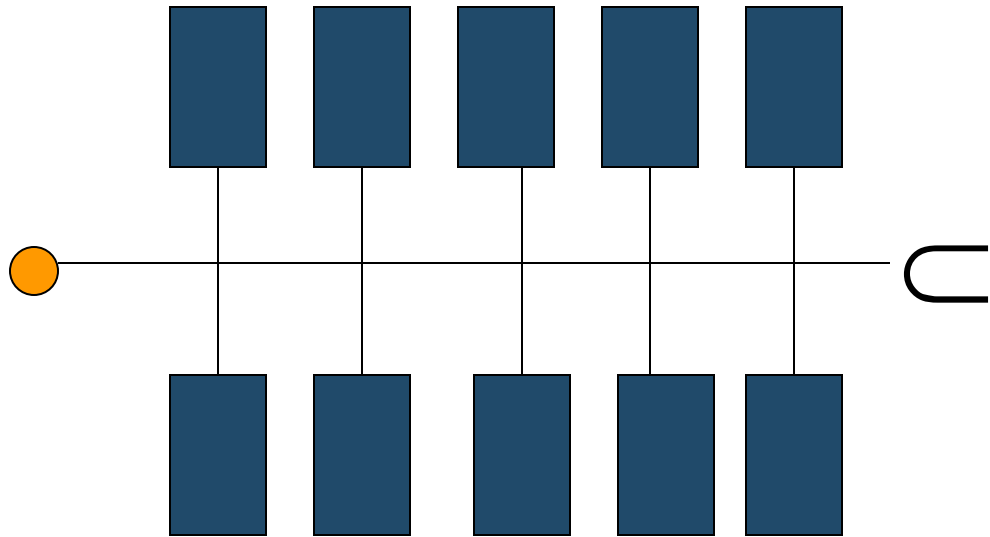
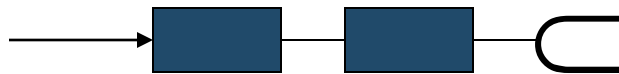
- Separate furcation from translation
- Least complicated assembly includes tubing needed to reach next assembly
- Use the highest possible degree of flow splitting ("X" instead of "T", 6-port instead of "X", etc.)
- Mold flow splitters where possible (Kynar, polypropylene), preferring injection molded stock pieces over custom molded TPE or silicone
- Minimize material types in each assembly
- Tubing mold at small ID ( $\leq 1/4''$ ); hose barbs/fasteners at intermediate ID's ( $1/4'' \leq \text{ID} \leq 3/4''$ ); TC connections at large ID ( $> 3/4''$ )

# Modular design enables management of single use components



# “Expand to Fit” Manifold is an example of modular design

*Filtration assembly  
(single, double, pre-  
filters, as required) Will  
have several options  
available as standards.*



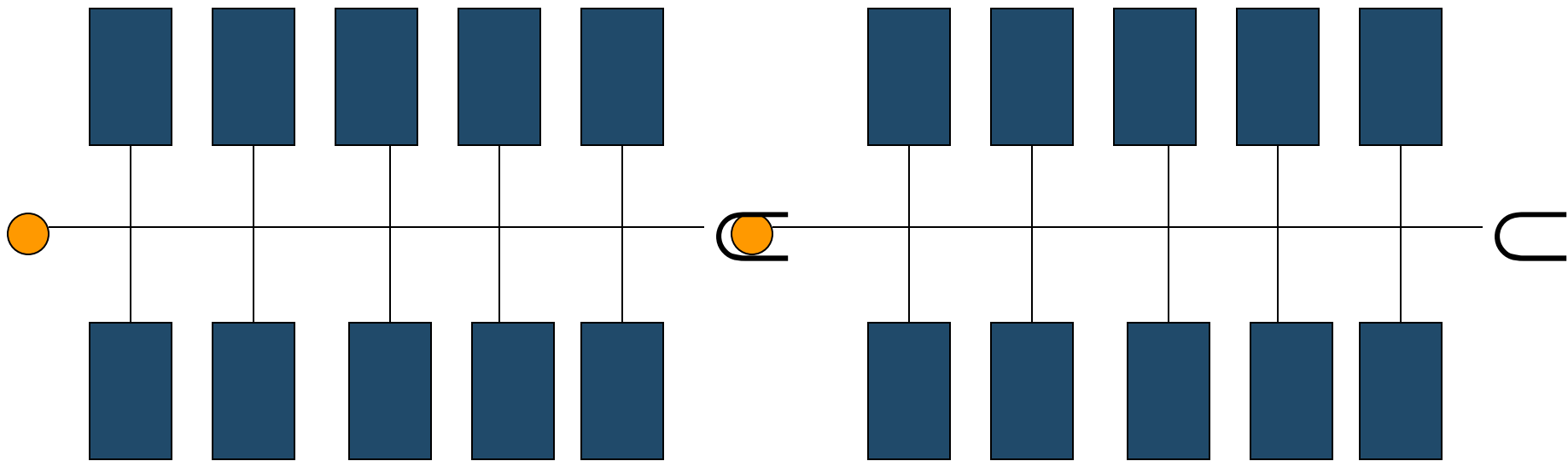
*Receiver manifold can  
contain any number of  
media bags attached to the  
“spine”. 10 bags illustrated  
here as an example.  
Provide a standard number  
in each bag size. For  
example, 10 @ 20-L, 6 @  
100-L.*

generic depiction of an  
aseptic connector pair:



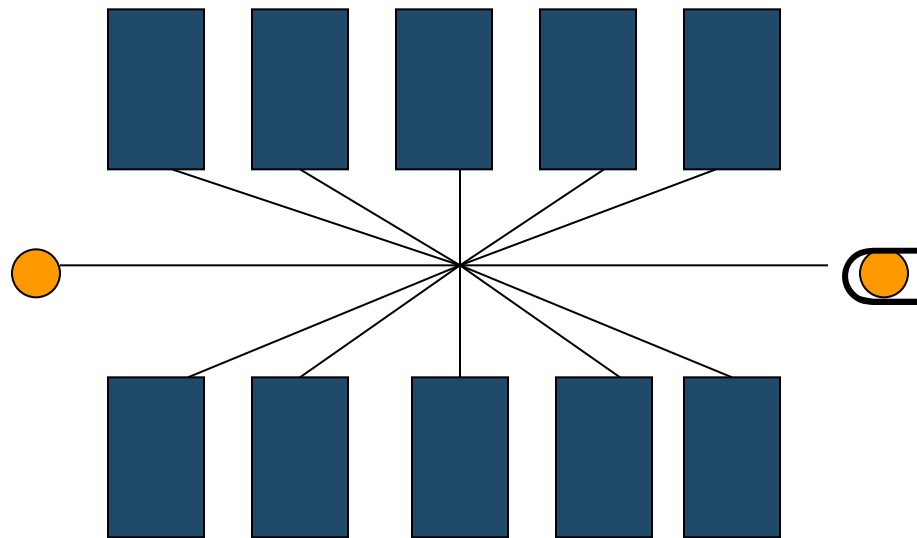
## Design once – use many

If more bags are needed, manifolds can be linked via the aseptic connector interface. The system size can be doubled, tripled, etc. as required.

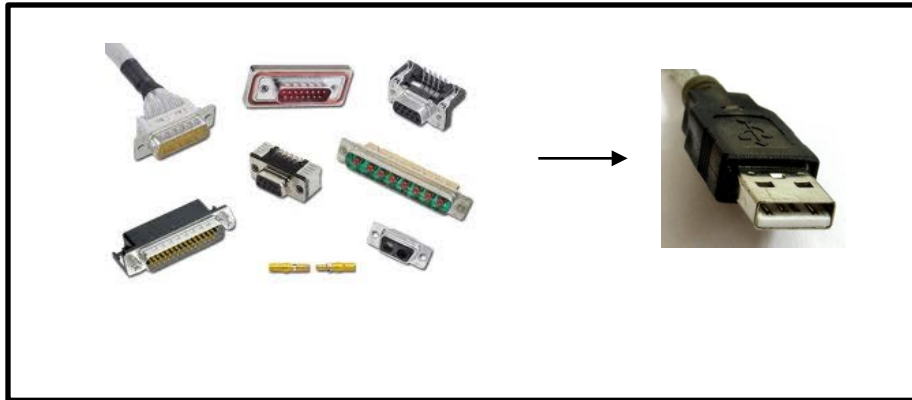


# Single use tubing is flexible

- “Hub” provides simplified fluid network architecture
- Single use assembly structure should be decoupled from operational layout.



If the parts don't fit together, the concepts won't work.



## Summary: Making single use technology work

- Design to meet requirements; source standard supplier products where possible
- Define internal standards and stick to them
- Develop a strategy that works for your manufacturing and supply chain management capabilities
- Deploy single use products properly
- Recognize single use technology management as a professional discipline and staff appropriately

