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Interchangeability of SUS – Functional Specifications and Materials of Construction

Christopher J. Smalley

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Global Technical Operations - Sterile & Validation CoE

MERCK

Be well

Discussion points

- What does existing industry guidance say about this?
- How does “interchangeability” relate to standards and good engineering practice?
- Why and when do we have to deal with this?
- How do we benefit from interchangeability?

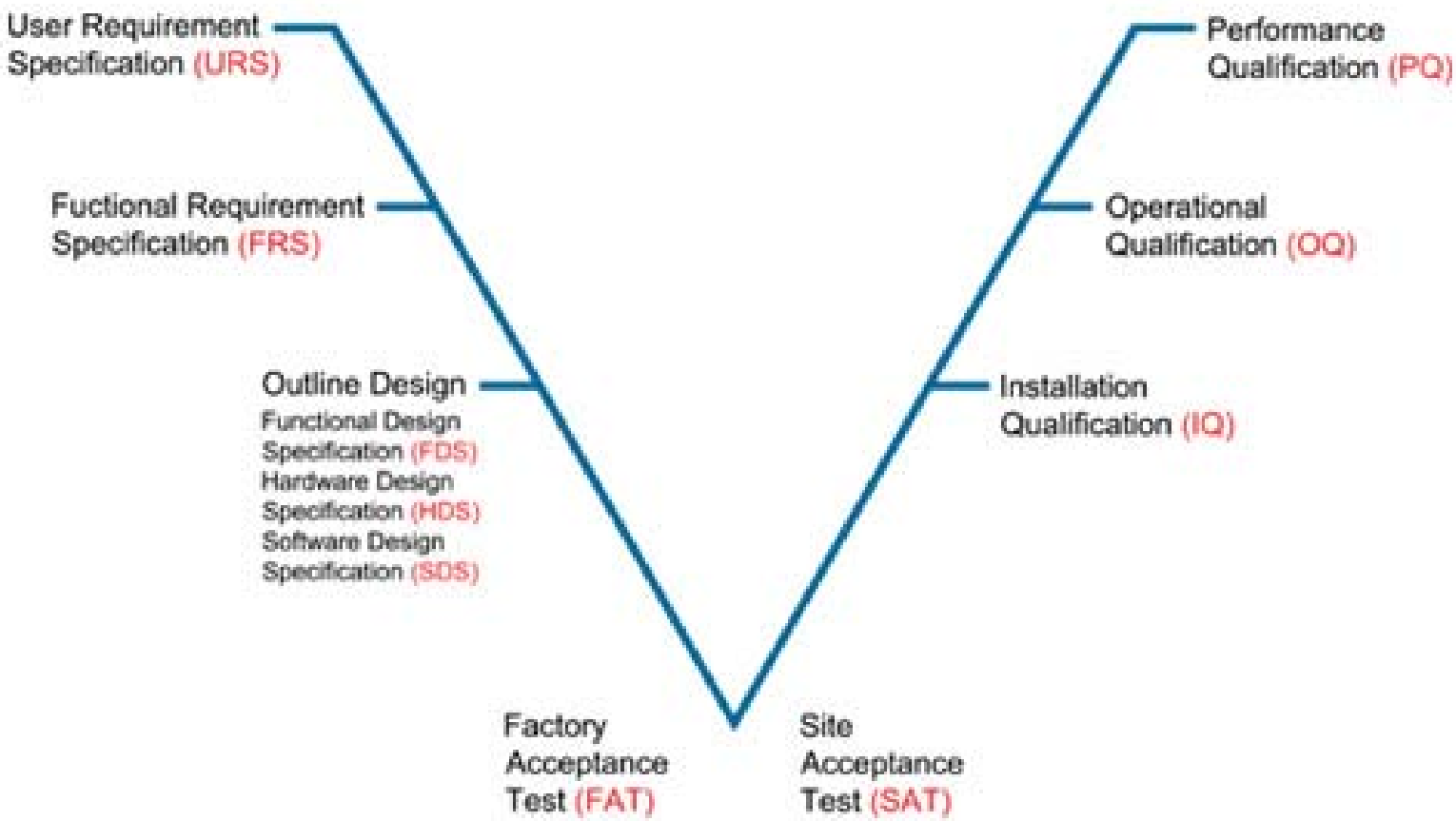
PDA Technical Report 66

- Many mentions of interchangeability and “functionally equivalent”
- Supply reliability and sourcing flexibility are benefits.
- Other benefits?
- What are the costs of establishing interchangeability?

Good engineering practices lead to project success.

- Start with user requirements
- Provide credible specifications for all components
- Use a readily accessible knowledge repository
- Encourage selectivity in the component list
- Meet user requirements with intelligent component sourcing and management strategy.

Getting from requirements to a validated system



source: http://www.tqcmedical.com/validation.htm

User Requirement vs. Functional Requirement

- Must be able to drive in the rain while seeing the road clearly.

- A mechanical wiping system will be implemented that does not cause damage to the windshield and can accommodate differing weather-related rain loads. An area of the windshield will be cleared providing adequate forward viewing.

Detailed Design

- Manufacture a flexible carbon steel wiper blade, 20 inches in length, clad in EPDM rubber and shaped to match the profile of the windshield.
- The blade will be attached via a movable hinge to a carbon steel driver arm 24 inches in length protected from the elements by powder coated paint and attached to an oscillating motor of adjustable speed causing the arm and blade to traverse across the windshield through a 180° arc.
- Contact between the rubber blade and the windshield must be maintained throughout the full range of motion and a minimum effective clearance path of 80% of the windshield area is required.
- The speed of the arc oscillation must be controllable by the driver within the vehicle at variable speed up to 1 cycle per second.

When is interchangeability evaluated?

- Process design – setting up redundant supply chains
- Processing and handling improvements

- Supplier changes
- Supplier's supplier changes

- Transportation changes
- Other situations that differ from original design and qualification conditions

Users are advised to have backups.

- From TR66, 7.7.2

- A backup policy of sourcing the same component from at least two different vendors should be adopted, and the suitability for the backup to be interchangeable with the original must be defined.

What qualifies as a “backup”?

- Functionally equivalent substitutions
- User requirements lead to functional specifications (FS)
- FS need to match in order to call parts interchangeable; FS include “the basics”
- FS must be respected as detailed designs and manufacturing instructions are produced or modified

Table 5.5.2-1 Component Interchangeability Evaluation

Change	Description	Risk Assessment Focus*	Performance Verification
Like-for-like	Identical components, dimensions, and materials of construction made by more than one supplier for the same processing conditions	1, 2	Design and user specification monitored through change control
Functionally equivalent	Combinations of materials with the same performance but different material suppliers (e.g., bag/filter/tubing) or processing conditions	1, 2, 3, 4, 6	Monitor performance attributes, leachables, and CQAs
Process or functional modification or improvement	Similar function or performance with different design and materials of construction and may require some process or equipment modification for operation (e.g., virus filter housing changed)	1, 2, 3, 4, 5, 6	Monitor performance attributes, leachables, and CQAs in a scaled-down development study

***Risk Assessment Focus Descriptions**

1. Design, dimension, performance, and materials claims of the proposed substitute (form, fit, and function)
2. Materials of construction and process contact fluid compatibility, contact area, and time

   Availability and extent of supplier biosafety (USP <87> and/or <88>, as appropriate for the application) and extractables data *(24,25)*
4. Suitability of supplier extractables data to bracket process fluid and conditions
5. Application and potential for subsequent leachable removal or dilution
6. Product impact assessment

source: PDA, TR66

Table 5.2-1 Risk Complexities of SUS Items and Applications

		System Complexity				
		Low	Moderate	High		
Impact to Process	Low	Buffer/Storage	UF*/DF†/ Concentration	Clarification/ Recovery	Low	Impact to Process
	Moderate	Transport/ Shipping	Connectors/Mixing/ Medium Storage	Cell Culture/ Fermentation	Moderate	
	High	Freeze/Thaw	Purification/ Product Storage	Fill and Finish	High	

*UF – ultrafiltration †DF – diafiltration

Interchangeability needs to be assessed at different levels

- Different supplier or supply chain
- Different materials of construction
- Different parts that can accomplish process intention

- Different lots?
- Different items in same lot?

Control what we can. Plan for what we can't.

"Variation is the root of all evil"

– J. Edwards Deming

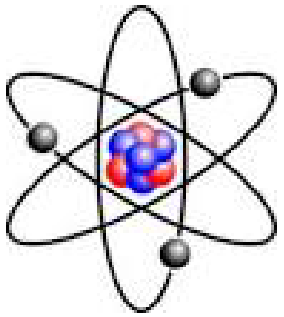
- Materials of construction
- Manufacturing processes for SU components
- Connection design (tubing, fittings, fasteners)
- Assembly operations
- Packaging and shipping
- Storage and un-packaging
- Use in biopharmaceutical manufacturing

Good engineering practices lead to operations success.

- Configuration Management: change evaluations, technical updates, response to user feedback and evolving requirements
- Process controls at SUS manufacturer
- Feedback to supplier
- “Continuous Supplier Qualification”
- Sourcing updates

Components: The building blocks of SUS

- Tubing
- Connectors/Connections
- Fasteners

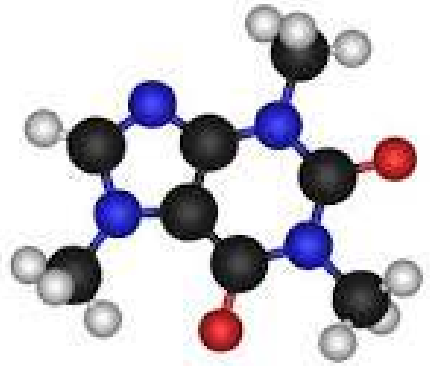


Standards should define:

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

Assemblies: Collections of Components

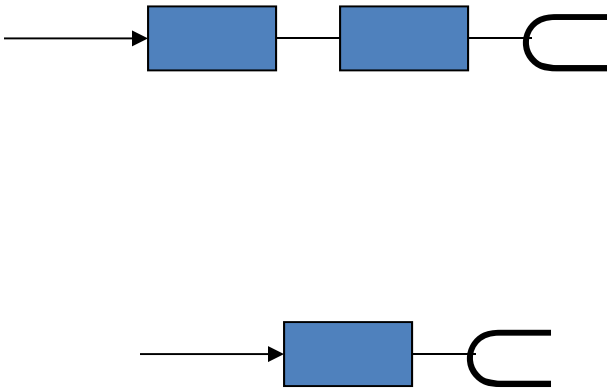
- Buy connections or make connections?
- Buy vs. make from scratch vs. “cake mix”
- If make, then how?
- Need a strategy: standard modules is one idea

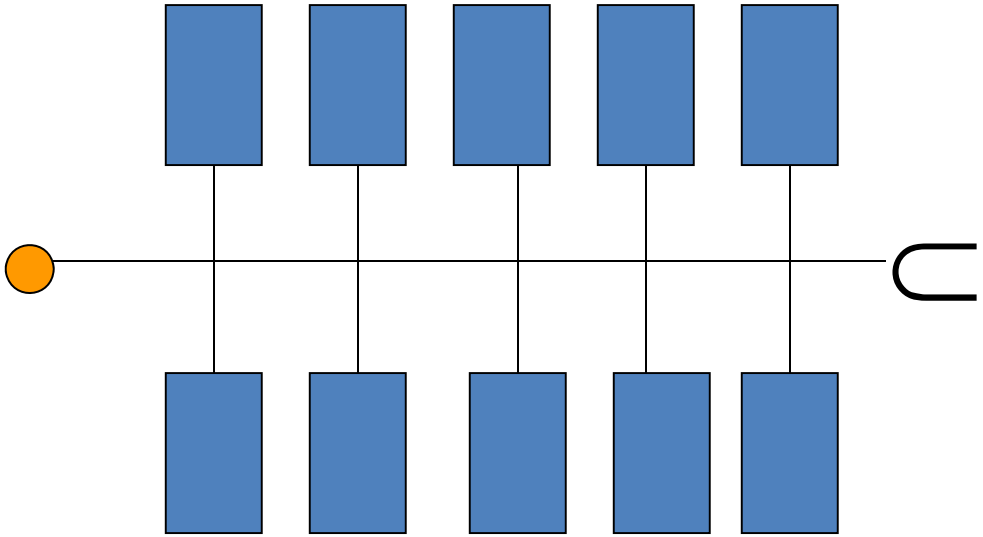


Standard will define:

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

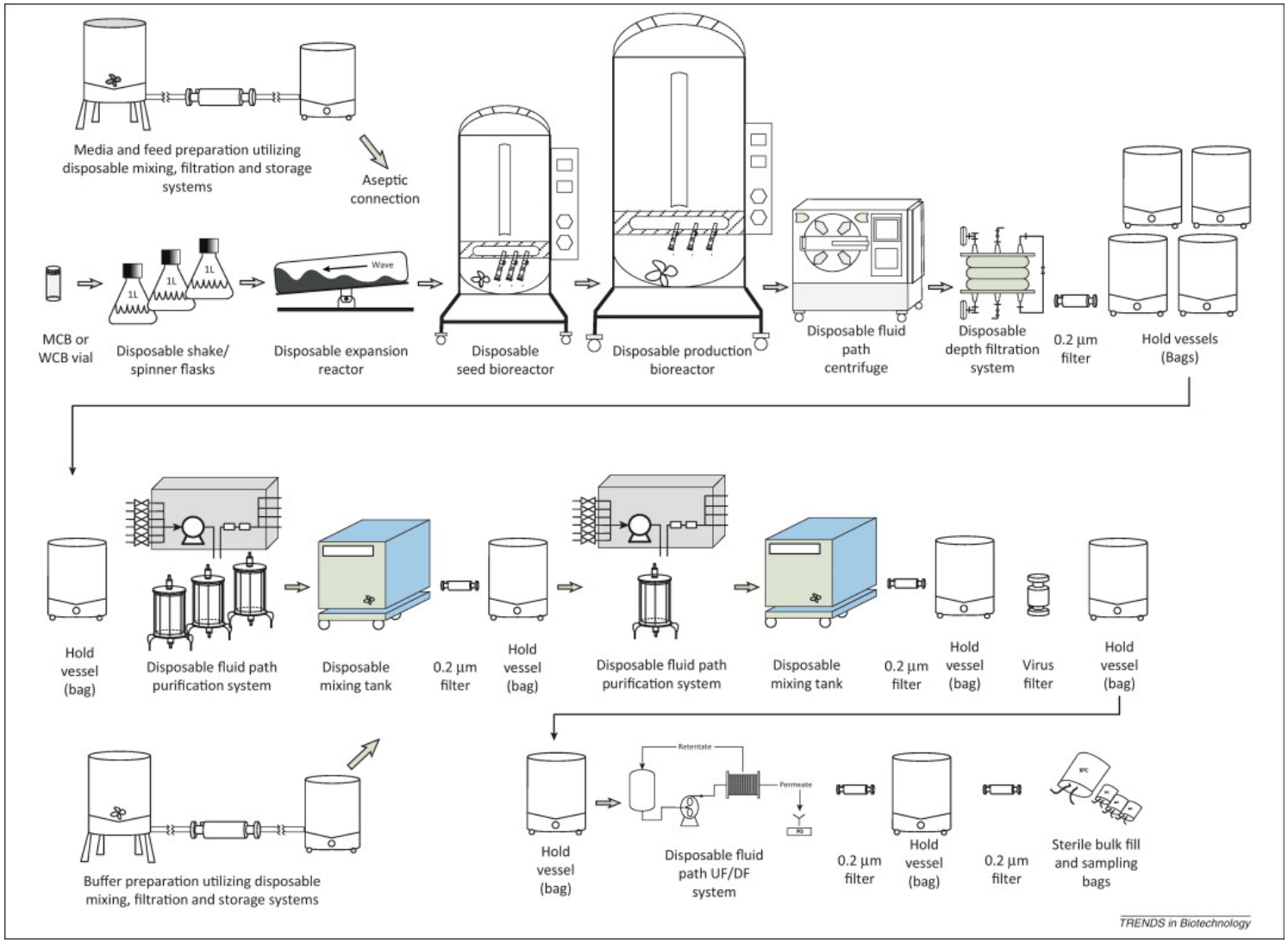
Effective modular design requires interchangeability



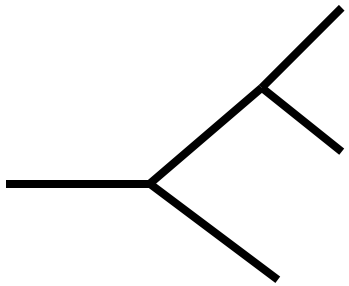


generic depiction of an aseptic connector pair:

Assemblies unite to form process trains

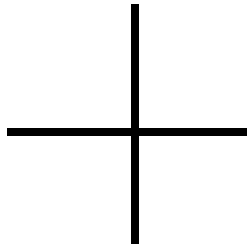


Equivalent?



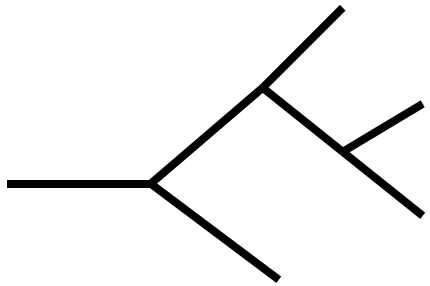
6 fasteners required, or

2 molded junctions



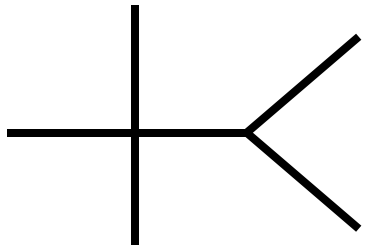
4 fasteners required, or

1 molded junction



9 fasteners required, or

3 molded junctions

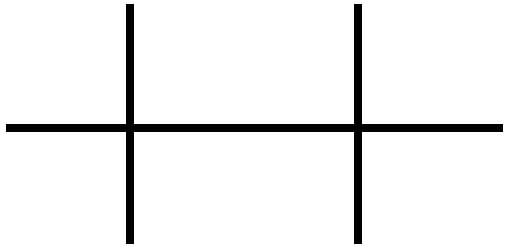


7 fasteners required, or

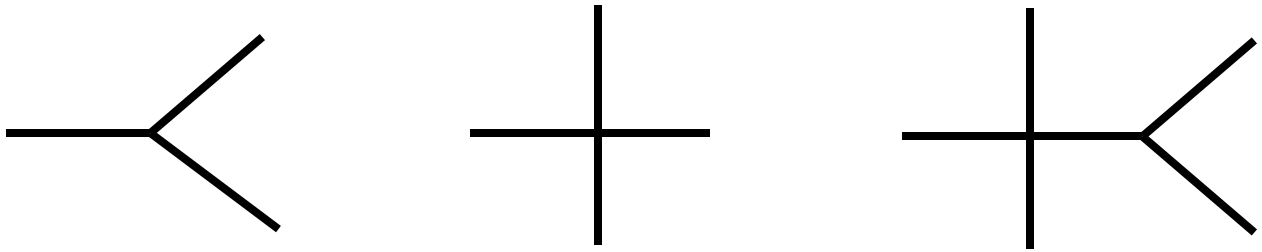
2 molded junctions

Functional equivalence – tubing manifolds

Could this:

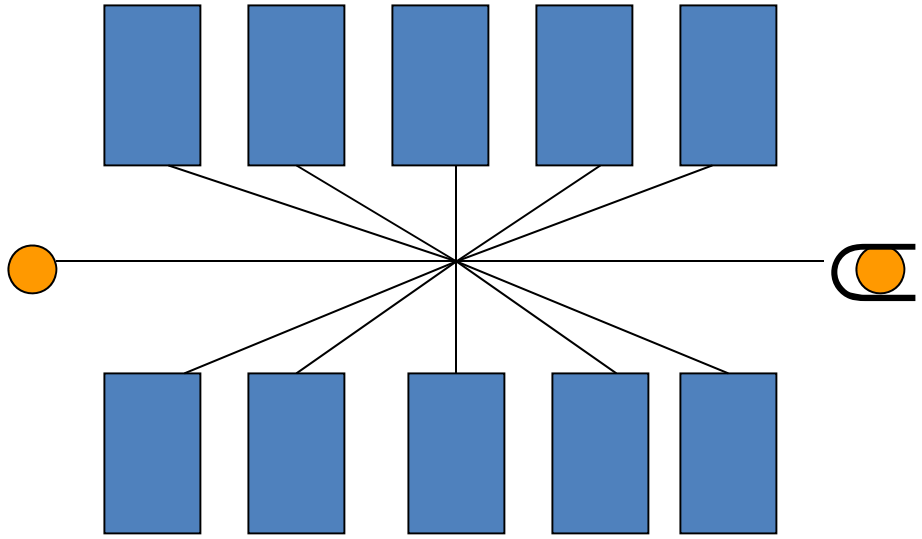


Replace all of these?:



Adaptable parts reduce number of parts.

- “Hub” provides simplified fluid network architecture; coils eliminate need for precise lengths
- Single use assembly structure can be decoupled from operational layout.



Summary: Interchangeability in SUS

- Keep user requirements in mind when assessing interchangeability
- Prepare a strategy for assessing interchangeability as part of the design process
- Be flexible in your thinking about what “the same” means

Thank you!

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Global Technical Operations - Sterile & Validation CoE

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PDA Technical Report 66 – Section 2, glossary

SUS Interchangeability

Functionally equivalent substitution of an alternative SUS, for an existing SUS design providing a contingency or process improvement with equivalent process performance and product quality. The end user is responsible to evaluate and determine if appropriate quality requirements are met for their application.