Facility Design and Resource Optimisation for Multi-Product Vaccine Manufacturing

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Imagination at work

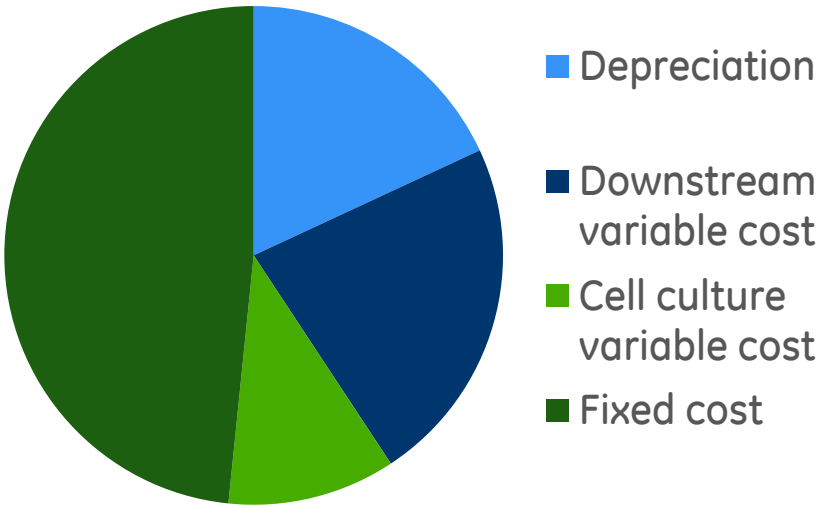
Overview

- Understanding manufacturing costs
- Case study - Facility design and operation
  - Impact of single-use systems
  - Impact of segregated processing areas
  - Impact of changeover scheduling strategies
- Summary

Understanding manufacturing costs

Classic biomanufacturing costs

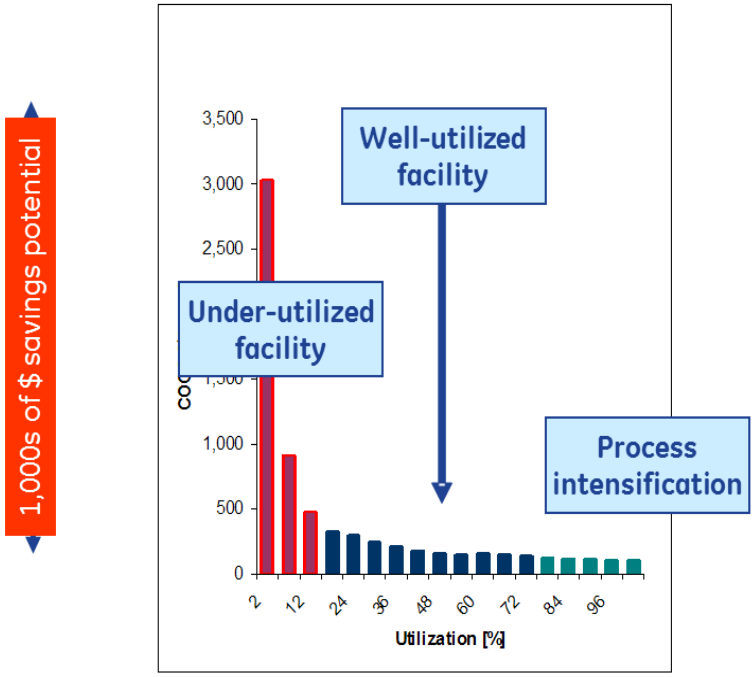
Manufacturing cost distribution



Classic scenario for biomanufacturing

- Single product: low flexibility
- Capital intensive
- Long construction lead time
- Fixed costs dominate
- Major gamble prior to launch

Facility utilization is key to minimizing production costs



The negative effect of under-utilization can hardly be compensated elsewhere, unless one builds small and (partly) disposable to reduce fixed cost by any feasible means.

Scenario in flexible facilities

- High degree of utilization due to process flexibility
- Output scale and demand match
- Multi-product production possible to drive further utilization improvements

Observations on cost drivers form a basis for facility design strategies

Observations

- Fixed costs dominate costs in conventional facilities
- Facility utilization is the dominating cost driver

Strategies for improved facility utilization

- Implementation of single-use systems
- Facility design to improve utilization
- Changeover scheduling

Single-use

Single-use technologies

Unit Operation	Single-use option availible	Comment
Cell culture	Yes	Options exist from multiple vendors, but limited in size.
Microbial fermentation	Yes	A few options exist, limited in size.
High pressure homogenizer	No	
Mixing	Yes	Mature application. Many options from different vendors, limited in size.
Liquid handling	Yes	Mature application. Many options from different vendors, limited in size.
Clarification	Yes	Depth filtration - Mature application. Many options from different vendors. Centrifugation – Options exist
Chromatography	Yes	Options exist, both for skids and columns (columns are typically used several times), but limited size range.
TFF	Yes	Options exist, both for skids and filters but limited size range.
Ultracentrifugation	No	

Claims made related to single-use systems

On costs

- Reduce capital investments (20-50% from comparable stainless facility)
- Delay investments
- Reduce validation cost (e.g. CIP methods)
- Reduce cleaning costs – personnel, water, steam and chemicals
- Increase some consumables costs (for disposables)
- Add and take away as needed - avoid cost of a rebuild
- Standardize and modularize – cheap to change, cheap to operate

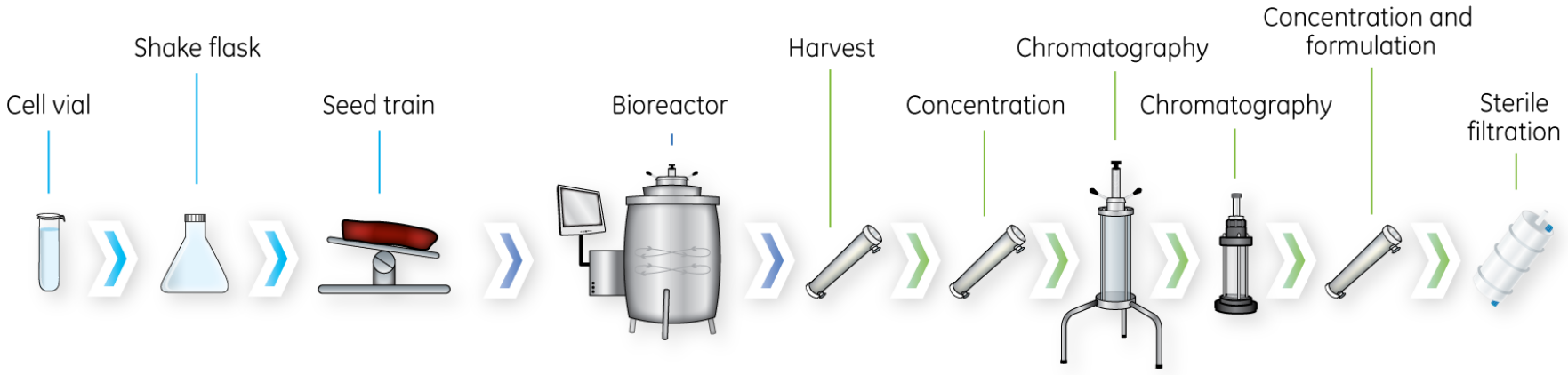
On revenue

- Shorten time to readiness of facility
- More product, especially for multi-product facility
- Flexible. Be alert for the next challenge.

Case study: Facility design and operation in stick-build facility

Case study design: Cell-based vaccine facility

- 500L scale cell-based vaccine
- Vial-to-reactor upstream process
- Filtration and chromatography downstream
- Single- or multi-purpose



Evaluating the impact of single-use systems

Two possible process designs

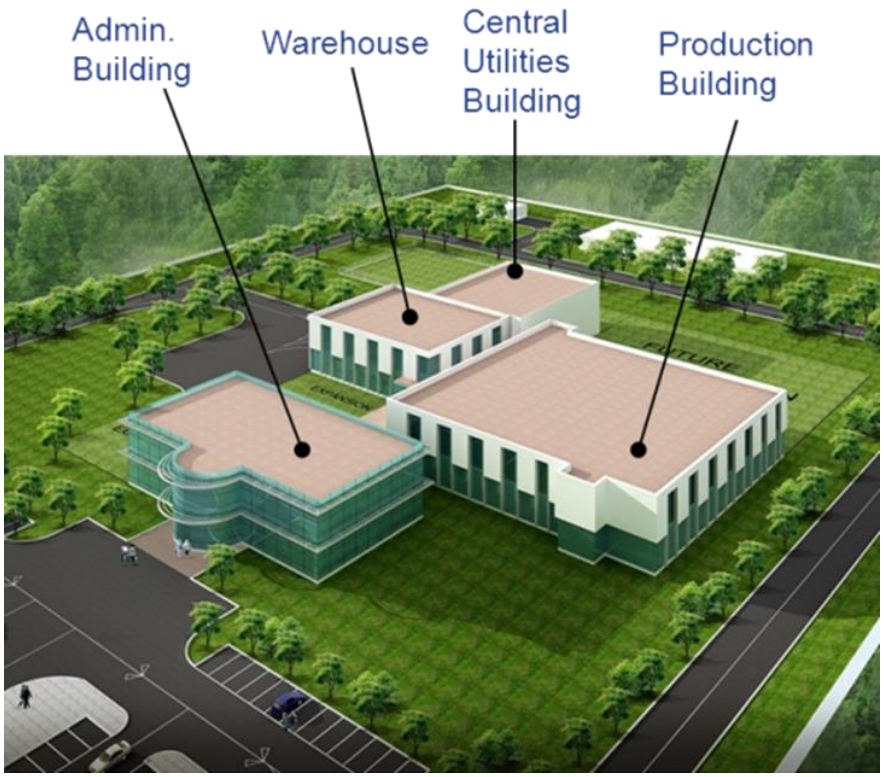
Stainless Steel

Conventional process equipment, but single-use buffer hold bags

Single-Use

Single-use equipment where possible

Basic facility design requirements



- Production Building - production and clean utilities
- Warehouse – raw material, consumables, product
- Central Utilities Building – Non GMP utilities
- Administration Building - Offices, QC Laboratory, Canteen

Facility and utility design differences when implementing single-use

Facility

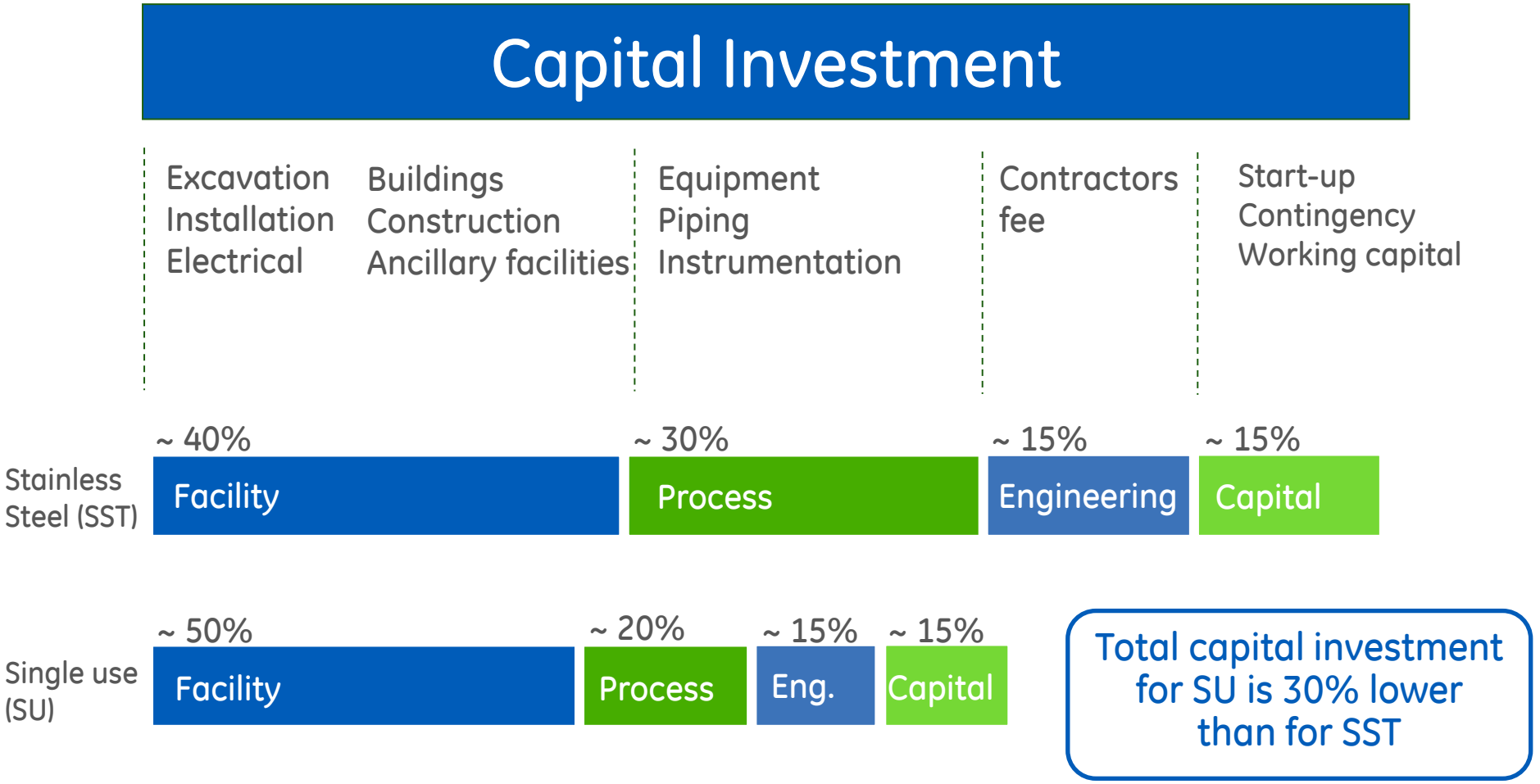
	Floor area (m^2)		SST-SU difference
	SST	SU	
Production building	2580	1968	-24%
Admin & lab building	1111	1111	0%
Warehouse	337	611	+81%
Central Utilities Building	325	325	0%
Total	4353	4015	-8%

Utilities

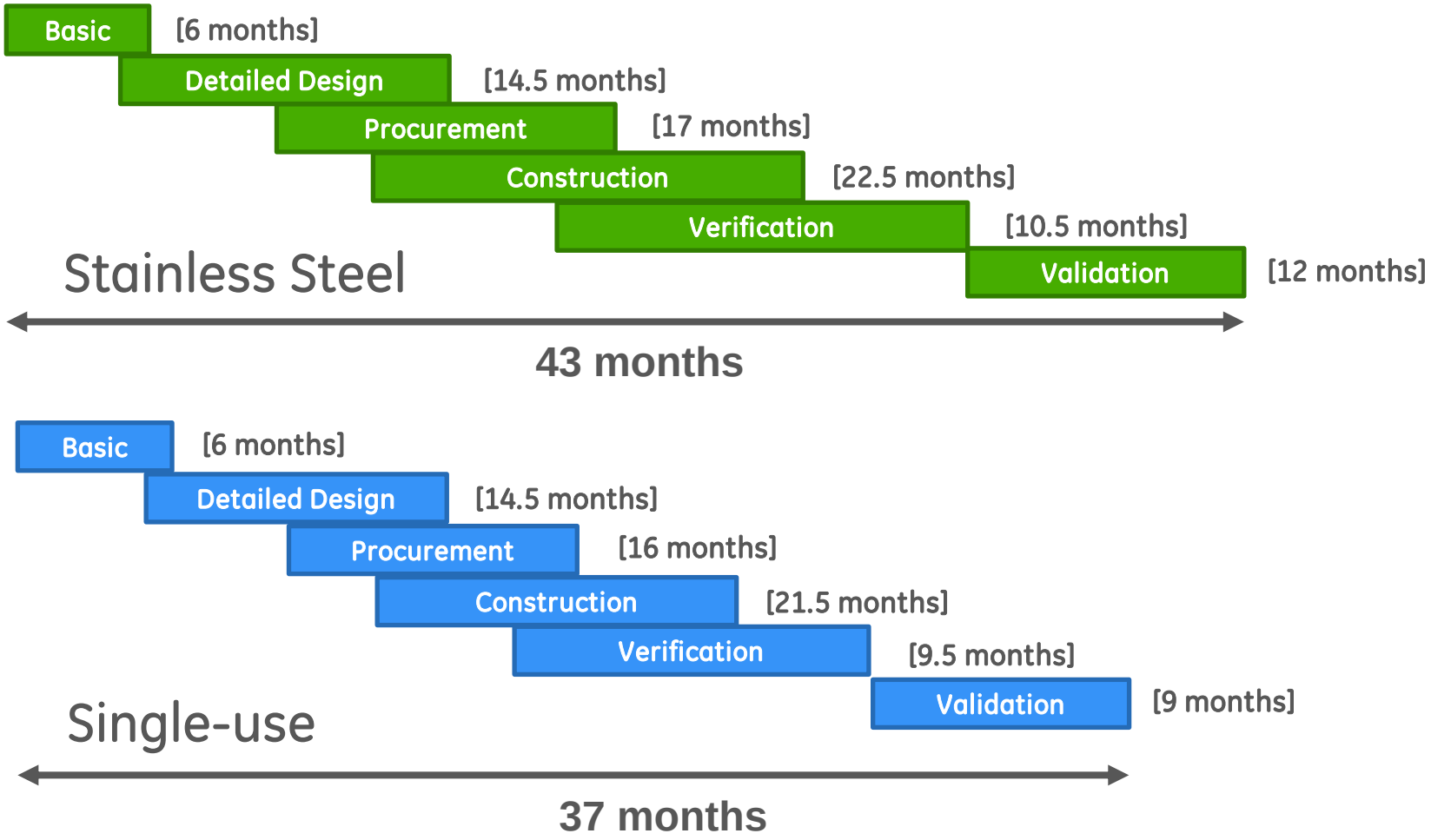
	Generator capacity		SST-SU difference
	SST	SU	
Purified Water generator (L/day)	18000	2200	-88%
WFI generator (L/day)	14000	1300	-91%
Clean Steam Generator (kg/h)	87	17	-80%

SST = Stainless Steel
SU = Single-use

Capital investment distribution when implementing single-use



Project execution comparison when implementing single-use systems



Drivers for project timeline reductions

A Single-Use strategy means

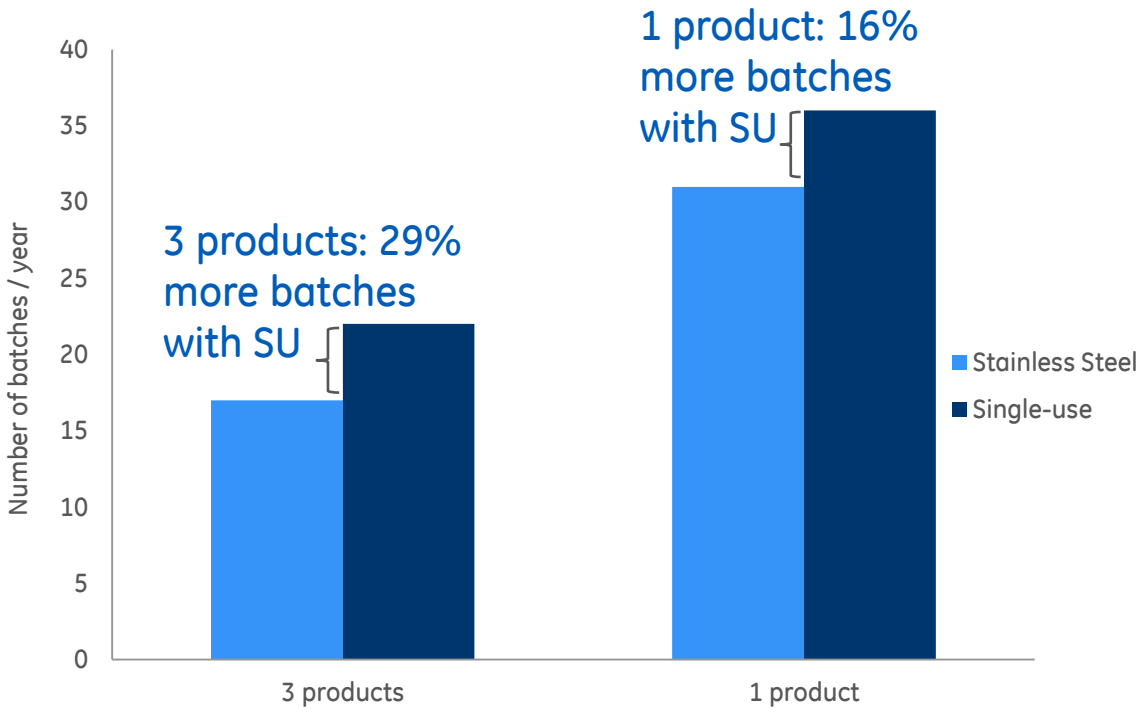
- More standard, off-the-shelf equipment units
- Few long lead equipment items
- Less complexity in facility
- Less installation work

The Effects

- Facility construction will set the time frame
- Time saving in cleaning validation
- Less risk of delays

Shorter project adds value if on critical time-line
Time saved frees up resources for other activities

A single-use strategy provides a strong throughput benefit in multi-product facilities



Summary of Findings: Single-use system implementation

- Facility size is similar, but distribution of clean room and warehouse space is different
- Capital investment and project timelines are reduced
- Higher impact on output in a multi-product facility compared to a single-product facility

Thank you

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