

ISPE-CASA PRESENTS “CLEAN & GREEN”

DEVELOPING A PROCESS MODEL FOR SINGLE-USE TFF CASSETTES

By: Mark A. Perreault



CLEAN AND GREEN TECHNOLOGIES FOR PURE WATER AND PROCESS TECHNOLOGIES

Effects of Single Use Technology

● Where has single-use technology effected Bio-Processing?

Then...



- **Bioreactors**
- **Media Storage**
- **Aseptic Filtration**



Now...



Effects of Single Use Technology

- Single-use technology has made bioprocesses:
 - Cleaner
 - Safer
 - More Efficient
- Single-use technology has enabled a typical purification process to eliminate numerous costly clean in place (CIP) operations



Considerations for Single Use TFF

- Tangential Flow Filtration (TFF) is a very common process step used during purification to concentrate and diafilter process streams
- When developing a process model for single use TFF, consider its purpose, function, and scale
- Only implement a single use process step if it makes “good sense” and can be justified.

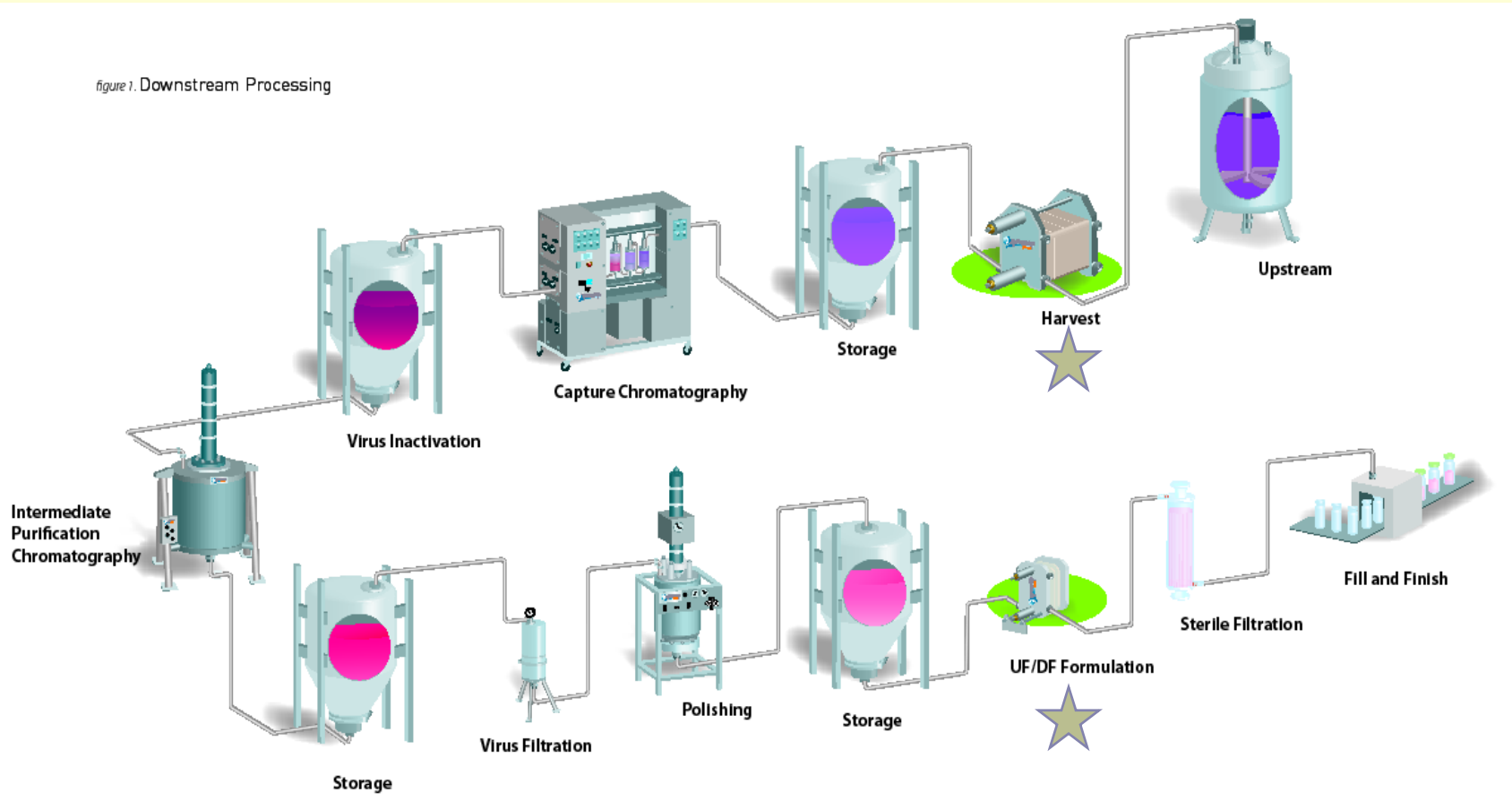


Developing a Process Model for Single Use TFF

- Begin by identifying the TFF steps in your purification process

Developing a Process Model for Single Use TFF

figure 1. Downstream Processing





Developing a Process Model for Single Use TFF

- Several key parameters will quickly identify which TFF steps are a good candidate for single use and ones that are not
- Consider the following:



Developing a Process Model for Single Use TFF

- Comparison of System Design
- Labor
 - Reusable TFF Process
 - Single Use TFF Process
- Consumables
 - Reusable TFF Process
 - Single Use TFF Process
- Economic Process Model Comparison

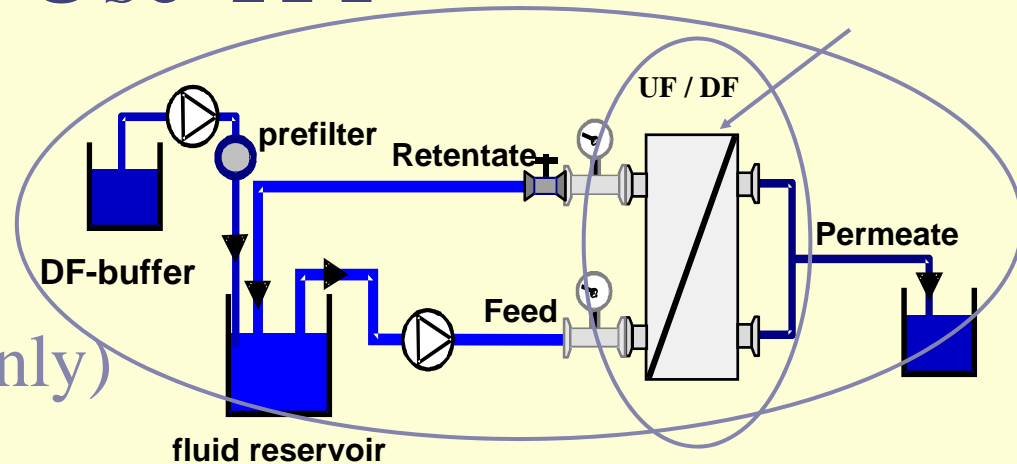


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Developing a Process Model for Single Use TFF

- System Design
- Single Use Options
 - Filtration Cassettes (only)
 - Cassette and Holder
 - Complete Single Use System



Developing a Process Model for Single Use TFF

● Examples of System Design

Reusable TFF System



Single Use TFF System



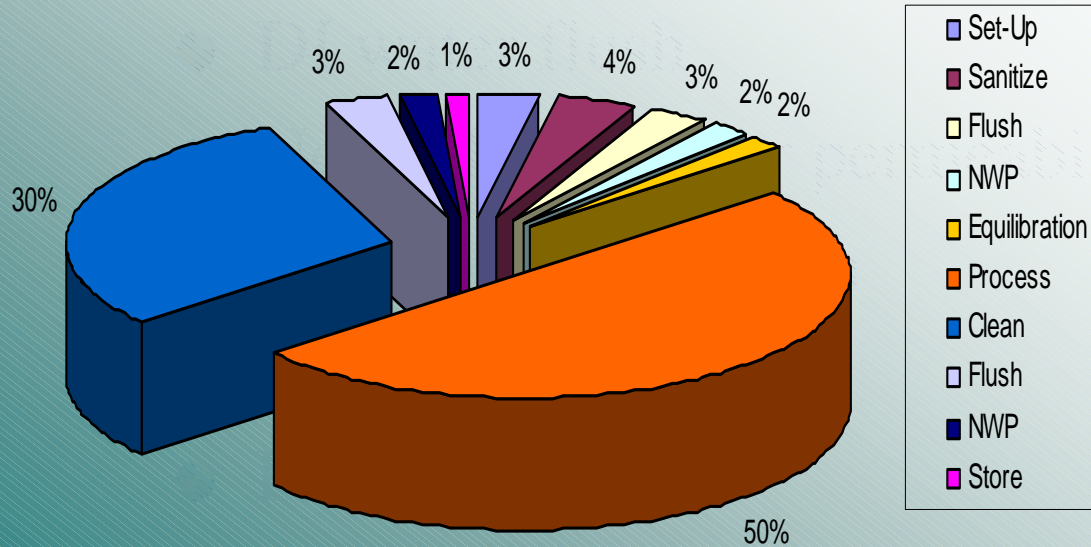


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Developing a Process Model for Single Use TFF

● Labor required for a reusable TFF Process

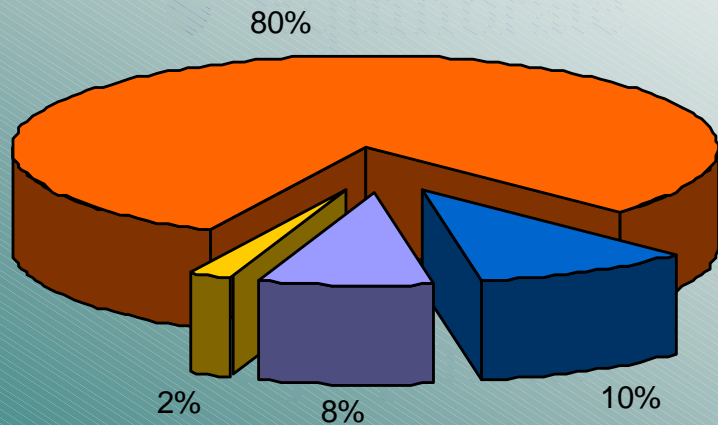


Reusable TFF Cassette Process

- Time and labor are consumed both before and after use
- Recourses are needed for cleaning validation
- A significant volume of purified water is needed for CIP and flushing
- Membrane performance can decrease after repeated use

Developing a Process Model for Single Use TFF

● Labor required for a Single Use TFF Process



Single-Use TFF Process

- A greater portion of time and resources can be devoted to processing
- Both labor and system size are minimized
- Reduced risk of cross contamination
- Utility requirements are lower
- Greater manufacturing flexibility is created



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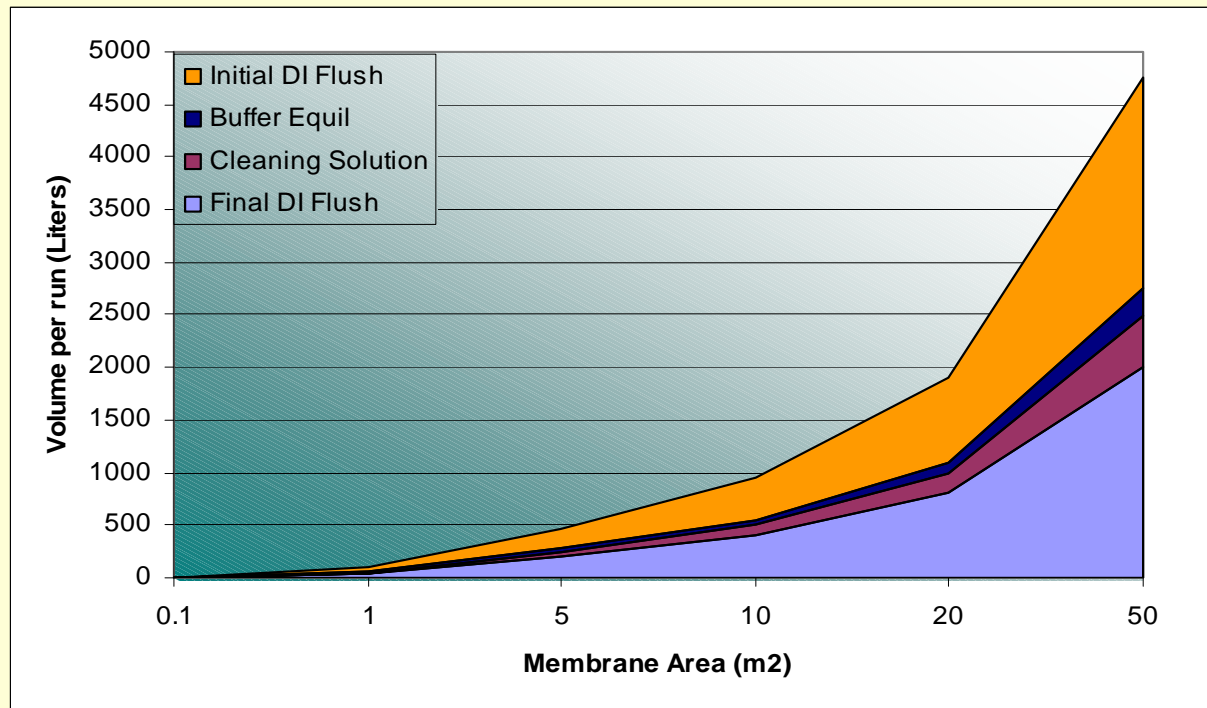
Developing a Process Model for Single Use TFF

Consumables for a TFF Process

- Purified Water – Added equipment costs and power requirements
- Equilibration Buffer – Pre-made buffers are expensive and making buffers are labor intensive
- Cleaning Solutions – Requires labor and equipment for preparation of CIP solutions
- Filtration Cassettes – Costs for initial investment of reusable vs. reoccurring costs of single-use

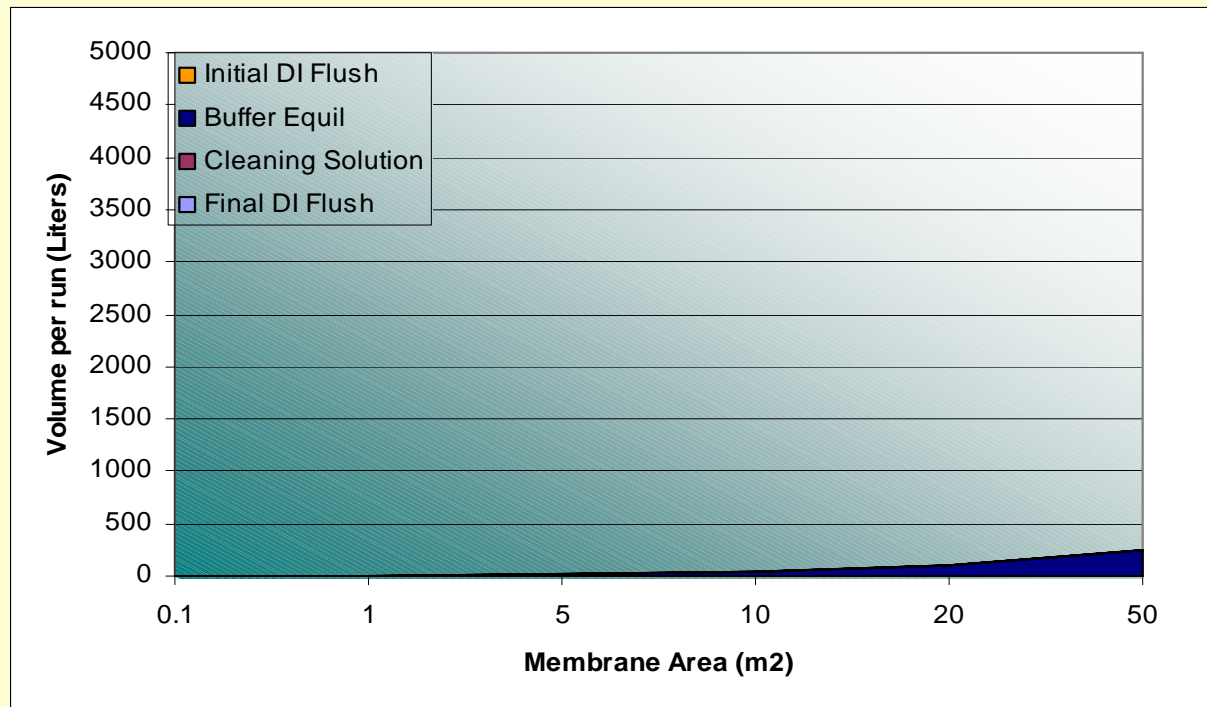
Developing a Process Model for Single Use TFF

- Purified water requirements for a **reusable** TFF Process



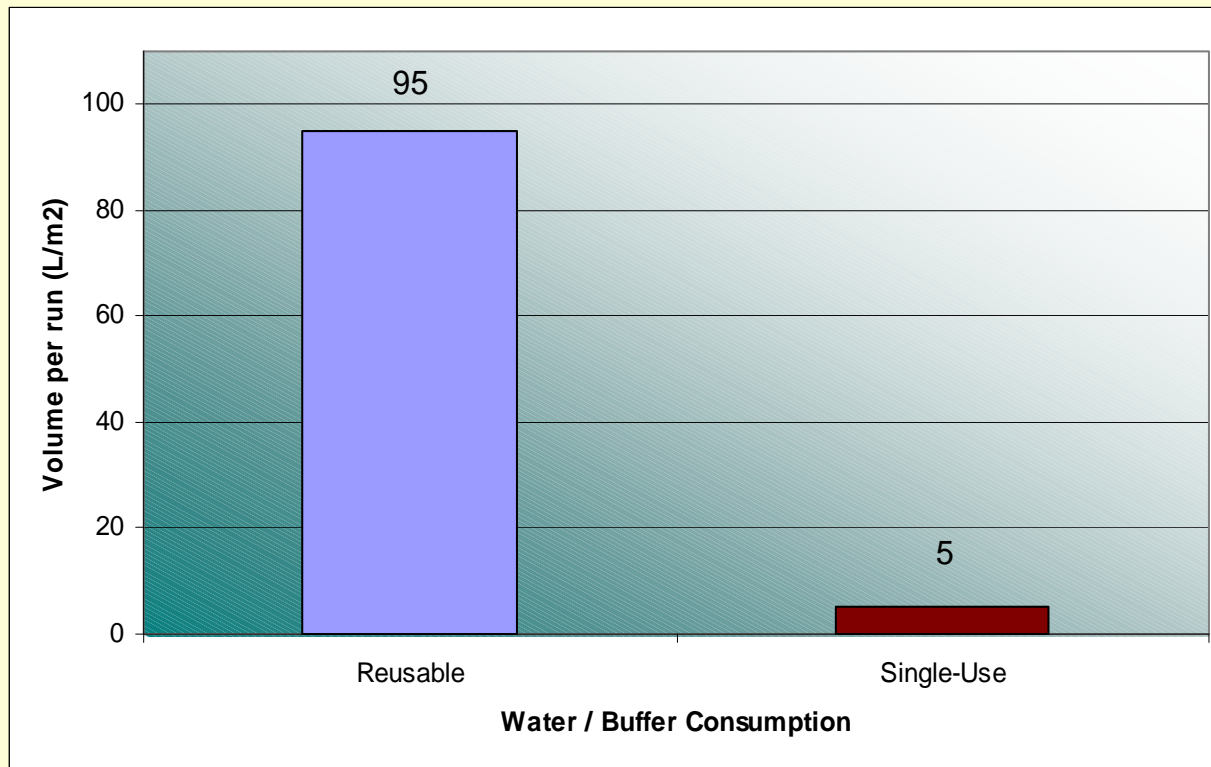
Developing a Process Model for Single Use TFF

- Purified water requirements for **single-use** TFF



Developing a Process Model for Single Use TFF

Water / Buffer Consumption Comparison





Developing a Process Model for Single Use TFF

- Single-use TFF has a significant impact on TFF process models
- Cleaning solutions are eliminated
- Water consumption is greatly reduced when using single-use TFF



Developing a Process Model for Single Use TFF

Consumables for a TFF Process

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- Equilibration Buffer – Pre-made buffers are expensive and making buffers are labor intensive
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Developing a Process Model for Single Use TFF

- Is there an economic benefit to using traditional cassettes as a “single-use” product?
- If not, can a feasible target cost of single-use cassettes be determined?
- One must consider major variables such as:
 - Equipment cost
 - Cleaning validation
 - Labor
 - Consumables
- Reusable and single-use cassette cost can be weighed against the percent savings of a single-use TFF process

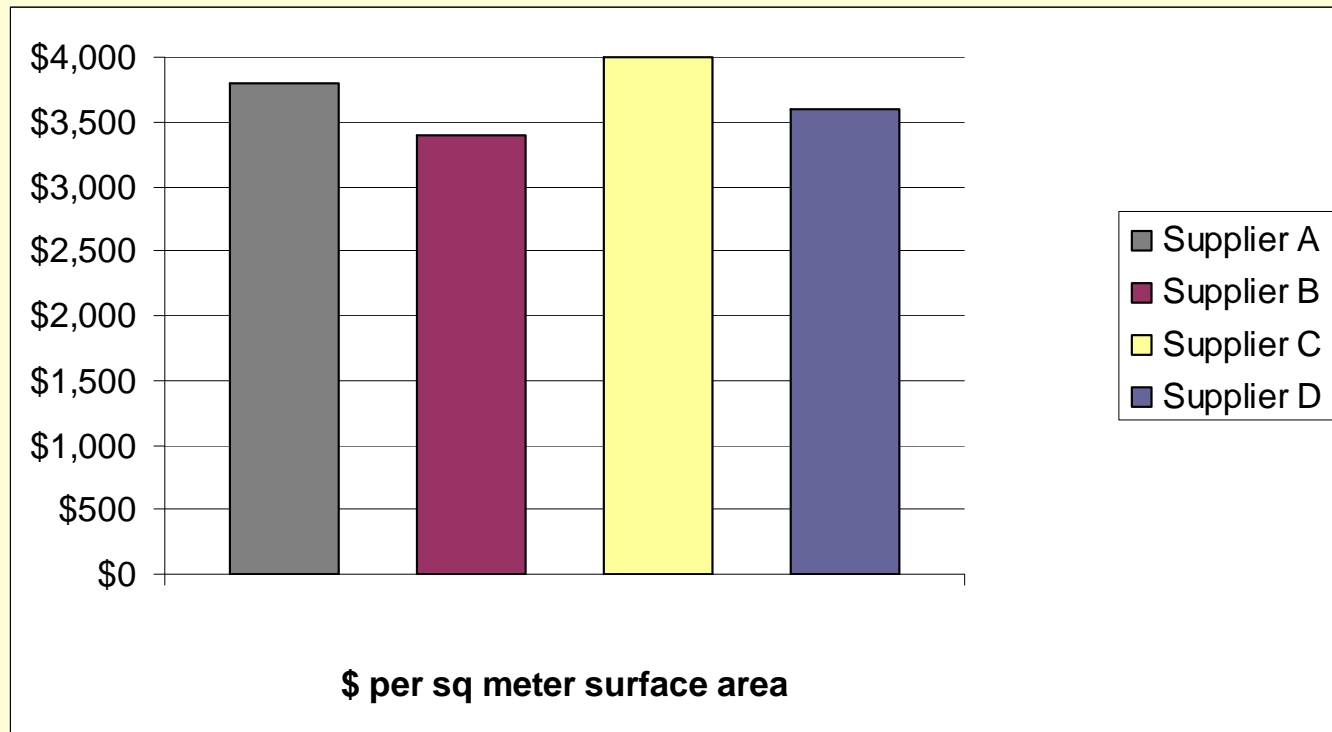


Developing a Process Model for Single Use TFF

- What are the costs of **reusable** TFF cassettes?
- Traditional reusable cassette costs are well established.
- Typical costs are as follows:

Developing a Process Model for Single Use TFF

Filtration cassette costs for reusable TFF

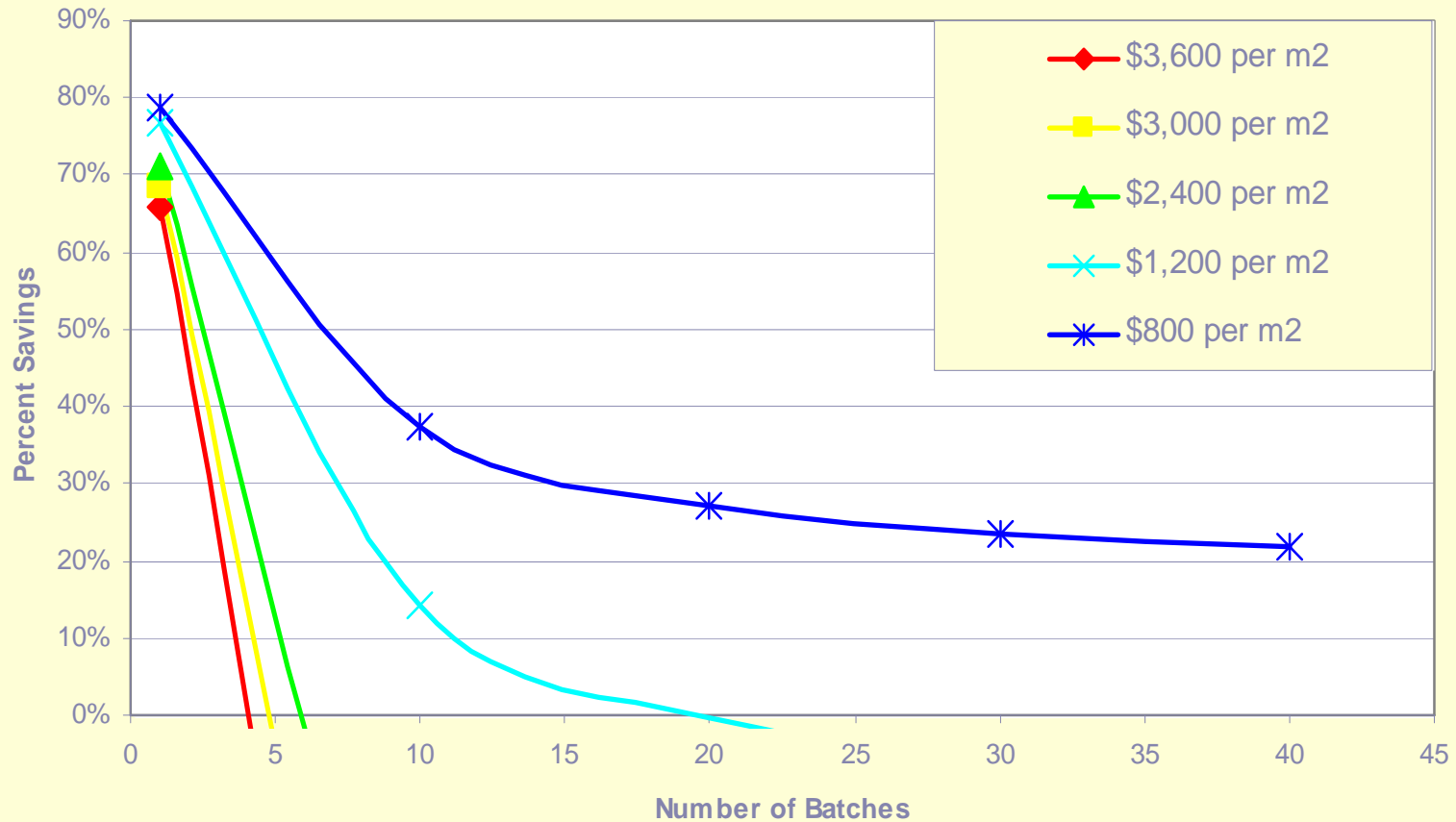




Developing a Process Model for Single Use TFF

- Can one anticipate cassette costs for a **single-use** TFF process that can trigger a “go” or “no go” decision?
- Consider the following:
 - Number of batches (or uses) per campaign
 - The average savings of using single-use cassettes per batch
 - The cost of the cassettes per batch
- What is that anticipated target cost for **single-use** TFF ?

Developing a Process Model for Single Use TFF





Developing a Process Model for Single Use TFF

- The target cost of a single-use TFF cassette should be no greater than \$800 / m² based on this model.
- The cost of traditional reusable cassettes can potentially limit the feasibility of single-use.
- Is there an economic model that can predict which processes are suited for single-use TFF?



Developing a Process Model for Single Use TFF

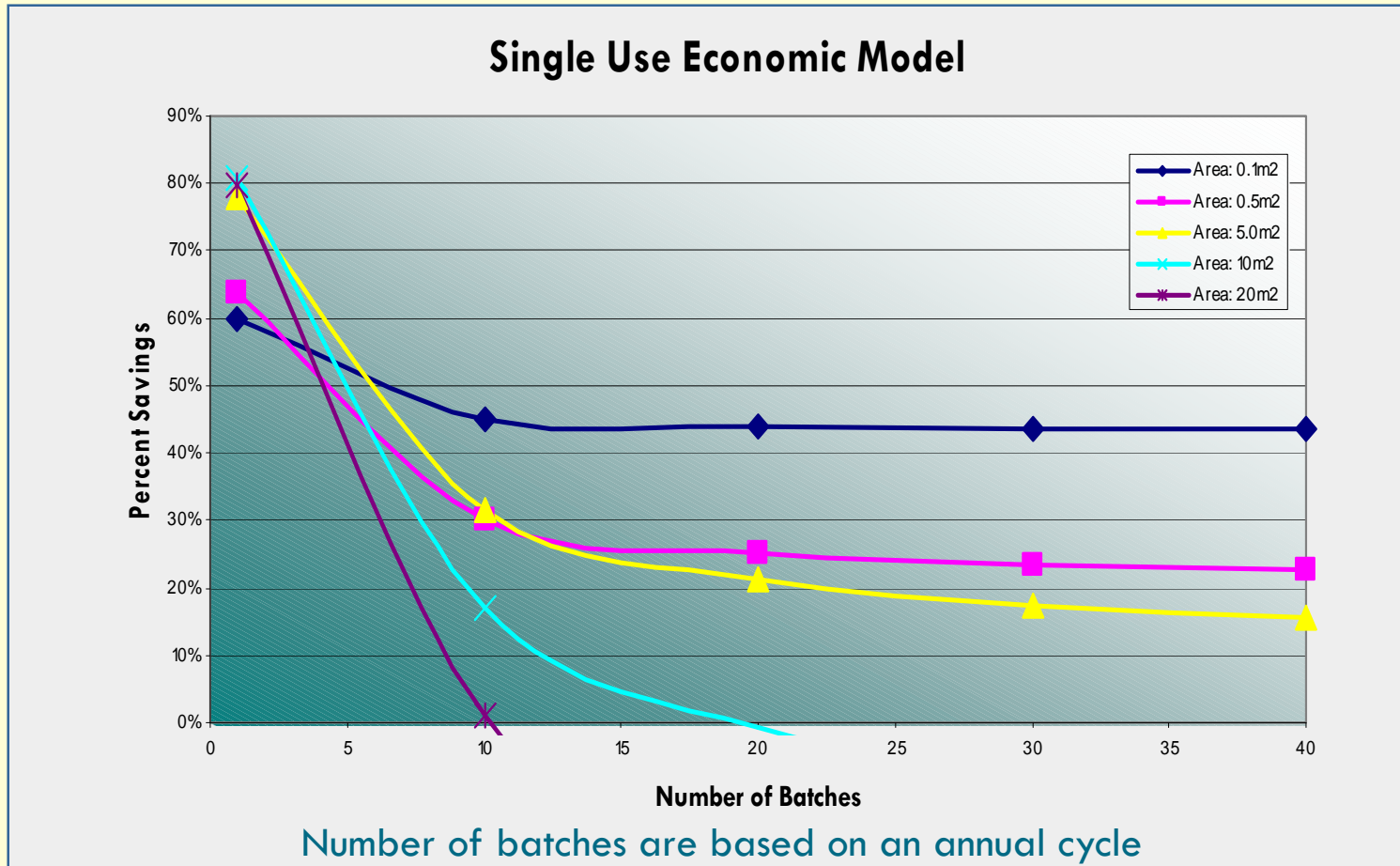
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Developing a Process Model for Single Use TFF

- Single-use TFF provides measurable benefits in many circumstances, however it can potentially have economic limitations depending on the scale and frequency of the operation.
- Two key factors affect the economy of single use TFF are:
 - Membrane area of the operation
 - The number of cycles the membrane is reused
- The following graph shows the relationship between the number of annual process cycles and the economic benefit (percent savings) associated with single-use TFF at several different process scales.

Developing a Process Model for Single Use TFF





Developing a Process Model for Single Use TFF

- The general trend shows single-use TFF technology is most beneficial at smaller scales, i.e. less than 5m².
- As the scale grows to 10m², this model predicts the break even point occurs at approximately 20 reuse cycles.
- Larger scale operations benefit when the number of annual process cycles is fewer than 20 reuse cycles.



Developing a Process Model for Single Use TFF

- Model accounts for:
 - System Design & Fabrication
 - Validation
 - CIP Cycles
 - Labor & Overhead Costs
 - Consumables



A Case Study for Single Use TFF

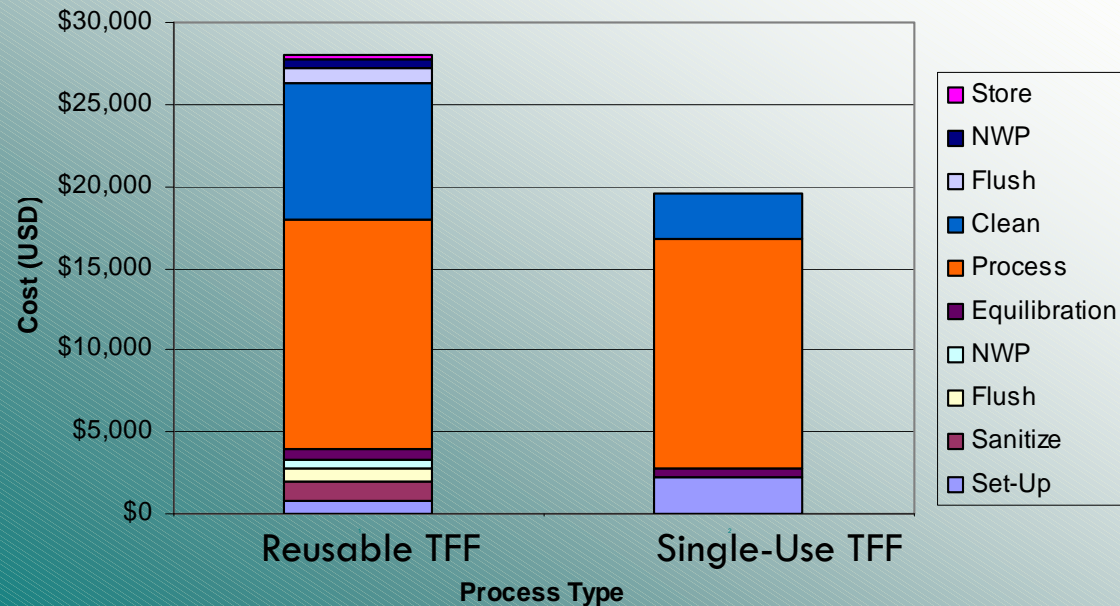
- A case specific analysis can be generated factoring these five parameters.
- A 50ft² (5m²) concentration and diafiltration process was modeled.
- Primary process steps were analyzed for the level of support required from the standpoint of labor and the facility.
- The following graph compares the sum of labor, facility, water, and consumable costs associated with a reusable TFF process vs. a single use one.

A Case Study for Single Use TFF

Labor Costs

- Labor rate includes overhead costs of a typical GMP BioPharm process facility
- A greater portion of time and resources can be devoted to processing
- Greater manufacturing flexibility is created

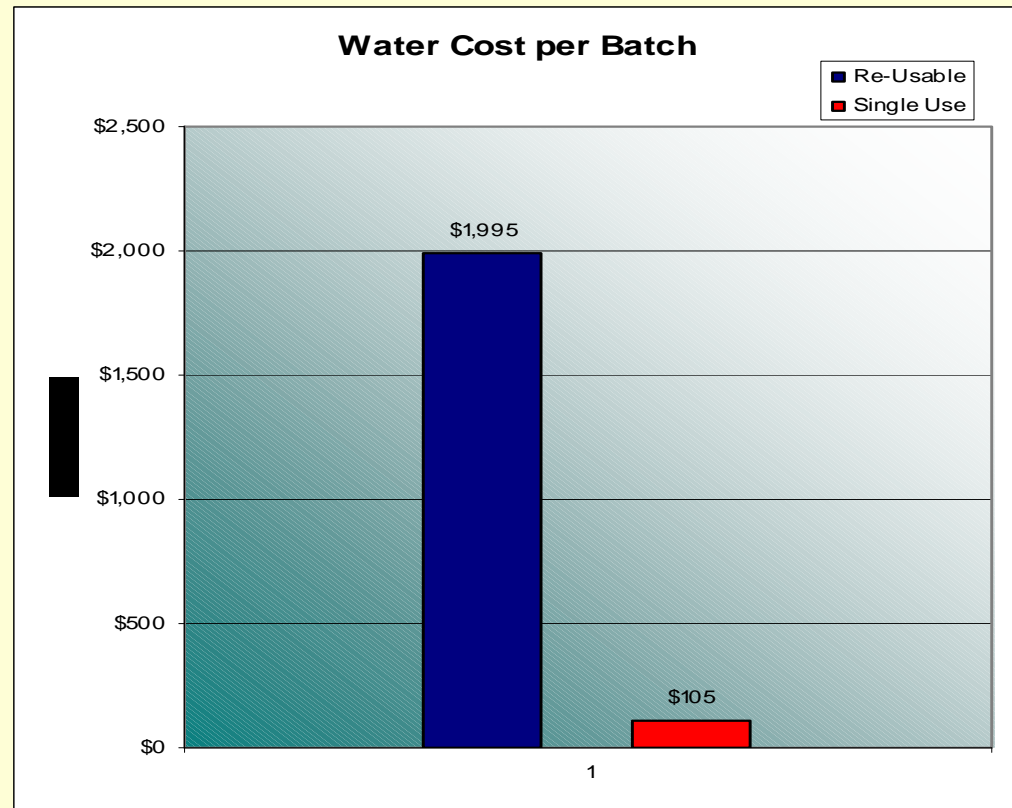
Reusable vs. Single-Use Process Cost / Batch



A Case Study for Single Use TFF

Water / Buffer Costs

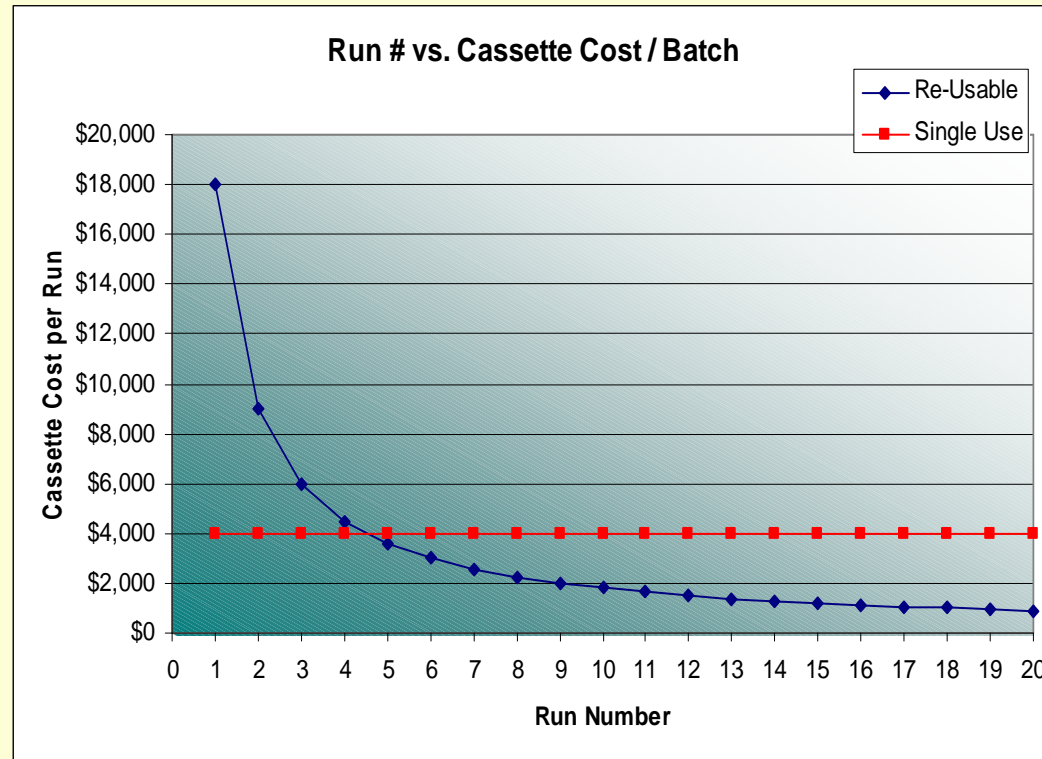
- Water / buffer costs include equipment, monitoring, preparation, and disposal
- Purified water system size can be greatly reduced with single-use TFF
- Disposal is also minimized



A Case Study for Single Use TFF

Consumable Costs

- Consumable costs are based on current TFF cassette prices
- Re-Usable cassette cost occurs once and is then divided over the total number of uses
- Single Use cassette cost occurs once for each run



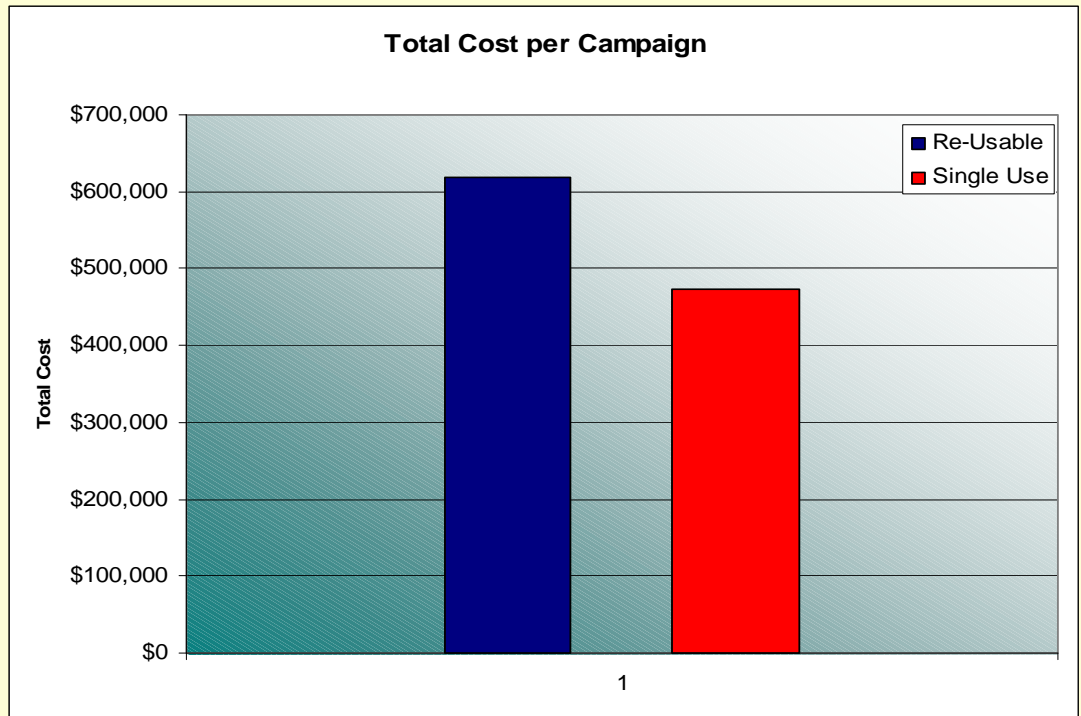
A Case Study for Single Use TFF

Re-Usable			Single Use		
Run #	Cost / run	Total Cost	Run #	Cost / run	Total Cost
Overhead & Labor	\$28,000	\$560,000	Overhead & Labor	\$19,600	\$392,000
Water Usage	\$1,995	\$39,900	Water Usage	\$105	\$2,100
Consumables	\$900	\$18,000	Consumables	\$4,000	\$80,000
TOTAL COST	\$30,895	\$617,900		\$23,705	\$474,100



Total Campaign Cost

- One campaign is defined by 20 individual process batches
- Total surface area was fixed at 5m² for each process
- A sum of labor w/overhead, water usage, and consumables constitute the total campaign cost





A Case Study for Single Use TFF

- Facility requirements were specified and an overhead rate was determined based on the service required for each process step.
- Labor rates were determined in a similar manner; management, operators, and quality personnel were all factored in on a weighted basis.
- Although operating costs vary from site to site, the savings associated with single use is measurable.
- Operating costs for a reusable TFF process is \$30,895 per run as compared to the cost of a single-use process of \$23,705 per run. Approximately \$7,200 USD is saved per run (or approximately 30%).
- The total savings of just this one TFF process is approximately \$143,000 per campaign, assuming a total of 20 discrete batches.



Single Use TFF - Summary

- Single-Use TFF eliminates the need to flush with costly purified water or measure water permeability rates, saving time and resources.
- Pre-Sanitized cassettes are installed, equilibrated with buffer, and used in processing.
- Development work, scale up and processing can be conducted nearly 50% faster without the need for membrane cleaning and measurement or water flux recovery.
- Cassette performance is more consistent from run to run as each process occurs using a new membrane.
- Cross-contamination is minimized with single-use cassettes.

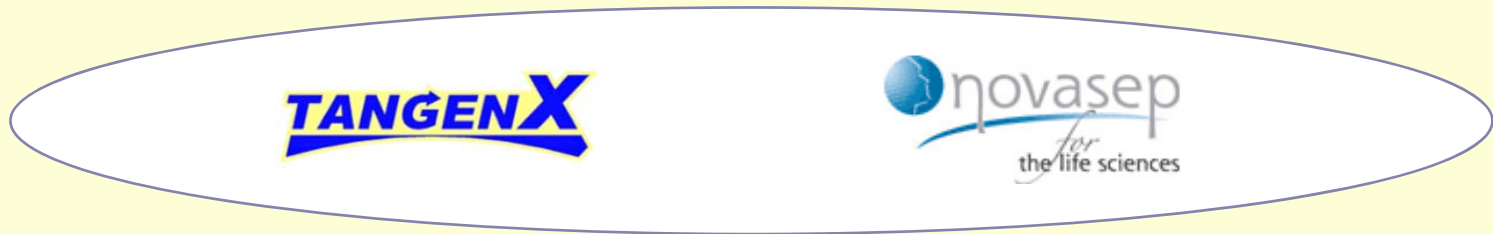


Single Use TFF - Conclusions

- Single-Use TFF provides the greatest benefit at small to moderate scales
- Contract manufacturing suites are ideal candidates for Single-Use TFF
- Many intangible benefits are also realized
 - Cross-Contamination
 - Batch to batch reproducibility
 - Manufacturing Flexibility
- Single-Use TFF provides both environmental and economic savings over traditional Reusable TFF

Thank you for your attention.

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