

Developing an Economic Model for Single-Use Tangential Flow Filtration

Cassettes

BioProcess International Conference, September 22-26, 2008 Anaheim, CA

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Introduction

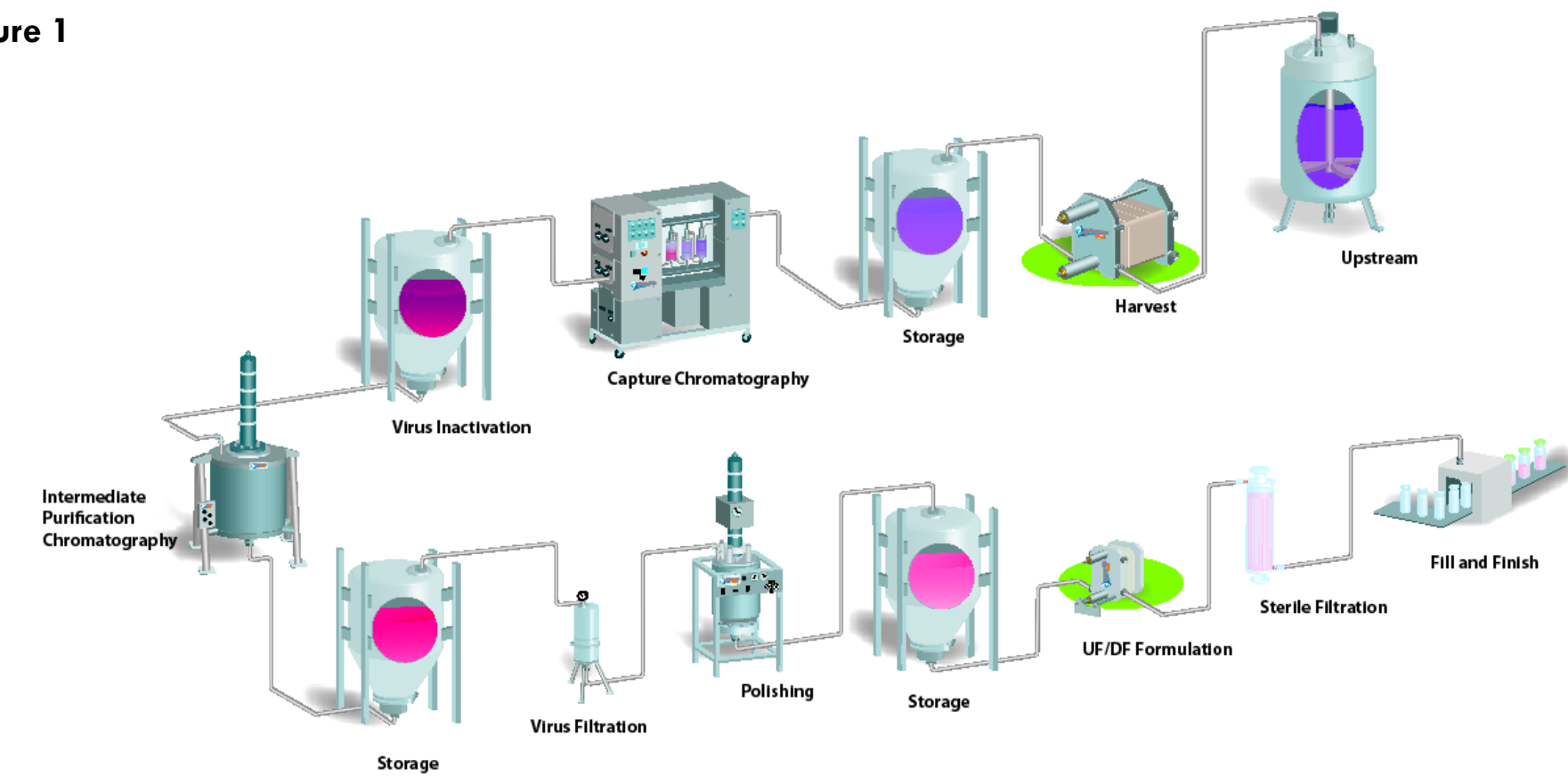
Developing an economic model for downstream purification processing steps is a critical task that is important when scaling a process from benchtop to process scale. Preparing an accurate economic model must include all critical aspects of the process. Considerations of labor, utilities, and waste contribute to the complexity of an accurate process model. It is here that the benefits of single-use technologies must be weighed against traditional reusable process steps. Novasep via TangenX Technology Corp. offers the first pre-sanitized, purposely built single-use tangential flow filtration cassette for the bio-pharmaceutical industry.

Understanding the Purification Process

Prior to creating an accurate economic model for tangential flow filtration (TFF), a thorough understanding of the process where TFF is used is essential. A process model is a valuable tool when properly executed, it must accurately include all critical aspects of the purification process. Considerations of labor, utilities, overhead, consumables, and waste all contribute to the complexity of an accurate process model. All aspects of the process must coalesce into a robust operation that easily scales up to a commercial manufacturing process. Typically, single-use technologies must be weighed against traditional reusable process steps during this planning phase.

When creating a process model, the various processing steps may be graphically depicted in a process flow diagram as shown in figure 1. Once the diagram has been created, the details of each step are considered and an economic model may be generated.

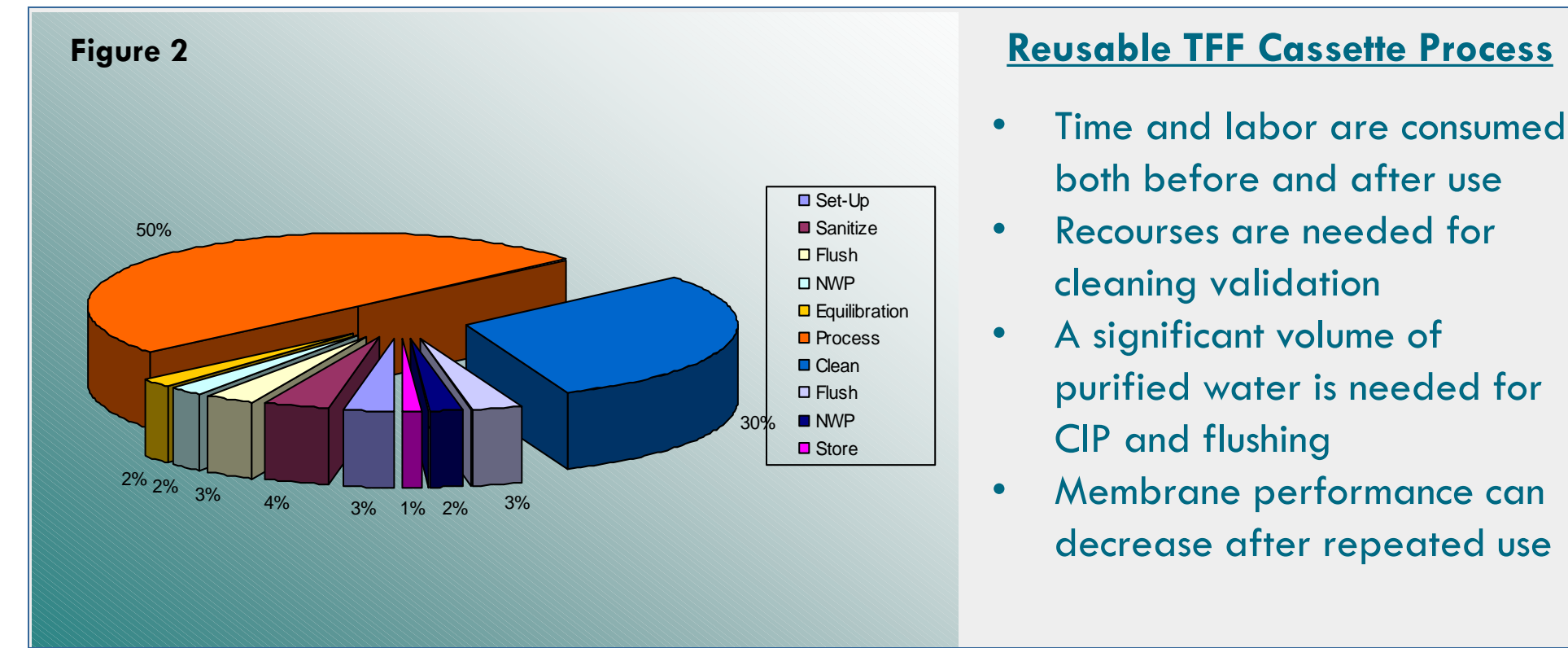
Figure 1



Benefits of Single-Use TFF

The biotechnology industry immediately recognized the benefits of single-use products for their ability to provide significant savings in time, labor and capital. Furthermore, single-use disposables are considered to be a scalable technology, and this flexibility increases production while eliminating the need for CIP cleaning, product validation. Since sanitization steps are not required, the use of caustic chemicals and purified water is minimized or eliminated, also reducing the risk of cross contamination. A similar philosophy can be applied to tangential flow filtration as well.

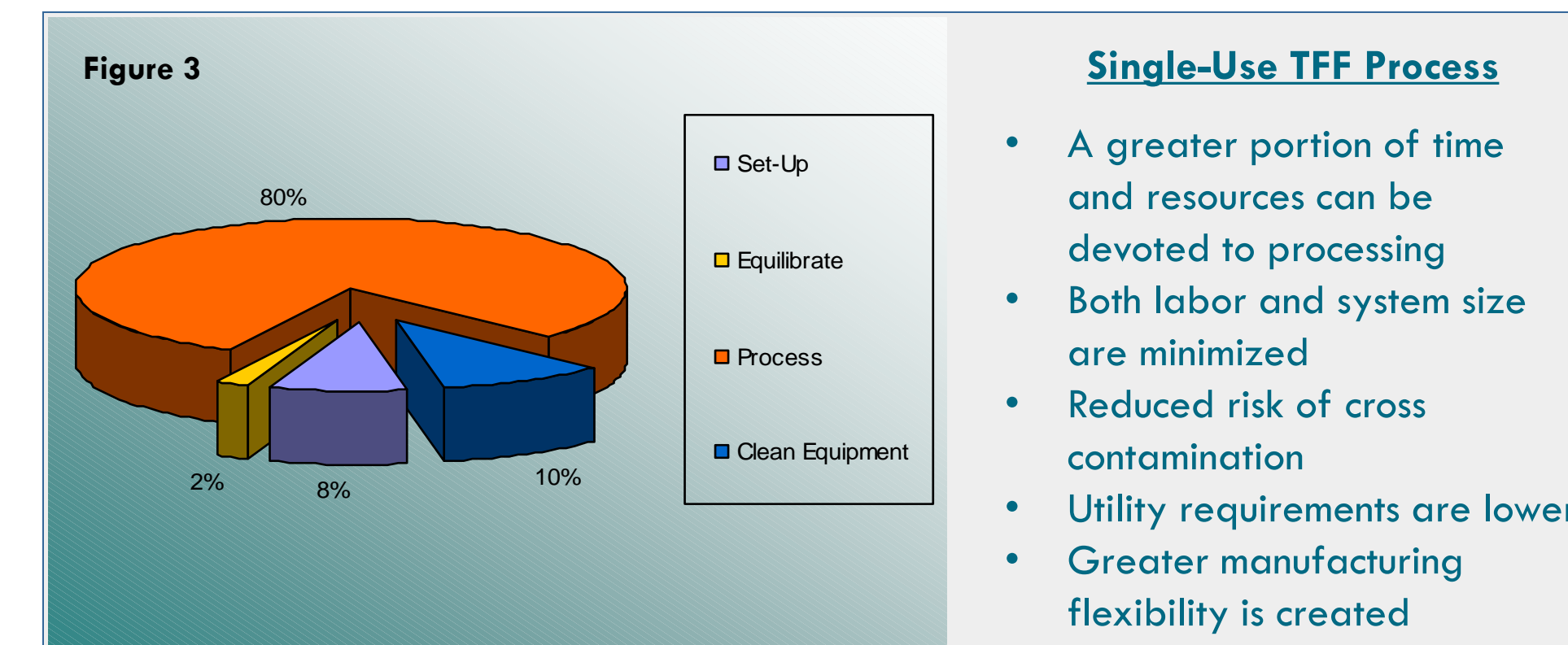
A typical downstream purification process often includes several TFF unit operations. Under suitable circumstances a significant amount of time and resources can be conserved when implementing a single-use TFF process. Typically a TFF process contains basic operations that include pre-use activities, process, and post-use activities. Each of these activities are shown in Figure 2 and are assigned a percentage that is proportional to the time required to perform. Only 50% of the total process time is devoted to processing the product, the remaining time is spent preparing and cleaning the TFF system.



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

Likewise, a single-use TFF process can be evaluated. Each of its activities are shown in Figure 3 and assigned a percentage that is proportional to the time required to perform. In this situation 80% of the total process time is devoted to processing the product, increasing process efficiency over a more traditional reusable 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

As most process engineers would agree, time and labor savings often times lends itself to the largest economic savings. Figure 4 compares the sum of facility and labor costs associated with a reusable TFF process and a single use one. A 50ft² (5m²) concentration and diafiltration process was modeled and primary process steps were analyzed for the level of support required from the standpoint of labor and the facility. The facility requirements were then specified and an overhead rate was determined based on the service required for each particular 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. In this particular case operating costs for a reusable TFF process is \$28,000 USD as compared to the cost of a single-use process of \$19,600; approximately \$8,400 USD is saved per run (or approximately 30%). The annual savings of just this one TFF process is approximately \$500,000 USD assuming one run per week.

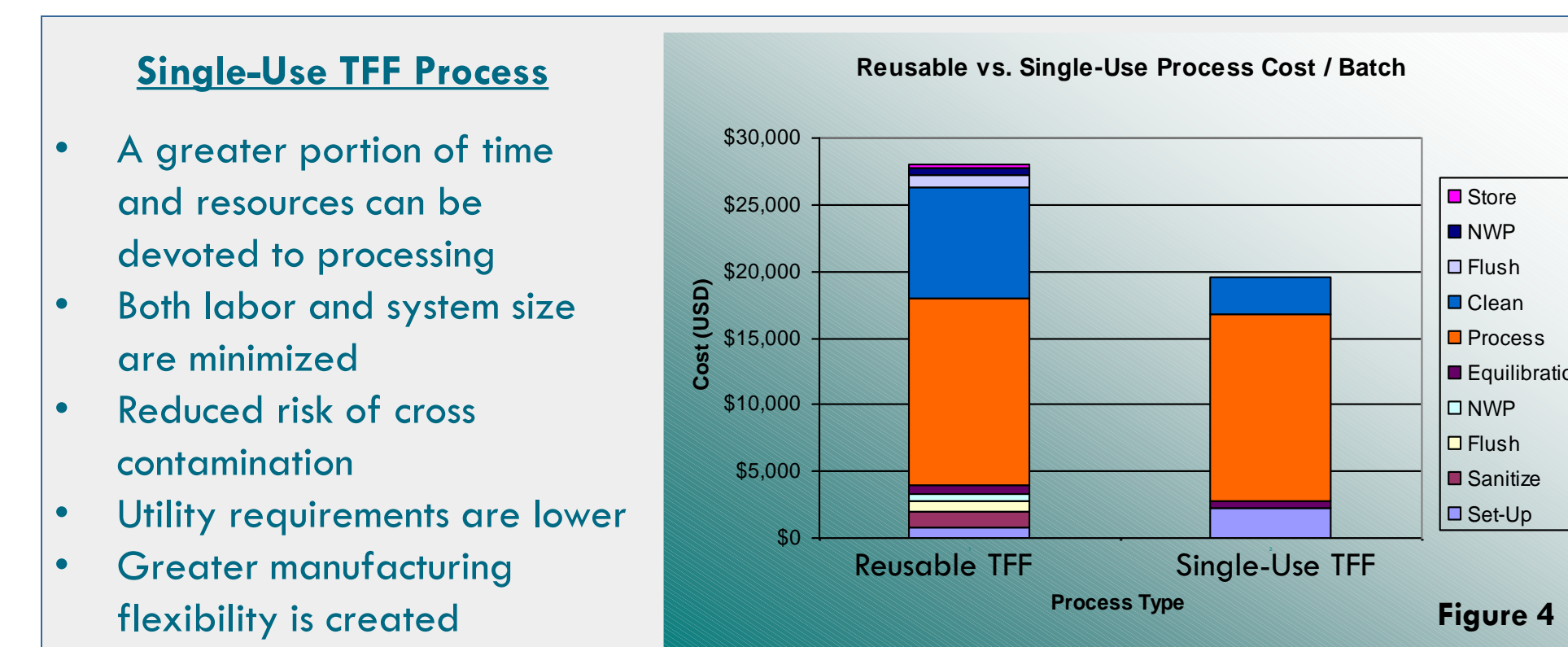


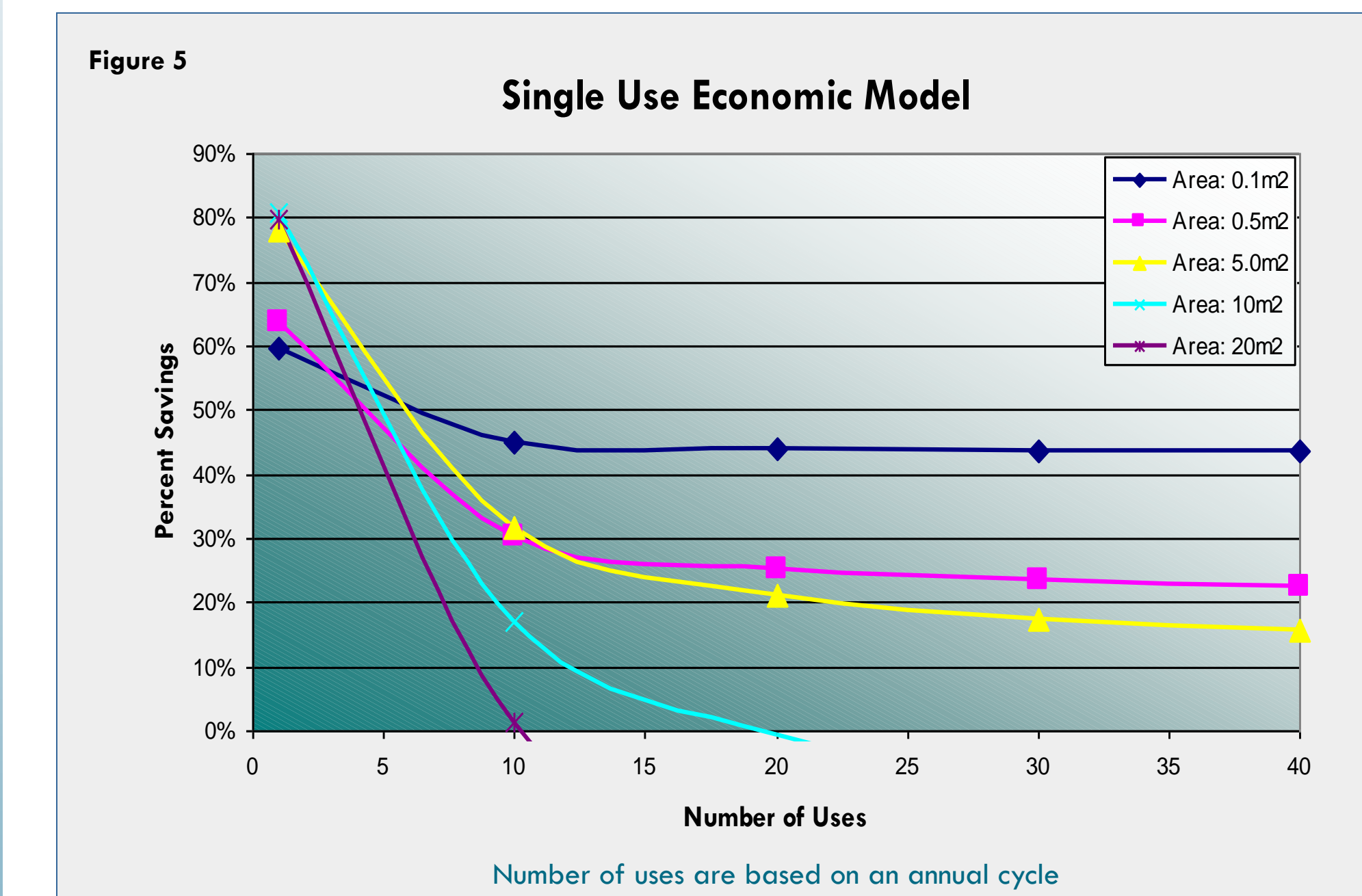
Figure 4

Single-Use TFF Process

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Single-Use Economic Model for TFF

Although single-use TFF provides measurable benefits in many circumstances, it can potentially have economic limitations depending on the scale and frequency of the operation. Several key factors affect the economy of single use TFF, two of which are the membrane area of the operation and the number of cycles the membrane is reused. Figure 4 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. 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.



Many intangible benefits will certainly outweigh additional costs associated with single-use TFF, but are not accounted for in this model. This model primarily accounts for system design, fabrication, facility, validation, labor, utilities, consumables, and waste disposal. This economic model is most useful when planning TFF process and making the decision of whether to use reusable or single-use cassettes for a given process scale.

Economic Model Summary:

- Single-Use TFF provides economic savings over traditional Reusable TFF
- 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
- Model accounts for:
 - System Design & Fabrication
 - Validation
 - CIP Cycles
 - Labor & Overhead Costs
 - Consumables

Conclusion

Single-use cassettes offer exceptional economic value when compared to re-usable TFF cassettes. Pre-Sanitized cassettes are installed, equilibrated with buffer, and used in processing. No need to flush with DI water or measure water permeability rates, saving time and resources. Development work, scale up and processing can be conducted nearly 50% faster without the need for membrane cleaning and measurement of 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.

Literature Cited

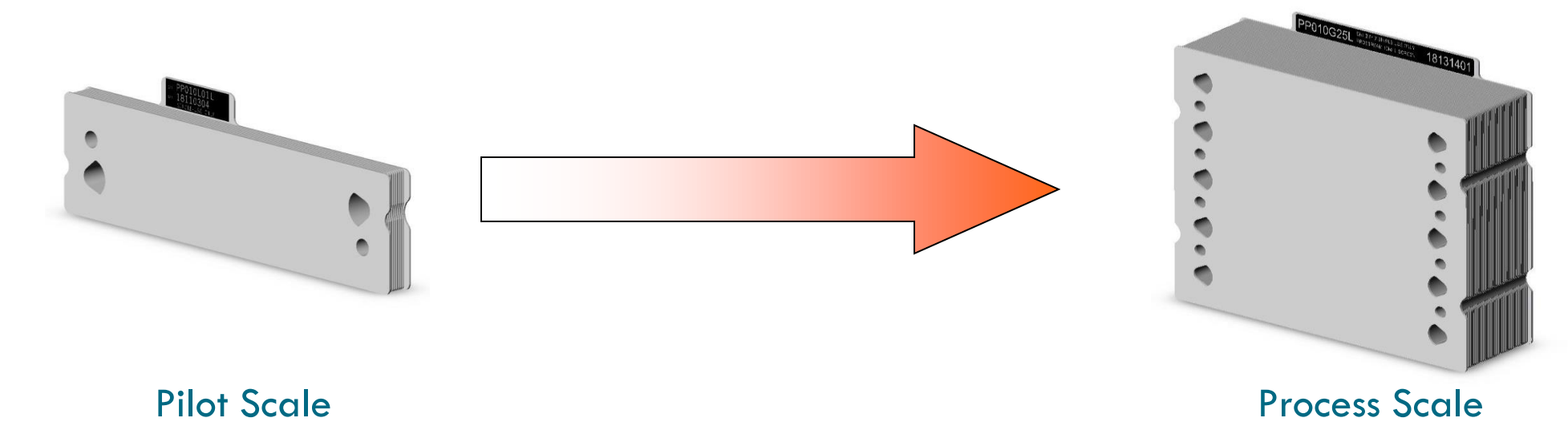
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Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

Sius™: Single-Use TFF Cassettes



The Sius™ family of single-use cassettes has been designed to offer comparable performance to reusable products at a fraction of the cost. Each cassette arrives pre-sanitized, ready to be equilibrated with buffer and used for processing. Prior to shipment, each cassette is 100% integrity tested and certified for low TOC and low endotoxin. Sius™ cassettes are available in a range of product surface areas from 0.01 m² to 5 m². These cassettes have been developed using an innovative manufacturing approach that provides an efficient production process yielding a single-use cassette costing significantly less than the comparably sized reusable product. Most important of all, the cassettes are completely interchangeable with existing cassette hardware making them an ideal choice for many TFF processes.



Novasep Process is leader in delivering innovative purification solutions for life sciences applications.

