



a Hepalink Company

Economic Impact of Adopting Single-use TFF Flat Sheet Cassettes

Stephanie Wickham and Brent VanRite

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Who We Are

- Biopharma Contract Development & Manufacturing Organization (CDMO)
 - Serving the pharmaceutical industry from drug development to vial filling
 - Clinical material supply for biological drug developers: antibodies, therapeutic proteins and enzymes
 - Mammalian, microbial, transgenic, and flex project manufacturing platforms
- 180+ employees with 28 PhDs
- 100,000 ft² of laboratories and manufacturing facilities with expansion space



A Brief History



2005 2006 2007

2008 2009

2010 2011

2012

2013

2014

2015

2005 - 2007

Process Development, cGMP Cell Banking, Analytical Lab Services.

885 Mammalian Manufacturing Facility built and commissioned

Added 100 L & 500 L Mammalian Bioreactors

2008 - 2009

Continued growth in

- Process & Analytical Development
- Quality Services
- Manufacturing
- CYT employees

Multiple 100 L & 500 L Phase I/II Clinical GMP Runs

2010 - 2011

Introduced Microbial Manufacturing Services

PD & MFG expansion into Genzyme labs and cleanrooms

Great Point Partners capital Infusion

2012

1,000 L Bioreactor brought online

Increased purification capacity

Added 50 L & 200 L Sartorius Disposable Bioreactors (SUB)

2013

200 L Microbial Manufacturing Expansion

Added 250 L & 1,000 L Hyclone Single Use Bioreactors Systems

Validated Transgenic DSP Manufacturing Facility

2014

Automated Fill Finish Service Validated and Online

Phase III CTM production

Process Validation (Conformance) Campaign Performed

2015

3500 Facility Online

Process Characterization Online

1,000 L Microbial Expansion Underway

5,000 L Bioreactor Project Initiated

Hepalink Purchases Cytovance

Cytovance: One-stop-shop



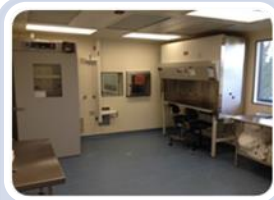
R&D Services



GMP
Mammalian
Manufacturing



GMP Microbial
Manufacturing



GMP Flex Suite
Manufacturing



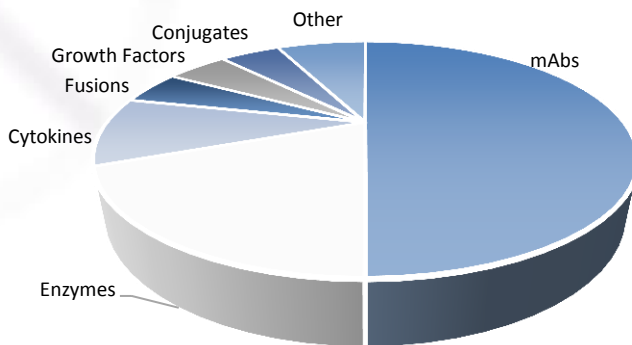
GMP Clinical
Drug Product
Vial Filling



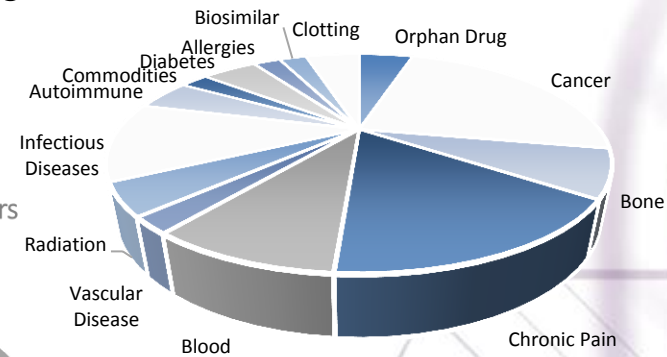
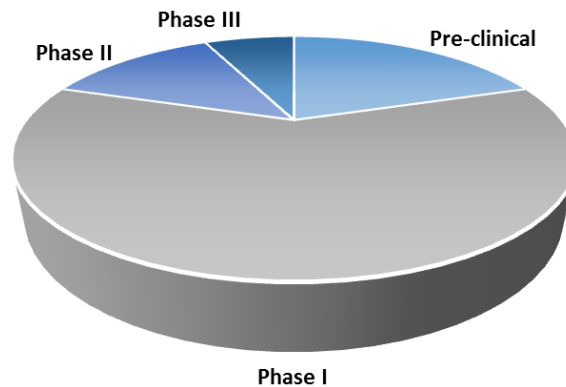
Drug
Substance and
Drug Product
Release and
Stability
Testing

Cytovance Biologics Experience

- Our scientists have developed processes for a wide variety of biologics using both microbial and mammalian platforms
- >50 Biologics and >14 Disease Areas
- Biosimilars
- Transgenic
- Fusion



Clinical Phase Profile of Cytovance Partners



Benefits of Single-Use TFF Technologies

1. Scalability
2. Efficiency
3. Decreased production time
4. Cost Comparison

Scalability

Traditional TFF Cassettes:

1. 0.01-2.5m² bricks
2. CRC and PES Membranes

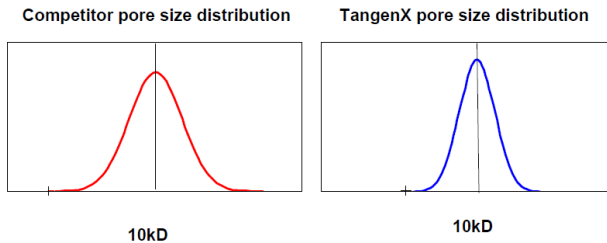


Image from millipore.com

Repligen TFF Cassettes:

1. 0.01-2.5m² bricks
2. PES membranes
 - A. Prostream
 - B. Hystream

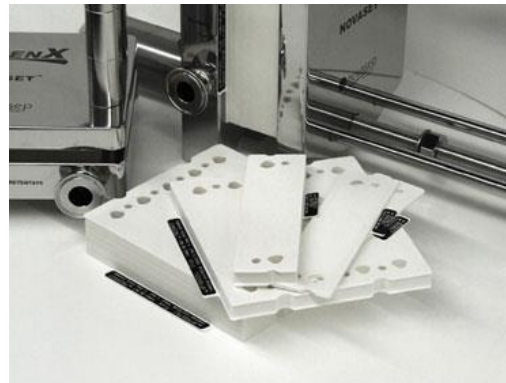


Image from tangenx.com

Competitors Single-Use TFF Cassettes:

1. 0.01-2.5m² bricks
 - A. Not always stackable
2. PES membranes



Image from pall.com

Efficiency

Traditional TFF Cassettes Operations

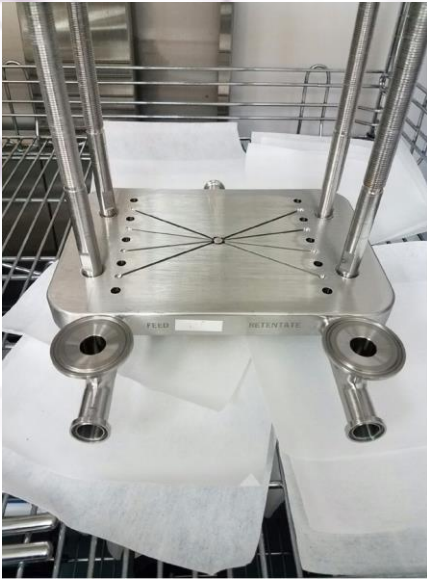
1. Installation and Pressure hold
 2. WFI Flush
 3. Sanitization
 4. WFI Flush and NWP Testing
 5. Equilibration
 6. Concentration
 7. Diafiltration
 8. Cleaning
 9. WFI Flush and NWP Testing
 10. Storage
- 2-3hours
- 1-2hours

Single-Use TFF Cassettes Operations

1. Installation and Pressure hold
2. WFI Flush
3. Equilibration
4. Concentration
5. Diafiltration

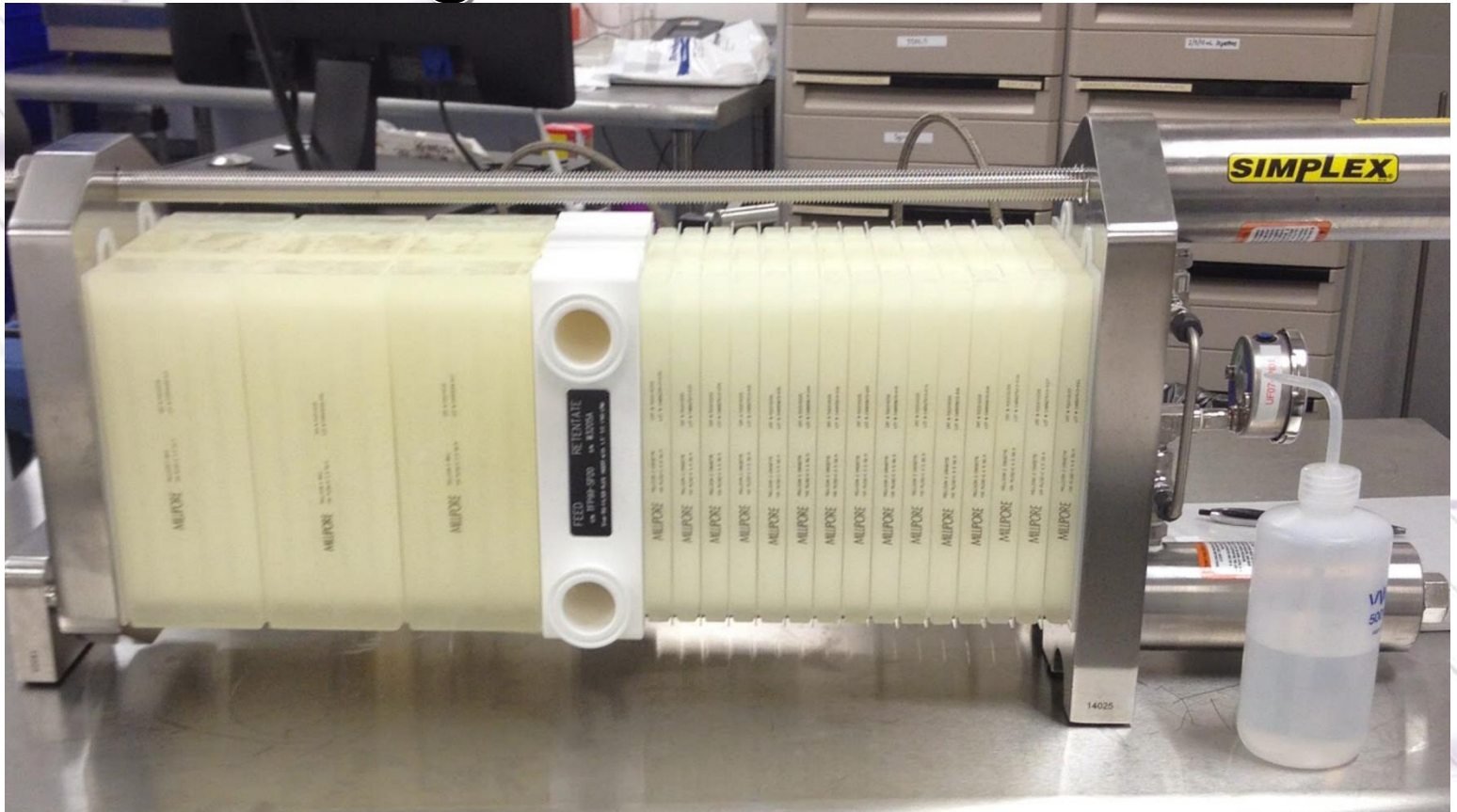
Single-use TFF cassettes increase efficiency in eliminating pre- and post-use cleaning and storage

Change Over



- Use of Repligen's TFF insert has eliminated the need for cleaning and testing of the TFF holder.
- **No Cleaning Validation required for membranes or holder.**

CYT Usage of TFF Cassettes



- Usage of TangenX holder with filter plate insert allows flexibility in configuration customized per project.

Cost Comparison

Converting an existing traditional CRC TFF process to TangenX PES TFF.

Traditional Cassettes

6x2.5m² bricks = ~\$11.2k each =



TangenX Cassettes

6x2.5m² bricks = ~\$2.5k each =



Case Study

Converting an existing traditional CRC TFF process to TangenX PES TFF.

Traditional CRC Cassettes had a capacity of 65L/m² with 3 uses before NWP dropped below 70%.

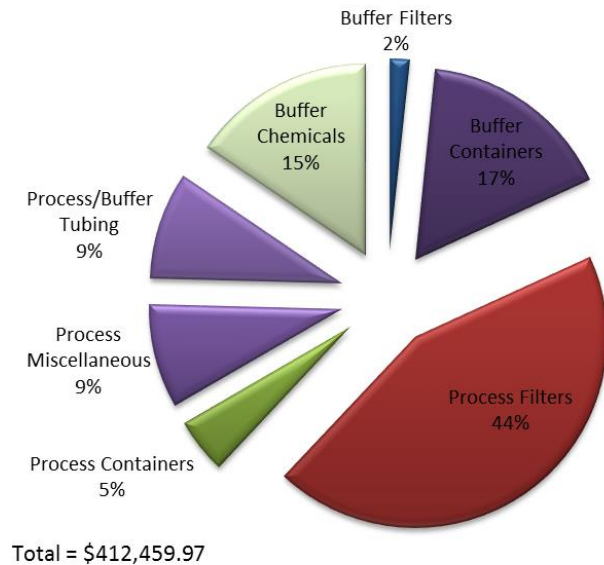
6x2.5m² bricks = ~\$11.2k each = ~\$67k

TangenX PES Cassettes had a capacity of 72L/m²

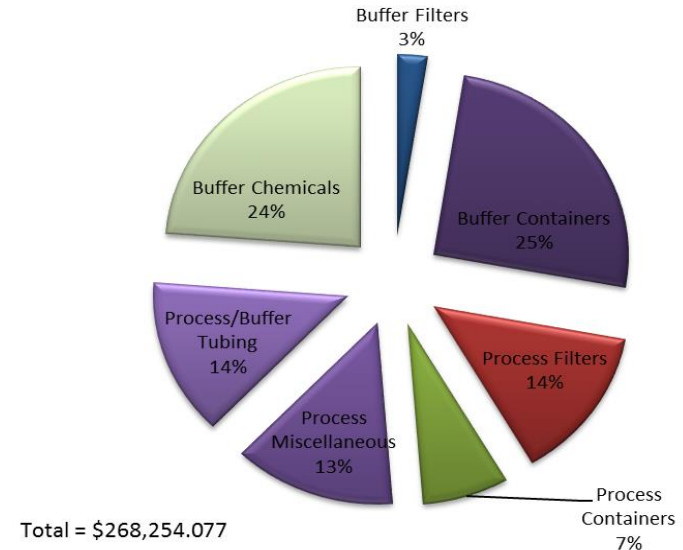
5x2.5m² bricks = ~\$2.5k each = ~\$12.5k x 3 = ~\$37.5k

Case Study

DSP Raw Materials with CRC Membranes



DSP Raw Materials with TangenX PES Membranes



Converting an existing traditional CRC TFF process to TangenX PES TFF dropped raw materials cost by almost ½ and removed days of suite time for cleaning results.

Summary

- Repligen's Single-Use TFF cassettes exhibit the same scalability as traditional TFF cassettes
- Repligen's Single-Use TFF cassettes exhibited the same if not slightly better capacity for processes transferred with the traditional CRC membranes.
- Single-Use TFF cassettes and Filter Plate Inserts offer:
 1. Increased efficiency in the reduction of pre-use and post-use steps
 2. Increased efficiency in the reduction of equipment cleaning
 - A. No cleaning validation
 3. Decreased single cost compared to traditional TFF Cassettes
 4. Decreased cost for fouling prone TFFs like microbial refold
 5. No validation of storage of cassettes post-use