

Performance and Economic Advantages of Single Use Flat Sheet Tangential Flow Filtration

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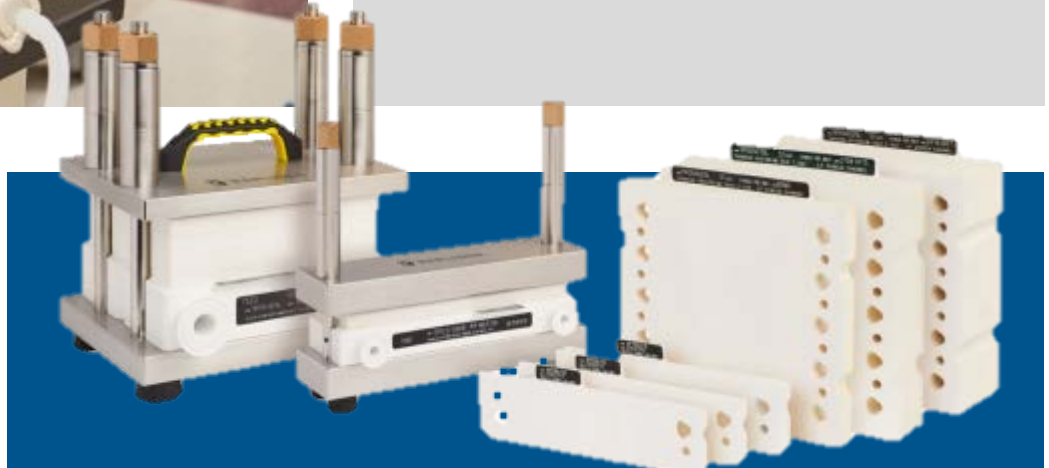


TangenX™ TFF Cassettes

Reliable, scalable, cost-effective solutions for tangential flow filtration

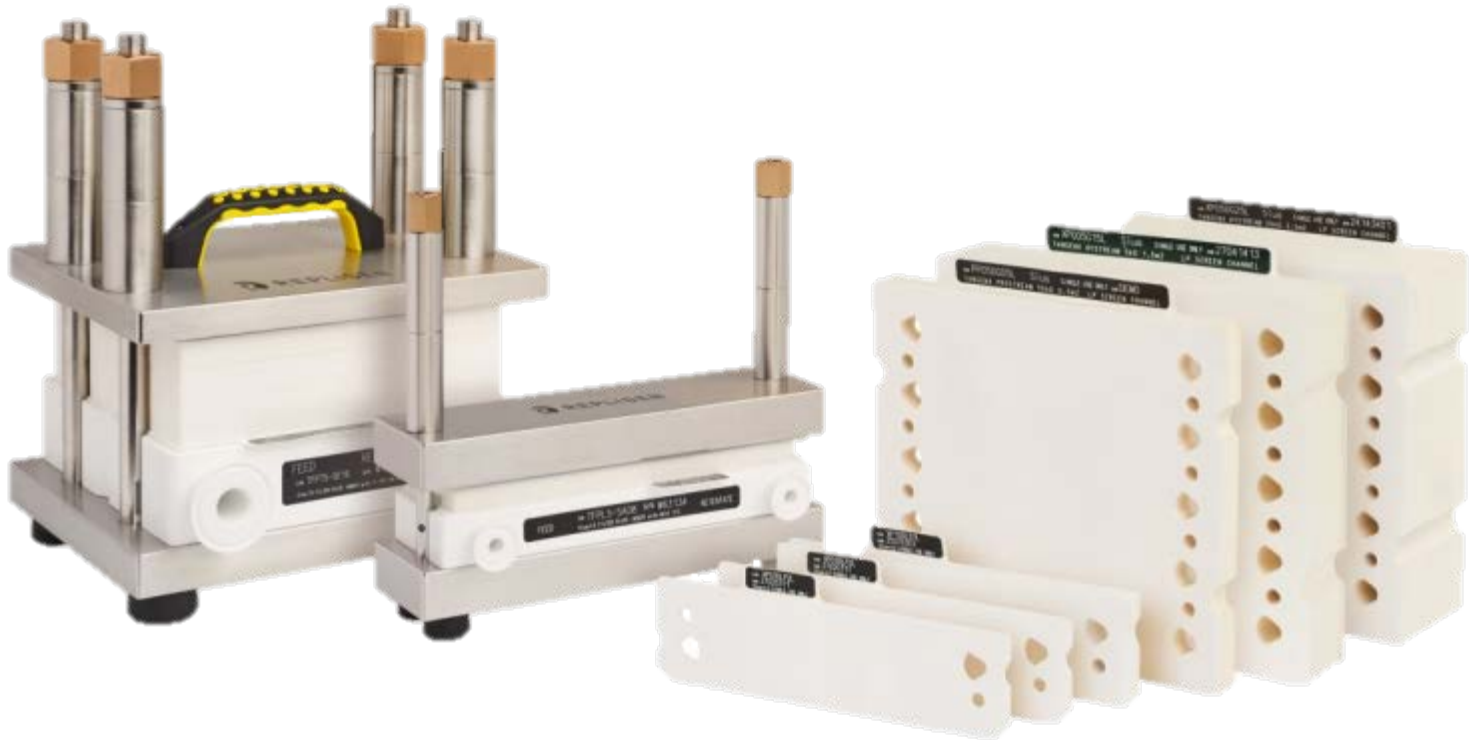


Featuring the first purpose-built single-use cassettes for tangential flow filtration



- Reliable, consistent performance since 2007
- 80% reduction in filter cost
- 50% reduction in labor use
- 75% reduction in buffer use
- Interchangeable, single-use, and reusable formats
- Scalable from bench to production

TangenX™ TFF Cassettes



Proven TFF cassettes in single-use and reusable formats

- Reliable, consistent performance since 2007
- Used in 200 Phase 1-3 processes and 5 commercial processes
- Scalable from bench to production
- Interchangeable single-use and reusable formats
 - TangenX™ SIUS™ and SIUS™ PD Single-use TFF Cassettes
 - TangenX™ PRO and PRO PD Reusable TFF Cassettes
- Two membrane chemistries: ProStream and HyStream

Reliable, scalable, cost-effective solutions for tangential flow filtration

First single-use TFF cassettes

Increase process efficiency



- Pre-sanitized, ready-to-use
- Scalable from bench to production
- Faster campaign turnarounds

Optimize process economics



- 80% reduction in filter costs
- 75% reduction in buffer use
- 50% reduction in labor use

Quality and risk mitigation



- Complete documentation package for GMP use
- Compliant with USP Class VI
- BSE / TSE Free

TangenX™ Ultrafiltration Membranes

Modified Polyethersulfone (mPES) Membranes

ProStream

Molecular Weight Cutoffs (MWCO)

- 1kD, 3kD, 5kD, 10kD, 30kD, 50kD, 100kD, 300kD
- Neutrally balanced charge / Low protein binding
- Comparable to Millipore Biomax and Pall Omega membranes

HyStream

Molecular Weight Cutoffs (MWCO)

- 5kD, 10kD, 30kD, 50kD, 100kD, 300kD, 0.1 μ m, 0.2 μ m, 0.45 μ m, 0.65 μ m
- Hydrophilic – Minimal fouling with hydrophobic molecules / Low protein binding
- Comparable to Millipore Ultracel and Sartorius Hydrosart

Molecular weight cutoffs suit most operations

TangenX™ Membranes

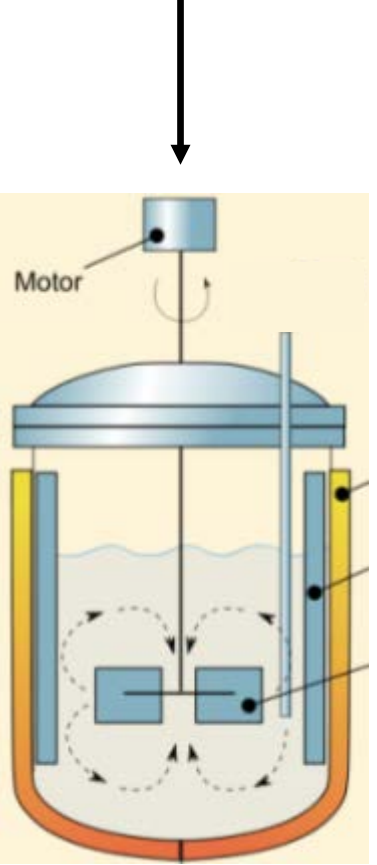
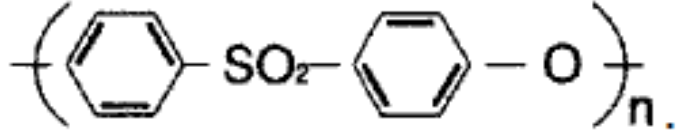
Validated manufacturing process

TangenX™ Ultrafiltration Membranes



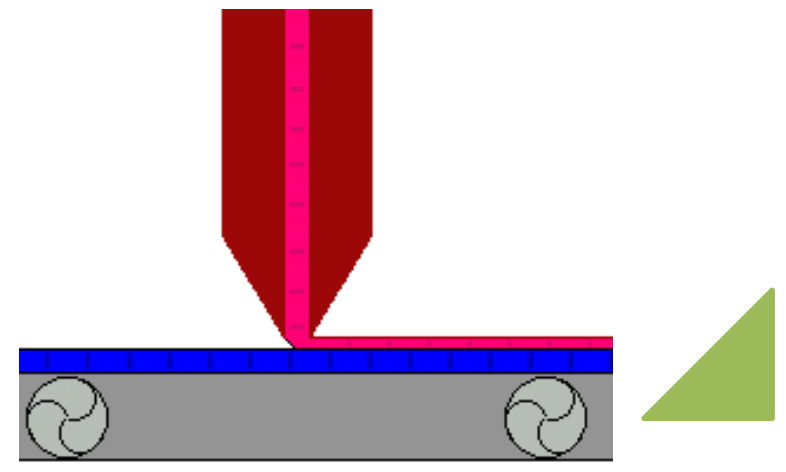
Modified Polyethersulfone (mPES) Membranes

Polyethersulfone + Non-Polar Solvent



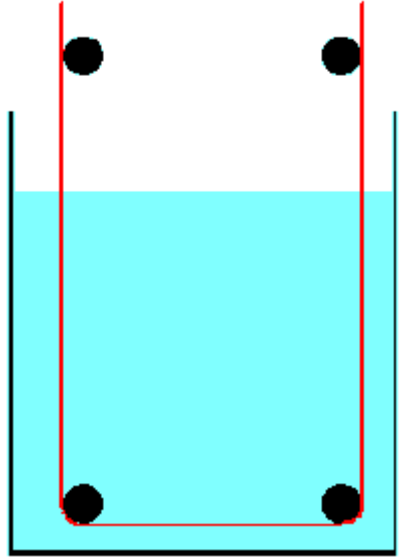
Step 1

- Polyethersulfone is dissolved in a solvent to create a casting solution



Step 2

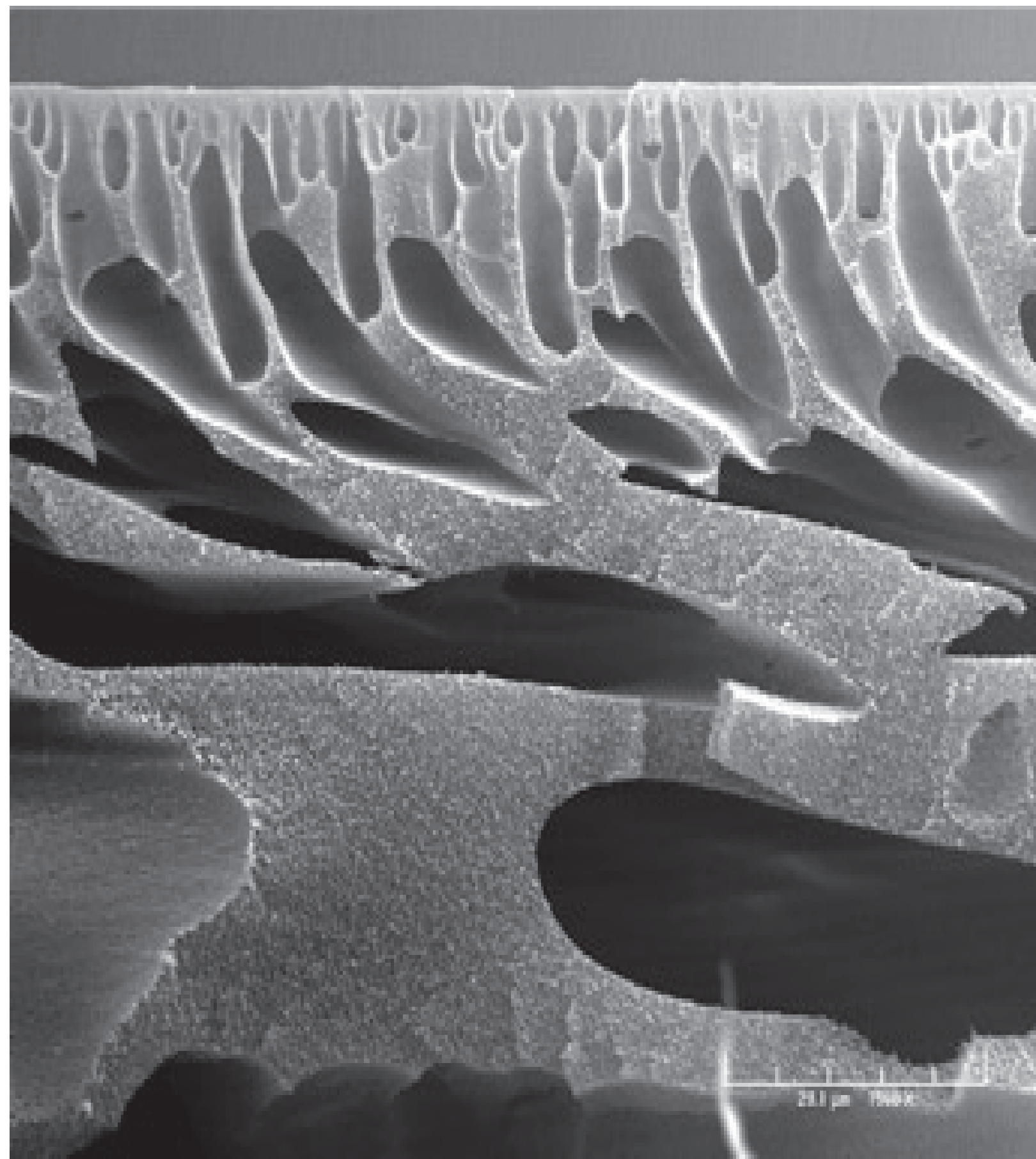
- The casting solution is coated onto a non-woven carrier



Step 3

- The coated substrate is immersed in a polar solvent (water) and solidifies forming a porous membrane

Efficient and robust membrane structure



TangenX™ Ultrafiltration Membranes

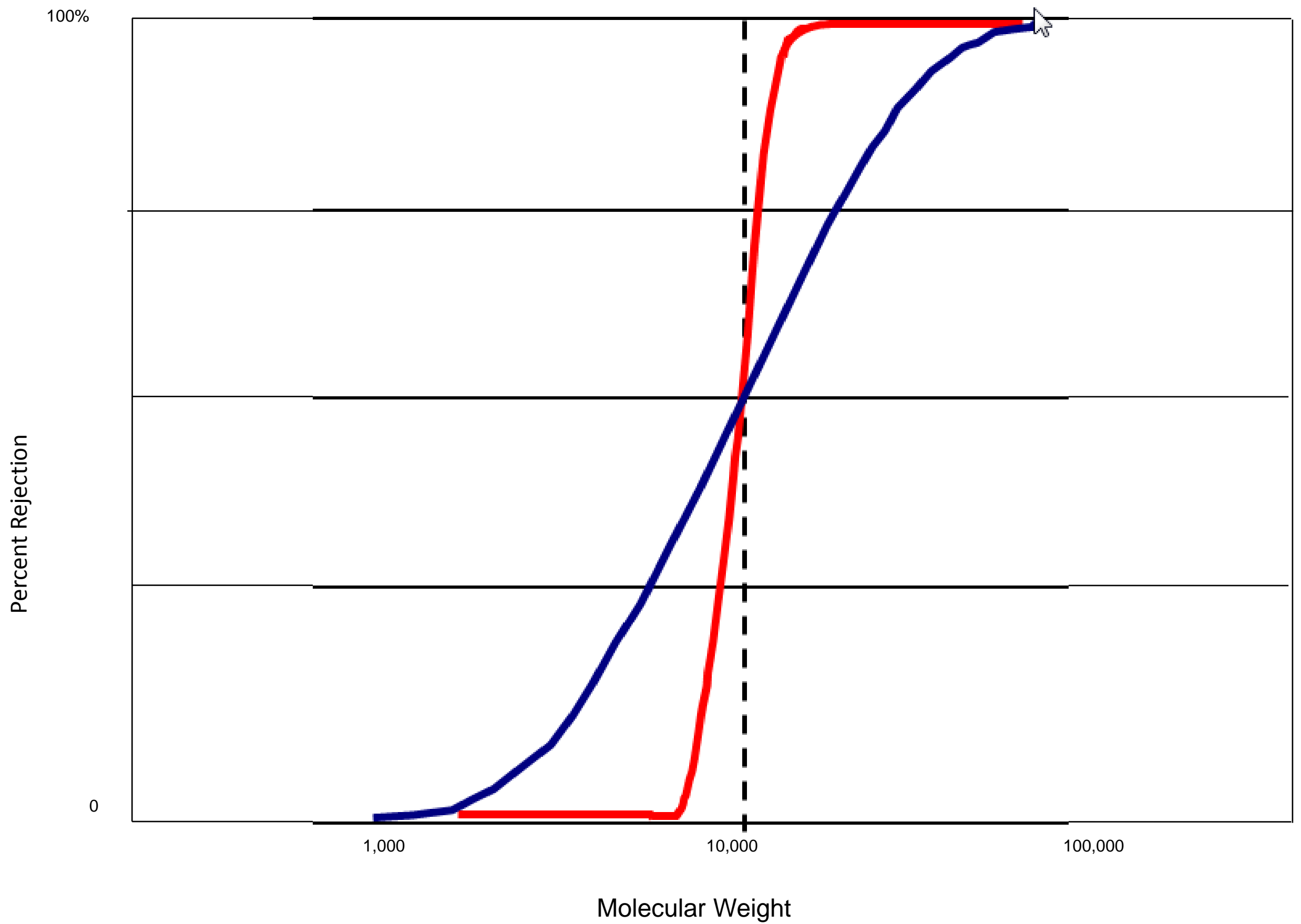
Balanced flux and selectivity are achieved using a controlled manufacturing process that enables tight control of the membrane pore size.

The manufacturing process ensures a controlled transition from the selective surface to the microporous support.

- No breakthrough of the UF skin, which maximizes selectivity performance
- Enhanced microporous substructure pore size and even transition, which maximize flux
- Reduced number of manufacturing steps, which reduces cost and promotes excellent consistency and reliability

Comparable rejection criteria with superior selectivity

TangenX™ Ultrafiltration Membranes

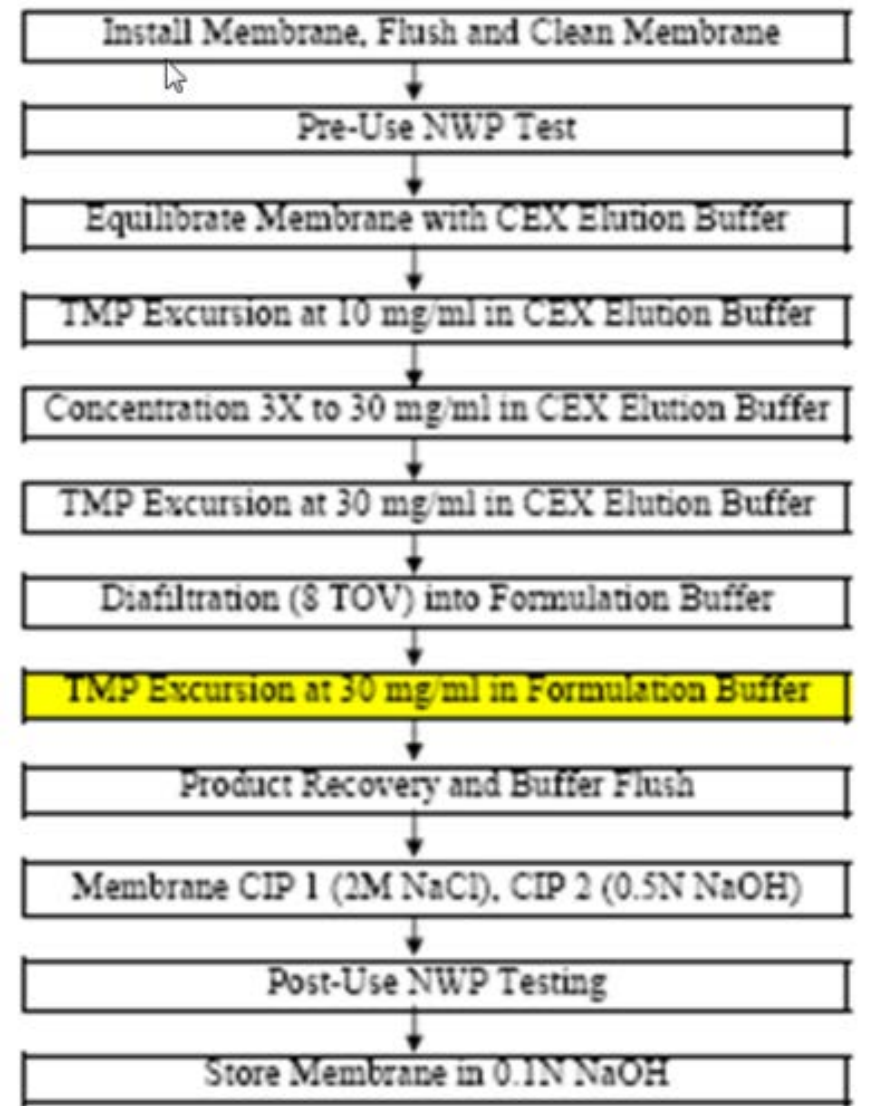
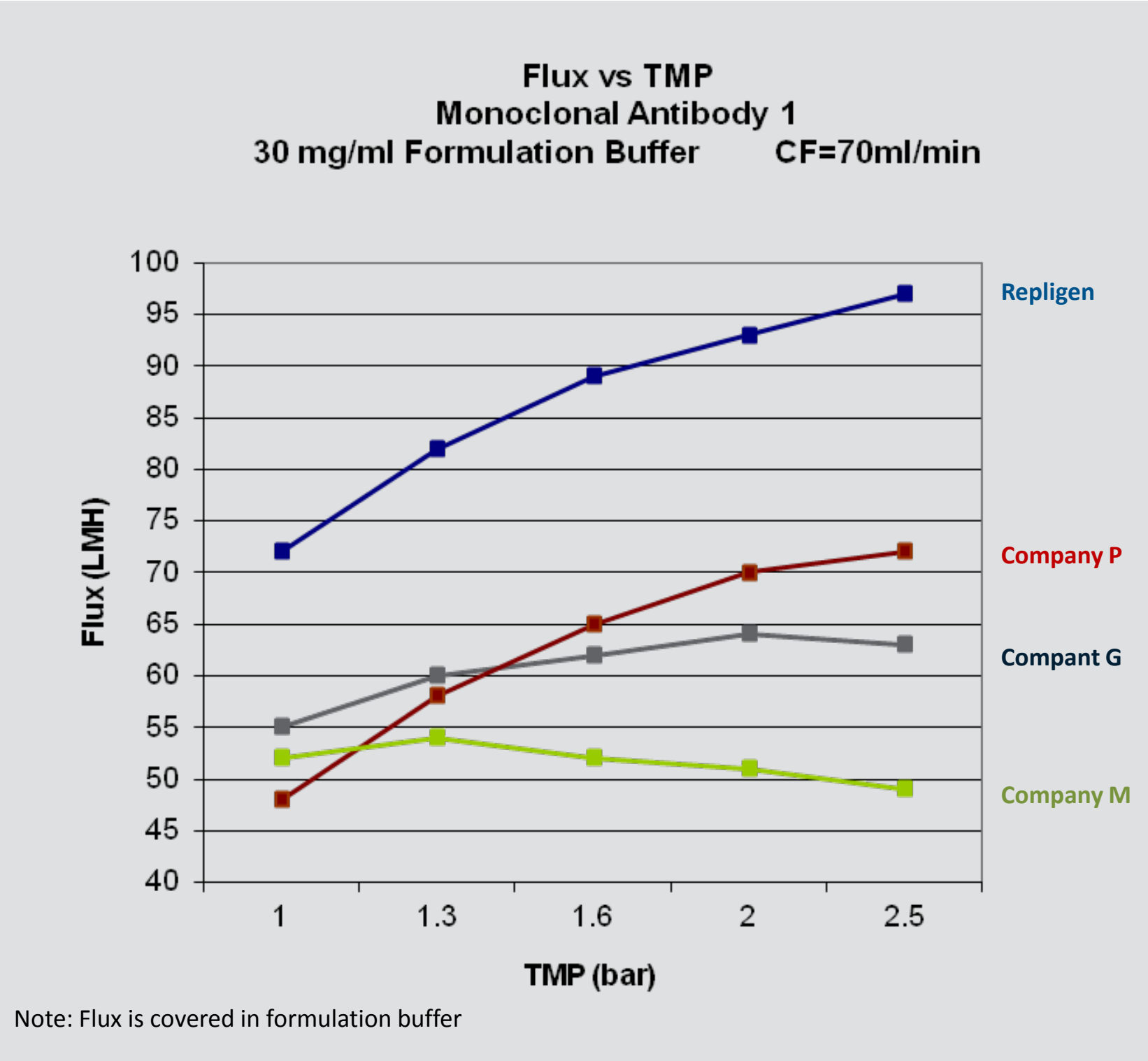


Highest flux at 30 mg/ml MAb

Modified Polyethersulfone (mPES) Membrane



TangenX™ Ultrafiltration Membranes



Source: IBC Applications for Biopharmaceuticals, La Jolla, CA, June 1-3 2009.

TangenX™ SIUS™ Single-use TFF Cassettes

TangenX™ SIUS™ Single-use TFF Cassettes

First purpose-built
single-use cassettes for
tangential flow filtration



TangenX™ SIUS™ PD



Membrane Surface Areas
0.01 m² 0.02 m² 0.10 m²

Cassette Clamp
Disposable Filter Plate Insert

TangenX™ SIUS™

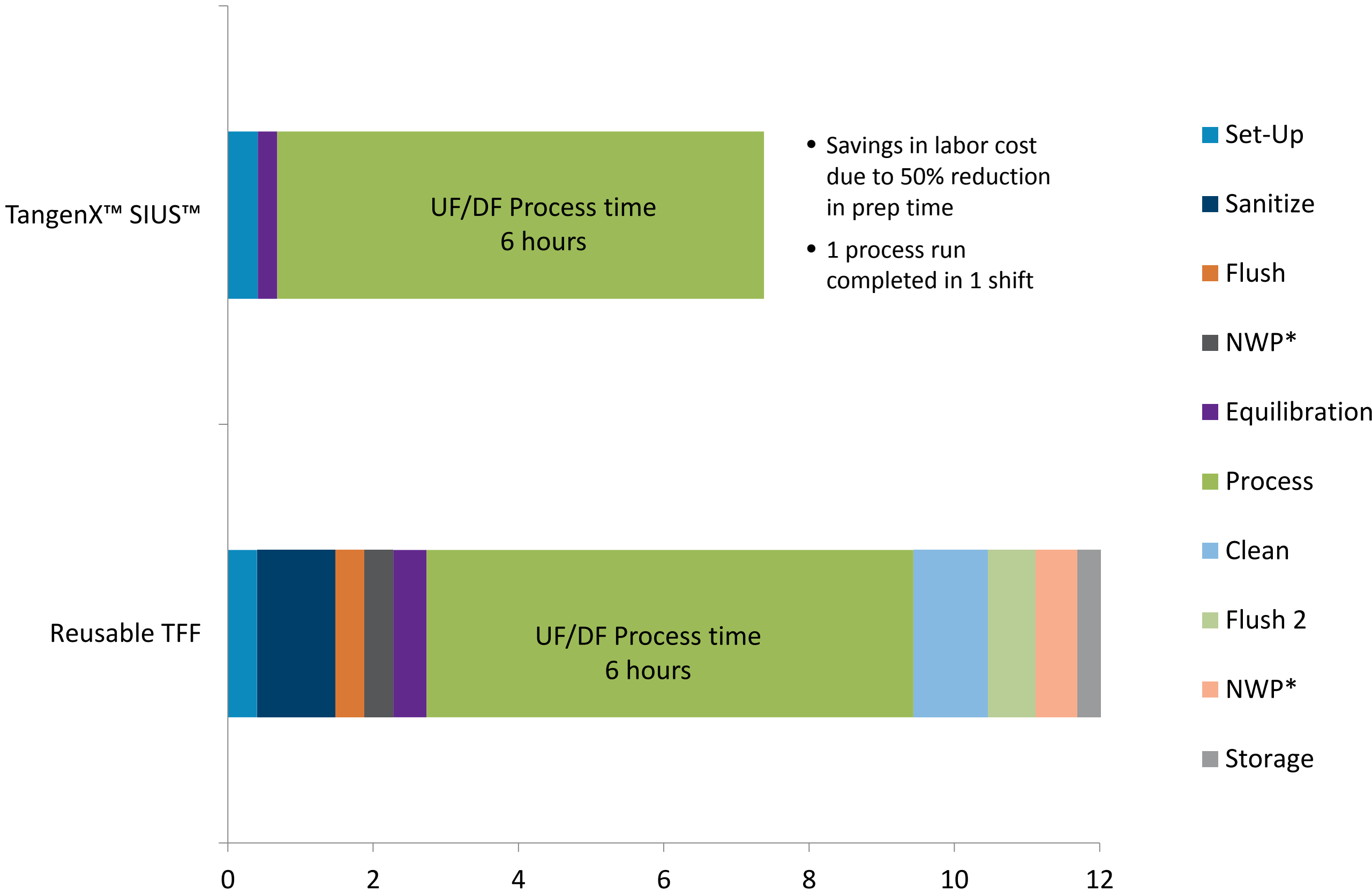


Membrane Surface Areas
0.5 m² 1.5 m² 2.5 m²

Cassette Clamp
Disposable Filter Plate Insert

Up to 50% Reduction in labor cost

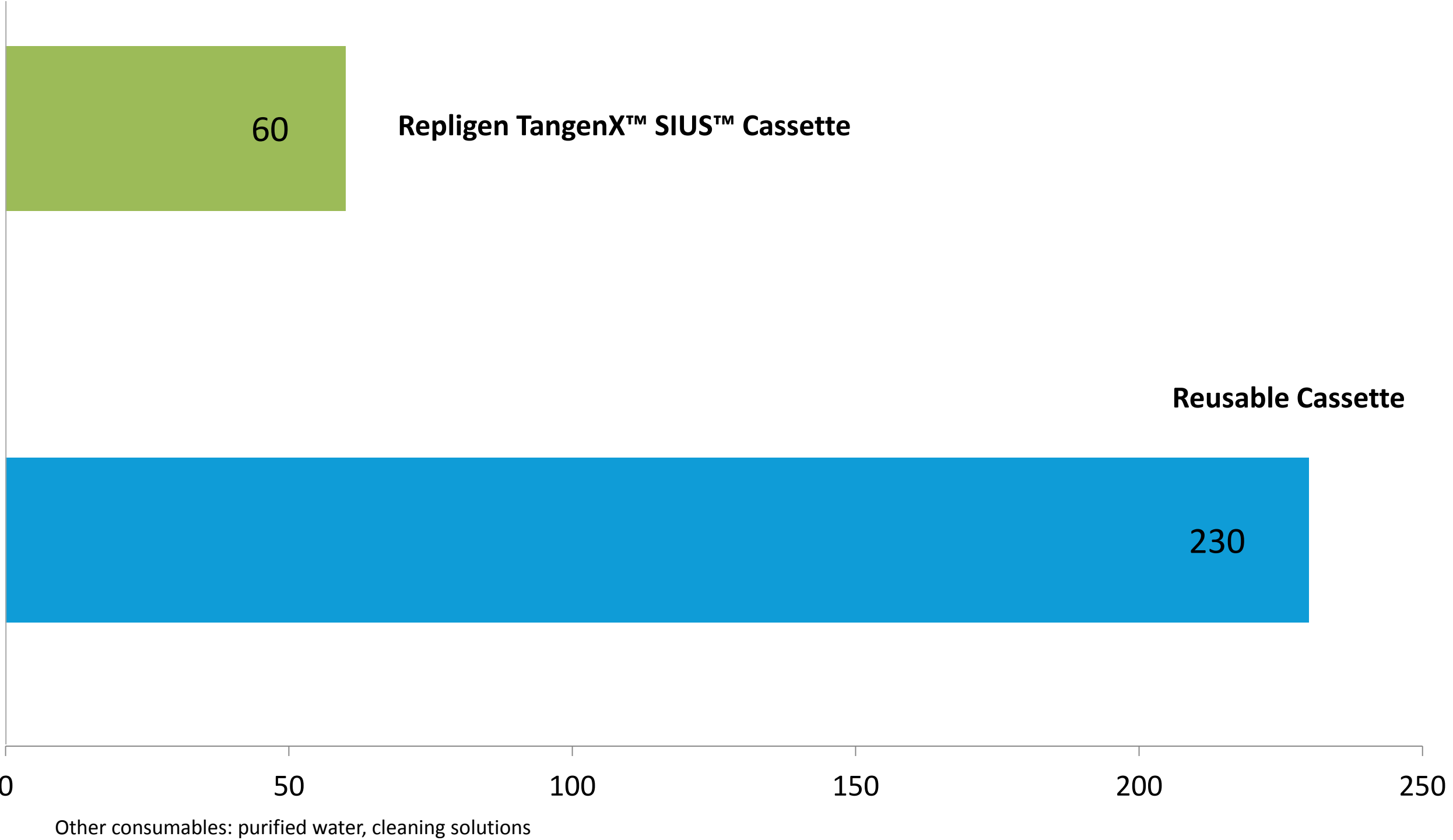
TangenX™ SIUS™
Single-use TFF Cassettes vs.
Reusable TFF Cassettes



* Normalized water permeability

75% reduction in buffer use

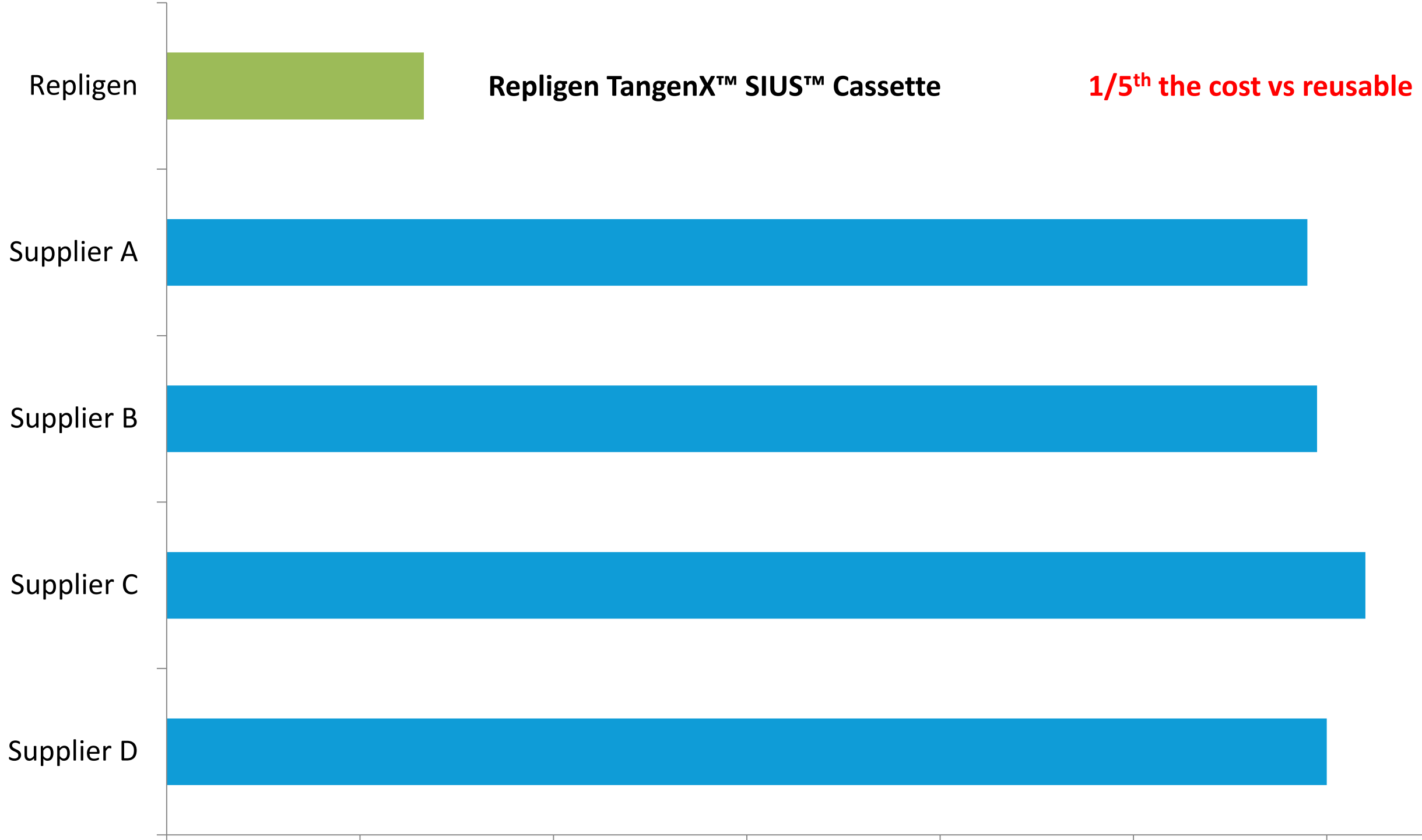
Buffer Usage (Liter / square meter of membrane area)



TangenX™ SIUS™
Single-use TFF Cassettes vs.
Reusable TFF Cassettes

80% Reduction in filter cost

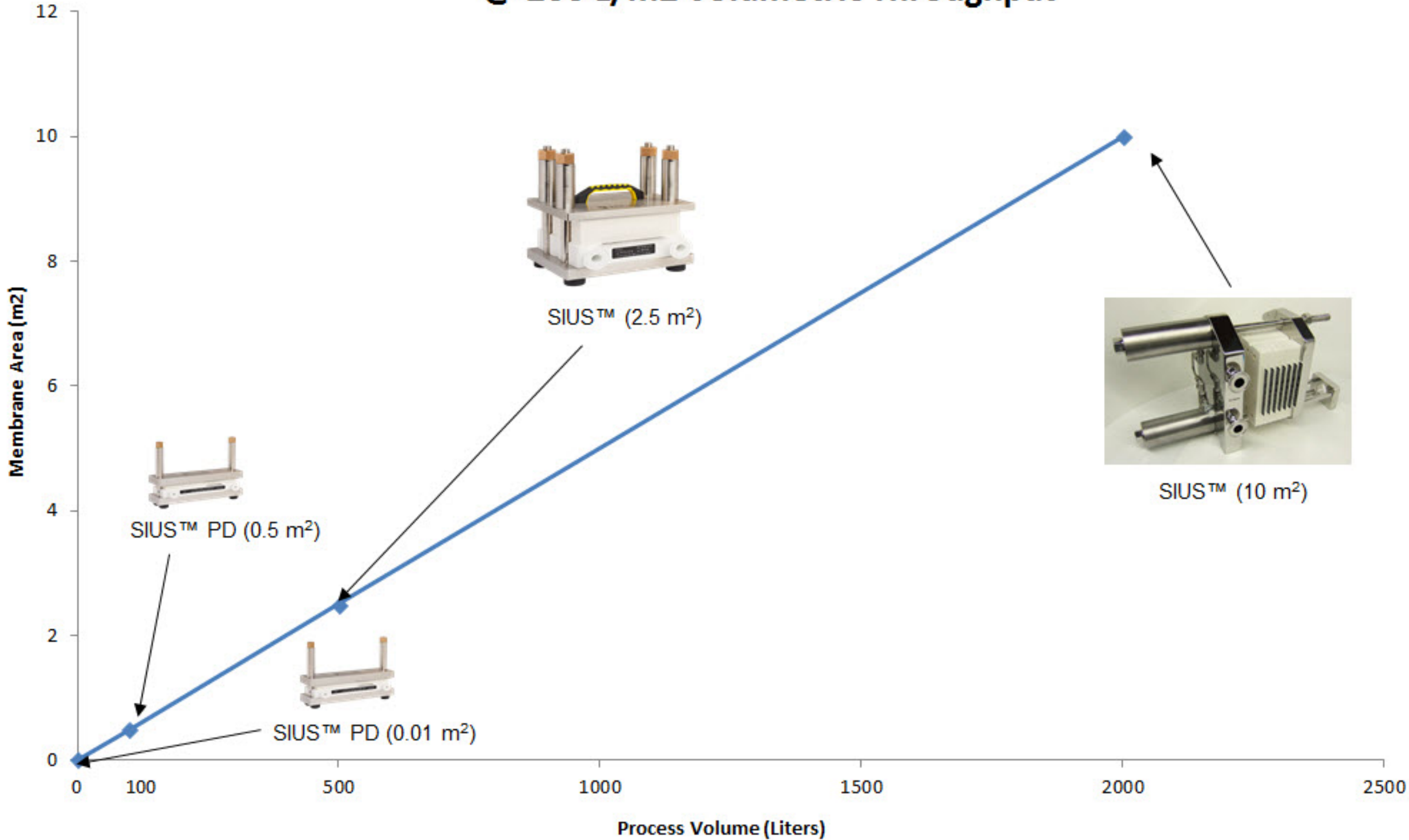
Cost / square meter



TangenX™ SIUS™
Single-use TFF Cassettes vs.
Reusable TFF Cassettes

Process volume and membrane area determine scale-up

Process Volume vs. Membrane Area @ 200 L/m² Volumetric Throughput



TangenX™ SIUS™ Single-use TFF Cassettes

First purpose-built
single-use cassettes for
tangential flow filtration

FEATURES

- Pre-sanitized, ready to use
- Compatible with holders from major suppliers (Millipore, Pall, Sartorius)
- Uses high-performance TangenX™ mPES membranes
 - ProStream (low binding)
 - HyStream (hydrophilic)
- Full range of formats and pore sizes

BENEFITS

- Reliable performance
- Scalable from bench to production scale
- 80% reduction in filter cost
- 50% reduction in labor cost
- 75% reduction in buffer use
- Reduced risk of cross-contamination



TangenX™ SIUS™ TFF Hardware

Compatible with
commercially available
holders (Millipore,
Pall, Sartorius)



SIUS™ PD
Horizontal
clamp



SIUS™
Horizontal
clamp



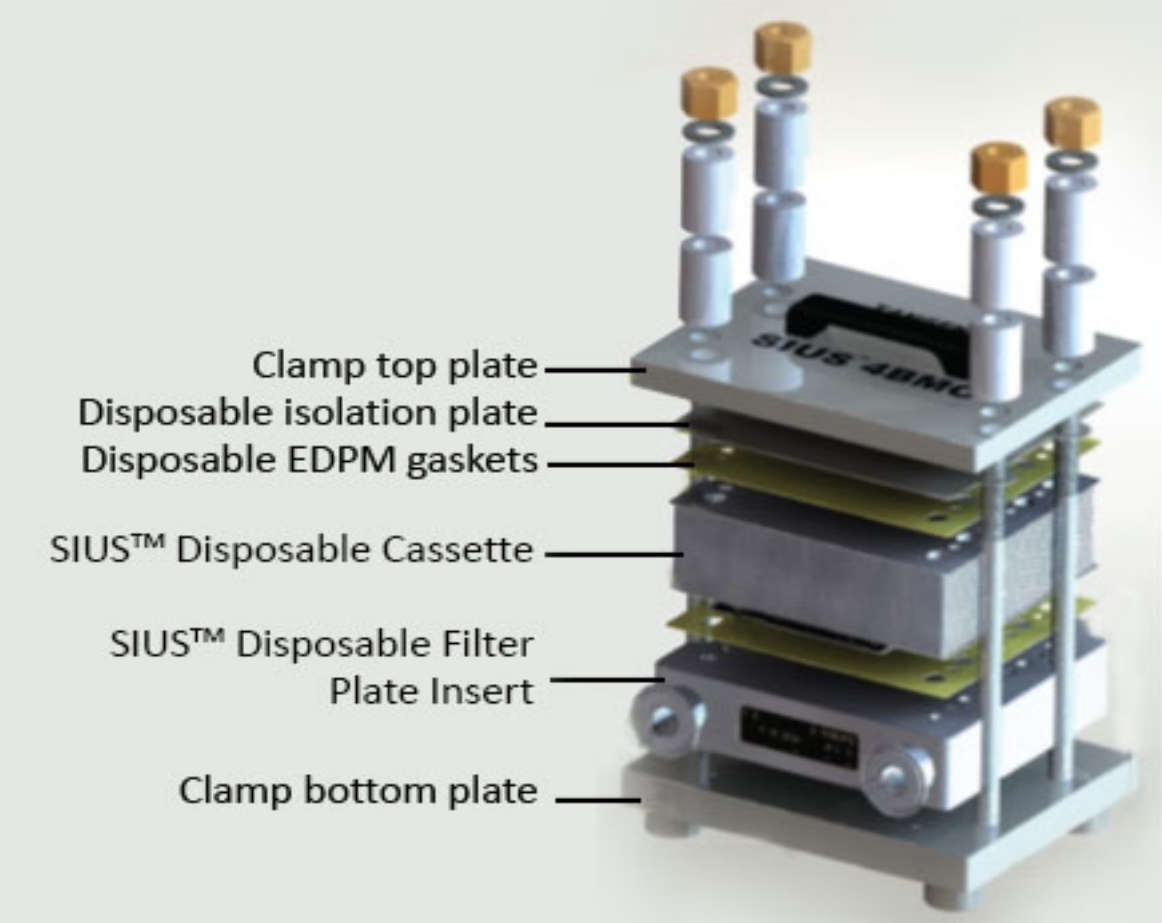
SIUS™
Vertical
clamp



SIUS™ PD
Filter
plate
insert



SIUS™
Filter
plate
insert



- Clamp top plate
- Disposable isolation plate
- Disposable EDPM gaskets
- SIUS™ Disposable Cassette
- SIUS™ Disposable Filter Plate Insert
- Clamp bottom plate

TangenX™ PRO Reusable TFF Cassettes

TangenX™ PRO
Reusable
TFF Cassettes

TangenX™ PRO PD



Membrane Surface Areas
0.01 m² 0.02 m² 0.10 m²

Cassette Holder

TangenX™ PRO



Membrane Surface Areas
0.5 m² 1.5 m² 2.5 m²

Cassette Holder

Interchangeable with SIUS™ Single-use Cassettes

TangenX™ SIUS™
Single-use TFF Cassettes

TangenX™ PRO
Reusable TFF Cassettes



Seamless transition from
bench-scale to
production-scale

Same channel geometry (ΔP and crossflow rate)

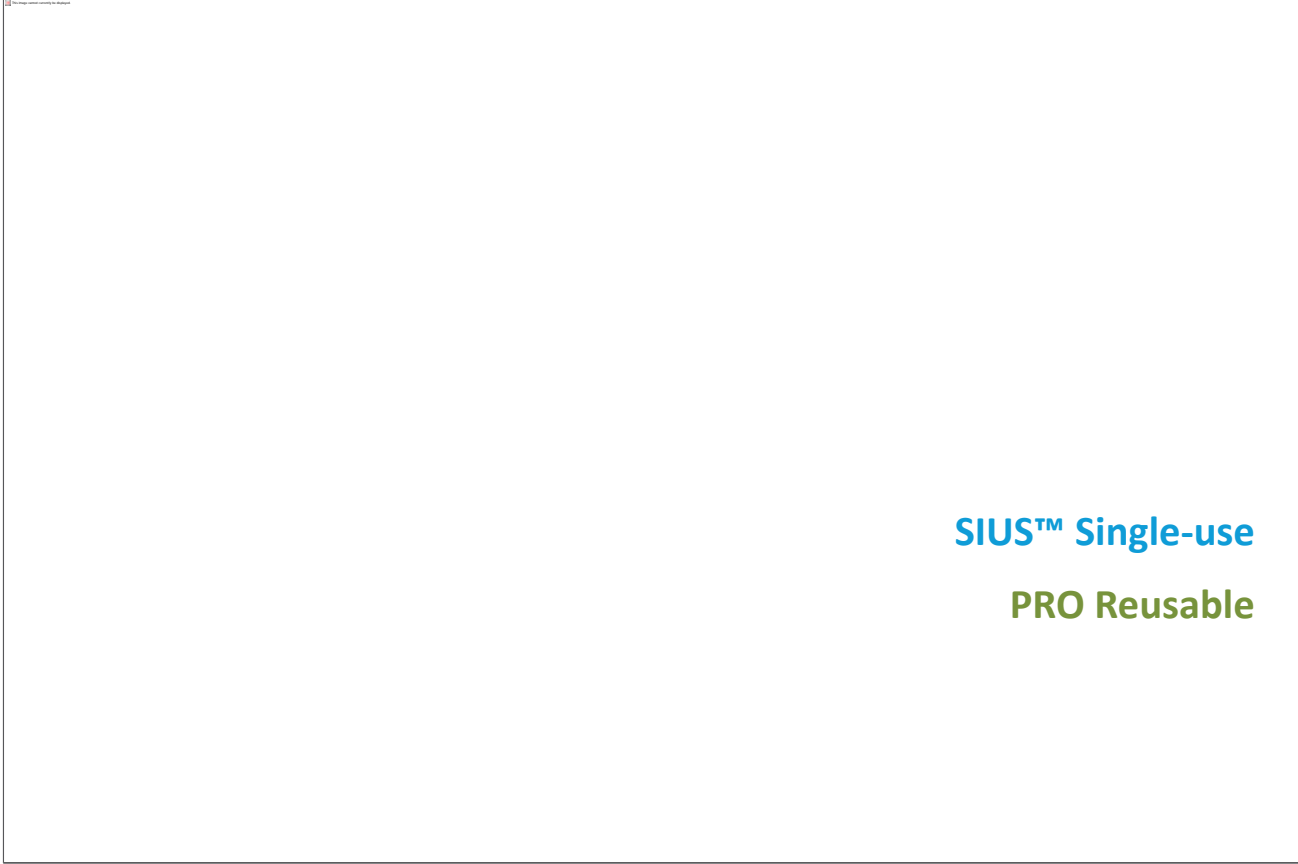
Same membrane chemistry (ProStream and HyStream)

Process volume and membrane area determine scale-up from TangenX™ SIUS™ to TangenX™ PRO

Membrane area: 2.5 m²



Membrane area: 40 m²



- ✓ Single-use TFF provides the greatest benefit for small to moderate scale operations
- ✓ Reusable TFF is optimal for large production scale operations
- ✓ Contract manufacturing organizations are ideal candidates for single-use TFF

Cost per run includes system design and fabrication, validation, CIP cycles, labor and overhead costs, consumables. Not included are reduced cross contamination, batch to batch reproducibility, increased manufacturing flexibility.

Comprehensive Regulatory Support Files for each cassette

Product information

- Cassette design
- Materials of construction

Product performance

- Membrane performance
- Cassette performance
- Cassette integrity
- Cassette pre-flushing study
- Cassette leachables
- Robustness study
- Shelf life study

Safety information

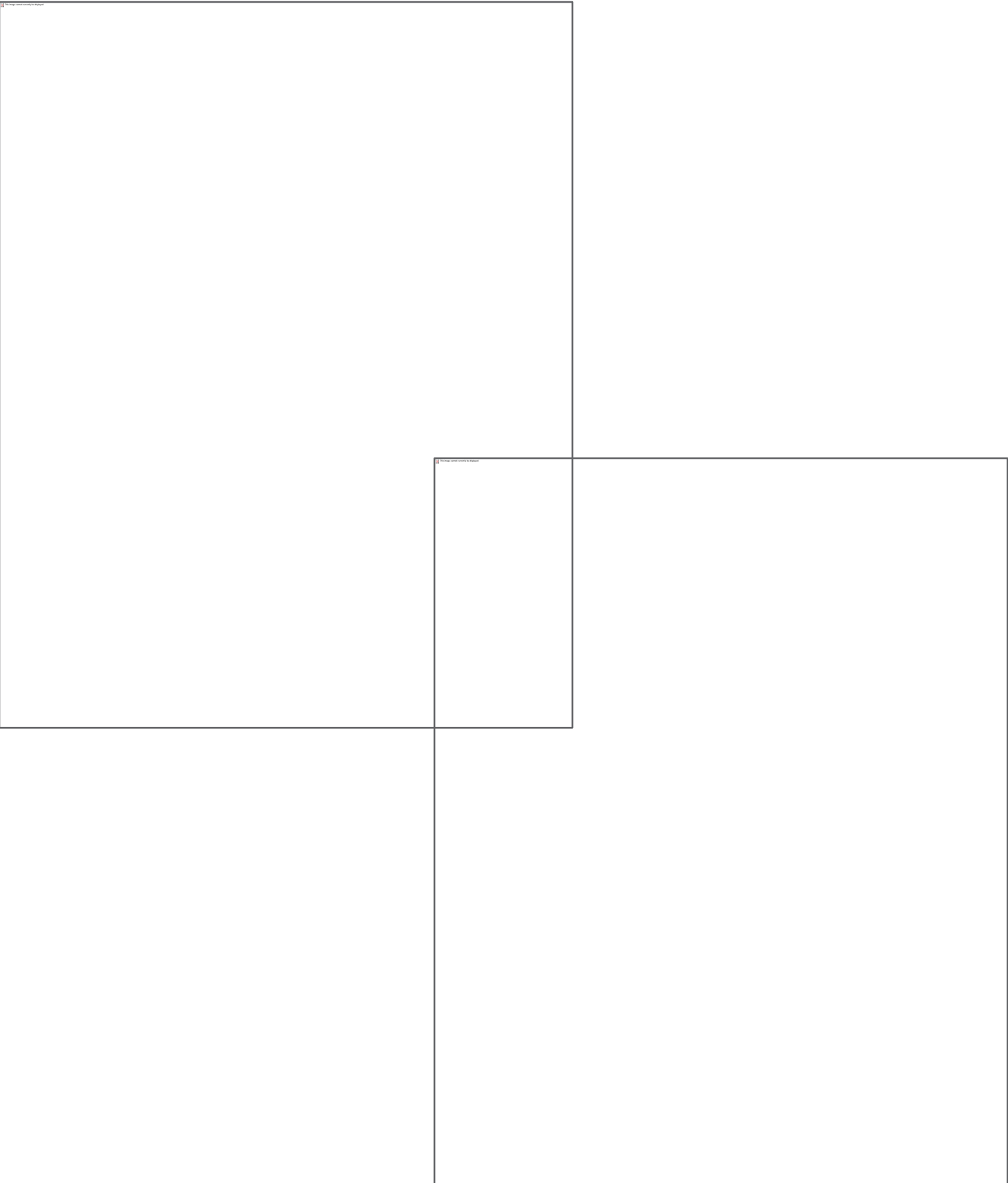
Documentation system

Product Manufacturing

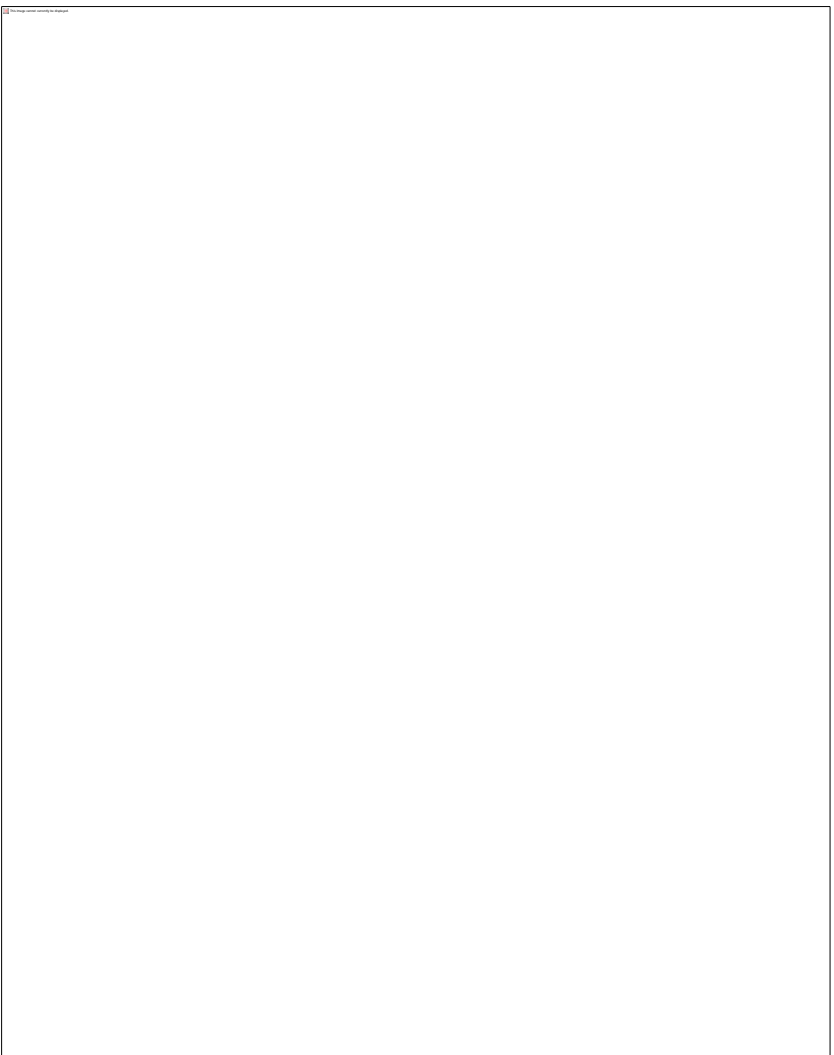
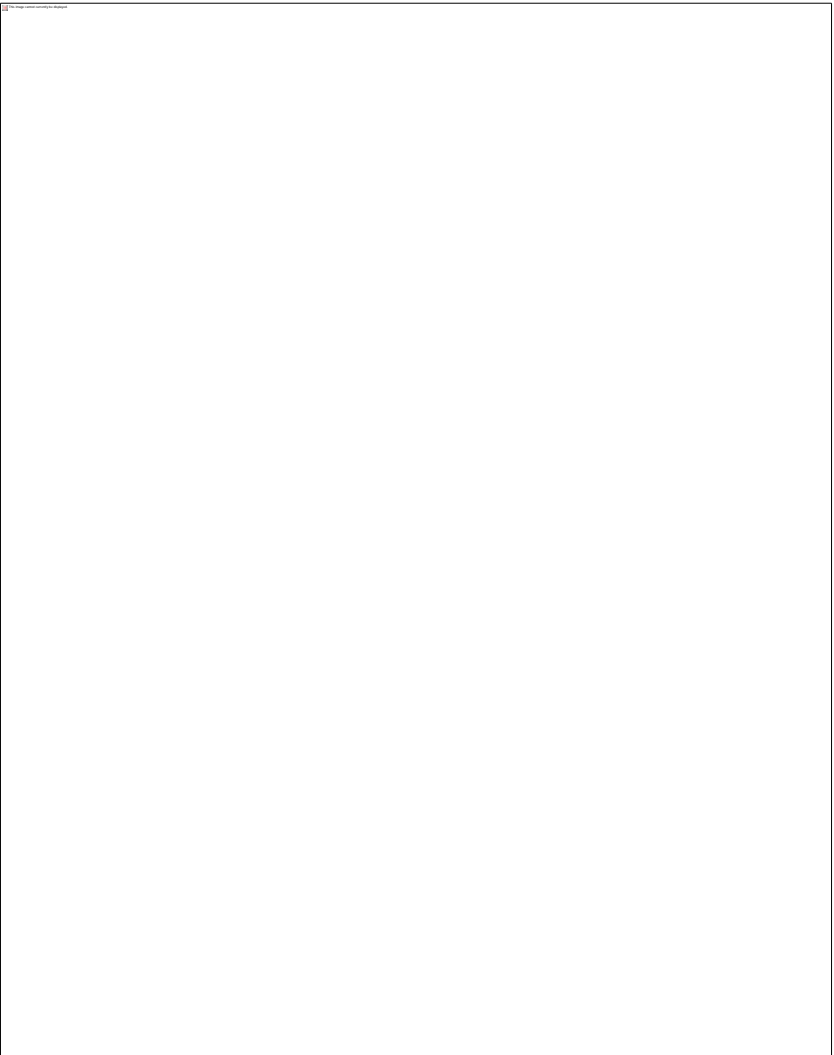
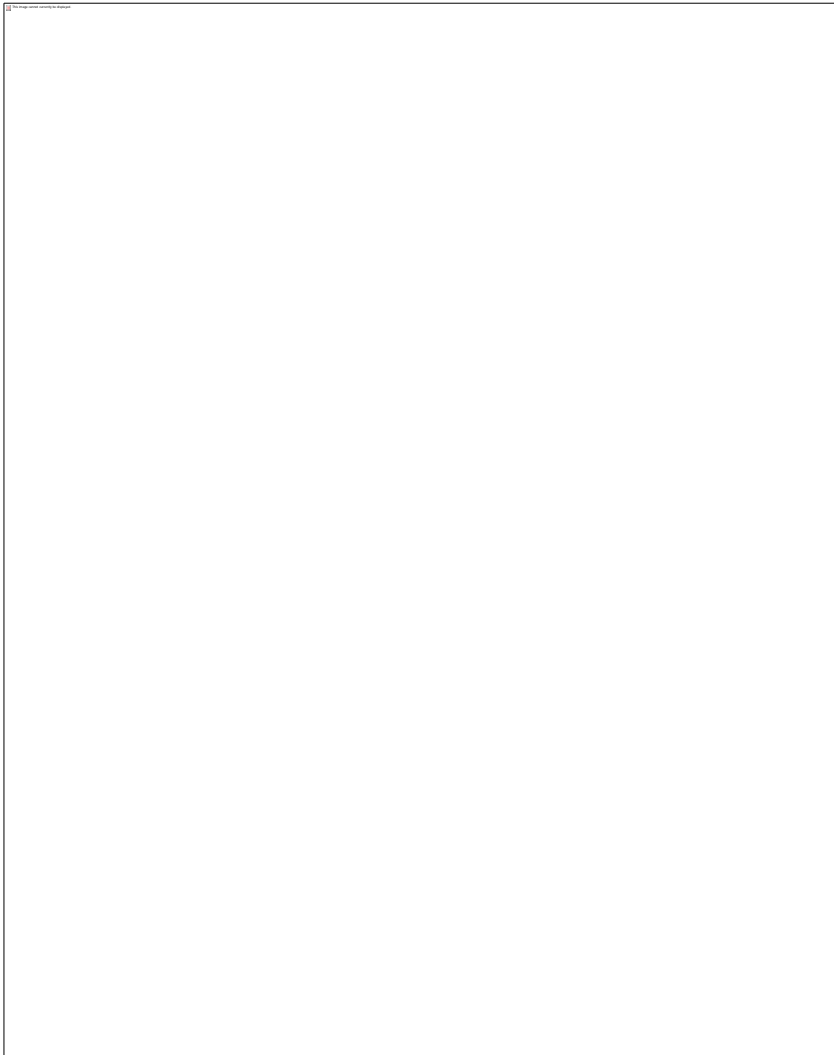
Qualification

Manufacturing Process Validation

Release Testing

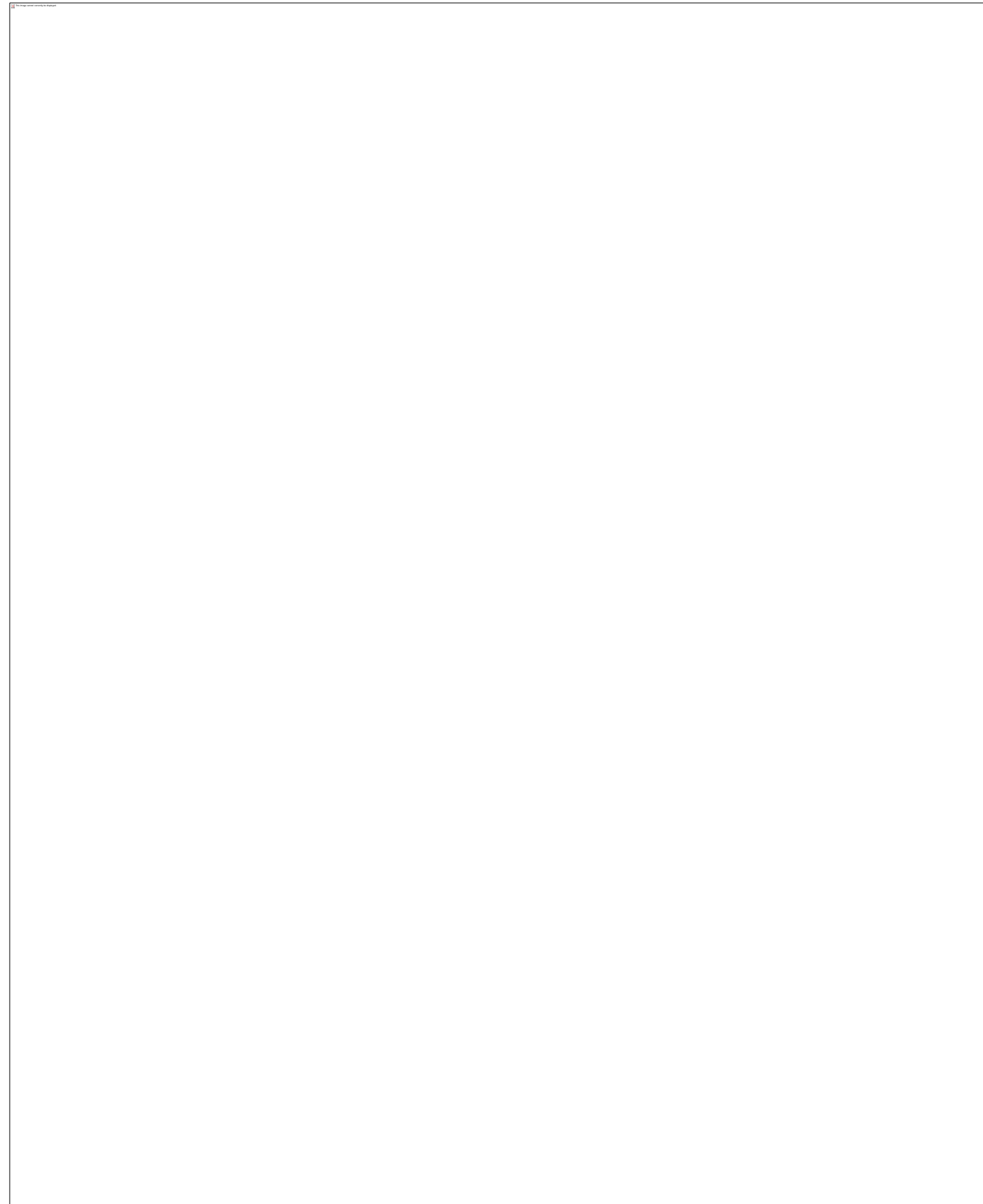


Quality manufacturing



Manufactured in a fully validated and documented manufacturing process according to the principles of cGMP

Reliable, scalable, cost-effective solutions for tangential flow filtration



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