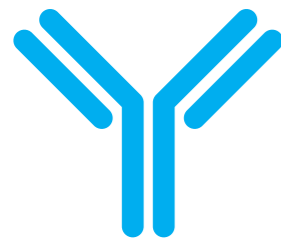


Harvesting Technology Guide for mAb Processes

Accelerated process development through the identification of optimal platform solutions





Accelerate Your Process Development

Your guide to cell harvesting using Pall technology

Higher cell densities increase the challenge for harvest clarification technologies. Evaluating every harvesting technology may be time-consuming and can delay process development.

Use the guide to:

- rapidly identify the most suitable platform technology
- compare the latest, single-use harvesting technologies

Introduction

The continuing optimization of cell culture processes leads to increases in the productivity of mammalian cell cultures producing higher cell titers and higher monoclonal antibody (mAb) concentrations.

These advances are accompanied by an increasing biomass, including in cell debris and other impurities that combine to increase the practical challenges of clarifying these fluids in preparation for downstream purification.

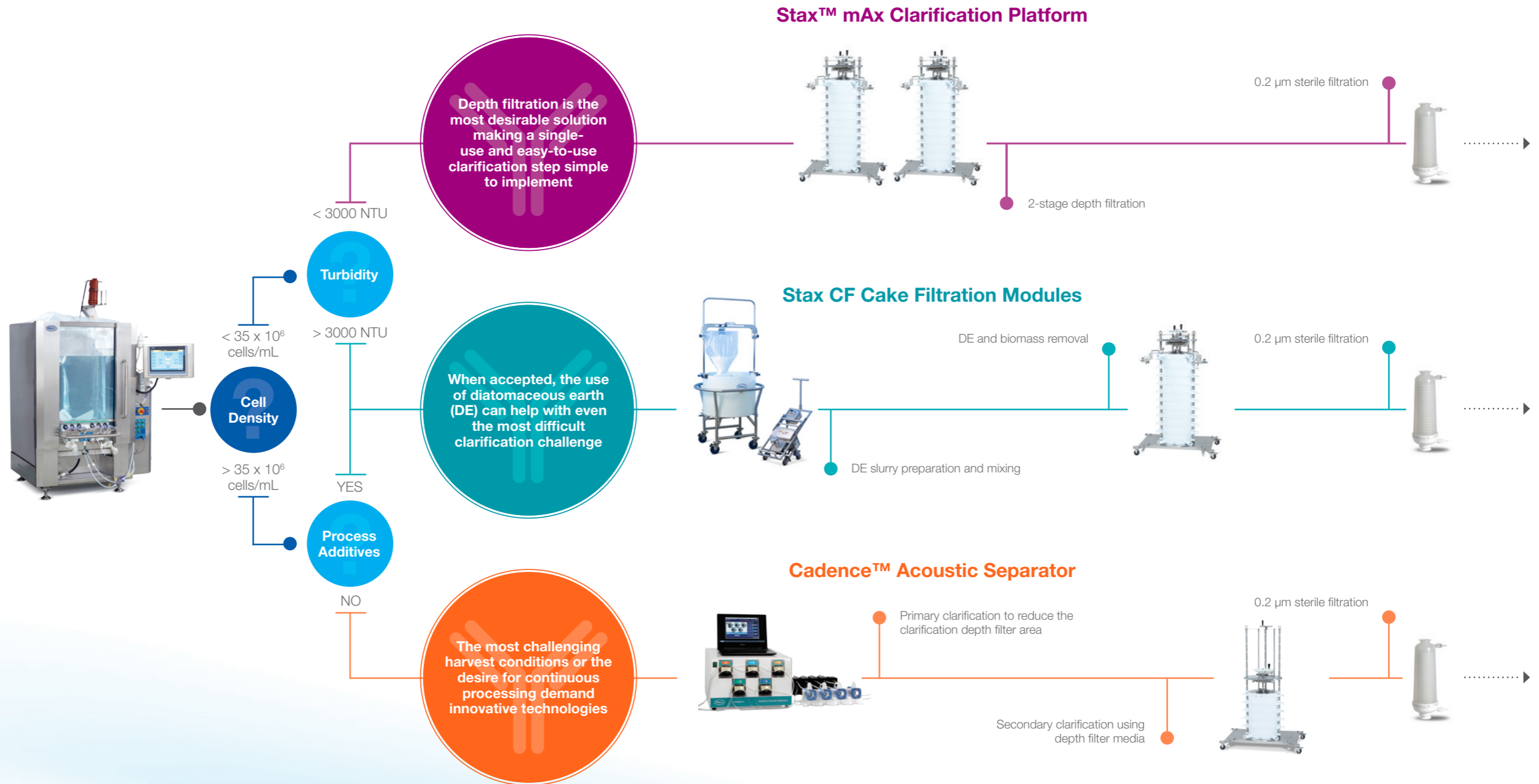
Extensive evaluation of multiple technologies to identify a single robust platform that will work well across a wide range of process, especially those with higher cell densities, is time and fluid intensive. This is often not practical. The selection process is then complicated further when expanding the review to include the scalability of the technology, the simplicity of installation or, operation and ultimately the economy, including the scale of capital investment required and ongoing consumable costs.

This guide provides a technology orientation to rapidly identify the best-fit technology, enable quick selection, and fast-track process development. Each of three technology platforms are aligned with known cell culture characteristics and process preferences, and deliver scalable economic solutions to meet your process demands.

Harvesting Guide for mAb Processes

Rapid Process Development with Optimal Platform Solutions

High cell density cell lines increase productivity but significantly increase the biomass challenge for the harvest clarification technology. Small differences in cell density and viability can have a significant impact on the performance of older technology. All Pall options are robust and each accommodate these variations to work as platform technology or individually optimized operations as needed.



Direct Clarification Using Depth Filtration

The Stax mAx Clarification Platform

Depth filtration is an established and easy-to-use solution for the clarification of cell cultures.

The Stax mAx clarification platform is a single-use, robust, depth filtration solution for the economic clarification of cell cultures used in the production of monoclonal antibodies without the need for centrifugation or process additives.

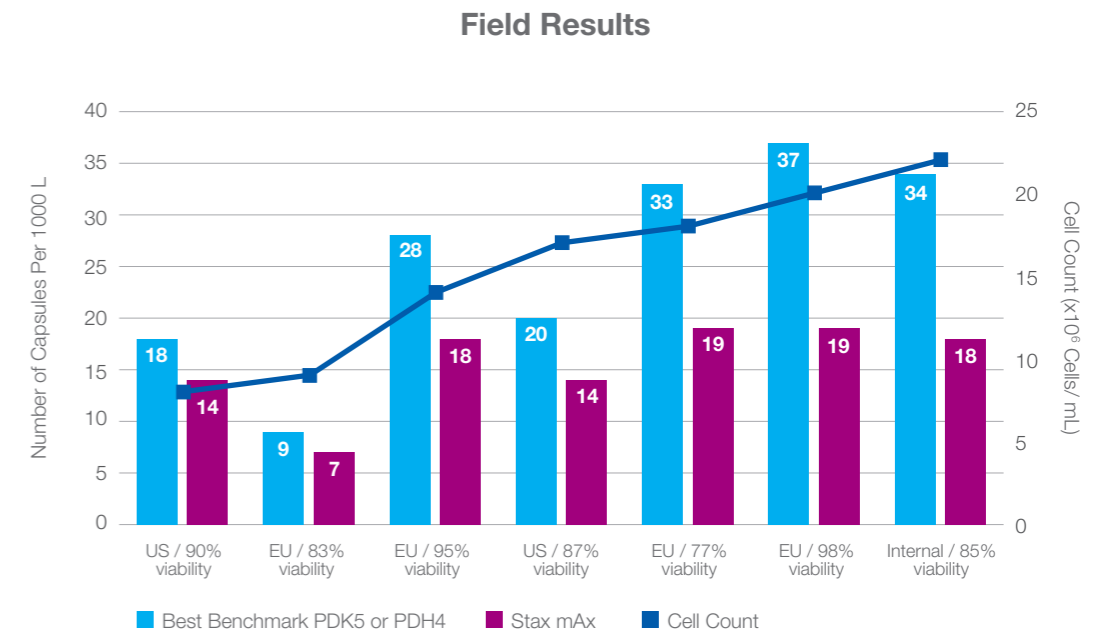
The two double-layer filtration stages are optimized for cell densities for up to 35×10^6 cells/mL and for culture turbidity of up to ~3000 NTU, and to maintain high capacity as cell density and viability change. This robust performance minimizes the impact of feed stream variations and delivers a wide platform performance that works across a broad range of cell cultures. It delivers high throughput in a small footprint.

The platform grades are available in a wide a range of formats and sizes to directly scale from bench-top testing up to large-scale clinical production.

- Robust performance for reliable processing
- High capacity, maintaining a small footprint even with high cell density cultures
- Simple, scalable and single-use technology for process flexibility

Robust performance and economic systems even with higher cell counts

Extensive field trials with a wide variety of cell culture feeds have shown that Stax mAx delivers the required performance across the broadest range of cell cultures. Figure 1 illustrates this data and shows the robustness of the performance with increased cell density.

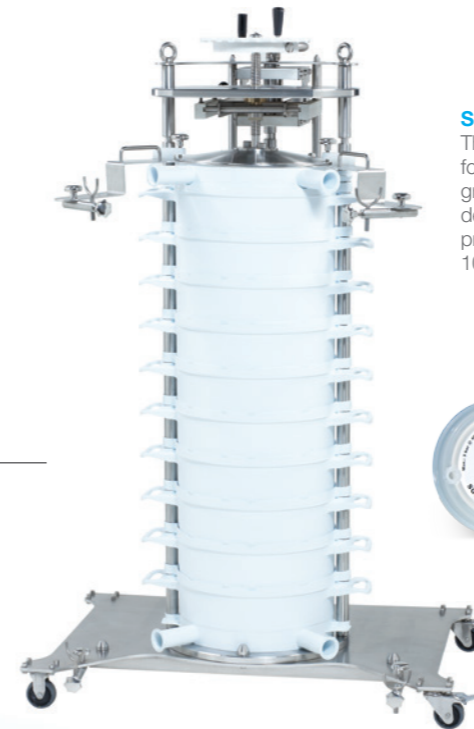


Allegro Bioreactor



Stax Depth Filtration

The Stax mAx clarification platform grows as your process scales to deliver clarification using the same format from 25 L to 1000 L.



Supracap™ 50 Capsules

The Supracap™ 50 and 100 capsule format uses the same Stax mAx filter grades and is the perfect process development tool, accurately predicting process performance with as little as 100 mL to 5 L of cell culture fluid.



Sterile Filtration

The high quality filtrate minimizes the size of subsequent bioburden control filters. Supor® filter capsules ensure the clarified harvest cell culture fluid is ready for downstream processing.



Clarification Using Acoustic Separation

The Cadence Acoustic Separator

For Chinese Hamster Ovary (CHO) cell cultures with very high cell densities of up to 50×10^6 cells/mL and where the use of process additives such as flocculating agents or DE is undesirable, few processing options exist without returning to centrifugation and accepting the challenges and compromises associated with this technology.

secondary clarification using Pall's range of HP-series, depth filter media this provides the consistent high quality filtrate necessary for bioburden control filtration and downstream processing.



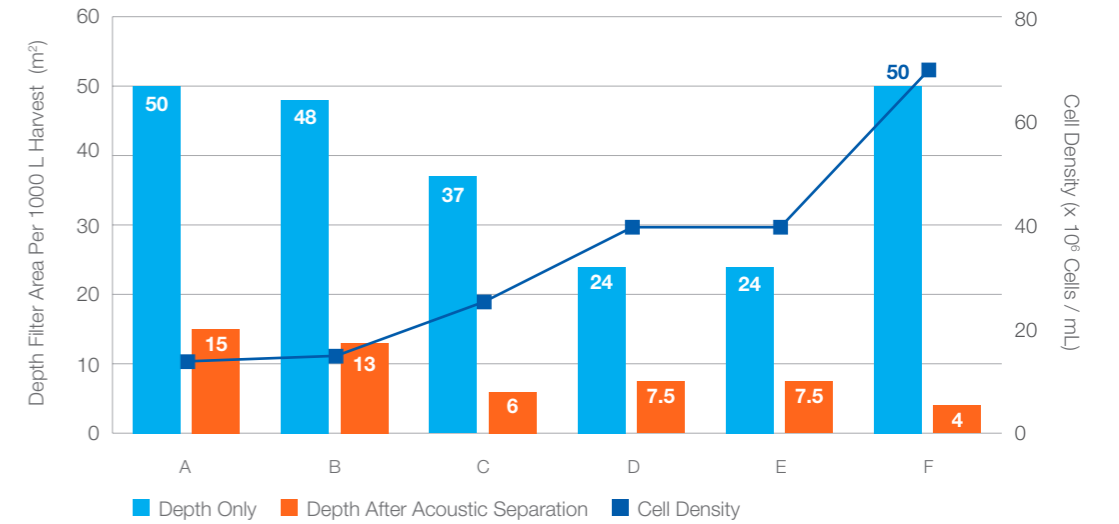
The Cadence Acoustic Separator uses a series of single-use acoustic chambers to achieve an effluent quality that is equivalent to centrifugation either in batch mode, or as part of a continuous clarification process. This primary clarification technology significantly reduces the number of depth filters required and when coupled with a

- Robust performance to minimize depth filter requirements for very high cell density cultures
- Scalable from <math><50\text{ L/h}</math> up to - Compatible with single-use and continuous manufacturing paradigms

Depth filter area reduction using the Cadence Acoustic Separator

Applying the Cadence Acoustic Separator for the primary clarification of very high cell density and highly turbid cell cultures can reduce the overall depth filtration requirements by as much as 90%. When combined with depth filtration, this assures high quality filtrate in even the most challenging of cell cultures with both technologies scaling together from process development to full scale clinical manufacturing.

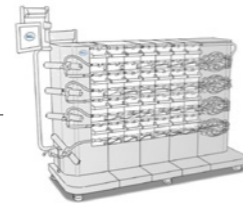
Depth Filter Area Reduction Post Acoustic Separation



Large Scale Production



Allegro Bioreactors



Acoustic Wave Separation
The Cadence Acoustic Separator typically operates at 3.6 L/h at process development scale. Larger scale systems will scale to flow rates of up to 350 L/h



Depth Filtration
Secondary clarification using HP-series depth media. Total depth filtration area may be reduced by 75% when compared to traditional depth filter solutions



Sterile Filtration
The high quality filtrate minimizes the size of subsequent bioburden control filters. Supor filter capsules ensure the clarified harvest cell culture fluid is ready for downstream processing

Development & Small Scale Production



The Continuous Ready trade mark identifies the Pall Life Sciences systems and consumables that enable the biopharmaceutical industry to adopt Continuous Bioprocessing in the manufacture of modern day medicines.

Direct Clarification Using Body-Feed Stax CF Cake Filtration Module

Where the cell culture characteristics lead to an uneconomic, or impractical system sizing using depth filtration alone, the addition of process additives such as diatomaceous earth (DE) assists in the removal of biomass and acts to reduce the filter area required.

Stax CF cake filtration modules use the same easy-to-use, Stax platform and are configured to retain up to 13 L of solids per module. This makes them ideally suited to accommodate the high-solid-load content present when using DE.

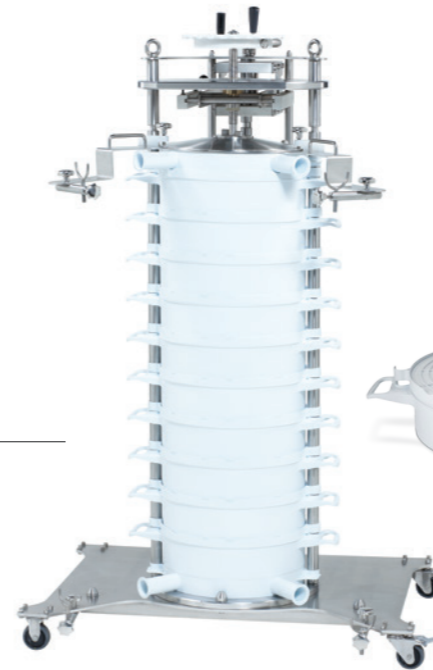
Preparation of the cell harvest slurry using single-use technology can be supported using the Pall Magnetic Mixer, which can achieve a uniform suspension in minutes with process volumes from 30 L to 2000 L. The addition of DE to the mixer can be supported with the use of Pall PD2 powder handling bags, lifting devices and filling hardware.

Stax CF modules deliver the clean retention of biomass and additives in a small footprint with filtrate quality ready for subsequent bioburden filtration and downstream processing.

- Proven technology ensuring the clean retention of biomass and DE
- Single-stage filtration delivering consistent filtrate clarity
- Simple scalability linked directly to the mass of diatomaceous earth used



DE Slurry Preparation
Single-use mixing and powder handling solutions support and control the operation to minimize the impact on the process area and assist with cGMP compliance



Cake Filtration
Each Stax CF modules can retain 3.8 kg of DE, enough for 150 L of cell culture with a typical biomass of 10%



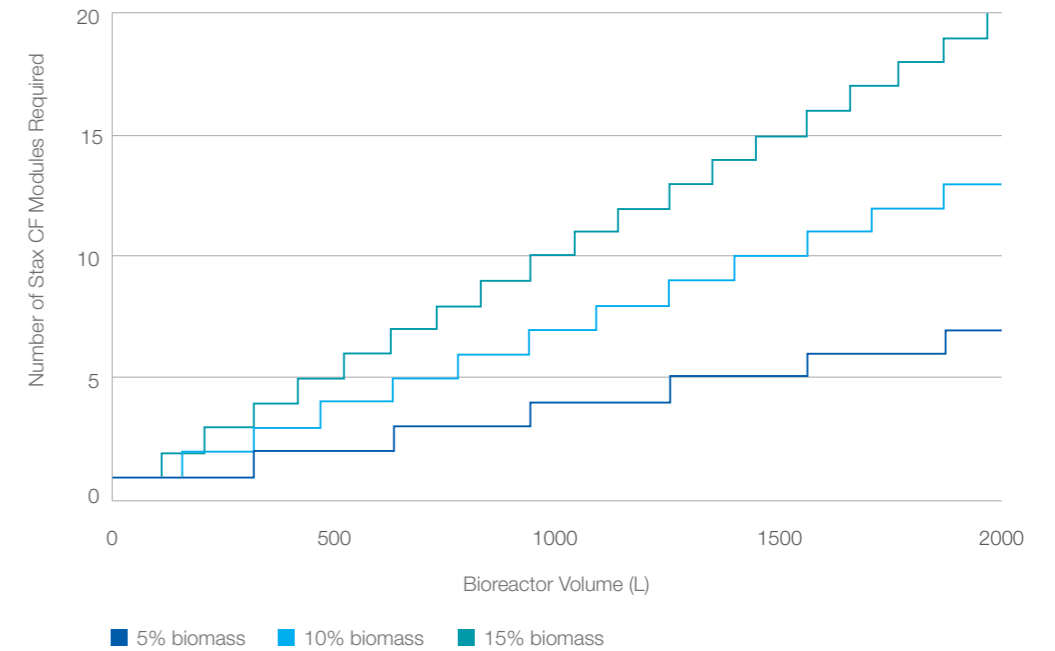
Sterile Filtration
The high quality filtrate minimizes the size of subsequent bioburden control filters. Supor filter capsules ensure the clarified harvest cell culture fluid is ready for downstream processing



Nominal Stax CF System Sizing

Nominal system sizing

At pH 5, an optimal DE: biomass ratio is typically 1:4. For a typical cell culture with a biomass of 10% this equates to a DE addition of approximately 25 g/L





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