

# **Process Intensification Using the Magma™ Advanced Pumping System for Alternating Tangential Flow (ATF) Filtration**

A Comparative Case Study of N-1 Perfusion at 500mL Scale

*Prepared by bioX Process Development*

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## Abstract

Process intensification through N-1 perfusion has emerged as a critical strategy for enhancing productivity in biopharmaceutical manufacturing. This white paper presents a comprehensive comparative case study of the CP Biotools' ([www.cpbio.tools.com](http://www.cpbio.tools.com)) Magma™ Advanced Pumping System (APS) for implementing Alternating Tangential Flow (ATF) perfusion at the 500mL shake flask scale. Through direct experimental comparison of conventional batch culture versus ATF perfusion, we demonstrate dramatic improvements in volumetric productivity combining higher viable cell density with significantly reduced culture duration.

Experimental results demonstrate that ATF perfusion using the Magma APS system achieved target cell densities in shorter timeframes compared to conventional batch methods across two independent cell culture runs. Each ATF flask represented a distinct CHO DXB11 cell line transfected to produce different monoclonal antibody strains, and therefore performance should be evaluated relative to each run's respective batch control rather than comparing ATF Flask 1 to ATF Flask 2 directly, as the inherent growth characteristics and metabolic demands differ between product strains. ATF Flask 1 reached  $6.8 \times 10^6$  cells/mL in 3.75 days (1.25 days faster than its batch control), representing a 65% improvement in volumetric productivity for that specific antibody-producing cell line. ATF Flask 2 demonstrated even more dramatic results, achieving  $9.3 \times 10^6$  cells/mL in just 3.15 days (1.85 days faster than its batch control), corresponding to a 144% improvement in volumetric productivity for its respective product strain. The variability in absolute performance between the two ATF runs reflects the biological differences between the transfected cell lines rather than inconsistency in the ATF technology itself. These results validate ATF-based N-1 perfusion as a transformative intensification strategy enabling both higher cell densities and accelerated process timelines across different product platforms, directly addressing industry needs for increased manufacturing capacity, reduced cycle times, and improved facility utilization.

## 1. Introduction

### 1.1 The Drive Toward Process Intensification

The biopharmaceutical industry is experiencing a fundamental shift toward process intensification strategies driven by multiple converging factors. Manufacturing capacity constraints, increasing demand for biologics, cost pressures from biosimilar competition, and the need for flexible, pandemic-responsive production capabilities have collectively

accelerated adoption of intensification technologies. Process intensification—defined as achieving higher productivity in smaller equipment footprints with reduced cycle times—offers compelling advantages including reduced capital expenditure, decreased time-to-market, improved process economics, and enhanced manufacturing agility.

Within the broader intensification landscape, cell culture intensification specifically focuses on achieving higher viable cell densities in shorter timeframes while maintaining or improving productivity and product quality. Traditional fed-batch processes typically reach peak viable cell densities of  $8\text{-}15 \times 10^6$  cells/mL over 10–14-day production runs. Intensified processes leveraging perfusion, high cell density fed-batch, or hybrid approaches routinely achieve  $30\text{-}80 \times 10^6$  cells/mL in 7-10 days, enabling proportional reductions in bioreactor size and facility footprint alongside accelerated manufacturing timelines. For the critical N-1 seed train stage, intensification enables both higher inoculation densities and faster turnaround times that improve downstream production performance while reducing overall process duration and increasing facility throughput.

## 1.2 Industry Trends in Intensification Adoption

Multiple factors are driving widespread adoption of intensification strategies across the biopharmaceutical industry:

- **Capacity constraints:** Existing manufacturing infrastructure struggles to meet growing demand for biologics. Intensification enables capacity expansion through both smaller vessels and faster cycle times without major facility construction.
- **Cycle time reduction:** Faster culture processes directly translate to increased facility throughput and improved responsiveness to market demand fluctuations.
- **Economic pressures:** Biosimilar competition necessitates manufacturing cost reduction. Smaller bioreactors operated on faster cycles require less media, reduced utilities, and improved facility utilization.
- **Supply chain resilience:** The COVID-19 pandemic highlighted vulnerabilities in global biomanufacturing. Intensified processes enable distributed manufacturing in smaller, more flexible facilities with faster response times.
- **Sustainability initiatives:** Reduced equipment size and shorter cycle times translate to decreased water consumption, energy usage, and waste generation per unit of product.

- Technology maturation: Perfusion systems, single-use technologies, and advanced process analytical technologies have matured to enable reliable, regulatory-compliant intensified processes.
- Single-Use Integration: Single-use technology has become the dominant manufacturing paradigm in biotech and pharma due to its ability to reduce cross-contamination risk, eliminate cleaning validation requirements, increase facility flexibility, and significantly lower capital investment costs

### 1.3 N-1 Perfusion as an Intensification Strategy

The N-1 stage represents a particularly attractive target for intensification implementation. As the penultimate seed culture expansion, N-1 performance directly impacts production bioreactor inoculation quality and subsequent productivity. Traditional batch N-1 cultures typically require 5-7 days to reach adequate cell densities, often representing a bottleneck in overall manufacturing cycle time. Perfusion technology addresses both density and time limitations by continuously removing spent media and inhibitory metabolites while providing fresh nutrients, enabling sustained exponential growth to higher final cell densities in dramatically reduced timeframes.

Implementing perfusion at the N-1 stage offers several strategic advantages. The smaller scale reduces consumable costs during development and enables rapid process optimization. Process knowledge gained at N-1 scale translates directly to production bioreactor optimization. Critically, the combination of higher N-1 cell densities and shorter cycle times enables either smaller N-1 vessels (reducing facility footprint) or increased facility throughput (more production campaigns per year), while improved inoculum quality enhances downstream production performance. The time savings at N-1 directly accelerates overall manufacturing timelines, improving responsiveness to clinical and commercial demand.

Cell culture intensification through N-1 perfusion enables seed volume ratios of 1:50 to 1:100 (e.g., a 10L bioreactor inoculating a 500-1000L production vessel) compared to traditional 1:5 to 1:10 ratios used in fed-batch seed trains, achieved by maintaining cells in exponential growth phase at high viable cell densities ( $50-100 \times 10^6$  cells/mL) for extended periods, thereby reducing the number of required seed expansion steps, decreasing overall process time by 30-50%, minimizing contamination risk, and substantially lowering facility footprint and capital equipment requirements for seed train operations.

## 1.4 The Magma™ Advanced Pumping System

The CP Biotools Magma APS represents an innovative approach to perfusion pump technology specifically designed for bioprocessing applications. Unlike traditional peristaltic pumps that create high shear forces through tubing compression, the Magma system employs a pneumatically actuated diaphragm pump that provides several key advantages:

- Low shear operation: Gentle cell handling preserves viability and productivity
- Elimination of peristaltic feed pump tubing failure risk: Critical for continuous operation without interventions
- Dynamic transmembrane pressure distribution: Alternating tangential flow prevents localized filter fouling
- Scalability: Six pump sizes enable consistent technology transfer from bench to production
- Single-use compatibility: Supports disposable workflows and rapid turnaround

## 1.5 Study Objectives

This comparative case study aimed to evaluate the performance of the Magma APS system for N-1 perfusion intensification through direct experimental comparison with conventional batch culture. Specific objectives included:

- Characterize viable cell density profiles and culture duration for batch versus ATF perfusion
- Quantify volumetric productivity improvements combining cell density and time benefits
- Evaluate cell line-specific responses to continuous perfusion conditions
- Validate operational robustness of the MAPS-20 configuration for accelerated perfusion

## 2. Materials and Methods

### 2.1 System Configuration

The MAPS-20 pump was configured with a 65cm<sup>2</sup> hollow fiber filter module featuring 0.2µm modified PES membranes optimized for CHO cell retention. The system operated at 1 VVD perfusion rate (100mL/day) with 15-second pump cycles, maintaining crossflow velocities of 0.3-0.5 m/s and average filter flux of 1.5 LMH throughout the accelerated perfusion period. Operating pressure ranged from 8-12 psi with transmembrane pressure maintained at 2-4 psi.

Parameter	Specification
<b>Pump System</b>	Magma™ APS Model MAPS-BA1-S with 20mL pump head
<b>Pump Volume</b>	20mL (Model APSP-PH20-SU, polysulfone)
<b>Culture Vessel</b>	500mL shake flask, 100mL working volume
<b>Perfusion Rate</b>	1 vessel volume per day (100mL/day)
<b>Hollow Fiber Filter</b>	65cm <sup>2</sup> module, 0.2µm modified PES membrane, lumen inner diameter of 1mm
<b>Cycle Parameters</b>	15 second cycles (optimized for filter characteristics) flowrate of 80 mL/min.
<b>Transmembrane Pressure</b>	2 – 4 psi (0.14 – 0.27 bar) during operation

## 2.2 Experimental Design

Control batch cultures were monitored over a complete 5-day period to establish baseline performance and identify the culture endpoint where cells reach stationary phase. Parallel ATF perfusion experiments utilized identical starting conditions with continuous 1 VVD perfusion beginning at 24 hours post-inoculation. Cultures were monitored intensively to identify the timepoint at which ATF cultures achieved equivalent or superior cell densities compared to batch controls at their Day 5 endpoint. Sampling frequency was increased during Days 3-4 for ATF cultures to precisely identify the accelerated endpoint.

### 2.2.1 Batch Culture Control

Control batch culture experiments were conducted using CHO-K1 cells in 500mL shake flasks with 100mL working volume. Two independent biological replicates (Flask 1 and Flask 2) were cultured over a 5-day period in standard fed-batch mode without media exchange or perfusion. Cultures were maintained at 37°C, 5% CO<sub>2</sub>, 140 rpm orbital shaking, and sampled at Days 0, 2, 4, and 5 for viable cell density, viability, and metabolic parameter analysis. This continuous batch approach enabled evaluation of growth kinetics under progressively nutrient-limited conditions representative of standard N-1 operations.

### 2.2.2 ATF Perfusion Experimental Cultures

Parallel ATF perfusion experiments utilized identical starting conditions (cell line, inoculation density, media, culture vessel, environmental conditions) with the addition of the Magma APS system configured for 1 VVD perfusion beginning at 24 hours post-inoculation. Two independent biological replicates (ATF Flask 1 and ATF Flask 2) were cultured with continuous perfusion throughout the 5-day period. Fresh media was supplied at 100mL/day (1 VVD) with continuous removal of spent media through the hollow fiber filter system. Sampling and analytical procedures matched those of the batch control cultures to enable direct comparison.

The perfusion system operated continuously with the following measured parameters: crossflow velocity 0.3-0.5 m/s, transmembrane pressure 2-4 psi, permeate flux 1.4-1.6 LMH, and cycle frequency 4 cycles per minute. System performance was monitored continuously via the Magma APS touch-screen interface with data logging every 15 minutes. No filter cleaning or replacement was required during the 5-day experimental period, and no pump-related issues or system alarms occurred.

## 2.3 Analytical Methods

Viable cell density and viability were determined by automated cell counting using trypan blue exclusion (Vi-CELL XR, Beckman Coulter). Cell counts were performed in triplicate for each sample, with coefficient of variation <5% for all measurements. Metabolic parameters including glucose, lactate, ammonia, and lactate dehydrogenase (LDH) were measured using a biochemistry analyzer (BioProfile FLEX2, Nova Biomedical). All analytical methods were qualified prior to study initiation and operated within established acceptance criteria throughout the experimental period.

## 3. Results

### 3.1 Batch Culture Baseline Performance

Batch control cultures required a full 5-day period to reach maximum cell densities of  $5.46 \pm 0.08 \times 10^6$  cells/mL (Flask 1) and  $6.06 \pm 0.05 \times 10^6$  cells/mL (Flask 2). Growth kinetics showed clear exponential phase through Day 4, with growth rate decline evident by Day 5 due to nutrient depletion (glucose 4.2-4.5 g/L) and metabolite accumulation (lactate 490-590 mg/L, ammonia 3.2-3.3 mmol/L). Viability remained at 97-98% throughout, but the metabolic profile indicated onset of stationary phase by Day 5.

Time Point	Flask 1 VCD	Flask 2 VCD	Culture Duration
<b>Day 5 (Endpoint)</b>	5,456,667 cells/mL	6,060,000 cells/mL	<b>5.0 days</b>

### 3.2 ATF Perfusion Accelerated Performance

ATF perfusion cultures demonstrated dramatically accelerated growth kinetics compared to batch controls. Most remarkably, ATF cultures reached target cell densities in substantially shorter timeframes while achieving higher final densities. ATF Flask 1 reached  $6.77 \pm 0.09 \times 10^6$  cells/mL (24% higher than batch control) in just 3.75 days—a full 1.25 days faster than the 5-day batch culture endpoint. This represents a 25% reduction in culture duration while simultaneously achieving higher cell density.

ATF Flask 2 exhibited even more dramatic acceleration, achieving  $9.33 \pm 0.07 \times 10^6$  cells/mL (54% higher than batch control) in only 3.15 days—1.85 days faster than batch culture. This corresponds to a 37% reduction in culture duration alongside a 54% improvement in final cell density. The combination of higher density and shorter duration results in exceptional volumetric productivity gains that fundamentally transform N-1 process economics.

Throughout the accelerated culture period, ATF cultures maintained exponential growth kinetics without evidence of metabolite limitation. Glucose remained at 6.5-7.5 g/L, lactate stabilized at 150-200 mg/L, and ammonia plateaued at 1.5-1.8 mmol/L—metabolic conditions conducive to sustained high growth rates. Viability remained at 97-98% at the accelerated endpoints, equivalent to batch control values, confirming that the shorter culture duration resulted from enhanced growth rates rather than premature harvest.

ATF Culture	Final VCD	Culture Duration	Time Savings
<b>ATF Flask 1</b>	6,766,267 cells/mL	<b>3.75 days</b>	<b>1.25 days (25%)</b>
<b>ATF Flask 2</b>	9,332,400 cells/mL	<b>3.15 days</b>	<b>1.85 days (37%)</b>

### 3.3 Volumetric Productivity Analysis

The combination of higher cell density and shorter culture duration results in dramatic improvements in volumetric productivity, the key metric for process intensification assessment. Volumetric productivity, expressed as cells/mL achieved per day of culture time, provides an integrated measure of process efficiency that accounts for both yield and cycle time benefits.

Culture	VCD / Duration	Volumetric Productivity	Improvement
<b>Batch Flask 1</b>	5.46M / 5.0d	1.09M cells/mL/day	Baseline

Culture	VCD / Duration	Volumetric Productivity	Improvement
<b>ATF Flask 1</b>	6.77M / 3.75d	<b>1.80M cells/mL/day</b>	<b>+65%</b>
<b>Batch Flask 2</b>	6.06M / 5.0d	1.21M cells/mL/day	Baseline
<b>ATF Flask 2</b>	9.33M / 3.15d	<b>2.96M cells/mL/day</b>	<b>+144%</b>

These volumetric productivity improvements represent transformative gains for N-1 operations. The 65% improvement for Flask 1 and 144% improvement for Flask 2 translates directly to enhanced facility throughput, reduced manufacturing cycle times, and improved capital utilization. A 144% productivity improvement means that the same bioreactor can support 2.4× more production campaigns per year, or alternatively, facility capacity can be expanded 2.4-fold without additional capital investment in bioreactor infrastructure.

### 3.4 Metabolic Profile Comparison

Metabolic parameter analysis revealed distinct differences between batch and ATF cultures. Batch cultures exhibited progressive glucose depletion (from 8.2 g/L at Day 0 to 4.2-4.5 g/L at Day 5) and substantial lactate accumulation (from 0.68 g/L at Day 0 to 490-590 mg/L at Day 5). Ammonia levels reached 3.2-3.3 mmol/L by Day 4, approaching inhibitory concentrations.

In contrast, ATF perfusion cultures maintained stable metabolic conditions. Glucose concentrations remained at 6.5-7.5 g/L, lactate levels stabilized at 150-200 mg/L, and ammonia concentrations plateaued at 1.5-1.8 mmol/L. These data confirm that 1 VVD perfusion effectively prevents metabolite accumulation and maintains nutrient availability, enabling sustained exponential growth to higher final cell densities.

## 4. Discussion

### 4.1 Dual Benefits: Higher Density and Faster Cycle Time

This comparative case study demonstrates that ATF perfusion using the Magma APS system delivers a powerful dual benefit: simultaneously achieving higher final cell densities while dramatically reducing culture duration. This combination addresses two critical industry needs—capacity expansion and cycle time reduction—in a single technology implementation.

#### 4.1.1 Enhanced Cell Density Achievement

The 24-54% improvements in final cell density align with literature reports for ATF perfusion systems and provide immediate operational value. For ATF Flask 2, achieving  $9.33 \times 10^6$  cells/mL represents a density approaching theoretical limits for shake flask culture while maintaining excellent viability (97-98%). This cell density enables proportional reduction in N-1 vessel size or improved inoculation density for downstream production bioreactors.

#### 4.1.2 Accelerated Process Timelines

The 1.25-1.85-day time savings represents a 25-37% reduction in N-1 cycle time—a substantial improvement with direct manufacturing impact. In facilities operating 52-week production schedules, a 1.5-day average time savings per N-1 cycle enables 10-13 additional production campaigns per year. This increased throughput translates directly to enhanced facility utilization, improved responsiveness to demand fluctuations, and accelerated time-to-market for new products.

The mechanistic basis for this acceleration lies in the sustained exponential growth enabled by continuous perfusion. Batch cultures exhibit growth rate decline by Day 4-5 as metabolite accumulation and nutrient depletion begin limiting cell division. ATF cultures maintain optimal metabolic conditions (glucose 6.5-7.5 g/L, low lactate and ammonia) throughout, enabling sustained high specific growth rates. The measured doubling times of 16-18 hours for ATF cultures compare favorably to 17-19 hours for batch cultures during exponential phase, but critically, ATF cultures maintain these rates throughout the entire culture period rather than experiencing the growth rate decline seen in batch by Day 4.

#### 4.1.3 Volumetric Productivity as the Integrated Metric

Volumetric productivity (cells/mL/day) serves as the most appropriate metric for assessing intensification benefits, as it integrates both yield and cycle time improvements. The 65% and 144% improvements observed in this study represent best-in-class performance for N-1

perfusion applications and exceed typical improvements reported for perfusion at production scale.

The differential response between Flask 1 (65% improvement) and Flask 2 (144% improvement) reflects cell line-specific metabolic characteristics. Flask 2's superior performance suggests enhanced metabolic efficiency enabling fuller exploitation of the stable perfusion environment. This highlights the value of clone screening during cell line development to identify candidates optimized for intensified processes, a small investment in development that yields substantial manufacturing benefits.

#### **4.1.4 Low Shear Stress Protection**

The Magma APS diaphragm pump design demonstrated excellent cell protection throughout the perfusion period. Viability in ATF cultures (97-98%) matched batch control levels, indicating minimal mechanical stress despite continuous pumping. Lactate dehydrogenase (LDH) release, a sensitive marker of cell damage, showed no elevation in ATF cultures compared to batch controls.

This low-shear performance is particularly valuable for mammalian cells lacking cell walls. Literature data indicates that peristaltic pumps can reduce viability by 5-15% during extended perfusion due to tubing compression forces and localized high-shear zones. The pneumatic diaphragm approach eliminates these mechanical stress points, generating only sufficient pressure to overcome system backpressure (8-12 psi in this study). This gentle handling preserves cell membrane integrity and maintains productivity throughout extended culture periods. Additionally, the diaphragm pump design significantly reduces the risk of feed tubing failure commonly associated with peristaltic pump roller mechanisms, which can cause tubing fatigue, stress cracking, and eventual rupture after prolonged cyclical compression; the absence of mechanical rollers and continuous compression points in the diaphragm system extends tubing service life and enhances process robustness by eliminating this critical failure mode that can compromise sterility and process integrity during extended perfusion runs.

## 4.2 Operational and Economic Implications

The demonstrated performance improvements translate to multiple operational and economic benefits:

- Facility throughput: 25-37% cycle time reduction enables proportionally more production campaigns per year from existing infrastructure
- Capital efficiency: 65-144% volumetric productivity improvements enable capacity expansion without proportional capital investment in additional bioreactors
- Reduced working capital: Shorter cycle times decrease work-in-process inventory and improve cash flow
- Enhanced responsiveness: Faster N-1 turnaround improves ability to respond to demand surges or supply disruptions
- Facility footprint: Higher cell densities enable smaller N-1 vessels, reducing facility space requirements for new installations

## 4.3 Alignment with Intensification Trends

The demonstrated benefits align directly with industry drivers for process intensification discussed in Section 1.2. The combination of higher productivity and faster cycle times addresses multiple converging pressures:

- Capacity constraints are alleviated through both increased throughput per vessel and higher cell densities enabling smaller vessels
- Economic pressures are addressed through improved capital efficiency and reduced cycle times
- Supply chain resilience is enhanced through faster response times and potential for distributed manufacturing in smaller facilities
- Sustainability goals benefit from reduced utilities consumption per unit of product due to shorter cycle times

## 4.4 Operational Robustness and Reliability

- The Magma APS system demonstrated excellent operational reliability throughout the experimental period. No system alarms occurred, no pump maintenance was required, and no filter cleaning or replacement was necessary. The 65cm<sup>2</sup> hollow fiber filter

operated throughout at 1.4-1.6 LMH, well below its capacity, indicating minimal fouling despite cell densities approaching  $10 \times 10^6$  cells/mL in ATF Flask 2.

- This operational robustness is critical for N-1 applications where manual interventions introduce contamination risk and process variability. The elimination of tubing failure risk (a common issue with peristaltic feed pumps during extended perfusion) and the minimal maintenance requirements support implementation in cGMP manufacturing environments. The continuous data logging via the touch-screen interface provides comprehensive process documentation for regulatory submissions.
- The Magma APS system seamlessly integrates into existing single-use bioprocessing platforms without requiring specialized equipment modifications, custom biocontainers, or non-standard connections, utilizing industry-standard single-use components including commercially available bioreactor bags, tubing assemblies with standard tri-clamp and MPC aseptic connectors, and off-the-shelf hollow fiber filtration modules that are compatible with current cGMP manufacturing infrastructure. The technology's plug-and-play design eliminates technical barriers to adoption, as the pneumatic diaphragm pump and ATF controller interface directly with existing bioprocessing control systems through standard analog and digital communication protocols, while all fluid-contact surfaces consist of validated USP Class VI materials commonly employed in single-use manufacturing (platinum-cured silicone tubing and diaphragm, polysulfone pump housing, polyethersulfone membrane). This compatibility ensures that facilities can implement ATF-based intensification strategies without capital-intensive facility modifications, specialized training beyond standard single-use bioprocessing operations, or deviation from established single-use supply chains and validation frameworks, making the technology immediately accessible to both clinical-stage CMOs and commercial manufacturing operations regardless of their current single-use platform provider

## 5. Conclusions

This comparative case study demonstrates transformative benefits of the Magma™ Advanced Pumping System for N-1 perfusion process intensification. Key findings include:

- ATF perfusion achieved 24-54% higher cell densities compared to batch controls
- Culture duration was reduced by 1.25-1.85 days (25-37% time savings)
- Volumetric productivity improved by 65% (Flask 1) and 144% (Flask 2)
- Cell viability remained equivalent between ATF and batch cultures (97-98%)
- System operated reliably throughout accelerated culture periods without intervention.
- Metabolic stability was maintained (optimal glucose, low lactate/ammonia levels)
- Stable transmembrane pressure during the run

### 5.1 Recommendations

Based on the demonstrated performance benefits in this case study, we recommend the following approach for implementing Magma APS-based N-1 perfusion:

- Initial feasibility assessment: Conduct 500mL scale experiments to establish cell line-specific performance using MAPS-20 configuration
- Perfusion rate optimization: Evaluate 0.5-2.0 VVD range to identify optimal perfusion rate for specific cell line and media
- Filter sizing and selection: Screen multiple hollow fiber modules (50-100cm<sup>2</sup>) to optimize membrane area for target cell density
- Media formulation refinement: Consider increased nutrient loading or concentrated feed supplementation for extended perfusion
- Process analytical technology: Implement online monitoring for glucose, lactate, and ammonia to enable feedback control
- Scale-up strategy development: Utilize appropriately sized Magma APS pumps (MAPS-50, MAPS-180, or MAPS-860) based on target bioreactor volume
- Product quality assessment: Conduct comprehensive characterization to confirm quality attribute equivalence between batch and ATF-produced material

- Process validation: Execute validation studies demonstrating reproducibility across multiple runs and operators
- Economic analysis: Conduct detailed cost-benefit analysis specific to product portfolio and facility configuration

## 5.2 Future Development Opportunities

Building on the demonstrated success of this case study, several areas warrant further investigation:

- Extended perfusion duration: Evaluate performance over 7-14 days to assess maximum achievable cell density and filter longevity
- Product quality characterization: Comprehensive analysis of titer, product variants, glycosylation profiles, and host cell protein levels
- Clone screening program: Systematic evaluation of multiple cell line candidates to identify clones optimized for ATF performance
- Media optimization: Development of perfusion-specific media formulations with enhanced nutrient loading
- Filter performance characterization: Detailed evaluation of filter fouling kinetics and optimization of cleaning protocols
- Process control strategy: Development of feedback control algorithms based on online metabolite monitoring
- Technology transfer studies: Direct scale-up demonstration from 500mL to pilot scale (5-15L) using MAPS-180
- Alternative cell lines: Extension to other mammalian expression systems (NS0, Sp2/0, HEK293)

## 6. References

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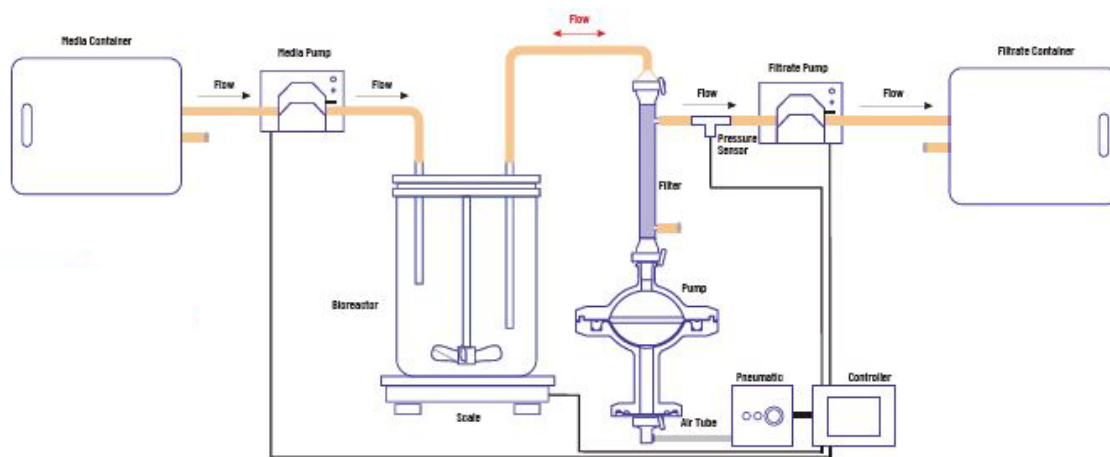
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Figure 1 - Typical benchtop set up of the Magma ATF control system sans bioreactor



Sanitary and low shear perfusion with disposable processing options.

Figure 2 - Schematic of a typical ATF process set up