ABZENA

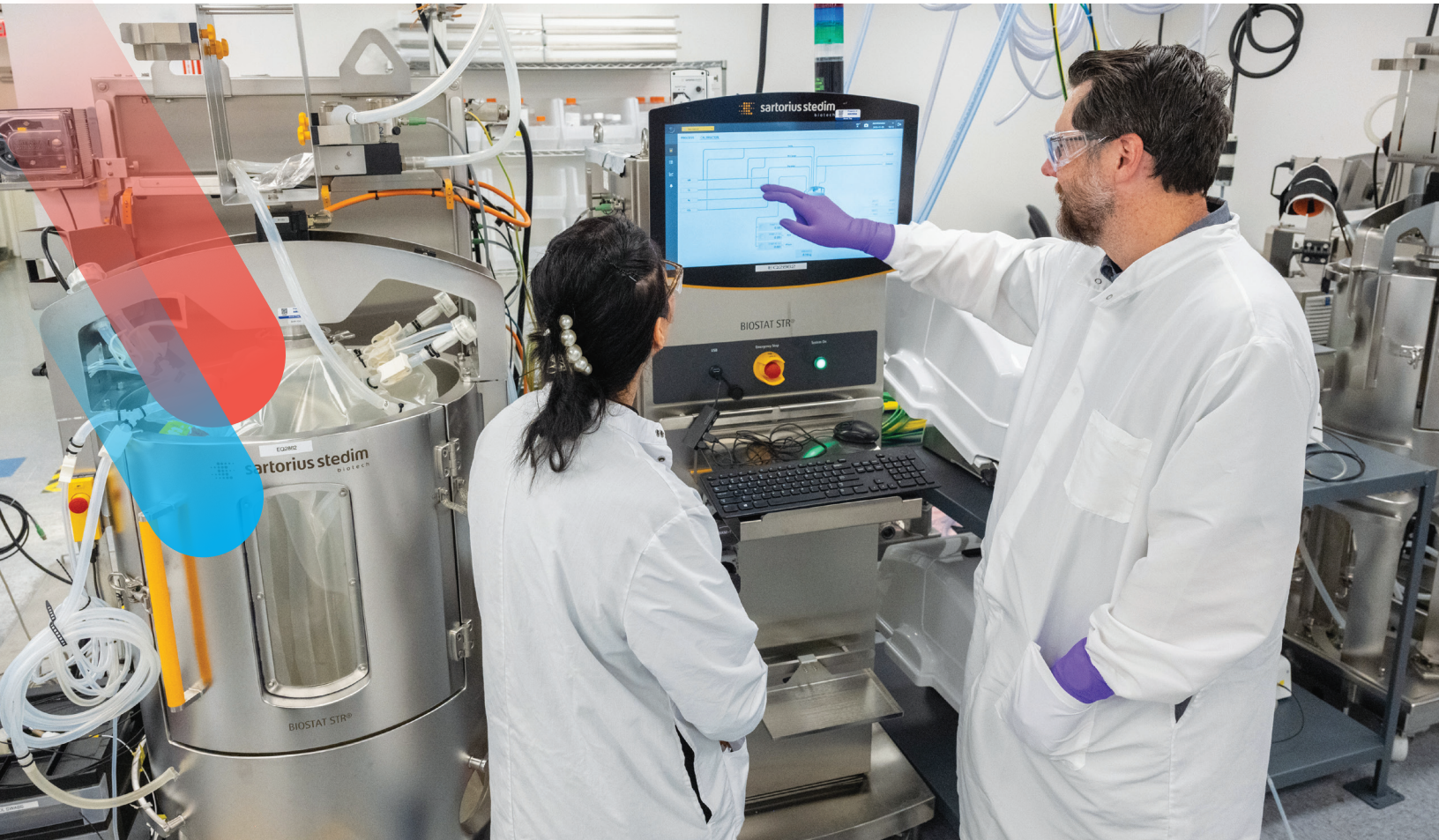
Process Development for Biologics

Developing biologic therapeutics presents unique challenges due to the intricate nature of large biomolecules and the variability inherent in biological systems. Optimizing production processes to ensure consistent product quality, scalability, and regulatory compliance requires specialized expertise and advanced technologies.

At Abzena, we offer comprehensive process development services tailored to the specific needs of your biologic therapeutics. Our integrated approach combines advanced cell culture and purification techniques to deliver scalable solutions as you progress your program onwards toward GMP manufacturing.

Support Across a Broad Array of Biologics

- mAbs and FAbs
- Antibody-Drug Conjugates (ADC)
- Antibody-Oligonucleotide Conjugates (AOC)
- Bispecifics
- Fusion Proteins
- Virus Like Proteins
- Viral Envelope Protein Antigens
- Immunotherapeutic Vaccine
- Bifunctional Immunotherapeutics



Expertise and Capabilities

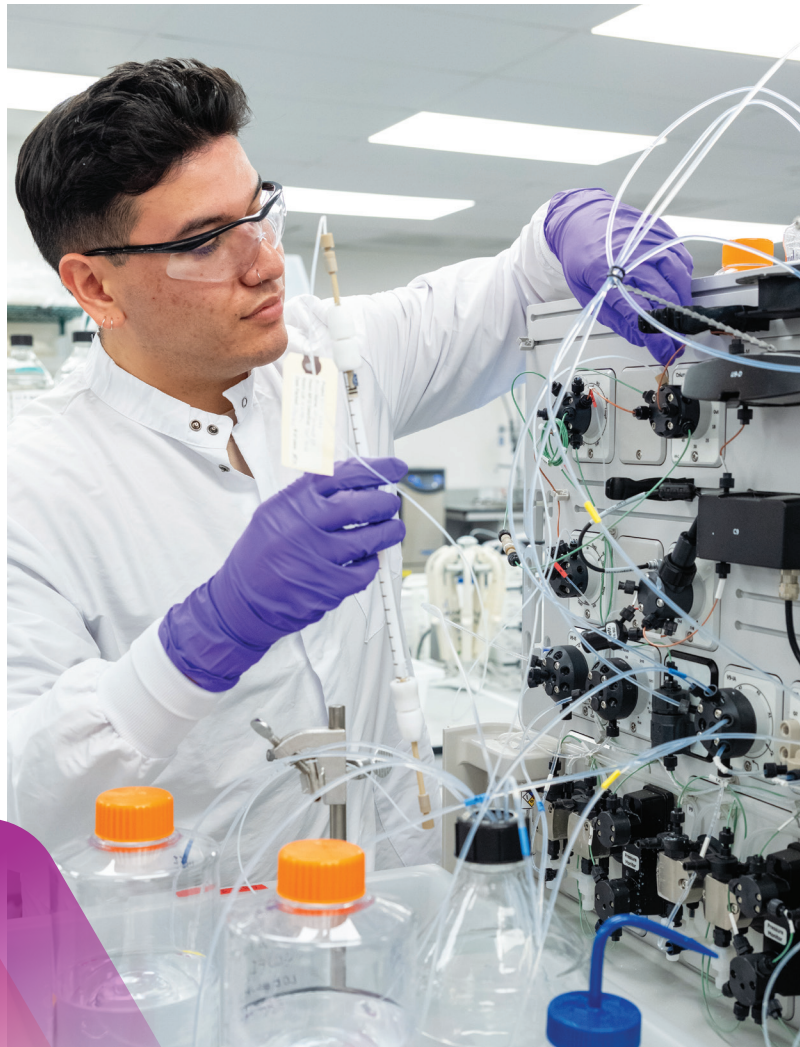
Our team brings extensive expertise in the following areas:

Cell Culture Process Development: We optimize upstream processes to enhance cell growth, productivity, and product quality.

- **Clone Selection and Media Screening:** Utilizing high-throughput screening platforms to identify optimal cell clones and media formulations that maximize protein expression and maintain desired quality attributes. Detailed analyses of cell line stability, growth kinetics, and metabolite profiles guide the selection of the best production clone.
- **Seed Train Development:** Establishing robust seed train protocols to ensure consistent inoculum quality and viability for large-scale bioreactor runs. Optimization of cryopreservation methods, numbers of passages, and seeding densities maintains cell health and performance.
- **High-Throughput Bioreactor Parameter Screening:** Employing scale-down bioreactor systems to rapidly optimize critical process parameters such as dissolved oxygen (DO), pH, temperature profiles, agitation rates, and feed strategies. This accelerates process development and identifies optimal conditions for large-scale production.
- **Centrifugation Development:** Optimizing cell harvest techniques by evaluating centrifugation conditions (e.g., g-force, flow rates) to maximize cell removal efficiency while minimizing shear stress and product loss.
- **Production Scale Bioreactors:** Our capabilities range from benchtop (250 mL) to pilot and GMP manufacturing scales (2L, 50L, 200L, 500L, 2000L) using single-use bioreactor systems. We ensure seamless scale-up by maintaining geometric and kinematic similarity across scales.
- **Cell Culture Parameter Optimization:** Fine-tuning culture conditions, including nutrient feed compositions, feeding strategies (fed-batch, perfusion), culture duration, and metabolic control to enhance titre and product quality.
- **Toxicology Production:** Producing GLP preclinical batches for toxicology studies, ensuring material consistency with future GMP batches regarding glycosylation patterns, charge variants, and impurity profiles.
- **Pilot Scale Confirmation Batches:** Executing pilot-scale runs to confirm process scalability and reproducibility, assessing mixing times, oxygen transfer rates (kLa), and shear effects on cell culture performance.
- **Scale-Down Model Development:** Creating and qualifying representative models to facilitate process characterization, optimization, and troubleshooting. These models are essential for risk mitigation and efficient process validation.
- **Process Characterization:** Performing statistical design of experiments (DoE) to identify critical process parameters (CPPs) to maintain critical quality attributes (CQAs) and develop in-process controls (IPCs), establishing a robust design space and control strategy.
- **Process Transfer:** Managing seamless technology transfer of processes into and out of process development to manufacturing facilities. We prepare comprehensive process descriptions, and transfer protocols to ensure efficient and accurate knowledge transfer.

Purification Process Development: Our downstream processing expertise ensures high purity and yield while maintaining critical quality attributes.

- **Chromatography Resin Screening:** Evaluating various chromatography resins (e.g., Protein A, ion exchange [IEX], hydrophobic interaction chromatography [HIC], mixed-mode [MMC]) for binding capacity, selectivity, and scalability. This identifies optimal purification strategies tailored to your molecule.



- **Filter Screening and Sizing:** Determining optimal filtration strategies, including depth filtration (e.g., diatomaceous earth, cellulose-based filters) and standard flow filtration (NFF) membranes. We aim to achieve the desired purity and clarity while maximizing product recovery.
- **Virus Filter Sizing:** Selecting virus filtration membranes (e.g., Planova™ filters, Viresolve® Pro) to ensure robust viral clearance, meeting regulatory requirements for product safety.
- **Tangential Flow Filtration (TFF) Development:** Optimizing ultrafiltration/diafiltration processes for concentration and buffer exchange. We select appropriate membrane materials (e.g., polyethersulfone, regenerated cellulose), molecular weight cut-offs (MWCO), and operating parameters such as transmembrane pressure (TMP) and crossflow rates.
- **Chromatography Parameter Screening and Optimization:** Fine-tuning chromatographic conditions such as pH, conductivity, gradient elution profiles, isocratic elution profiles, and flow rates. This improves separation efficiency, resolution, and product purity while minimizing process-related impurities and aggregates.
- **Toxicology Production:** Purifying bulk drug substance for preclinical evaluations, ensuring that material represents clinical-grade product in terms of purity, potency, and impurity profiles.
- **Pilot Scale Confirmation Batches:** Conduct purification runs at pilot scale to verify scalability, assess impurity profiles, confirm viral clearance steps, and verify process performance under GMP-like conditions.
- **Scale-Down Model Development:** Establishing and qualifying laboratory-scale models of downstream processes that replicate large-scale performance. This enables process optimization, and characterization with reduced material requirements.
- **Process Transfer:** Providing comprehensive documentation, including process descriptions, and detailed protocols to support the efficient transfer of purification processes to manufacturing facilities.
- **Support for Viral Clearance Studies:** Collaborating with Contract Research Organizations (CROs) to design and execute viral clearance validation studies. This includes small-scale spiking studies, scale-down model qualification, and preparation of regulatory documentation.

Advanced Analytical Support: Our state-of-the-art analytical capabilities support every stage of process development:

- **Analytical Method Development and Validation:** Developing and validating robust, phase-appropriate analytical methods for product characterization, including:
  - **Purity and Impurity Analysis:** High-performance liquid chromatography (HPLC), capillary electrophoresis sodium dodecyl sulfate (CE-SDS), size-exclusion chromatography (SEC), and reverse-phase (RP) HPLC.
  - **Identity and Structural Analysis:** Peptide mapping, intact mass analysis, N-terminal sequencing, and mass spectrometry (MS).
  - **Potency Assays:** Cell-based bioassays, binding assays (e.g., ELISA, surface plasmon resonance [SPR]), and enzymatic activity assays.
  - **Safety Testing:** Quantification of residual host cell proteins (HCPs) via ELISA, host cell DNA using quantitative PCR (qPCR), endotoxins through Limulus Amebocyte Lysate (LAL) assays.
- **Product Characterization:** Comprehensive analysis of biologic products, including:
  - **Glycosylation Profiling:** Analysis of glycan structures using techniques such as hydrophilic interaction liquid chromatography (HILIC)-UPLC-FLR-MS.
  - **Charge Variant Analysis:** Isoelectric focusing (IEF), imaged capillary isoelectric focusing (icIEF), and ion-exchange chromatography.
  - **Post-Translational Modifications:** Identifying and quantifying oxidation, deamidation, glycation, and other modifications that may affect product efficacy and stability.

Regulatory Compliance and Quality Assurance: Abzena adheres to the highest standards of regulatory compliance and quality assurance:

- **cGMP Compliance:** Our facilities and processes comply with current Good Manufacturing Practices, ensuring that all materials produced meet regulatory requirements for clinical use.
- **Quality Management Systems:** Robust quality |management systems are in place, including SOPs, deviation management, change control, document control, and comprehensive training programs to ensure compliance and data integrity.
- **Regulatory Support:** Providing support for regulatory submissions, including preparation and review of Chemistry, Manufacturing, and Controls (CMC) sections for Investigational New Drug (IND) applications, Biologics License Applications (BLA), and Marketing Authorization Applications (MAA).
- **Auditing and Inspections:** Experience with regulatory audits and inspections from agencies such as the FDA and EMA, ensuring readiness and compliance throughout the development process.

Summary

Partnering with Abzena accelerates your biologic therapeutic programs by delivering optimized, scalable, high-quality processes. Our specialized expertise reduces development and manufacturing risks, enhances efficiency, and positions your biologic for successful clinical and commercial outcomes. We navigate the complexities of biologic development so you can focus on bringing innovative therapies to patients faster.

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Advance your biologic therapeutics with confidence. Contact us to discuss how Abzena's customized process development solutions can drive your project forward and bring your product to market.

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