Miltenyi Bioindustry

Enhancing preclinical cell therapy development for clinical trial readiness

The transition from preclinical development to clinical trials is pivotal for cell therapy innovations. For many companies, the challenges of scaling processes, ensuring regulatory compliance, and maintaining consistency can hinder clinical trial readiness. This article explores how Miltenyi Bioindustry addresses these challenges through a holistic approach to process and analytical optimization.

The challenges of preclinical development

Limitations of manual and fragmented processes

The journey from preclinical development to clinical readiness is fraught with complexities. While the scientific promise of cell-based treatments continues to grow, the underlying processes often struggle to keep pace with the demands of scalability, consistency, and regulatory compliance.

One of the most significant challenges lies in the reliance on manual and modular processes. These methods, which may be adequate for early-stage experiments, introduce variability that can affect product quality and reproducibility. The use of open systems further compounds risks, such as contamination and extended timelines, which can jeopardize project milestones and clinical readiness . This variability is particularly evident at the cellular level, where ensuring consistency and reliability in assays requires rigorous controls.

Dirk Windgassen, who leads the Analytical Development team within Product Development/Process Sciences at Miltenyi Bioindustry, explains, “There’s variability in cells, so to ensure the assay is truly reproducible and reliable, and testing the intended markers, people have started using more controls in these assays, such as suitability criteria for the assay itself.”

Analytical frameworks present another critical hurdle. Many early-stage analytics are not designed with scalability in mind, creating bottlenecks when processes need to be qualified for clinical readiness.

The lack of robust assays to measure potency, purity, and stability often results in inefficiencies that delay progress and increase costs.

“If analytics are not considered early, we lose momentum and timelines. Timelines are critical for filings, and analytics need to be worked on from the start, in parallel with process development,” Windgassen adds.

Early optimization of both process and analytical frameworks is key to overcoming these barriers. By identifying and addressing these limitations at the preclinical stage, companies can establish a stronger foundation for clinical trial readiness, ensuring a smoother transition to clinical development.

Miltenyi Bioindustry's approach to holistic process optimization

Addressing the inherent challenges of preclinical development requires more than integrated solutions. Miltenyi Bioindustry takes a collaborative, client-focused approach that combines process optimization with advanced analytical development, ensuring clients are prepared for clinical success.

Automation is a powerful tool in Miltenyi Bioindustry's methodology, minimizing variability, reducing contamination risks, and optimizing timelines. However, true optimization also involves tailoring processes to the unique needs of each therapy.

“We start with an initial consultative evaluation of relevant client information, product data, workflows, and preclinical or R&D studies,” explains Kunal Patel, Head of Process Engineering.

“From there, we develop a comprehensive product development plan that is phase-appropriate and

follows quality-by-design principles." This collaboration ensures that early decisions support both scalability and compliance.

A platform-based perspective enhances Miltenyi Bioindustry's flexibility. Their platforms adapt to diverse cellular therapeutics, spanning autologous and allogeneic therapies.

"By using a platform-based approach, clients can leverage existing process knowledge and characterization that we've already performed on the platform," explains Patel.

"This allows us to tremendously shorten development time while ensuring a robust process with reproducible results." This adaptability extends to custom applications when standard workflows do not meet specific product requirements.

The platform approach also extends to analytical development, establishing control and consistency in assays to demonstrate potency, purity, and stability. As Windgassen explains, "In flow cytometry assays, for example, we have established reagent panels and workflows using automated analysis tools. These tools reduce inefficiencies while meeting regulatory standards."

By embedding compliance considerations into every step, Miltenyi Bioindustry ensures alignment with Good Manufacturing Practice (GMP) standards, minimizing risks during regulatory review.

"At the end of the development phase, after we have a design freeze and ensured consistency, we move into GMP activities, leading to process qualification and IND- or CTA-enabling runs," notes Patel. This seamless transition supports regulatory success while enabling efficient scale-up.

Ensuring preclinical success

Preclinical development sets the stage for every breakthrough in cell therapy. Miltenyi Bioindustry's commitment to process and analytical optimization ensures that clients are equipped not only to achieve clinical trial readiness but also to build scalable, compliant processes that support long-term clinical and commercial success.

By combining expertise, innovation, and flexibility, Miltenyi Bioindustry offers a clear path through the complexities of cell therapy development. To learn how Miltenyi Bioindustry can help streamline your preclinical journey, explore their approach to process and analytical optimization today.

Case Study: Automating an autologous cell therapy process

Client X's initial autologous cell therapy process aimed to restore fetal hemoglobin (HbF) production in patient hematopoietic stem cells. This 4-day manufacturing workflow relied on open, manual methods across multiple platforms, creating inefficiencies and risks. Key steps included CD34$^+$ cell enrichment on the CliniMACS® Plus instrument, manual washes and resuspensions, and mRNA electroporation using the MaxCyte GT system. The process concluded with manual formulation and cryopreservation.

Miltenyi Bioindustry collaborated with Client X to automate and close this workflow using the CliniMACS® Prodigy platform. A custom application program increased CD34$^+$ enrichment capacity by 50%, while temperature control, media washes, and culturing were fully automated. For electroporation, Miltenyi Bioindostry integrated a CliniMACS® Electroporator to automate rebuffering, electroporation, and recovery of gene edited product, while improving the editing efficiency and cell viability. For formulation, a CliniMACS® Formulation Unit was employed to streamline drug product bag filling.

This transition reduced hands-on time, minimized contamination risks, and enhanced scalability, aligning the process with IND & CTA requirements. While a custom wash buffer was needed to address challenges with cell recovery, the overall targeting efficiency remained consistent. The outcome demonstrates Miltenyi Bioindustry's ability to optimize complex cell therapy workflows for regulatory and clinical success.

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Miltenyi Biotec Inc. | Phone +1 866 811 4466 | Fax +1 530 745 2806 | bioindustry@miltenyi.com | **www.miltenyibioindustry.com**
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