Miltenyi Biotec

Unlocking cell & gene therapy performance: proven strategies for modern operations

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Building a scalable global T cell manufacturing platform

See how a complex T cell process was streamlined into a scalable model built for growth, consistency, and global rollout.

How it's done: building a scalable, global manufacturing platform for TCR-T cell manufacturing

- **Boost batch yield 3x:** deliver sufficient viable T cells per batch to meet solid tumor TCR-T cell demand.
- **Cut manual handling by >70%:** free expert capacity and increase process quality.
- **Build scheduling agility:** use cryopreserved starting material and drug product to align production with patient treatment timelines and increase accessibility.
- **Scale globally with confidence:** transfer standardized processes across GMP manufacturing sites without quality loss.
- **Lock in quality at every run:** automated flow cytometry delivers critical insights and drives faster, evidence-based decisions during process optimization.

The bottleneck

A clinical-stage biotech company advancing a TCR-T cell program for solid tumors, recognized its manual manufacturing model could not meet the scale, quality, or global footprint required for late-phase clinical trials. Initial workflows had been built for blood cancers and relied on modular, operator-intensive methods that struggled with batch variability, cleanroom dependency, and tech transfer inefficiencies. These limitations placed the success of clinical expansion and eventual cost efficiency at risk.

The breakthrough

In order to meet the requirements, a standardized, scalable solution using the **T Cell Transduction – Large Scale (TCT-LS)** process on the **CliniMACS Prodigy® Platform** was developed and implemented, accompanied by **automated QC testing** on the **MACSQuant® Analyzer.**

Strategic outcomes

Operational efficiency at scale

Manufacturing of TCR-T cells involves multiple complex steps that traditionally require extensive manual labor and increase the risk for batch failure. However, integrating six critical operations into one automated, closed system not only simplified the process but also significantly reduced hands-on time and substantially increased cell production capacity:

- Six core steps (including T cell selection, activation, transduction, expansion, formulation, and cryopreservation) ran seamlessly on the CliniMACS Prodigy Platform.
- Hands-on operator time dropped by >70% thanks to end-to-end automation.
- Process automation enabled consistent manufacturing of the target dose of TCR-T cells, from leukapheresis starting material to final product.
- Expanded cultivation chamber increased batch yield 3-fold, exceeding 1.5×10^{10} viable T cells.

Enhanced flexibility, consistent quality, built for scale

Uncompromising quality while scaling is critical for meeting both regulatory expectations and patient needs. The process protocol was optimized by adapting critical process parameters to meet acceptance criteria and relevant product attributes:

- Consistently achieved >98% $CD3^+$ T cell purity with balanced $CD4^+/CD8^+$ T cell ratios.
- Preserved critical T cell phenotypes (T stem cell memory subset) and post-thaw viability of the drug product.
- Enabled automated manufacturing from cryopreserved apheresis material, improving scheduling, logistics, and re-manufacturing resilience.

Global consistency, local delivery

Ensuring patient access and consistent product quality was central to the tech transfer strategy. The robustness of the standardized TCT-LS process enabled the tech transfer into three GMP manufacturing sites across North America and Europe:

- All sites achieved equivalent performance with minimal rework.
- Lower cleanroom classification requirements enabled faster facility ramp-up.
- 72 production runs received a batch success rate of 89%, here deviations could be traced back to source material, not process design.
- Introduced a semi-automated fill strategy for early-stage trials.

The impact

This case study demonstrates that targeted process optimization, harmonization, and technology integration can fundamentally strengthen the scalability, reliability, and resilience of cell and gene therapy (CGT) manufacturing. By enabling high-dose therapy production at commercial scale without sacrificing quality, the company has set the path for a new operational benchmark for the industry. Looking ahead, embedding these capabilities across the full CGT value chain – from early development to global distribution – will be critical to meet rising patient demand, accelerate commercialization timelines, and expand access. Future advancements will hinge on further automation, digital integration, and data-driven process control, ensuring that the transformative potential of CGT is delivered to patients with consistency, speed, and uncompromising quality.

QC-ready assays by design

Explore how early analytical alignment can turn one of CGT's biggest bottlenecks into a development accelerator.

What is in it for you?

- **Accelerate IND submission by >6 months:** early definition of analytical requirements and using a standardized analytical platform reduced development-to-submission time.
- **Cut flow cytometry gating setup time by 40%:** gating setup time reduced significantly through an automated, site-agnostic assay setup, streamlining tech transfer.
- **Avoid redundant validation repeats:** streamlined, pre-validated platforms prevented costly rework.
- **Support global reproducibility:** site-agnostic methods minimized requalification efforts.
- **Ensure regulatory readiness:** develop a clear and gap-free analytical package to answer authority queries promptly without costly delays.

The bottleneck

Experience across multiple cell and gene therapy (CGT) programs shows that analytical methods developed in Research and Development often fail to meet GMP QC expectations, where stringent regulatory requirements like ICH Q2 (R2) and USP <1220> apply. Missing controls, undefined sample-suitability limits, loose development protocols, and poorly defined acceptance criteria are common pitfalls that can cause costly delays when transferring assays from analytical development (AD) to QC, jeopardizing regulatory submissions and slowing patient access to life-saving therapies.

The breakthrough

To shift analytical developments from a fragmented to a streamlined process, the **Analytical Target Profile (ATP)** was defined early in collaboration with all stakeholders. Key parameters, including instrument assay setup, gating strategies, and reagents were standardized from the start using the **MACSQuant® Analyzer** flow cytometry platform.

Strategic outcomes

Accelerating timelines with ATP-driven design and early alignment

Late-stage surprises are a major source of risk to program timelines and regulatory milestones. These often occur when reproducible data are missing for critical assay parameters such as reagent concentration, incubation time, and instrument settings.

Embedding ATP rigor early and aligning key stakeholders across AD, QC, and specialized teams like Analytical Science & Technology (ASAT) on assay purpose, precision limits, reportable range, and constraints before lab work starts significantly reduces these risks and accelerates progress.

- Avoid costly delays through cross-functional ATP planning and save validation repeats .
- Using both ATP and ASAT expertise accelerates IND timelines up to 40%.
- Eliminate rework and last-minute corrective and preventive actions (CAPAs) through early cross-functional alignment between AD, QC, ASAT and CDMO partners.
- Increase confidence in data packages by building reproducibility and robustness in from the start, so teams spend less time troubleshooting.
- Reduce requalification through early platform alignment, streamlining qualification across AD and QC teams.

De-risking assay transfer through platform standardization

Assay variability is one of the biggest risks during tech transfer in CGT. Inconsistent gating strategies, manual reagent preparation, and instrument drift introduce delays, requalification work, and regulatory uncertainty.
The standardized MACSQuant Analyzer flow cytometry platform addresses this by locking gating strategies,

instrument assay setup, and reagents from the start for faster and reproducible assay transfer:

- Higher consistency across sites with operator-independent, algorithm-driven gating and analysis using Express Modes.
- Reduced gating setup time and analyst workload by 40% using Express Modes for automated flow cytometry analysis.
- Streamlined multi-instrument harmonization and assay transfer with Smart Gain technology adjusting PMT voltages to predefined target values automatically.
- Simplified workflow and drastic time savings with ready-to-use dry antibody cocktails, like StainExpress™ Dry Antibody Cocktails.
- Harmonized technologies, between the MACSQuant Analyzer and CliniMACS Prodigy Platform, run across AD, QC, and GMP suites, enabling closed, automated cell processing and flow analysis while reducing requalification during scale-up.

The impact

This case study demonstrates that embedding ATP diligence and platform standardization early transforms analytical tech transfer to QC from a potential bottleneck into a strategic accelerator. IND readiness was achieved more than six months ahead of schedule, giving programs a critical head start in clinical development.

Validation hurdles that previously required duplicate cycles were streamlined, reducing both costs and operational strain. Standardized, site-agnostic methods ensured assays ran consistently across sites, removing the bottleneck of requalification and strengthening global scalability.

With robust, regulatory-ready datasets in place, FDA queries were addressed proactively. The result is not just faster timelines, but a competitive edge where speed, reliability, and regulatory confidence converge to bring transformative therapies to patients worldwide.

Implementing scalable training excellence in CGT manufacturing

Discover how a modern, lifecycle-aligned training platform turns CGT operators into confident, compliant specialists.

Structured training for scalable CGT manufacturing excellence

- **Stage-aligned capabilities:** modular training builds critical skills when and where they are needed across the CGT lifecycle.
- **Faster onboarding, consistent execution:** standardized content accelerates ramp-up and ensures reliable performance across sites.
- **Reduced risk, higher output:** fewer deviations and batch failures lower costs and increase manufacturing productivity.

The bottleneck

Working in the CGT field means facing unique challenges every day. From the complexity of advanced therapy medicinal products (ATMPs) to the pressure of accelerating timelines, the journey from discovery to commercialization is anything but straightforward. Operator training remains one of the most underestimated bottlenecks in CGT manufacturing. Rapidly evolving technologies, frequent process changes, and stringent regulatory requirements demand a workforce that is not only qualified, but continuously upskilled. Additionally, traditional training approaches often struggle to keep pace, leading to extended onboarding times, inconsistent execution, and increased risk of deviations or batch failures, which ultimately raises production costs.

The breakthrough

Providing high-quality therapies requires being an expert in every aspect of the cell manufacturing process and associated analytics. To address these challenges, a comprehensive and agile training platform was developed, designed specifically for CGT manufacturing environments. This breakthrough approach delivers extensive operator training and continuous support through a structured program, ensuring knowledge is effectively transferred and sustained across teams. Training is embedded at every stage of the product lifecycle – from process development through clinical manufacturing and into commercial production – providing operators with the right skills at the right time. Fully aligned with site-specific standard operating procedures (SOPs) and tailored to each unique manufacturing process, the program offers highly customized training pathways that reflect real-world operations. Built to evolve alongside technologies, processes, and regulations, the platform enables rapid updates and continuous improvement, ensuring operators remain competent, compliant, and confident as CGT manufacturing scales.

Strategic outcomes

The program aligns with the drug development path and focuses on what operators must execute at each phase:

- Pre-clinical phase: **Essential Training** – standardized courses for quick adoption during process development.
- Clinical/Commercial phases: **High-Compliance Training (HCT)** – tailored training for the execution of manufacturing process-specific SOP & Manufacturing Batch Records (MBR), as well as deviation handling.
- Clinical/Commercial phases: **Train-the-Trainer (TTT) program** – certify trainers to sustain in-house knowledge and deliver standardized operator training with quality of the technology supplier.

Training development journey

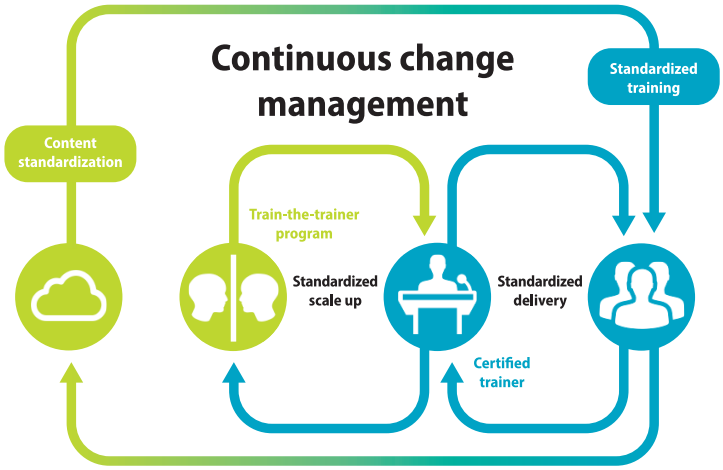

Figure 1:
The training development journey supported by Miltenyi Biotec. Training development can be initiated alongside the development of a manufacturing process. Upon finalizing the manufacturing process, the training is standardized and implemented at the manufacturing site. To accommodate the increase in new operators during manufacturing scale-up, the TTT program supports the development of in-house trainer candidates, enabling them to deliver standardized training with the quality of certified Miltenyi Biotec trainers. Additionally, process changes are systematically integrated into standardized training content by continuous change management.

A fast and efficient training roll-out

This case summarizes a multi-site implementation of the training platform within a European CGT manufacturing network. Implementation began mid-2022 with content standardization and SOP author training completed within three months. In the following five months, 18 operators had already received the standardized training. In 2023, the program scaled significantly, onboarding 36 additional operators. Early 2024 marked a major expansion: 69 operators completed training alongside 24 expert-level participants, while 18 operators underwent retraining. The TTT program was launched in March 2024 with two candidates, and within six months, certified trainers were delivering sessions independently. By late 2024, all operator training had transitioned fully in-house. In 2025, the program continued to grow, adding 1 certified trainer, 27 operators, and 18 experts, with additional sites reporting 69 operator trainees and further retraining planned.

Impact

By targeting the right competencies at each development stage, the platform accelerates onboarding, increases operator productivity, and lowers the likelihood of deviations. The TTT program sustains knowledge in-house, supports scale-up, and preserves performance as teams expand and processes evolve. Ultimately, training shifts from a bottleneck to a strategic enabler for reliable, compliant CGT manufacturing.

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