

Miltenyi Biotec

Large-scale manufacturing of gene-engineered hematopoietic stem cells

CliniMACS Prodigy® HSC Transduction – Large Scale Process

Application

The CliniMACS Prodigy Hematopoietic Stem Cell Transduction – Large Scale (HSCT-LS) Process allows a simplified, closed, and automated gene engineering of human CD34⁺ cells from patient material for large-scale manufacturing of gene-engineered hematopoietic stem cells (HSCs).

This application sheet provides an overview of the specifications, required materials, and setup configuration to run the large-scale HSC transduction process using the CliniMACS Prodigy Tubing Set (TS) 620. Furthermore, it outlines the complete workflow and presents performance data.

Specifications

Cellular starting material:	CD34⁺ cells, e.g., enriched from mobilized leukapheresis
Starting cell number:	Minimum 2×10^7 cells, scalable up to 2.4×10^9 cells
Starting sample volume:	40–2280 mL
Culture volume:	40*–600 mL
Final product:	Gene-engineered CD34⁺ cells
Final product volume:	Four different harvest types available (see user manual): • Optional rebuffering step • Optional transfer of cells into Target Cell Bag
Process time:	2–3 days

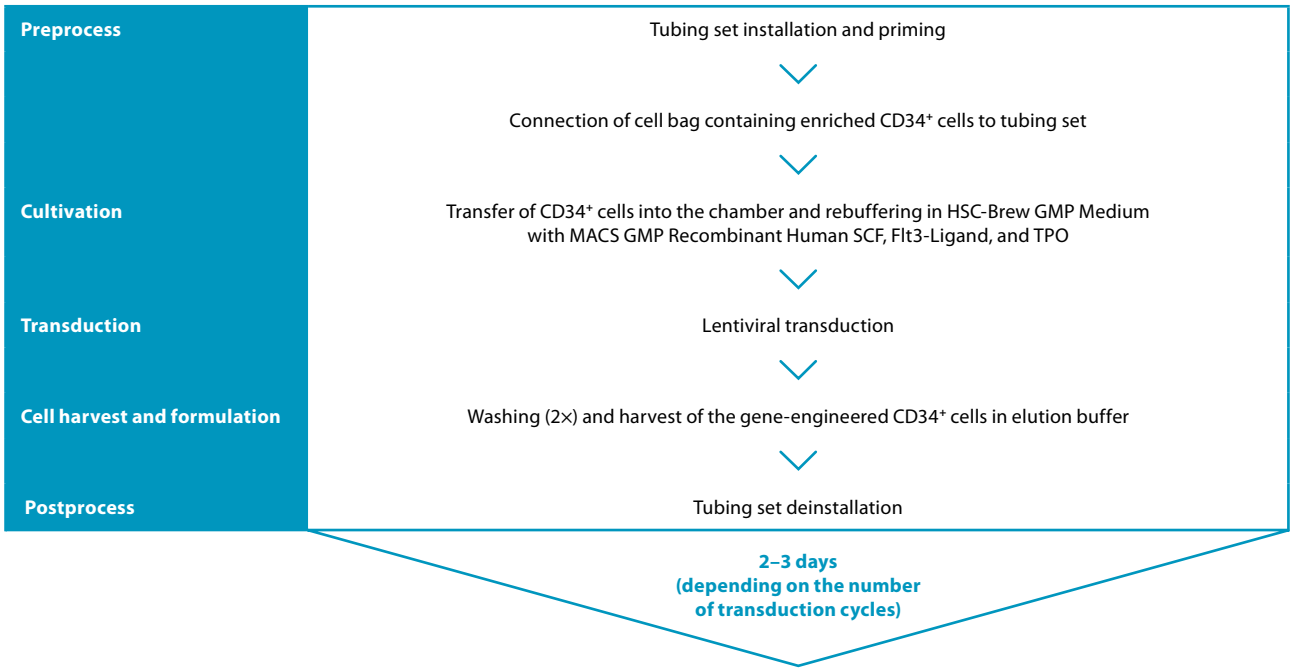
*For smaller cultivation volumes, small adjustments are needed. Please contact Miltenyi Biotec's Technical Support for more information.

Products required

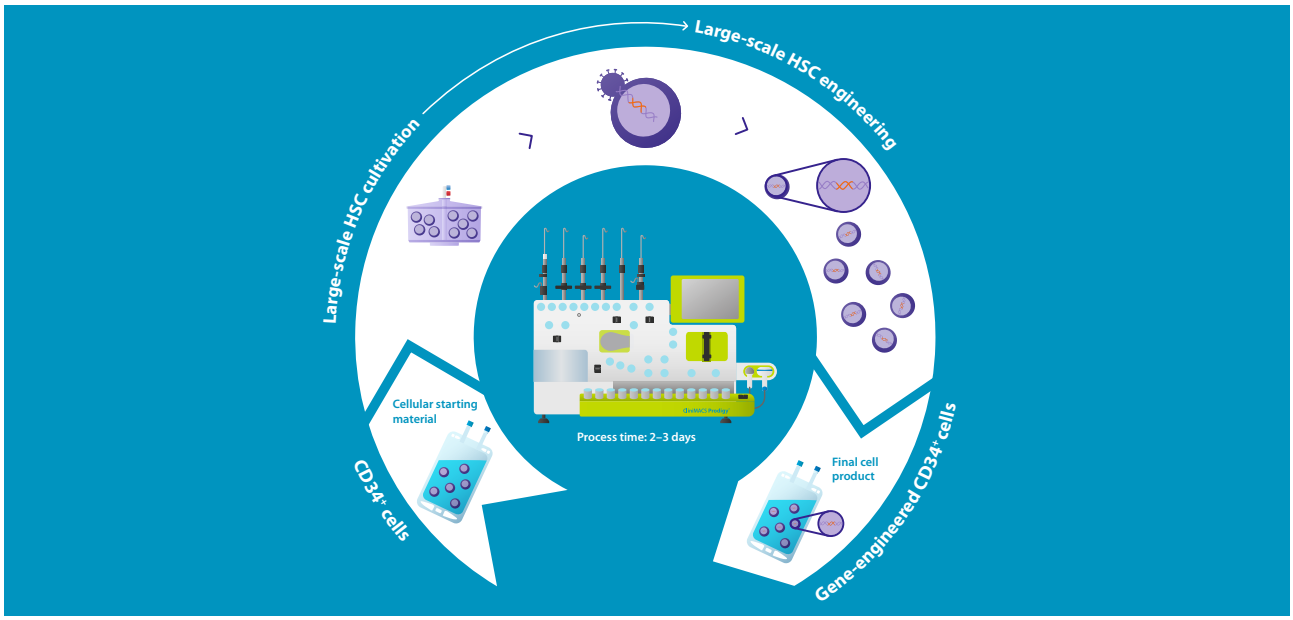
Products	Quantity*
CliniMACS® and MACS® GMP Products	
CliniMACS Prodigy Instrument	1 piece
CliniMACS Prodigy TS 620	1 set
HSC-Brew GMP Medium	Up to 2 L
MACS GMP Recombinant Human SCF*	2.00×10^5 *U*
MACS GMP Recombinant Human Flt3-Ligand*	1.44×10^5 *U*
MACS GMP Recombinant Human TPO*	8.00×10^5 *U*
Additional materials	
1 m Tube Extension (Miltenyi Biotec)	1 piece
3-way Tube Adaptor (Miltenyi Biotec)	At least one piece
Luer/Spike Interconnector (Miltenyi Biotec)	At least one piece
Elution solution (physiological sodium chloride solution with 0.5% (w/v) human serum albumin)	1 L
Viral vector	10 mL recommended
20 mL Reagent Bag (Miltenyi Biotec)	1 bag
Disposable bags	At least 1 bag
Syringes	Depending on use
Human serum albumin (HSA)**	Use according to the instructions for use

*Quantities recommended for a one-hit transduction of 1×10^8 cells in a 100 mL cultivation without stage load during culture setup, ending in end of culture type 1. Specific material quantities depend on the process configuration, setup, and protocol. For alternative process configurations, consult the user manual or your Miltenyi Biotec representative.
**Only HSA approved for clinical use in your country should be used.

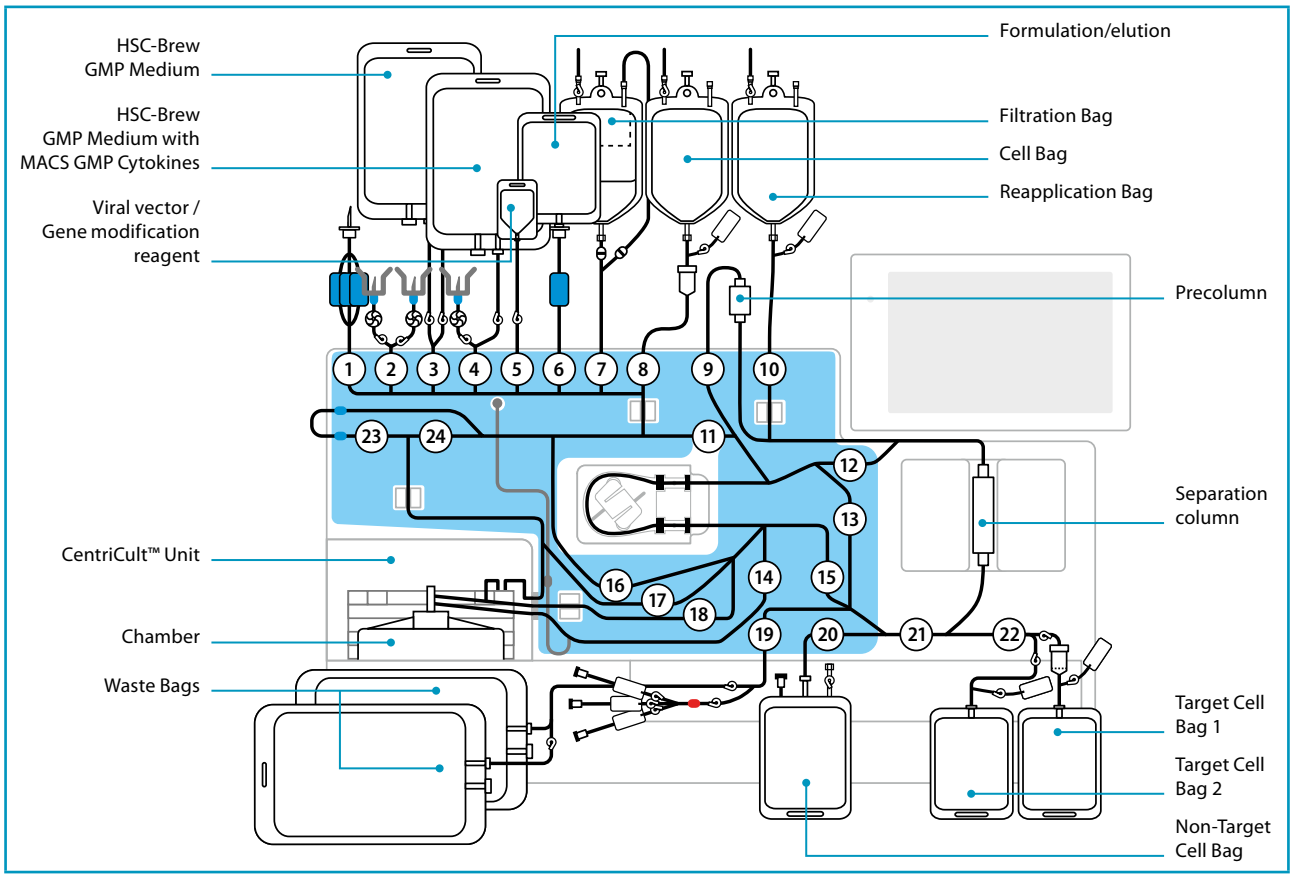
Process overview: CliniMACS Prodigy HSC Transduction – Large Scale Process



Workflow overview



CliniMACS Prodigy TS 620 setup for HSC Transduction – Large Scale



Performance data

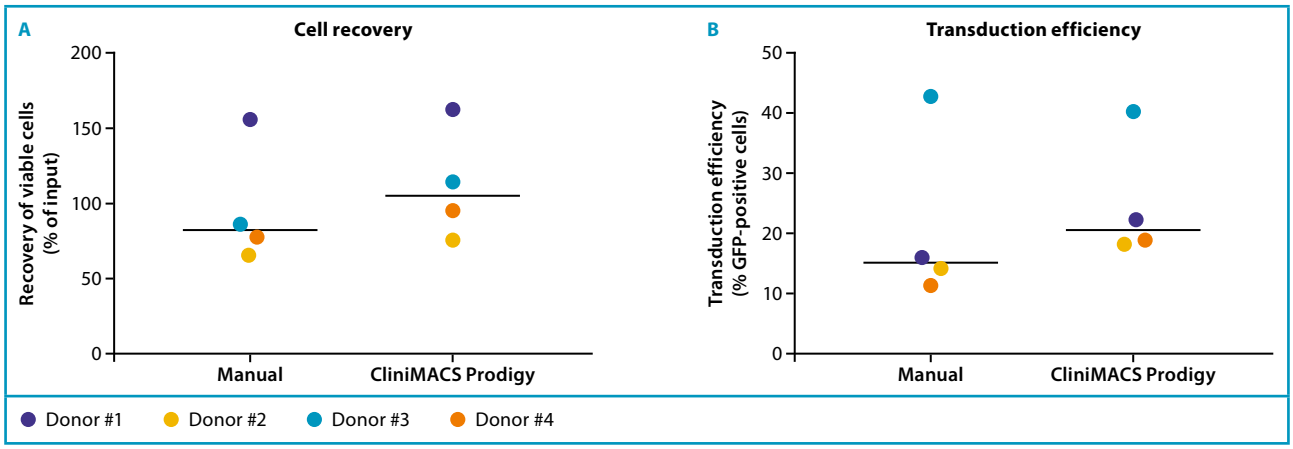


Figure 1: Both cell recovery and transduction efficiency were comparable between automated processing on the CliniMACS Prodigy and the corresponding manual protocols. Human CD34⁺ cells enriched from mobilized leukapheresis products of four donors were transferred into HSC-Brew GMP Medium supplemented with MACS GMP Recombinant Human Flt3-Ligand, SCF, and TPO on day 0. Culture volumes for the four donors were larger than 350 mL. On day 1, cells were transduced with a GFP-encoding lentiviral vector (MOI 30) using the CliniMACS Prodigy HSCT-LS Process. In parallel, the same workflow was performed manually using a standard protocol with 24-well plates. Cell recovery was evaluated on day 2 (A). Harvested gene-engineered CD34⁺ cells were further cultured manually in 96-well plates, and transduction efficiency was assessed on day 6 (B).

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In the EU, the CliniMACS System components are available as CE-marked medical devices for their respective intended use, unless otherwise stated. The CliniMACS Reagents and Biotin Conjugates are intended for *in vitro* use only and are not designated for therapeutic use or direct infusion into patients. The CliniMACS Reagents in combination with the CliniMACS System are intended to separate human cells. Miltenyi Biotec as the manufacturer of the CliniMACS System does not give any recommendations regarding the use of separated cells for therapeutic purposes and does not make any claims regarding a clinical benefit. For the manufacturing and use of target cells in humans, the national legislation and regulations – e.g., for the EU the Directive 2004/23/EC ("human tissues and cells"), or the Directive 2002/98/EC ("human blood and blood components") – must be followed. Thus, any clinical application of the target cells is exclusively within the responsibility of the user of a CliniMACS System.
In the US, the CliniMACS CD34 Reagent System, including the CliniMACS Plus Instrument, CliniMACS CD34 Reagent, CliniMACS Tubing Sets TS and LS, and the CliniMACS PBS/EDTA Buffer, is FDA approved as a Humanitarian Use Device (HUD), authorized by U.S. Federal law for use in the treatment of patients with acute myeloid leukemia (AML) in first complete remission. The effectiveness of the device for this indication has not been demonstrated. Other products of the CliniMACS Product Line are available for use only under an approved Investigational New Drug (IND) application, Investigational Device Exemption (IDE) or FDA approval.
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