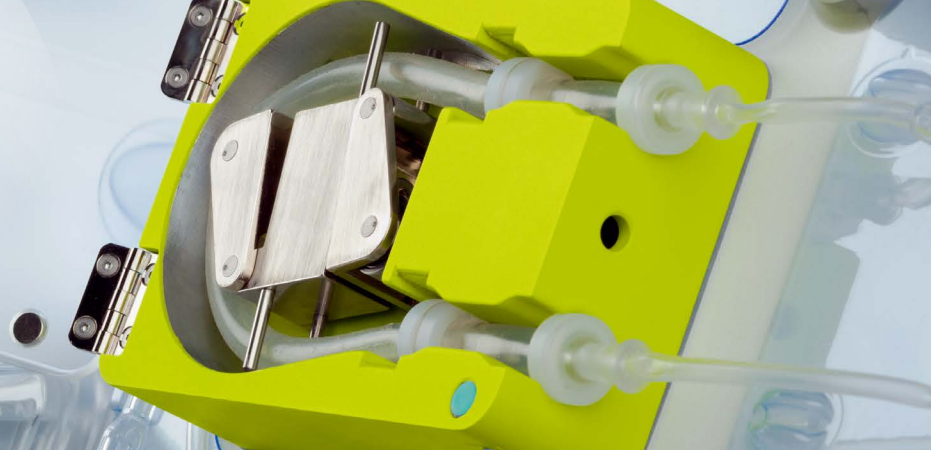




Miltenyi Biotec



CliniMACS Prodigy® Adherent Cell Culture System

GMP-compliant human mesenchymal stem cell expansion process

Application

The CliniMACS Prodigy® Adherent Cell Culture System allows GMP-compliant and clinical scale human mesenchymal stem cell (MSC) expansion starting from 30–100 mL human bone marrow (BM) samples.

This application sheet gives an overview of the entire process and provides information about the required materials and the subsequent quality control assays. In addition, it elucidates the setup of the tubing set CliniMACS Prodigy TS 730 and the performance data.

Specifications

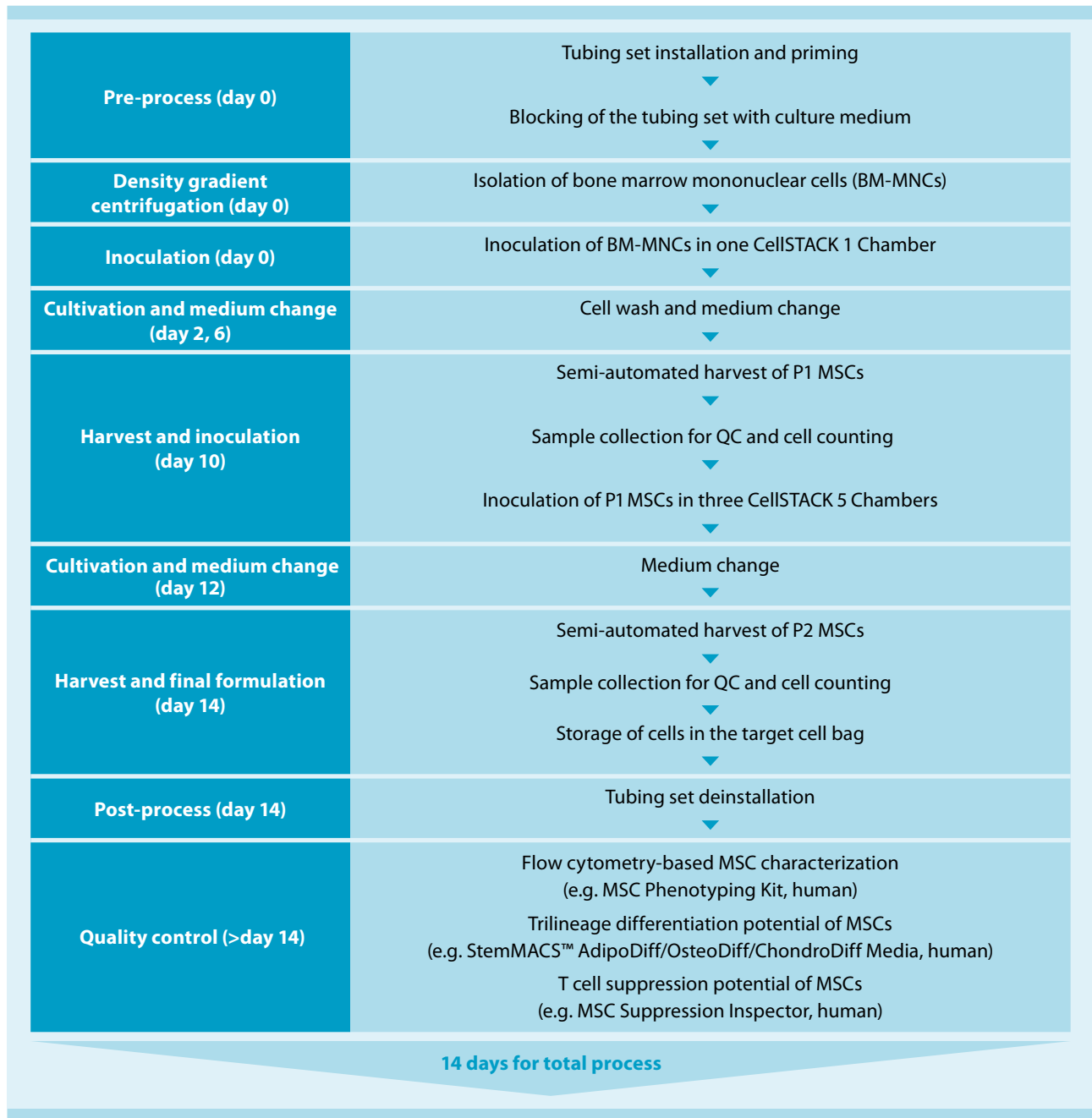
Process capacity:	scalable (up to 4×10^9 P2 MSCs)
Starting sample volume:	30–100 mL human bone marrow sample
Final product volume:	approx. 110 mL
Total process time:	14 days
Total hands-on time:	approx. 2.8 h

Products

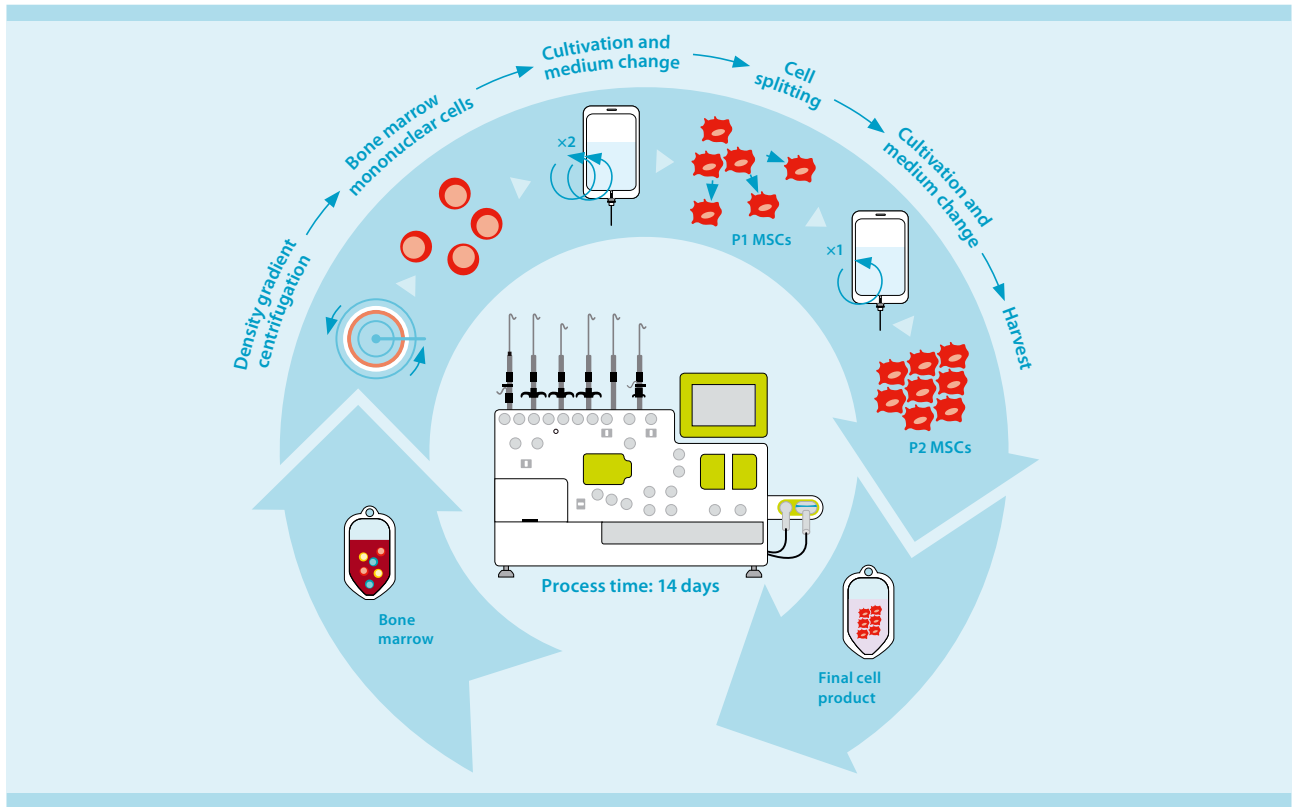
Consumables	Amount required
CliniMACS Prodigy® Instrument	1 piece
CliniMACS Prodigy TS 730	1 set
MSC-Brew GMP Medium	5 L
CliniMACS® PBS/EDTA Buffer (3×1 L)	2 L
CliniMACS® PBS/EDTA Buffer (2×3 L)	3 L
1 m Tube Extension	1 piece
3-way Tube Adapter	1 piece

Additional materials	Amount required
Corning® CellSTACK® accessories, fill cap, 3.2 mm I.D. tubing, female Luer Lock with male luer plug	4 pieces
Corning CellSTACK 5 Chamber	3 pieces
Corning CellSTACK 1 Chamber	1 piece
Luer/Spike Interconnector	3 pieces
Transfer Bag 600 mL	3 pieces
Ficoll®-Paque Premium, 100 mL, GE-Healthcare	160 mL
CTS™ TrypLE™ Select Enzyme, 100 mL, Thermo Fisher	800 mL
Defined Trypsin Inhibitor, 100 mL, Thermo Fisher	450 mL
HSA (to be added to the CliniMACS PBS/EDTA Buffer during the density gradient centrifugation)	final concentration 0.5% (w/v)

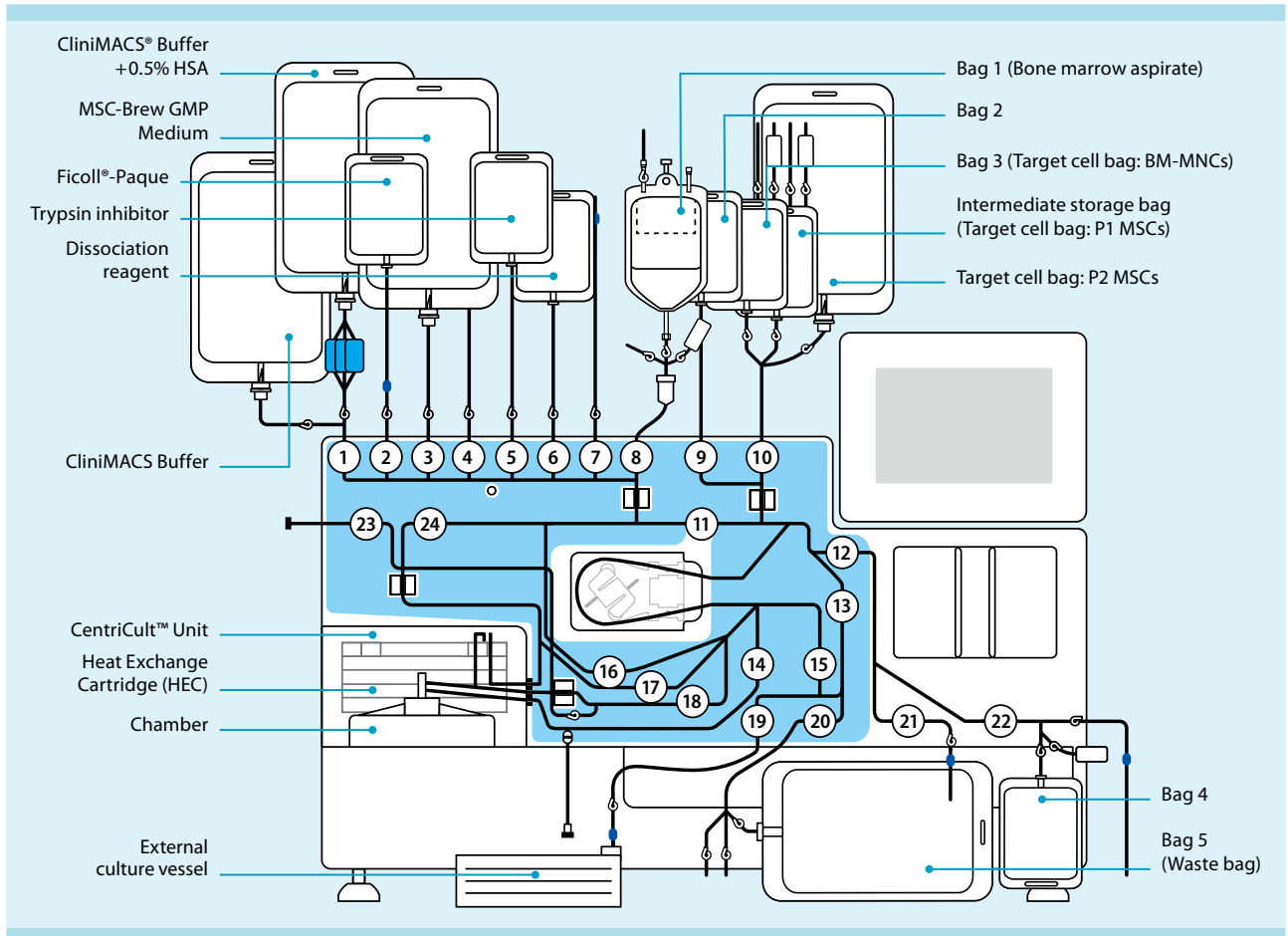
Process overview for MSC expansion



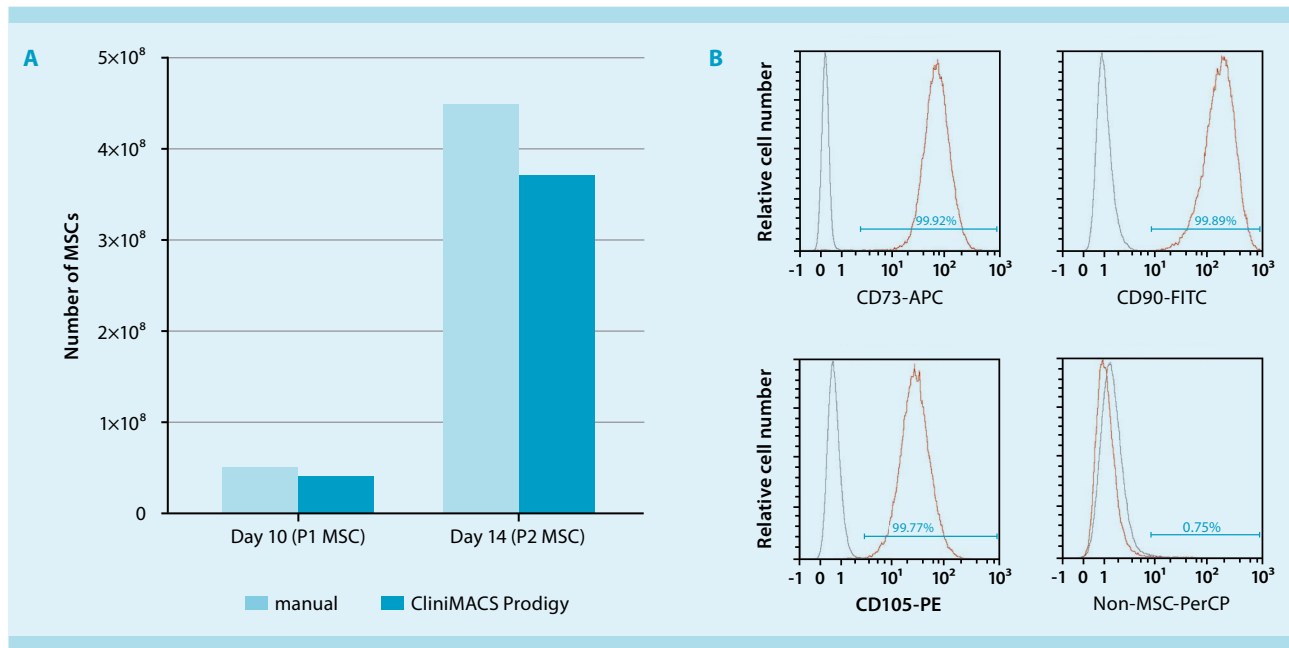
Principle of the MSC expansion process using the CliniMACS Prodigy®



CliniMACS Prodigy TS 730 setup for MSC expansion



Performance data



Human MSCs were isolated from bone marrow-mononuclear cells (BM-MNCs) and initially seeded in one CellSTACK 1 Chamber, then expanded in three CellSTACK 5 Chambers in MSC-Brew GMP Medium using the CliniMACS Prodigy® Adherent Cell Culture System. The same experiment was facilitated manually following a standard protocol using T175 flasks. (A) After 14 days of expansion, similar cell numbers of P2 MSCs were harvested by using the CliniMACS Prodigy Adherent Cell Culture System (3.8×10^8) compared to manual handling (4.5×10^8). (B) A flow cytometry-based quality control assay using the MSC Phenotyping Kit was performed to confirm the quality of resulting MSCs processed with the CliniMACS Prodigy Adherent Cell Culture System. Harvested MSCs met ISCT criteria showing high expression levels of MSC specific markers CD73, CD90, CD105, and very low expression of non-MS-C markers.



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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. CliniMACS GMP MicroBeads are for research use and *ex vivo* cell processing only. CliniMACS MicroBeads are for research use only and not for human therapeutic or diagnostic use. CentriCult, CliniMACS, CliniMACS Prodigy, MACS, the Miltenyi Biotec logo, and StemMACS are registered trademarks or trademarks of Miltenyi Biotec and/or its affiliates in various countries worldwide. Ficoll and Ficoll-Paque are trademarks of GE Healthcare companies. All other trademarks mentioned in this document are the property of their respective owners and are used for identification purposes only. Copyright © 2020 Miltenyi Biotec and/or its affiliates. All rights reserved.