Miltenyi Biotec

MACS® GMP Products

Facilitate *ex vivo* processing for cell manufacturing

Raw and ancillary materials

Complete cell product manufacturing solutions

Quality management and regulatory support

Advancing cell therapies

Quality assurance: where it counts

The success of your cell product depends on the quality of the raw materials. MACS® GMP Products are designed for *ex vivo* processing of human cells and are manufactured in compliance with relevant GMP-guidelines.

Rely on MACS® GMP Products. Quality guaranteed.

Contents

Raw and ancillary materials

Facilitate *ex vivo* processing for cell manufacturing

The quality of raw or ancillary materials used for the manufacture of cell-based and gene therapy products such as

- Fluorescent antibodies
- Antigens
- Cell culture bags
- Cell culture media
- Cytokines

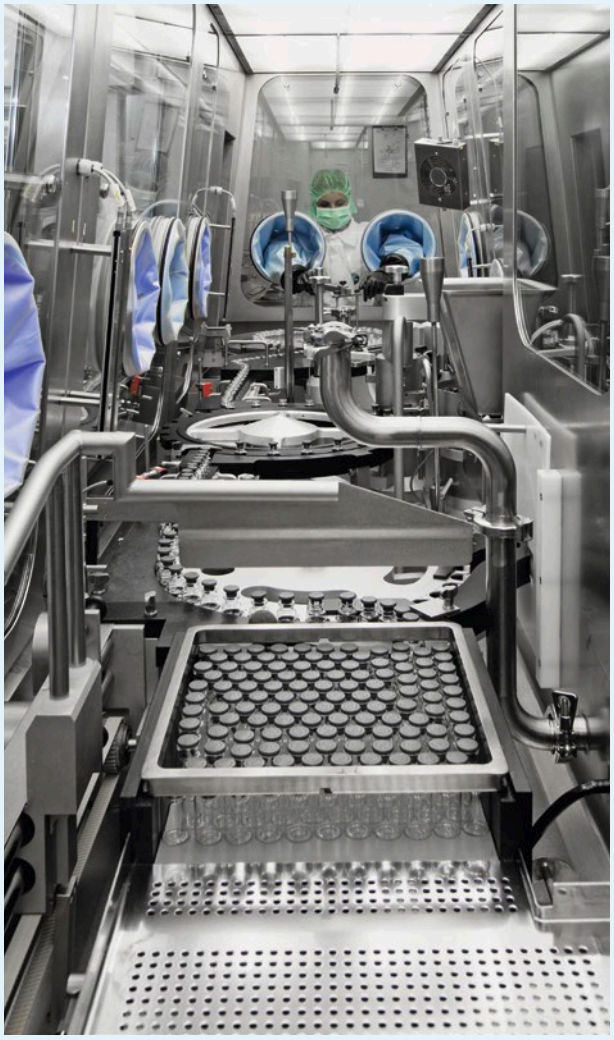
need to meet regulatory specifications in order to ensure quality, safety, and efficacy of the final product. Only a qualified vendor can guarantee compliance to these regulatory requirements and provide supply assurances.

In order to minimize risk, raw materials free of animal substances are preferred.

It should also be noted that changes in raw materials during the lifecycle of a cell-based product may affect the quality of the final product and thus may require additional studies to demonstrate comparability.

Regulatory background

The regulatory requirements for raw materials in the manufacturing process of cells are partly covered in the U.S. Pharmacopeia <1043> on Ancillary Materials and the draft EU Pharmeuropa 26.4; 5.2.12: Raw material for the production of cell-based and gene therapy medicinal products.



Aseptic filling

GMP manufacturing of MACS® GMP Products

Excellence at Miltenyi Biotec

Our products are manufactured using the highest quality standards:

- Produced in a modern GMP-certified facility, including a full quality management system according to ISO 9001 & ISO 13485
- EU GMP certificates for manufacturing of monoclonal antibodies (phase I/II), infusion solutions and aseptic filling
- FDA-inspected for the CliniMACS® CD34 System
- Free of animal-derived components

Media and buffer production

MACS® GMP Products

Benefit from an extensive quality management system and regulatory support

Quality

MACS® GMP Products are manufactured and tested under a quality management system (ISO 13485) and are in compliance with relevant GMP guidelines. They are designed following the recommendations of USP <1043> on ancillary materials.

No animal-derived materials are used for manufacture of these products.

- Lot-to-lot consistency
- Tested to regulatory standards
- Extensive stability studies
- Assured supply
- Vendor qualification of raw materials

MACS GMP Products support the transition from research to clinic and help make cell therapies a clinical reality.

Regulatory Support

Product-specific documentation

- Package Insert
- Batch-specific Certificate of Analysis (CoA) including animal component free statement
- Certificate of Compliance (CoC)/TSE (transmissible spongiform encephalopathies)
- Product Information File (PIF)

USA

- Type II Master File or Safety Master File (for cross-reference) for selected MACS GMP Products

Worldwide (ex USA)

- Regulatory Support File (equivalent to Master File, for cross-reference)

Company Information and Quality System

Self Survey and Customer Questionnaires as part of a customer vendor qualification program

Expert consultation

Miltenyi Biotec actively interacts with regulatory agencies and notified bodies. Please ask us about customized support for your clinical study.

Complete manufacturing solutions

GMP-compliant tools for cell therapy products





Leukapheresis, blood, bone marrow, tissue	Cell separation	Cell expansion or differentiation	Cell analysis	Cryopreservation	Final cellular product
gentleMACS™ Dissociators (RUO)	CliniMACS® Instruments	MACS GMP Cell Culture Media	MACSQuant Instruments (RUO)	CryoMACS® Freezing Bags	
	CliniMACS Reagents	MACS GMP Activation Kits	MACS Antibodies (RUO)	CryoMACS DMSO 10 (EP, USP)	
	MACS® GMP Fluorescent Antibodies	MACS GMP Expansion Tools			
		MACS GMP Antigens			
		MACS GMP Cytokines			
		MACS GMP Cell Culture Bags			

RUO = Research Use Only
EP = European Pharmacopoeia
USP = United States Pharmacopeia

See the full GMP portfolio at
www.miltenyibiotec.com/gmp

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.

MACS® GMP Product Portfolio

Advancing cell therapies

Activation and expansion tools

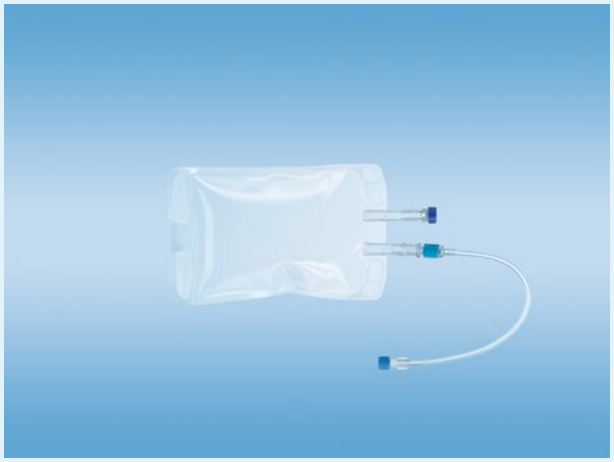
Antibodies, as well as antibody-coated particles (ExpAct™ Treg Beads), are suitable for the polyclonal *ex vivo* activation and expansion of cells. The MACS® GMP TransAct™ CD3/CD28 Kit is a new format for efficient T cell activation, transduction, and expansion. These products have been developed for today's clinical grade manufacturing of cellular products and are manufactured under strict quality assessment and in accordance with GMP guidelines.

Antigens

MACS GMP PepTivator® Peptide Pools consist of a pool of lyophilized overlapping oligopeptides (mainly 15-mers), covering the complete sequence of the protein antigen. PepTivator Peptide Pools and the unique GMP *A. fumigatus* Lysate have been designed for efficient *in vitro* stimulation and subsequent isolation of antigen-specific $CD4^+$ and $CD8^+$ T cells. They are also widely used for antigen loading of MoDCs and blood DCs.

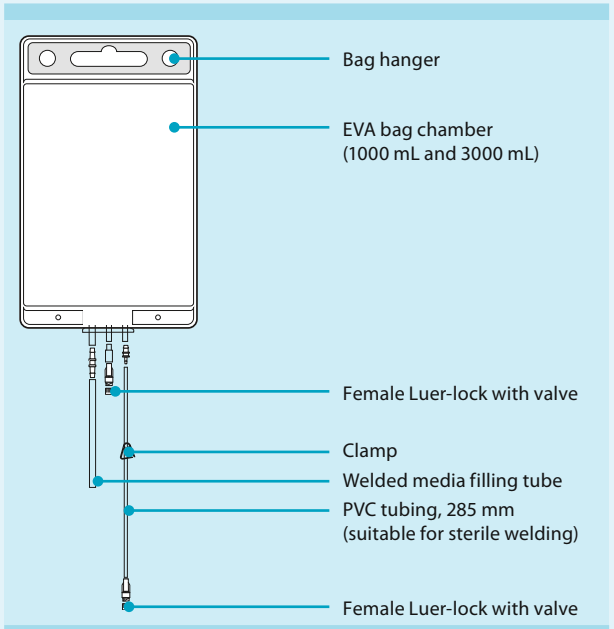
Cell culture bags

MACS® GMP Cell Culture Bags are made of polyolefin, making them gas-permeable and transparent for microscopy. All cell culture bags are individually packed, sterilized by e-beam, and tested for endotoxins. The integrated PVC tubing enables sterile connections to be made. The unique Cell Expansion Bag and Cell Differentiation Bags are available with volumes ranging from 100 to 3000 mL.



Cell culture media

MACS® GMP Media have been developed for the demands of specific cell types, such as dendritic cells, T cells, Treg cells, MSCs, HSCs, and iPSCs. These high performance media have been designed for excellent growth and differentiation, high cell viability, and consistency under serum-free conditions. Filling in flexible bags (see figure) ensures reliability and sterile connection during GMP manufacturing of cellular products. Customized formats are available on request.



MACS® GMP Product Portfolio

Advancing cell therapies

Cell sorting reagents

MACS® GMP Fluorescent Antibodies have been developed for flow cytometric analysis and sorting of cell populations from human blood products in the clinical setting. A large range of specificities and fluorochromes are available and a newly introduced program for customized specificities means manufacture of virtually any specificity is possible in MACS GMP Quality.

Cytokines

MACS GMP Cytokines and Growth Factors are highly active and pure recombinant proteins that enable consistent cell culture results. They are lyophilized without carrier protein or preservatives. Highest product standards are ensured by aseptic filling, lyophilization, and rigorous quality control tests. Biological activities are measured for each lot after lyophilization and normalized with the reference standards from NIBSC (IU/mg). Each product is supplied with a certificate of analysis that confirms the stringent specifications and states the lot-specific biological activity.

Your trusted partner in cell and gene therapy

Corporate information about Miltenyi Biotec

Miltenyi Biotec

- Founded in 1989
- Independent, privately owned biotech company
- >3,000 employees worldwide with 475 people in R&D and engineering
- Fully vertically integrated biotech company for biologics and devices
- Committed to advancing scientific understanding and medicine
- Providing innovative solutions for biomedical research and cell therapy
- Biotechnology Made in Germany

GMP Manufacturing

- Antibodies and antibody conjugates
- Proteins and peptide pools
- Media and buffers
- Medical devices
- Lentiviral vectors
- GMP single use plastic consumables

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Miltenyi Biotec B.V. & Co. KG, GMP-compliant manufacturing plant, Teterow, Germany

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