Miltenyi Biotec

# CliniMACS® Cell Separation System

## Product catalog 2008

# Product overview

| Page | Product | Regulatory status[1] | Availability | Order no. |
|---|---|---|---|---|
| | **CliniMACS® Plus Instrument** | | | |
| 7 | **CliniMACS Plus Instrument** | CE | Europe, CAN, AUS, US | **151-01** |
| 7 | **CliniMACS Plus Upgrade Kit "Software"** | | Europe, CAN, AUS, US[2] | **755-16** |
| | **CliniMACS® Service Contracts** | | | |
| 8 | **CliniMACS Full Service Agreement** | | Europe | **160-000-973** |
| 8 | **CliniMACS Maintenance** | | Europe | **160-000-974** |
| 8 | **CliniMACS Premium Service Agreement** | | CAN, US | **160-000-701** |
| 8 | **CliniMACS Basic Service Agreement** | | CAN, US | **160-000-702** |
| | **CliniMACS® Tubing Sets** | | | |
| 9 | **CliniMACS Tubing Set** | CE | Europe, CAN, AUS, US[2] | **161-01** |
| 9 | **CliniMACS Tubing Set LS** | CE | Europe, CAN, AUS, US[2] | **162-01** |
| 10 | **CliniMACS Tubing Set for Research Use** | For research use only, not for use in humans | US | **165-01** |
| 10 | **CliniMACS Tubing Set LS for Research Use** | For research use only, not for use in humans | US | **168-01** |
| 11 | **CliniMACS Depletion Tubing Set** | CE | Europe, US[2] | **261-01** |
| 11 | **CliniMACS Depletion Tubing Set for Research Use** | For research use only, not for use in humans | US, CAN, AUS | **266-01** |
| 12 | **CliniMACS Tubing Set 600 for Research Use** | For research use only, not for use in humans | Worldwide | **166-01** |
| 12 | **CliniMACS Tubing Set 150 for Research Use** | For research use only, not for use in humans | Worldwide | **167-01** |

**For availability in your country please contact your local representative**

1) The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE). CliniMACS MicroBeads are for research use only, and not for use in humans.

2) In the USA, the CliniMACS® System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

# Product overview

| Page | Product | Regulatory status[1] | Availability | | Order no. |
|---|---|---|---|---|---|
| | **Stem and progenitor cells** | | | | |
| 13 | **CliniMACS CD34 Reagent** | CE | Europe, CAN, AUS, US[2] | | **171-01** |
| 13 | **CliniMACS CD34 Complete Kit** | CE-marked components | Europe | | **178-01** |
| 13 | **CliniMACS CD34 Complete Kit with Accessories** | CE-marked components | Europe | | **177-01** |
| 13 | **CliniMACS CD34 Complete LS Kit** | CE-marked components | Europe | | **170-01** |
| 13 | **CliniMACS CD34 Complete LS Kit with Accessories** | CE-marked components | Europe | | **169-01** |
| 13 | **CliniMACS CD34 MicroBeads** | For research use only, not for use in humans | US | | **175-01** |
| 16 | **CliniMACS CD133 Reagent** | CE | Europe, US[2] | | **172-01** |
| 16 | **CliniMACS CD133 Complete Kit** | CE-marked components | Europe | | **196-01** |
| 16 | **CliniMACS CD133 Complete Kit with Accessories** | CE-marked components | Europe | | **198-01** |
| 16 | **CliniMACS CD133 Complete LS Kit** | CE-marked components | Europe | | **197-01** |
| 16 | **CliniMACS CD133 Complete LS Kit with Accessories** | CE-marked components | Europe | | **199-01** |
| 16 | **CliniMACS CD133 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | | **195-01** |
| 18 | **CliniMACS CD3/CD19 Reagent Combination** | CE-marked components | Europe | | **704-00** |
| 18 | **CliniMACS CD3/CD19 Complete Kit** | CE-marked components | Europe | | **740-01** |
| 18 | **CliniMACS CD3/CD19 Large-Scale Complete Kit** | CE-marked components | Europe | | **740-02** |
| | **T cells** | | | | |
| 20 | **CliniMACS CD3 Reagent** | CE | Europe, US[2] | | **273-01** |
| 20 | **CliniMACS CD3 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | | **176-01** |
| 21 | **CliniMACS CD4 Reagent** | CE | Europe, US[2] | | **276-01** |
| 21 | **CliniMACS CD4 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | | **304-01** |
| 22 | **CliniMACS CD8 Reagent** | CE | Europe, US[2] | | **275-01** |
| 22 | **CliniMACS CD8 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | | **308-01** |
| 23 | **CliniMACS CD25 Reagent** | CE | Europe, US[2] | ***NEW*** | **274-01** |
| 23 | **CliniMACS CD25 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | | **325-01** |
| | **CD3/CD19 combination products, please see chapter "Stem and progenitor cells"** | | | | |
| | **Antigen-specific T cells** | | | | |
| 25 | **CliniMACS Cytokine Capture System (IFN-gamma)** | CE | Europe, US[2] | | **279-01** |
| 25 | **CliniMACS Cytokine Capture System (IFN-gamma) MicroBeads** | For research use only, not for use in humans | US , CAN, AUS | | **287-01** |

**For availability in your country please contact your local representative**

1) The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE). CliniMACS MicroBeads are for research use only, and not for use in humans.

2) In the USA, the CliniMACS® System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

# Product overview

| Page | Product | Regulatory status[1] | Availability | Order no. |
|---|---|---|---|---|
| | **NK cells** | | | |
| 28 | **CliniMACS CD56 Reagent** | CE | Europe, US[2] | **271-01** |
| 28 | **CliniMACS CD3/CD56 Reagent Combination** | CE-marked components | Europe | **704-01** |
| 28 | **CliniMACS CD3/CD56 Complete Kit** | CE-marked components | Europe | **740-04** |
| 28 | **CliniMACS CD56 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | **194-01** |
| | **B cells** | | | |
| 30 | **CliniMACS CD19 Reagent** | CE | Europe, US[2] | **179-01** |
| 30 | **CliniMACS CD19 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | **193-01** |
| | **Dendritic cells** | | | |
| 32 | **CliniMACS CD14 Reagent** | CE | Europe, US[2] | **272-01** |
| 32 | **CliniMACS CD14 Complete Kit** | CE-marked components | Europe | **281-01** |
| 32 | **CliniMACS CD14 MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | **191-01** |
| 33 | **CliniMACS CD1c (BDCA-1)-Biotin** | CE | Europe, US[2] | ***NEW*** **277-01** |
| 33 | **CliniMACS CD1c (BDCA-1)/CD19 Complete Kit** | CE-marked component | Europe | ***NEW*** **740-03** |
| 33 | **CliniMACS CD1c (BDCA-1)-Biotin for Research Use** | For research use only, not for use in humans | US, CAN, AUS | **255-01** |
| 34 | **CliniMACS CD304 (BDCA-4) MicroBeads** | For research use only, not for use in humans | Worldwide | **291-01** |
| | **Flexible labeling system** | | | |
| 35 | **CliniMACS Anti-Biotin Reagent** | CE | Europe, US[2] | **173-01** |
| 35 | **CliniMACS Anti-Biotin MicroBeads** | For research use only, not for use in humans | US, CAN, AUS | **192-01** |
| 35 | **CliniMACS® Biotinylation Kit 500** | CE | Europe, US[2] | ***NEW*** **701-06** |
| 35 | **CliniMACS® Biotinylation Kit 500 for Research Use** | For research use only, not for use in humans | US, CAN, AUS | **257-01** |
| | **CliniMACS® Buffers** | | | |
| 36 | **CliniMACS PBS/EDTA Buffer** | CE | Europe, CAN, AUS, US[2] | **700-25** |
| 36 | **CliniMACS PBS/EDTA Buffer for Research Use** | For research use only, not for use in humans | US | **705-25** |

**For availability in your country please contact your local representative**

1) The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE). CliniMACS MicroBeads are for research use only, and not for use in humans.

2) In the USA, the CliniMACS® System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

# Product overview

| Page | Product | Regulatory status[1] | Availability | | Order no. |
|---|---|---|---|---|---|
| | **Accessories** | | | | |
| 38 | **Cell Expansion Bag (tube)** | CE[3] | Europe | | **200-074-301** |
| 38 | **Cell Expansion Bag (6 ports)** | CE[3] | Europe | | **200-074-302** |
| 38 | **Cell Expansion Bag (tube)** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-351** |
| 38 | **Cell Expansion Bag (6 ports)** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-352** |
| 39 | **Cell Differentiation Bag (tube) – 100** | CE[3] | Europe | | **200-074-101** |
| 39 | **Cell Differentiation Bag (tube) – 250** | CE[3] | Europe | | **200-074-102** |
| 39 | **Cell Differentiation Bag (tube) – 500** | CE[3] | Europe | | **200-074-103** |
| 39 | **Cell Differentiation Bag (6 ports) – 100** | CE[3] | Europe | | **200-074-201** |
| 39 | **Cell Differentiation Bag (6 ports) – 250** | CE[3] | Europe | | **200-074-202** |
| 39 | **Cell Differentiation Bag (6 ports) – 500** | CE[3] | Europe | | **200-074-203** |
| 39 | **Cell Differentiation Bag (tube) – 100** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-151** |
| 39 | **Cell Differentiation Bag (tube) – 250** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-152** |
| 39 | **Cell Differentiation Bag (tube) – 500** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-153** |
| 39 | **Cell Differentiation Bag (6 ports) – 100** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-251** |
| 39 | **Cell Differentiation Bag (6 ports) – 250** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-252** |
| 39 | **Cell Differentiation Bag (6 ports) – 500** | For research use only | US, CAN, AUS | ***NEW*** | **130-074-253** |
| 40 | **Pre-System Filter** | CE | Europe | | **181-01** |
| 40 | **Luer/Spike Interconnector** | CE | Europe | | **187-01** |
| 40 | **Sampling Site Coupler** | CE | Europe | | **189-01** |
| 41 | **Transfer Set Coupler/Needle** | CE | Europe | | **185-01** |
| 41 | **Transfer Set Coupler/Coupler** | CE | Europe | | **186-01** |
| 41 | **Transfer Set Needle/Needle** | CE | Europe | | **188-01** |
| 42 | **Transfer Bag 150 mL** | CE | Europe | | **183-01** |
| 42 | **Transfer Bag 600 mL** | CE | Europe | | **190-01** |
| 42 | **Transfer Bag 1000 mL** | CE | Europe | | **180-01** |
| 42 | **Transfer Bag 600 mL with 8 couplers** | CE | Europe | | **184-01** |

**For availability in your country please contact your local representative**

1) The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE). CliniMACS MicroBeads are for research use only, and not for use in humans.

2) In the USA, the CliniMACS® System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

3) The Cell Expansion Bags and the Cell Differentiation Bags are manufactured and controlled under an ISO 13485 certified quality system. These products are available in Europe as CE-marked medical devices.

## CliniMACS® Technology

The CliniMACS® Plus Instrument is an automated cell separation system based on MACS® Technology. It enables the operator to perform clinical-scale magnetic enrichment of target cells or depletion of unwanted cells in a closed and sterile system.

The cells are first magnetically labeled in the Cell Preparation Bag using an antigen-specific reagent. After labeling, the cells are washed to remove excess reagent. Then the Cell Preparation Bag containing the labeled cells is connected to the Tubing Set, which in turn is connected to the CliniMACS Buffer Bag and Cell Collection Bag. After starting, for example the enrichment program, the system automatically applies the cell sample onto the selection column. The sample application is followed by a series of washing steps depending on the chosen enrichment program. Finally, the target cells are eluted from the column. The CliniMACS Plus Instrument in combination with the CliniMACS® System separates large numbers of cells providing target cells with high purity and excellent yield.
A range of tubing sets optimized for different applications is available.

The CliniMACS System (CliniMACS Plus Instrument, CliniMACS Tubing Sets, CliniMACS Reagents, and CliniMACS PBS/EDTA Buffer) offers a flexible platform enabling the separation of many cell types as well as customized separation protocols according to specific sample requirements. Unique reagents and tubing sets also allow for the transition of promising research applications in innovative cell therapy concepts.

**Figure 1:** Cell Selection Column placed in the CliniMACS Magnetic Separation Unit.

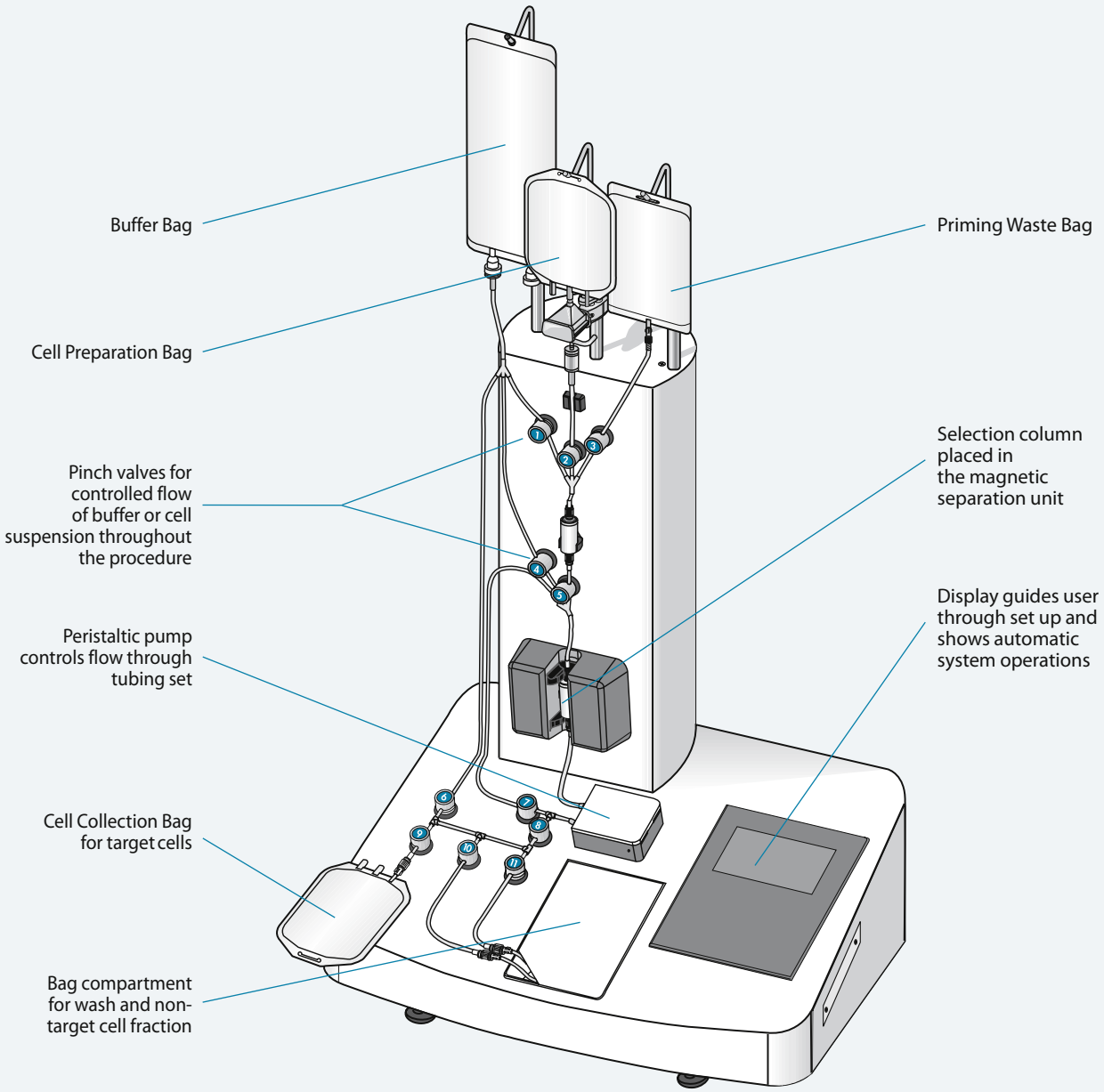
The CliniMACS Plus Instrument is CE-marked for clinical use in Europe and is used for the separation of a variety of human cell types in combination with a CliniMACS Tubing Set, a CliniMACS Reagent, and the CliniMACS PBS/EDTA Buffer. The portfolio of CliniMACS Reagents includes reagents for the separation of stem cells, monocytes, DCs, NK cells, B cells, and T cell subsets.
In the USA, the CliniMACS® System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).


**Figure 2:** The CliniMACS Plus Instrument with installed CliniMACS Tubing Set.

## CliniMACS® Plus Instrument

The key components of the CliniMACS® Plus Instrument are the integrated micro-computer, the magnetic separation unit, the peristaltic pump, and various pinch valves. The integrated computer controls all components of the instrument and directs the system to perform reproducible procedures in a standardized sequence. The magnetic separation unit includes a movable permanent magnet and a holder for the selection column. The peristaltic pump controls constant flow rates throughout the tubing set and ensures, together with the pinch valves, the controlled flow of buffer and cell suspension.

**Key components of the CliniMACS Plus Instrument with installed CliniMACS® Tubing Set.**



# CliniMACS® Plus Instrument

## CliniMACS® Plus Instrument

| Product | Regulatory status | Availability | Order no. |
|---|---|---|---|
| **CliniMACS Plus Instrument** | CE | Europe, CAN, AUS, US[1)] | **151-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CliniMACS® Plus Instrument is an enhanced version of the CliniMACS Cell Selection Device. While the basic CliniMACS Instrument was designed to enrich stem and progenitor cells, the CliniMACS Plus Instrument provides an open platform technology enabling additional isolation strategies for many cell types, such as monocytes, dendritic cells, NK cells, T cells, and B cells (see chapter "CliniMACS Reagents" or call for application updates).

The combination of immunomagnetic reagent and tubing set offers high flexibility and versatility for individual separation strategies. Different-scale applications from rare-cell enrichment to bulk depletion are feasible.

### Technical specifications

CliniMACS Plus Instrument

| | |
|---|---|
| Model: | CS2 CE/UL |
| Size: | 70 cm (w) × 60 cm (d), 90–130 cm (h) |
| Weight: | 35 kg |
| Input voltage: | 100–240 V AC |
| Power consumption: | 180 VA |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

## CliniMACS® Plus Upgrade Kit "Software"

| Product | Availability | Order no. |
|---|---|---|
| **CliniMACS Plus Upgrade Kit "Software"** | Europe, CAN, AUS, US[1)] | **755-16** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS System components including the CliniMACS Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

All CliniMACS® Plus Instruments can be upgraded to the latest status of the software.

The upgrade is CE-compliant.

Existing basic CliniMACS Instruments can be upgraded.

### Kit components

**CliniMACS Plus Upgrade Kit "Software" (755-16):**

- Software Card
- CliniMACS User Manual
- 2 Bag Hanger assemblies
- Stabilization foot

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

# Service contracts

## CliniMACS® Service Contracts

| Product | Availability | Order no. |
|---|---|---|
| **CliniMACS Full Service Agreement** | Europe | **160-000-973** |
| **CliniMACS Maintenance** | Europe | **160-000-974** |
| **CliniMACS Premium Service Agreement** | CAN, US | **160-000-701** |
| **CliniMACS Basic Service Agreement** | CAN, US | **160-000-702** |

For availability in your country please contact your local representative.

# CliniMACS® Tubing Sets

## CliniMACS® Tubing Set and Tubing Set LS

| Product | Components | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|---|
| **CliniMACS Tubing Set** | 1 Tubing Set | CE | $60\times10^9$ total cells [2)] | Europe, CAN, AUS, US [1)] | **161-01** |
| **CliniMACS Tubing Set LS** | 1 Tubing Set | CE | $120\times10^9$ total cells [2)] | Europe, CAN, AUS, US [1)] | **162-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

2) Capacity (max.) of labeled cells depends on the software program used.

### Description

CliniMACS® Tubing Sets consist of pre-assembled tubing including a pre-column and a selection column. The fluid path of the tubing sets is sterile and non-pyrogenic.
One package unit contains one sealed tubing set for single use.

**The CliniMACS Tubing Set (161-01):** The CliniMACS Tubing Set was designed for the separation of cells from up to $60\times10^9$ total cells.

**The CliniMACS Tubing Set LS (162-01):** The CliniMACS Tubing Set LS was designed for the separation of cells from up to $120\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

The CliniMACS® Tubing Sets for clinical use were developed for the enrichment or depletion of cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

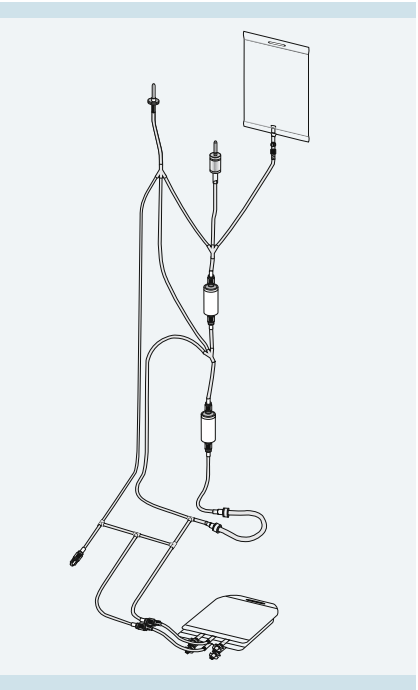


**Figure 1:** The CliniMACS Tubing Set.

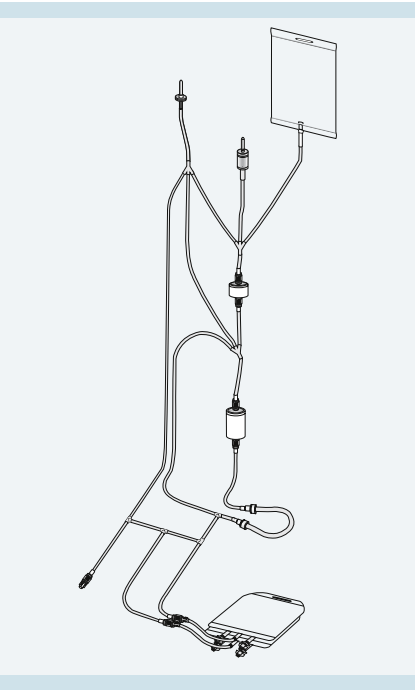


**Figure 2:** The CliniMACS Tubing Set LS.

# CliniMACS® Tubing Sets

## CliniMACS® Tubing Sets for Research Use

| Product | Components | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|---|
| **CliniMACS Tubing Set for Research Use** | 1 Tubing Set | For research use only, not for use in humans [2] | $60\times10^9$ total cells [1] | US | **165-01** |
| **CliniMACS Tubing Set LS for Research Use** | 1 Tubing Set | For research use only, not for use in humans [2] | $120\times10^9$ total cells [1] | US | **168-01** |

For availability in your country please contact your local representative.
1) Capacity (max.) of labeled cells depends on the software program used.
2) Manufactured by Miltenyi Biotec GmbH under an ISO 9001 certified quality system.

### Description

CliniMACS® Tubing Sets for Research Use consist of pre-assembled tubing including a pre-column and a selection column.
The fluid path of the tubing sets is sterile and non-pyrogenic.
One package unit contains one sealed tubing set for single use.

**CliniMACS Tubing Set for Research Use (165-01):**
The CliniMACS Tubing Set was designed for the separation of cells from up to $60\times10^9$ total cells.

**CliniMACS Tubing Set LS for Research Use (168-01):**
The CliniMACS Tubing Set LS was designed for the separation of cells from up to $120\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

The CliniMACS® Tubing Sets for Research Use were developed for the enrichment or depletion of cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

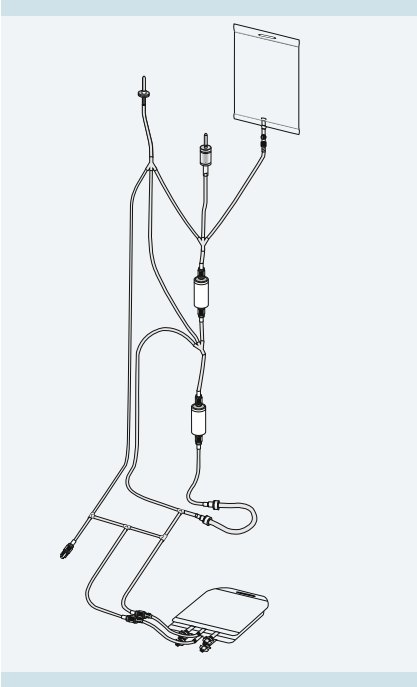


**Figure 1:** Schematic illustration of the CliniMACS Tubing Set for Research Use containing a pre-column and a selection column.

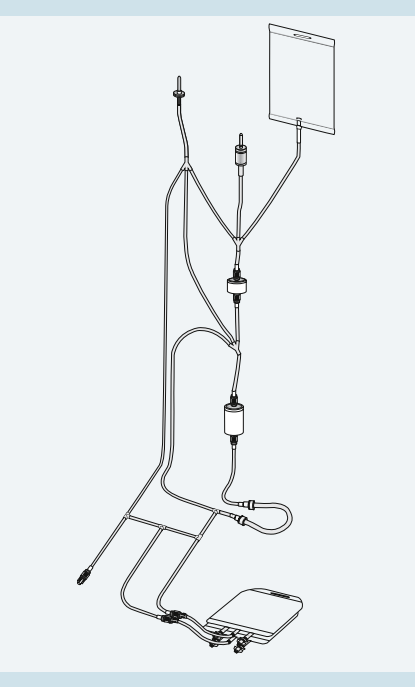


**Figure 2:** Schematic illustration of the CliniMACS Tubing Set LS for Research Use containing a pre-column and a selection column.

# CliniMACS® Tubing Sets

## CliniMACS® Depletion Tubing Sets

| Product | Components | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|---|
| **CliniMACS Depletion Tubing Set** | 1 Tubing Set | CE | $40\times10^9$ labeled cells from $120\times10^9$ total cells | Europe, US [1)] | **261-01** |
| **CliniMACS Depletion Tubing Set for Research Use** | 1 Tubing Set | For research use only, not for use in humans [2)] | $40\times10^9$ labeled cells from $120\times10^9$ total cells | US, CAN, AUS | **266-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

2) Manufactured by Miltenyi Biotec GmbH under an ISO 9001 certified quality system.

### Description

CliniMACS® Depletion Tubing Sets contain tubing with a pre-assembled Cell Collection Bag, Reapplication Bag, Non-Target Cell Bag, and Buffer Waste Bag. The fluid path of the tubing sets is sterile and non-pyrogenic.
One package unit contains one sealed tubing set for single use.

**CliniMACS® Depletion Tubing Set (261-01):**
The CliniMACS Depletion Tubing Set was designed for the depletion of up to $40\times10^9$ labeled cells from up to $120\times10^9$ total cells.

**CliniMACS® Depletion Tubing Set for Research Use (266-01):**
The CliniMACS Depletion Tubing Set for Research Use was designed for the depletion of up to $40\times10^9$ labeled cells from up to $120\times10^9$ total cells.

Please inquire about recommended device and accessories. The CliniMACS Plus Instrument with Software Version 2.40 or higher is required.

### Applications

The CliniMACS Depletion Tubing Set is specifically designed for depletion of large quantities of cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.
It is also designed for a faster depletion of more cells as compared to other CliniMACS Tubing Sets.[1,2]


**References**

1. Fritsch *et al.* (2004) Bone Marrow Transplant. 33 (Suppl.1): 595.
2. Fritsch *et al.* (2004) Cytotherapy 6(4): 432.


### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS Plus Upgrade Kit "Software" | 755-16 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

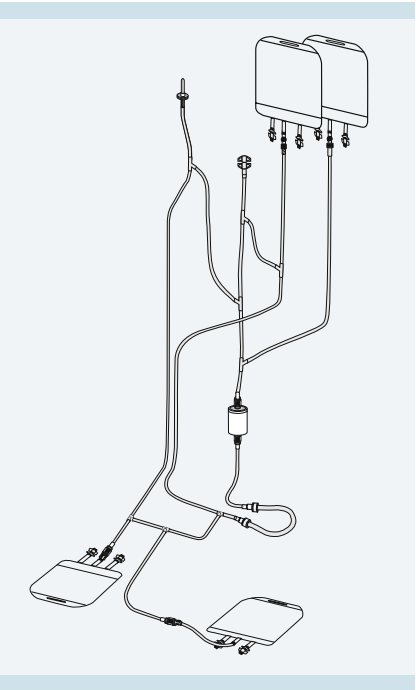


**Figure 1:** CliniMACS Depletion Tubing Set

# CliniMACS® Tubing Sets

## CliniMACS® Tubing Sets 150 and 600 for Research Use

| Product | Components | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|---|
| **CliniMACS Tubing Set 600 for Research Use** | 5 Tubing Sets | For research use only, not for use in humans[1)] | $20\times10^9$ total cells | Worldwide | **166-01** |
| **CliniMACS Tubing Set 150 for Research Use** | 5 Tubing Sets | For research use only, not for use in humans[1)] | $10\times10^9$ total cells | Worldwide | **167-01** |

For availability in your country please contact your local representative.

1) Manufactured by Miltenyi Biotec GmbH under an ISO 9001 certified quality system.

### Description

CliniMACS® Tubing Sets 600 and 150 for Research Use are ideal tools for pre-clinical cell separations on the CliniMACS Platform. The CliniMACS Tubing Sets for Research Use with reduced tubing geometry consist of a selection column without a pre-column. One package unit contains five separately sealed tubing sets for single use.

**CliniMACS Tubing Set 600 for Research Use (166-01):**
The CliniMACS Tubing Set 600 for Research Use was designed for the separation from up to $20\times10^9$ total cells.

**CliniMACS Tubing Set 150 for Research Use (167-01):**
The CliniMACS Tubing Set 150 for Research Use was designed for the separation from up to $10\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

The CliniMACS Tubing Sets 600 and 150 for Research Use can be utilized for various pre-clinical separations. The system allows for large-scale, sterile cell separation. The cells can be used, for example, for animal models, cell culture assays, or other research-related applications.

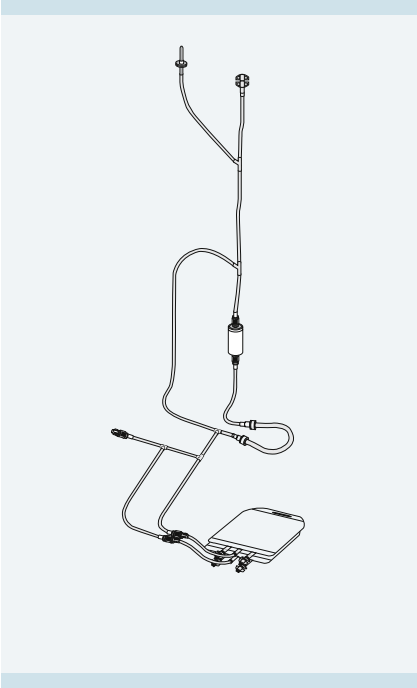


**Figure 1:** CliniMACS Tubing Set 600 for Research Use.

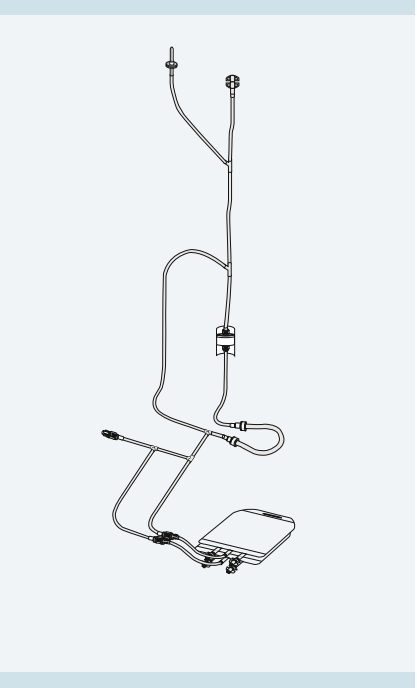


**Figure 2:** CliniMACS Tubing Set 150 for Research Use.

## CliniMACS® CD34 Enrichment

### Background

The CD34 antigen is expressed on hematopoietic progenitor cells constituting a small subpopulation of bone marrow cells and peripheral blood cells. After severe damage, for example, after myeloablative conditioning, the hematopoietic system can be reconstituted by transplantation of allogeneic or autologous $CD34^+$ hematopoietic progenitor cells. The concomitant removal of T cells and B cells is important especially for allogeneic grafts. CD34 enrichment of progenitor cells in the autologous setting may be used for removing contaminating tumor cells from the graft (purging).

### Performance

Since its introduction, CliniMACS® CD34 System has been used in numerous clinical trials to provide $CD34^+$ progenitor cells with high purity and yield in conjunction with excellent passive depletion of unwanted cells. A review of the performance in the allogeneic setting is shown in table 1.

### Clinical results

The concomitant T and B cell depletion may reduce the incidence of graft versus host disease (GVHD) and EBV-induced lymphoproliferative disease in allogeneic transplantation settings. This has been suggested in the HLA identical setting with related[1,2] as well as unrelated[3,4] donors. It is thought to be crucial in the haploidentical setting where, due to the high degree of HLA mismatch, GVHD is the major cause of transplantation-related mortality[5,6]. It has also been shown that CliniMACS CD34 Enrichment is a means to provide tumor cell-depleted stem cell grafts in lymphoma and neuroblastoma patients[7,8]. An emerging field for CD34-enriched cells has recently been seen in the depletion of autoreactive cells from stem cell grafts for diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and systemic sclerosis[9–12].

| | n = 32 | n > 500 | n = 293 | n = 136 | n = 30 |
|---|---|---|---|---|---|
| Purity CD34 (%) | 97.2 | 95 – 99 | 97.5 | 90 | 96 |
| Recovery CD34 (%) | 60 | 70 | 77 | 81 | 64 |
| CD3 log depletion | 4.6 | > 5 | 4.6 | 4.6 | 5 |
| CD19 log depletion | nd | < 0.5 % | nd | 3.2 | 3.2 |

**Table 1:** CliniMACS CD34 Enrichment results from PBSCs of allogeneic donors (nd = not determined). References 1, 13–16.


**References**

1. Elmaagacli *et al.* (2003) Blood 101(2): 446–453.
2. Urbano-Ispizua *et al.* (2001) Bone Marrow Transplant. 28: 349–354.
3. Bornhaeuser *et al.* (2000) Haematologica 85: 839–847.
4. Lang *et al.* (2003) Blood 101: 1630–1636.
5. Handgretinger *et al.* (2003) Pediatr Transplant. 7 (Suppl. 3): 51–55.
6. Aversa *et al.* (2004) Springer Semin Immunopathol. 26 (1–2): 155–68.
7. Flohr *et al.* (2002) Bone Marrow Transplant. 29: 769–775.
8. Handgretinger *et al.* (2002) Bone Marrow Transplant. 29: 731–736.
9. Snowden *et al.* (2004) J. Rheumatol 31: 482–488.
10. Jayne *et al.* (2004) Lupus 13: 168–176.
11. Carreras *et al.* (2003) Haematologica 88: 306–14.
12. Rosen *et al.* (2000) Arthritis Research 2: 327–336.
13. Handgretinger *et al.* (2003) Pediatr Transplant. 7 (Suppl. 3): 51–55.
14. Lang *et al.* (2004) ISCT Dublin, Miltenyi Biotec Satellite Symposium.
15. Falzetti *et al.* (2002) Bone Marrow Transplant. 29 (Suppl. 2): S199.
16. Martin-Henao *et al.* (2002) ISCT Barcelona, #100.


## CliniMACS® CD34 Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD34 Reagent** | CE | $0.6\times10^9$ $CD34^+$ cells from $60\times10^9$ total cells | Europe, CAN, AUS, US[1)] | **171-01** |
| **CliniMACS CD34 Complete Kit** | CE-marked components | $0.6\times10^9$ $CD34^+$ cells from $60\times10^9$ total cells | Europe | **178-01** |
| **CliniMACS CD34 Complete Kit with Accessories** | CE-marked components | $0.6\times10^9$ $CD34^+$ cells from $60\times10^9$ total cells | Europe | **177-01** |
| **CliniMACS CD34 Complete LS Kit** | CE-marked components | $1.2\times10^9$ $CD34^+$ cells from $120\times10^9$ total cells | Europe | **170-01** |
| **CliniMACS CD34 Complete LS Kit with Accessories** | CE-marked components | $1.2\times10^9$ $CD34^+$ cells from $120\times10^9$ total cells | Europe | **169-01** |
| **CliniMACS CD34 MicroBeads** | For research use only, not for use in humans | $0.6\times10^9$ $CD34^+$ cells from $60\times10^9$ total cells | US | **175-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD34 antigen is a single transmembrane glycoprotein that is mainly expressed on human hematopoietic stem and progenitor cells but is also present on endothelial progenitor cells. The CD34 antigen is involved in cell adhesion and is thought to function as a signaling molecule.

The CliniMACS® CD34 Products consist of superparamagnetic iron dextran particles directly conjugated to CD34 antibodies.

# Stem and progenitor cells

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $0.6 \times 10^9$ $CD34^+$ cells from up to $60 \times 10^9$ total cells.

Please inquire about recommended device and accessories.

## Applications

CliniMACS CD34 Products were developed for the enrichment of $CD34^+$ cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

## Referenced literature

CD34 enrichment of progenitor cells is performed to provide an allogeneic stem cell graft highly purified for $CD34^+$ cells and depleted of unwanted cells.[1–11] In autologous transplantation $CD34^+$ progenitor cells can be enriched in order to passively remove tumor cells from the graft (purging).[12–13]


**References**

1. Elmaagacli *et al.* (2003) Blood 101(2): 446–453.
2. Bornhaeuser *et al.* (2000) Haematologica 85: 839–847.
3. Lang *et al.* (2003) Blood 101: 1630–1636.
4. Handgretinger *et al.* (2001) Bone Marrow Transplant. 27: 777–783.
5. Aversa *et al.* (2002) Int. J. Hematol. 76(Suppl.1): 165–168.
6. Chakraverty *et al.* (2002) Blood 99(3): 1071–1078.
7. Craddock *et al.* (2000) Br. J. Haematol 111(3): 797–800.
8. Gaipa *et al.* (2003) Bone Marrow Transplant 31: 857–860.
9. Lang *et al.* (2004) Bone Marrow Transplant 33: 25–32.
10. Benesch *et al.* (2004) Br. J. Haematol 125(1): 58–63.
11. Handgretinger *et al.* (2003) Pediatr. Transplant. 7(Suppl.3): 51–55.
12. Flohr *et al.* (2002) Bone Marrow Transplant 29: 769–775.
13. Handgretinger *et al.* (2002) Bone Marrow Transplant 29: 731–736.

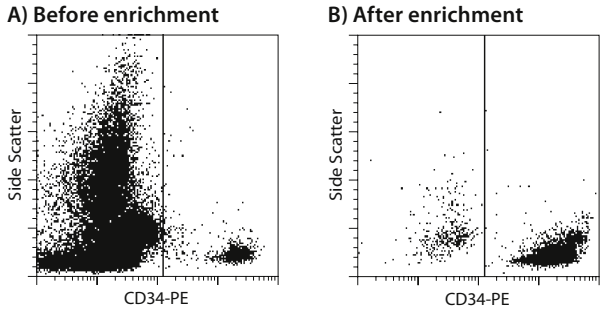




**Figure 1:** Flow cytometric analysis of CD34-enriched cells from mobilized leukapheresis product using the CliniMACS CD34 System. Cells are gated on viable $CD45^+$ cells.

## Kit components (not available in the US)

**CliniMACS CD34 Complete Kit (178-01):**

- 1 vial CliniMACS CD34 Reagent
- 1 CliniMACS Tubing Set
- 3×1L CliniMACS PBS/EDTA Buffer

**CliniMACS CD34 Complete Kit with Accessories (177-01):**

- 1 vial CliniMACS CD34 Reagent
- 1 CliniMACS Tubing Set
- 3×1L CliniMACS PBS/EDTA Buffer
- 1 Pre-System Filter
- 1 Luer/Spike Interconnector
- 1 Transfer Bag 150 mL

**CliniMACS CD34 Complete LS Kit (170-01):**

- 2 vials CliniMACS CD34 Reagent
- 1 CliniMACS Tubing Set LS
- 3×1L CliniMACS PBS/EDTA Buffer

**CliniMACS CD34 Complete LS Kit with Accessories (169-01):**

- 2 vials CliniMACS CD34 Reagent
- 1 CliniMACS Tubing Set LS
- 3×1L CliniMACS PBS/EDTA Buffer
- 1 Pre-System Filter
- 1 Luer/Spike Interconnector
- 1 Transfer Bag 150 mL

## Related MACS® Products

| | |
|---|---|
| CD34-FITC, human | 130-081-001 |
| CD34-PE, human | 130-081-002 |
| CD34-APC, human | 130-090-954 |
| CD133/2 (293C3)-PE, human | 130-090-853 |
| CD133/2 (293C3)-APC, human | 130-090-854 |
| CD45-FITC, human | 130-080-202 |

## CliniMACS® CD133 (AC133) Enrichment

### Background

The CD133 antigen has been identified as a stem cell marker. CD133 is specifically expressed on an immature subset of $CD34^+$ cells, on circulating endothelial progenitor cells, as well as on a $CD34^-$ stem cell subset (see figure 1)[1]. CD133 is a marker for very early hematopoietic stem cells with high proliferative activity[2].

The high potential for hematopoietic engraftment of isolated $CD133^+$ cells has been shown in NOD/SCID repopulation assays[3,4]. CD133-enriched cells have also been used as a starting fraction for the *ex vivo* expansion of hematopoietic progenitor cells from cord blood[5–8]. Clinically, CD133-enriched stem cell grafts have been employed in autologous[9,10] and allogeneic transplantation, not only in the haploidentical[11,12], but also in the HLA-matched[13] setting.

Additionally, $CD133^+$ stem cells can be utilized in non-hematological applications such as regenerative medicine. CD133 is expressed on stem/progenitor cells of different tissues including bone marrow, peripheral blood, cord blood, and liver. $CD133^+$ stem cells have been shown to harbor the capability to differentiate *in vitro* into cell types of various tissues.

Bone marrow-derived $CD133^+$ stem cells have come into focus in non-hematological applications, especially ischemic heart diseases. Clinical trials are currently being conducted to address safety and feasibility of this approach[14–18].

### Performance

Since its introduction, the CliniMACS® CD133 System has demonstrated excellent performance providing $CD133^+$ progenitor cells with high purity and yield in conjunction with excellent passive depletion of unwanted cells (see table 1).


**References**

1. De Wynter *et al.* (1998) Stem Cells 16: 387–396.
2. Goussetis *et al.* (2000) J. Hematother, & Stem Cell Res. 9: 827–840.
3. Kuci *et al.* (2003) Blood 101: 869–876.
4. Handgretinger *et al.* (2003) Ann. N. Y. Acad. Sci. 996: 141–151.
5. Pasino *et al.* (2000) Brit. J. Haematol. 108: 793–800.
6. Forraz *et al.* (2002) Brit. J. Haematol. 119: 516–524.
7. Kobari *et al.* (2001) J. Hematother. & Stem Cell Res. 10: 273–281.
8. Peled *et al.* (2004) Cytother, 6: 344–355.
9. Köhl *et al.* (2002) Bone Marrow Transpl. 29: 927–930.
10. Falzetti *et al.* (2002) Blood 100(11): 831a.
11. Lang *et al.* (2004) Brit. J. Haematol. 124: 72–79.
12. Lang *et al.* (2004) Bone Marrow Transpl. 33: 879–880.
13. Bornhaeuser *et al.* (2005) Leukemia 19: 161–165.
14. Pompilio *et al.* (2004) Ann. Thorac. Surg. 78(5): 1808–1812.
15. Klein *et al.* (2004) The Heart Surgery Forum. Vol. 7, Issue 5.
16. Ghodsizad *et al.* (2004) Cytotherapy. 6(5): 523–526.
17. Stamm *et al.* (2004) Thorac. Cardiovasc. Surg. 52(3): 152–158.
18. Stamm *et al.* (2003) Lancet. 361(9351): 45–46.
19. Gordon. *et al.* (2003) Bone Marrow Transpl. 31: 17–22.
20. Lang *et al.* (2004) ISCT Dublin, Miltenyi Biotec Satellite Symposium.
21. Bornhaeuser *et al.* (2005) Leukemia 19: 161–165.

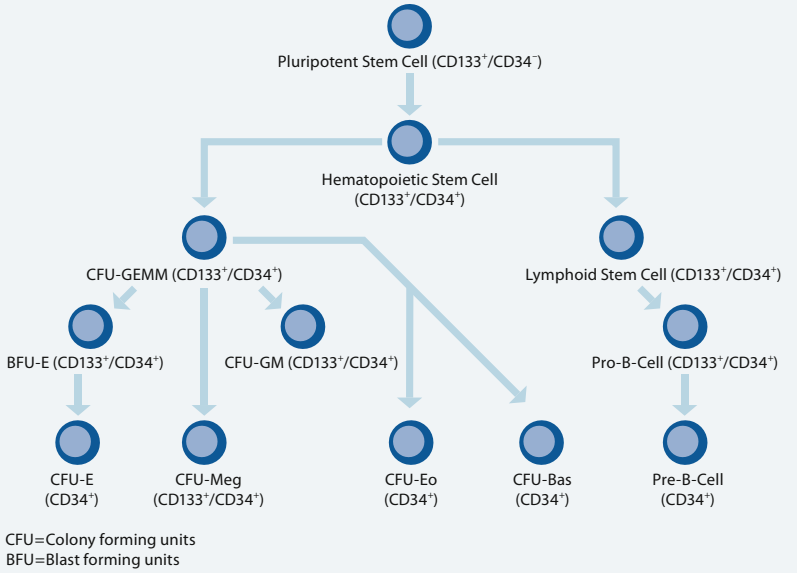




**Figure 1:** The early hematopoetic progenitor cell marker CD133 is ancestral to CD34.

| | n = 11 | n = 84 | n = 12 |
|---|---|---|---|
| Purity CD133 (%) | 94 | 93 | 97 |
| Recovery CD133 (%) | 69 | 81 | 69 |
| CD3 log depletion | 4.2 | 3.8 | nd |

**Table 1:** CliniMACS CD133 enrichment results from PBSCs of allogeneic donors (nd=not determined). References 19–21.

# Stem and progenitor cells

## CliniMACS® CD133 (AC133) Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD133 Reagent** | CE | $0.6\times10^9$ $CD133^+$ cells from $60\times10^9$ total cells | Europe, US [1)] | **172-01** |
| **CliniMACS CD133 Complete Kit** | CE-marked components | $0.6\times10^9$ $CD133^+$ cells from $60\times10^9$ total cells | Europe | **196-01** |
| **CliniMACS CD133 Complete Kit with Accessories** | CE-marked components | $0.6\times10^9$ $CD133^+$ cells from $60\times10^9$ total cells | Europe | **198-01** |
| **CliniMACS CD133 Complete LS Kit** | CE-marked components | $1.2\times10^9$ $CD133^+$ cells from $120\times10^9$ total cells | Europe | **197-01** |
| **CliniMACS CD133 Complete LS Kit with Accessories** | CE-marked components | $1.2\times10^9$ $CD133^+$ cells from $120\times10^9$ total cells | Europe | **199-01** |
| **CliniMACS CD133 MicroBeads** | For research use only, not for use in humans | $0.6\times10^9$ $CD133^+$ cells from $60\times10^9$ total cells | US, CAN, AUS | **195-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

CD133 is expressed on immature hematopoietic stem and progenitor cells but is not found on mature blood cells. In contrast to the CD34 antigen, CD133 is not expressed by late progenitors such as pre-B cells, CFU-E, and CFU-G. The stem cell marker CD133 was formerly known as AC133.

CliniMACS® CD133 Products consist of superparamagnetic iron dextran particles directly conjugated to CD133 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $0.6\times10^9$ $CD133^+$ cells from up to $60\times10^9$ total cells.
Please inquire about recommended device and accessories.

### Applications

CliniMACS CD133 (AC133) Products were developed for the enrichment of $CD133^+$ cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

### Referenced literature

CD133 enrichment of progenitor cells is performed to provide an allogeneic stem cell graft highly purified for $CD133^+$ cells and depleted of unwanted cells.[1–6] In autologous transplantation $CD133^+$ progenitor cells can be enriched in order to passively remove tumor cells from the graft (purging).[7] In addition, stem cells enriched for the CD133 antigen are being explored for use in regenerative medicine (e.g. cardiac diseases).[8–12]

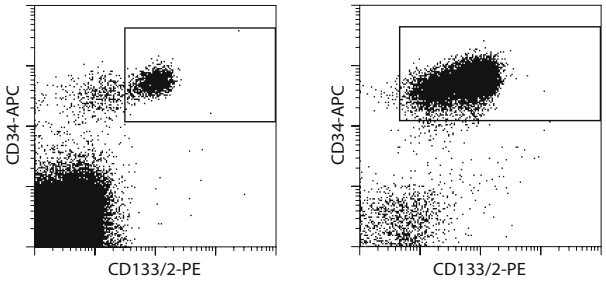



**Figure 1:** Flow cytometric analysis of CD133-enriched cells from a mobilized leukapheresis product using the CliniMACS CD133 System.

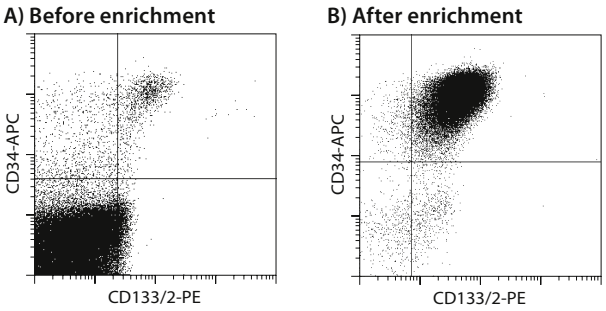



**Figure 2:** Flow cytometric analysis of CD133-enriched stem cells from a bone marrow aspirate using the CliniMACS CD133 System.


**References**

1. Bitan *et al.* (2005) Exp. Hematol. 33: 713–718.
2. Bornhäuser *et al.* (2005) Leukemia 19: 161–165.
3. Peled *et al.* (2004) Cytotherapy 6: 344–355.
4. Lang *et al.* (2004) Brit. J. Haematol. 124: 72–79.
5. Lang *et al.* (2004) Bone Marrow Transplant. 33 (1): 879–880.
6. Gordon *et al.* (2003) Bone Marrow Transplant. 31: 17–22.
7. Koehl *et al.* (2002) Bone Marrow Transplant. 29: 927–930.
8. Pompilio *et al.* (2004) Ann. Thorac. Surg. 78 (5): 1808–1812.
9. Klein *et al.* (2004) The Heart Surgery Forum. Vol. 7, Issue 5.
10. Ghodsizad *et al.* (2004) Cytotherapy 6 (5): 523–526.
11. Stamm *et al.* (2004) Thorac Cardiovasc. Surg. 52 (3): 152–158.
12. Stamm *et al.* (2003) Lancet 361 (9351): 45–46.

# Stem and progenitor cells

**Kit components** (not available in the US)

**CliniMACS CD133 Complete Kit (196-01):**
- 1 vial CliniMACS CD133 Reagent
- 1 CliniMACS Tubing Set
- 3×1L CliniMACS PBS/EDTA Buffer

**CliniMACS CD133 Complete Kit with Accessories (198-01):**
- 1 vial CliniMACS CD133 Reagent
- 1 CliniMACS Tubing Set
- 3×1 L CliniMACS PBS/EDTA Buffer
- 1 Pre-System Filter
- 1 Luer/Spike Interconnector
- 1 Transfer Bag 150 mL

**CliniMACS CD133 Complete LS Kit (197-01):**
- 2 vials CliniMACS CD133 Reagent
- 1 CliniMACS Tubing Set LS
- 3×1 L CliniMACS PBS/EDTA Buffer

**CliniMACS CD133 Complete LS Kit with Accessories (199-01):**
- 2 vials CliniMACS CD133 Reagent
- 1 CliniMACS Tubing Set LS
- 3×1 L CliniMACS PBS/EDTA Buffer
- 1 Pre-System Filter
- 1 Luer/Spike Interconnector
- 1 Transfer Bag 150 mL

**Related MACS® Products**

| | |
|---|---|
| CD133/2 (293C3)-PE, human | 130-090-853 |
| CD133/2 (293C3)-APC, human | 130-090-854 |
| CD34-FITC, human | 130-081-001 |
| CD34-PE, human | 130-081-002 |
| CD34-APC, human | 130-090-954 |
| CD45-FITC, human | 130-080-202 |
| CD45-PE, human | 130-080-201 |
| CD45-APC, human | 130-091-230 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

## CliniMACS® T and B cell depletion (CD3/CD19 combination)[1)]

Using the CliniMACS® System together with the CliniMACS CD3/CD19 Combination makes it possible to simultaneously deplete T cells and B cells from a graft.

In contrast to stem cell enrichment, this method preserves NK cells and other effector cells in the graft (see also table 1).[1]

Safety and feasibility of CD3/CD19-depleted grafts in the haploidentical and unrelated donor setting have been explored in a number of clinical studies[2–5].

Table 1 summarizes the CD3/CD19 depletion results with the CliniMACS System and the CliniMACS Tubing Set LS.

However, with the CliniMACS Tubing Set LS the depletion procedure is limited to a maximum of $20\times10^9$ labeled cells. Therefore, a new tubing set was developed, called the CliniMACS Depletion Tubing Set, which has been designed for depletion of up to $40\times10^9$ labeled cells with a reduced processing time. The new procedure uses the program DEPLETION 3.1 (software version 2.40 or higher).

| | n = 5 | n = 25 | n = 6 | n = 14 |
|---|---|---|---|---|
| Cell source | PBSCs | PBSCs | PBSCs | BM |
| Recovery CD34 (%) | 69 | 70 | 77 | 67 |
| Recovery NK cells (%) | 36 | nd | 67 | 75 |
| Remaining T cells (%) | 0.02 | 0.01 | nd | 0.11 |
| Remaining B cells (%) | 0.1 | 0.005 | nd | 1.6 |
| CD3 log depletion | 3.4 | 3.9 | 3.7 | 3 |
| CD19 log depletion | 2.2 | nd | 3.7 | nd |

**Table 1:** CliniMACS CD3/CD19 Depletion results from allogeneic settings (nd=not determined). References 1, 3–5.


**References**
1. Barfield *et al.* (2004) Cytother 6: 1–6.
2. Benaim *et al.* (2003) Blood 102(11): 969a.
3. Lang *et al.* (2004) ISCT Dublin, Miltenyi Biotec Satellite Symposium.
4. Fritsch *et al.* (2004) ISCT Dublin, Ireland #192.
5. Preijers *et al.* (2004) Bone Marrow Transplant. 33 (Suppl 1): S93.


**1) Not available in the United States.**

# Stem and progenitor cells

## CliniMACS® CD3/CD19 Depletion

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD3/CD19 Reagent Combination** | CE-marked components | $5\times10^9$ $CD19^+$ cells and $15\times10^9$ $CD3^+$ cells from $40\times10^9$ total cells | Europe | **704-00** |
| **CliniMACS CD3/CD19 Complete Kit** | CE-marked components | $5\times10^9$ $CD19^+$ cells and $15\times10^9$ $CD3^+$ cells from $40\times10^9$ total cells | Europe | **740-01** |
| **CliniMACS CD3/CD19 Large-Scale Complete Kit** | CE-marked components | $10\times10^9$ $CD19^+$ cells and $30\times10^9$ $CD3^+$ cells from $80\times10^9$ total cells | Europe | **740-02** |

For availability in your country please contact your local representative

### Description

The CliniMACS® CD3/CD19 Products consist of superparamagnetic iron dextran particles directly conjugated to CD3 and CD19 antibodies.

Each vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $15\times10^9$ $CD3^+$ cells and $5\times10^9$ $CD19^+$ cells from up to $40\times10^9$ total cells, respectively.

Please inquire about recommended device and accessories.

### Applications

The CliniMACS® CD3/CD19 Products were developed for the simultaneous depletion of unwanted T and B cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System. This approach keeps stem and progenitor cells untouched and leaves immune effector cells, such as NK cells and dendritic cells, in the cellular product.[1–2]

### Kit components (not available in the US)

**CliniMACS CD3/CD19 Reagent Combination (704-00):**
- 1 vial CliniMACS CD3 Reagent
- 1 vial CliniMACS CD19 Reagent

**CliniMACS CD3/CD19 Complete Kit (740-01):**
- 1 vial CliniMACS CD3 Reagent
- 1 vial CliniMACS CD19 Reagent
- 1 CliniMACS Depletion Tubing Set
- 3×1L CliniMACS PBS/EDTA Buffer

**CliniMACS CD3/CD19 Large-Scale Complete Kit (740-02):**
- 2 vials CliniMACS CD3 Reagent
- 2 vials CliniMACS CD19 Reagent
- 1 CliniMACS Depletion Tubing Set
- 3×1L CliniMACS PBS/EDTA Buffer

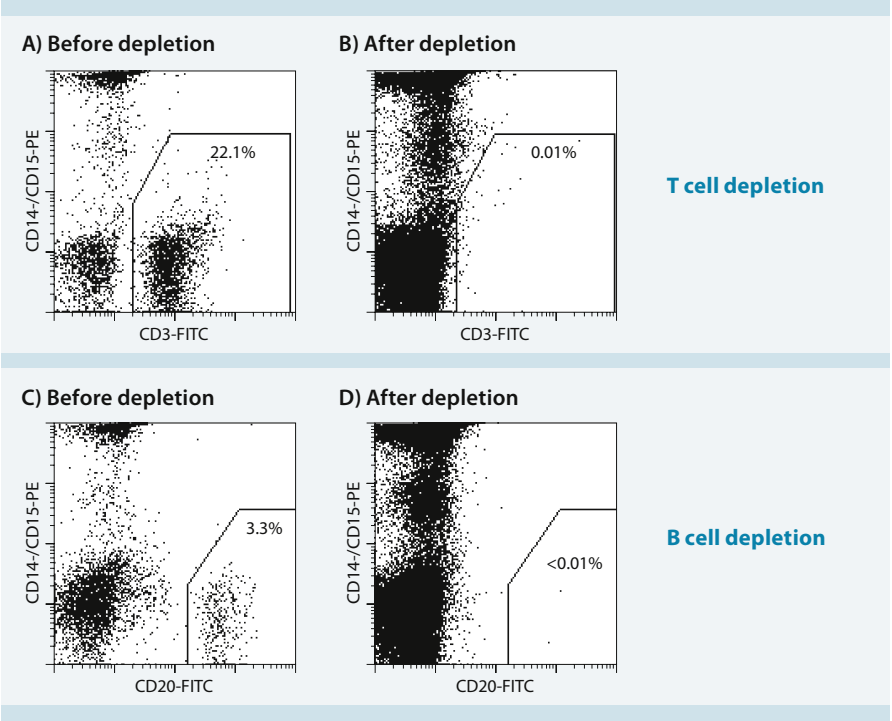



**Figure 1:** Flow cytometric analysis of simultaneous depletion of T and B cells from a buffy coat using the CliniMACS CD3/CD19 System.

### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS CD3/CD56 Reagent Combination[1)] | 704-01 |
| CliniMACS CD3 Reagent | 273-01 |
| CliniMACS CD19 Reagent | 179-01 |
| CliniMACS CD56 Reagent | 271-01 |

1) Not available in the US.

### Related MACS® Products

| | |
|---|---|
| CD14-PE, human | 130-091-242 |
| CD15-PE, human | 130-091-375 |
| CD20-FITC, human | 130-091-108 |
| CD45-FITC, human | 130-080-202 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.


**References**

1. Barfield *et al.* (2004) Cytotherapy 6: 1–6.
2. Gordon *et al.* (2002) Bone Marrow Transplant. 30: 69–74.

## CliniMACS® T Cell Separation

T cells play critical roles in the regulation of immune responses and are responsible for mediating both beneficial and harmful immune responses.
In the transplant setting, graft versus leukemia (GVL) effects and graft versus host diseases (GVHD) are in a large part conveyed by donor T lymphocytes as part of the unfolding adaptive immune response. New immunotherapy strategies have evolved, designed to separate GVL from GVHD, as well as to boost GVL and reduce GVHD.
The CliniMACS® System, together with the broadened CliniMACS T Cell Product portfolio, allows for enrichment or depletion of different T cell subsets providing the basis for a variety of different applications.
The CliniMACS CD3 Reagent was developed for the depletion of T cells from unmobilized as well as mobilized leukapheresis products. The rationale for this application is that the depletion of T cells may lower the risk of GVHD. Combined depletion of T and B cells from the graft using CliniMACS CD3 and CD19 Reagents leaves stem and progenitor cells and, in addition, provides a graft which contains NK cells[1]. Enrichment of NK cells can also be achieved using the CliniMACS CD56 Reagent after prior depletion of T cells with the CliniMACS CD3 Reagent.[2]
For certain oncological settings preliminary data suggest that T cells in a graft or as a donor lymphocyte infusion (DLI) may be beneficial.[3] In these settings a CD4 enrichment or CD8 depletion may be desired. $CD4^+$ T cells not only specifically help $CD8^+$ T cells during an immune reaction but also seem to support their prolonged survival in the recipient[4].
The depletion of $CD8^+$ T cells from DLI is described in various protocols for the prevention of GVHD.[5] The CliniMACS CD4 Reagent and CD8 Reagent are the reagents of choice for investigating potential applications based on such rationale.
CD25 was first described as a T cell proliferation marker. It is now regarded as a marker which defines activated/reactive T cells.
Alloreactive T cells can cause severe complications (GVHD) in transplantation.[6] Thus, it may be desirable to deplete $CD25^+$ T cells from apheresis products.
$CD25^{hi}CD4^+$ regulatory T cells are the focus of T cell research as they have been shown to be capable of specifically modulating immune reactions. For a variety of applications, these modulating capacities could potentially be utilized.[7]
The $CD25^+$ T cells can be depleted or enriched using the CliniMACS CD25 System.[8,9]
Antigen-specific T cells have become another focus in T cell research and opportunities for utilizing such cells for clinical-scale applications are being exploited. In order for an antigen-specific $CD8^+$ cell to survive long enough and thus be able to fight an infection or a tumor, the help of $CD4^+$ T cells is mandatory.
The CliniMACS Cytokine Capture System (IFN-gamma) is the first product developed that allows the concomitant clinical-scale enrichment of both $CD4^+$ and $CD8^+$ T cells specific for a given antigen.[10]

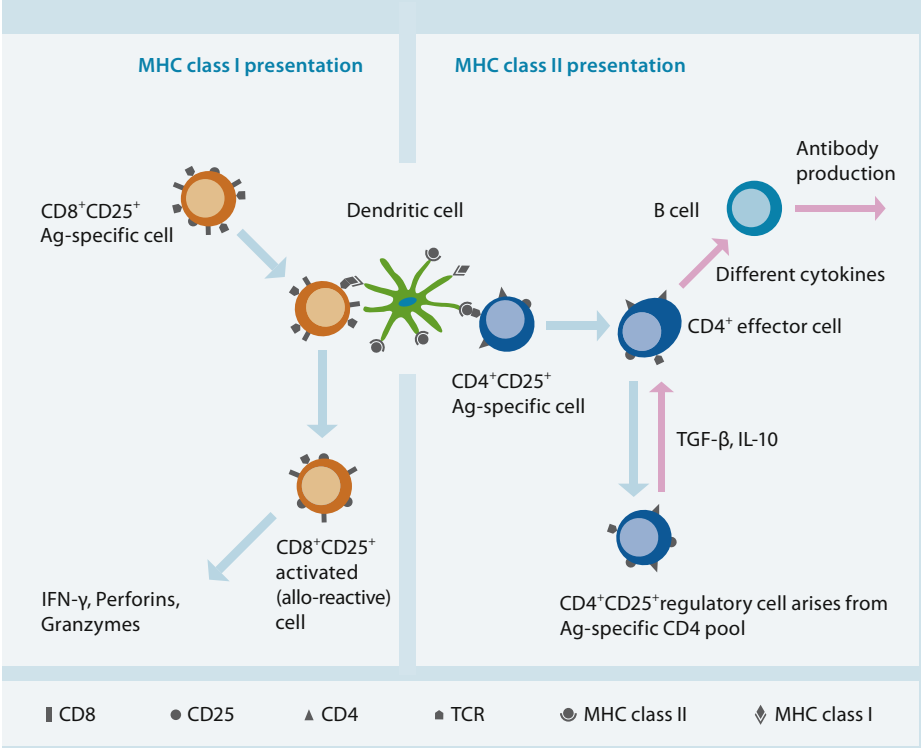



**Figure 1:** Schematic diagram of the interface between dendritic cells and T cells.

**References**
1. Barfield *et al.* (2004) Cytotherapy 6: 1–6.
2. Iyengar *et al.* (2003) Cytotherapy 5 (6): 479–484.
3. Falkenburg *et al.* (1999) Blood 94 (4): 1201–1208.
4. Rosenberg *et al.* (2004) PNAS, USA 101: 14639–14645.
5. Soiffer *et al.* (2002) Biol. Blood Marrow Transplant 8: 625–632.
6. André-Schmutz *et al.* (2002) Lancet 360: 130–137.
7. Hoffmann *et al.* (2004) Blood 104: 895–903.
8. Hoffmann *et al.* (2004) Blood 104: 2851.
9. Powell *et al.* (2005) J. Immunother. 28: 403–411.
10. Feuchtinger *et al.* (2004) Exp. Hem. 32: 282–289.

## CliniMACS® CD3 Cell Depletion

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD3 Reagent** | CE | $15\times10^9$ $CD3^+$ cells from $40\times10^9$ total cell | Europe, US [1)] | **273-01** |
| **CliniMACS CD3 MicroBeads** | For research use only, not for use in humans | $15\times10^9$ $CD3^+$ cells from $40\times10^9$ total cells | US, CAN, AUS | **176-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

CD3 is expressed on all T cells and is associated with the T cell receptor. Approximately 70–80% of human peripheral blood lymphocytes and 65–85% of thymocytes are $CD3^+$.

CliniMACS® CD3 Products consist of superparamagnetic iron dextran particles directly conjugated to CD3 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $15\times10^9$ $CD3^+$ cells from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS T Cell CD3 Products were developed for the depletion of unwanted T cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System. This approach maintains the stem cells and immune effector cells, such as NK cells, in the cellular product.[1,2]

**References**

1. Gordon *et al.* (2002) Bone Marrow Transplant. 30: 69–74
2. Chen *et al.* (2006) Brit. J. Haem. 135: 524–532.

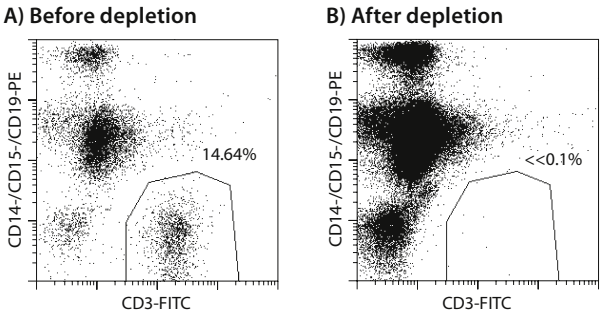



**Figure 1:** Flow cytometric analysis of CD3-depleted cells from a leukapheresis product using the CliniMACS CD3 System.

### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS CD19 Reagent | 179-01 |
| CliniMACS CD56 Reagent | 271-01 |
| CliniMACS CD3/CD19 Reagent Combination [1)] | 704-00 |

1) Not available in the US.

### Related MACS® Products

| | |
|---|---|
| CD14-PE, human | 130-091-242 |
| CD15-PE, human | 130-091-375 |
| CD19-PE, human | 130-091-247 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

## CliniMACS® CD4 Cell Separation

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD4 Reagent** | CE | $12\times10^9$ $CD4^+$ cells from $40\times10^9$ total cells | Europe, US[1)] | **276-01** |
| **CliniMACS CD4 MicroBeads** | For research use only, not for use in humans | $12\times10^9$ $CD4^+$ cells from $40\times10^9$ total cells | US, CAN, AUS | **304-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

CD4 is an accessory molecule in the recognition of foreign antigens in association with MHC class II antigens by T cells. T helper cells and to a lower degree monocytes and dendritic cells express CD4.

The CliniMACS® CD4 Products consist of superparamagnetic iron dextran particles directly conjugated to CD4 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $12\times10^9$ $CD4^+$ cells from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS® CD4 Products were developed for the depletion or enrichment of $CD4^+$ cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

### Referenced literature

In the allogeneic transplantation setting, $CD4^+$ T cells in donor lymphocyte infusions may be capable of mounting anti-tumor responses, concomitantly reducing the risk of GVHD[1] and reconstituting the recipient's immune system.[2]

Recently, TH2 cells have been successfully used to support stem cell grafts.[3]
In addition, the use of $CD4^+$ T cells may be the basis for various gene-therapeutic approaches such as in the HIV setting.[4–6]

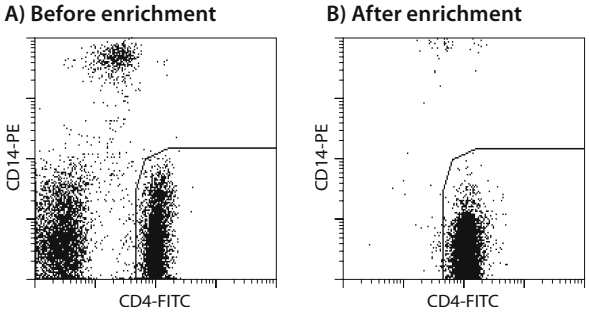



**Figure 1:** Flow cytometric analysis of CD4-enriched cells using the CliniMACS CD4 System.

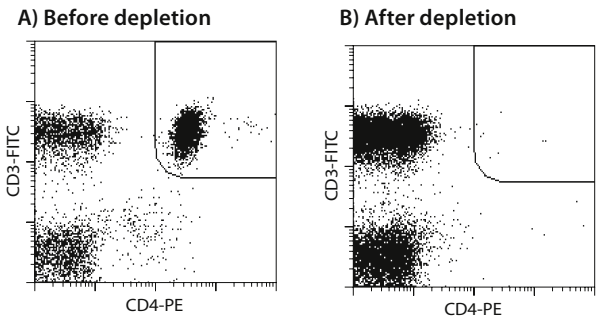



**Figure 2:** Flow cytometric analysis of CD4-depleted cells using the CliniMACS CD4 System.

**References**

1. Alyea *et al.* (1998) Blood 91: 3671–3680.
2. Bellucci *et al.* (2002) Blood 15: 4610–4617.
3. Fowler *et al.* (2004) Semin. Oncol. 31: 56–67.
4. Bernstein *et al.* (2004) Clin. Immunol. III: 262–274.
5. Levine *et al.* (2002) Nat. Med. 8: 47–53.
6. Davis *et al.* (2004) Mol. Ther. 9: 160–172.



### Related MACS® Products

| | |
|---|---|
| CD4-FITC, human | 130-080-501 |
| CD4-PE, human | 130-091-231 |
| CD4-APC, human | 130-091-232 |
| CD3-FITC, human | 130-080-401 |
| CD25-Biotin, human | 130-091-235 |
| Anti-Biotin-PE | 130-090-756 |
| Anti-Biotin-APC | 130-090-856 |
| CD8-FITC, human | 130-080-601 |
| CD30-PE, human | 130-081-401 |
| CD14-PE, human | 130-091-242 |
| CD25-PE, human | 130-091-024 |
| CD8-PE, human | 130-091-084 |
| CD8-APC, human | 130-091-076 |
| CD14-FITC, human | 130-080-701 |
| CD14-APC, human | 130-091-243 |
| Anti-Biotin-FITC | 130-090-857 |

## CliniMACS® CD8 Cell Depletion

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD8 Reagent** | CE | $4\times10^9$ $CD8^+$ cells from $40\times10^9$ total cells | Europe, US [1)] | **275-01** |
| **CliniMACS CD8 MicroBeads** | For research use only, not for use in humans | $4\times10^9$ $CD8^+$ cells from $40\times10^9$ total cells | US, CAN, AUS | **308-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD8 antigen, a co-receptor for MHC class I molecules, is expressed strongly on cytotoxic T cells and dimly on a subset of NK cells.

The CliniMACS® CD8 Products consist of superparamagnetic iron dextran particles directly conjugated to CD8 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $4\times10^9$ $CD8^+$ cells from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS CD8 Products were developed for depletion of $CD8^+$ T cells from human heterogeneous hematologic cell populations in combination with the CliniMACS System.

### Referenced literature

In the allogeneic transplantation setting $CD8^+$ T cells may be removed from a graft or DLI with the goal of preventing GVHD while maintaining GVL effects.[1–4] Additionally, the depletion of $CD8^+$ T cells might be part of a strategy for the enrichment of regulatory T cells. Enrichment of $CD8^+$ T cells is also an option for the generation of specific T cell lines.[5]


**References**

1. Nimer *et al.* (1994) Transpl. 57: 82–87.
2. Baron *et al.* (2003) Haematologica 88: 835–837.
3. Meyer *et al.* (2004) Blood 104: 5069.
4. Meyer *et al.* (2007) Blood 109: 374–382.
5. Savoldo *et al.* (2002) Blood 100: 4059–4066.


**A) Before depletion** **B) After depletion**

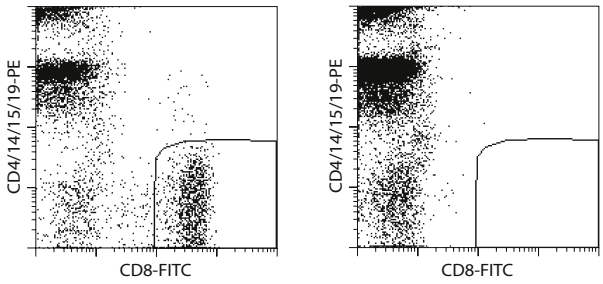



**Figure 1:** Flow cytometric analysis of CD8-depleted cells using the CliniMACS CD8 System.

### Related MACS® Products

| | |
|---|---|
| CD8-FITC, human | 130-080-601 |
| CD8-PE, human | 130-091-084 |
| CD8-APC, human | 130-091-076 |
| CD4-PE, human | 130-091-231 |
| CD4-APC, human | 130-091-232 |
| CD3-FITC, human | 130-080-401 |
| CD25-Biotin, human | 130-091-235 |
| Anti-Biotin-PE | 130-090-756 |
| Anti-Biotin-APC | 130-090-856 |
| CD30-PE, human | 130-081-401 |
| CD4-FITC, human | 130-080-501 |

## CliniMACS® CD25 Cell Separation

| Product | Regulatory status | Capacity (max.) | Availability | | Order no. |
|---|---|---|---|---|---|
| **CliniMACS CD25 Reagent** | CE | $6\times10^9$ $CD25^+$ cells (highly expressing CD25) from $40\times10^9$ total cells | Europe, US[1)] | ***NEW*** | **274-01** |
| **CliniMACS CD25 MicroBeads** | For research use only, not for use in humans | $6\times10^9$ $CD25^+$ cells (highly expressing CD25) from $40\times10^9$ total cells | US, CAN, AUS | | **325-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD25 antigen, the low affinity interleukin-2 receptor alpha chain (IL-2Rα), is expressed on activated T and B cells. In addition, CD25 is highly expressed on naturally occuring $CD25^{hi}CD4^+$ regulatory T cells.

The CliniMACS® CD25 Products consist of superparamagnetic iron dextran particles directly conjugated to CD25 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of $6\times10^9$ $CD25^+$ cells (highly expressing CD25) from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS® CD25 Products were developed for the enrichment or depletion of $CD25^+$ cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.

### Referenced literature

In the allogeneic transplantation setting a promising approach to reduce risk of severe GVHD may be the selective removal of $CD25^+$ alloreactive T cells.[1–3]

Studies in the mouse model paved the way to investigate the role of $CD25^{hi}CD4^+$ regulatory T cells for the improvement of stem cell transplantation. The addition of regulatory T cells, either to the graft or DLI may reduce the risk of GVHD.[4] $CD25^{hi}CD4^+$ regulatory T cells may also be depleted from patient's leukapheresis samples for immunotherapeutic approaches designed to favor anti-tumor responses.[5]

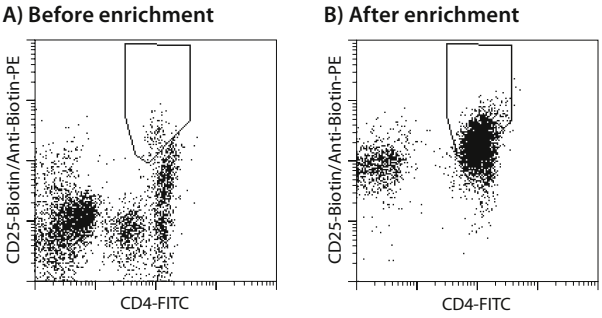



**Figure 1:** Flow cytometric analysis of CD25-enriched cells using the CliniMACS CD25 System.

Analysis of the content of $CD25^{hi}CD4^+$ regulatory T cells. For flow cytometric analysis a specific electronic window is defined. Regulatory T cells have been described as $CD4^+$ T cells which highly express CD25. The expression of CD4 is slightly reduced as compared to conventional $CD4^+$ T helper cells.[6]

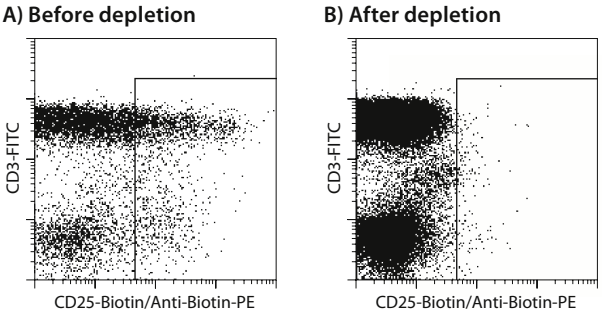



**Figure 2:** Flow cytometric analysis of CD25–depleted cells using the CliniMACS CD25 System.


**References**

1. Solomon *et al.* (2002) Cytotherapy 4 (5): 395–406.
2. André-Schmutz *et al.* (2003) Cytotherapy 7 (2): 102–108.
3. Amrolia *et al.* (2003) Blood 102 (6): 2292–2299.
4. Edinger *et al.* (2003) Nat. Med. 9: 1144–1150.
5. Powell *et al.* (2005) J. Immunother. 28(4): 403–11.
6. Baecher-Allen *et al.* (2001) J. Immunol. 167: 1245–1253.


### Related MACS® Products

| | |
|---|---|
| CD25-Biotin, human | 130-091-235 |
| Anti-Biotin-PE | 130-090-756 |
| Anti-Biotin-APC | 130-090-856 |
| CD3-FITC, human | 130-080-401 |
| CD4-FITC, human | 130-080-501 |
| CD8-FITC, human | 130-080-601 |

# Antigen-specific T cells

## CliniMACS® Antigen-specific T cell enrichment

Cytokine secretion is a hallmark of functionality of antigen-specific T cells. Large amounts of cytokines are produced by effector and memory T cells after short-term restimulation with "their" specific antigen.

For a multitude of challenges, it is of great interest to use antigen-specific T cells. Such applications could include prevention or managing of infection with Cytomegalovirus (CMV), Adenovirus, or Epstein-Barr Virus (EBV) [1, 2].
After immunosuppression (i.e. in the course of chemotherapy or organ-transplantation) such infections pose life-threatening complications, which sometimes are hard to fight by conventional means.

The treatment of tumors, which are resistant to conventional therapy, may become another field of application for antigen-specific T cells. Possible scenarios may also include autoimmune diseases such as rheumatoid arthritis and others.

It has been shown that optimal T cell immunity requires both $CD4^+$ helper T cells and $CD8^+$ cytotoxic T cells.[3] The CliniMACS® Cytokine Capture System (IFN-gamma) enables the enrichment of viable antigen-specific $CD4^+$ and antigen-specific $CD8^+$ T cells based on the cytokines they secrete.[4–6]

The CliniMACS Cytokine Capture System (IFN-gamma) offers unique reagents for clinical-scale enrichment of antigen-specific T cells, specifically developed for use exclusively on the CliniMACS® System.

Those cell preparations are the prerequisite for detailed analyses on the frequency and phenotype of the key players in a given immune response. Since the cells are viable after enrichment, subsequent *in vitro* steps such as expansion of the antigen-specific cells can be performed. Such an expansion step can also be performed "in the bag" to provide a greater degree of assurance of sterility.

The sensitivity and reliability of the assays have been demonstrated in a large panel of high-level scientific publications. These describe a variety of research applications from oncology or virology to autoimmune diseases.[4–6]

Using the CliniMACS Cytokine Capture System (IFN-gamma) the enrichment can be performed directly "in the bag" starting from up to $1 \times 10^9$ total cells. As for all CliniMACS applications, the entire process of cell enrichment is performed in a closed, sterile system. The resulting viable cells may be directly used in subsequent steps of the respective protocol. Alternatively, the cells may be manipulated or expanded *in vitro* or phenotypically analyzed.

**References:**
1. Cohen *et al.* (2002) Virology 304: 474.
2. Bissinger *et al.* (2002) Exp. Hematol. 30: 1178.
3. Dudley *et al.* (2002) Science 298: 850.
4. Campbell (2003) Methods 31: 150–159.
5. Feuchtinger *et al.* (2004) Exp. Hematol.32: 282–289.
6. Rauser *et al.* (2004) Blood 103: 3565–3572.

# Antigen-specific T cells

## IFN-γ-secreting antigen-specific T cells

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS Cytokine Capture System (IFN-gamma)** | CE | $1 \times 10^9$ total cells | Europe, US [1)] | **279-01** |
| **CliniMACS Cytokine Capture System (IFN-gamma) MicroBeads** | For research use only, not for use in humans | $1 \times 10^9$ total cells | US, CAN, AUS | **287-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

Interferon-gamma (IFN-gamma) is a cytokine secreted by $CD4^+$ and $CD8^+$ memory and effector T cells upon antigenic restimulation.

The CliniMACS® Cytokine Capture System (IFN-gamma) is comprised of the CliniMACS IFN-gamma Catchmatrix Reagent, consisting of CD45 antibodies conjugated to IFN-gamma specific antibodies, and the CliniMACS IFN-gamma Enrichment Reagent.
The CliniMACS IFN-gamma Enrichment Reagent consists of superparamagnetic iron dextran particles conjugated to IFN-gamma specific antibodies. The CliniMACS IFN-gamma Enrichment Reagent allows for magnetic selection of the IFN-gamma secreting cells.

One kit is suitable for processing up to $1 \times 10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

The CliniMACS® Cytokine Capture System (IFN-gamma) allows for the concomitant enrichment of viable antigen-specific $CD4^+$ and $CD8^+$ IFN-gamma secreting T cells.

### Referenced literature

Antigen-specific $CD4^+$ and $CD8^+$ T cells can be enriched using the CliniMACS Cytokine Capture System (IFN-gamma)[1]. T cells with specificity for CMV or Adenovirus could be expanded *in vitro*.[2–3]
The adoptive transfer of antigen-specific T cells may hold promise for the treatment of viral infections.[4–5]


**References**

1. Campbell (2003) Methods 31(2): 150–159.
2. Feuchtinger *et al* (2004) Exp. Hematol. 32 (3): 282–289.
3. Rauser *et al.* (2004) Blood 103 (9): 3565–3572.
4. Feuchtinger *et al.* (2005) Br. J. Haematol. 128: 503–509.
5. Feuchtinger *et al.* (2006) Br. J. Haematol. 134: 64–76.


### Related MACS® Products

| | |
|---|---|
| CD4-FITC, human | 130-080-501 |
| CD4-APC, human | 130-091-232 |
| CD8-FITC, human | 130-080-601 |
| CD8-APC, human | 130-091-076 |
| Large-Scale IFN-γ Secretion Assay – Enrichment Kit, human | 130-091-329 |
| T cell Expansion Bag (6 ports) | 130-091-459 |
| T cell Expansion Bag (tube) | 130-091-458 |
| T cell Activation/ Expansion Kit, human | 130-091-441 |
| Anti-IFN-γ-PE, human | 130-091-653 |

# Antigen-specific T cells

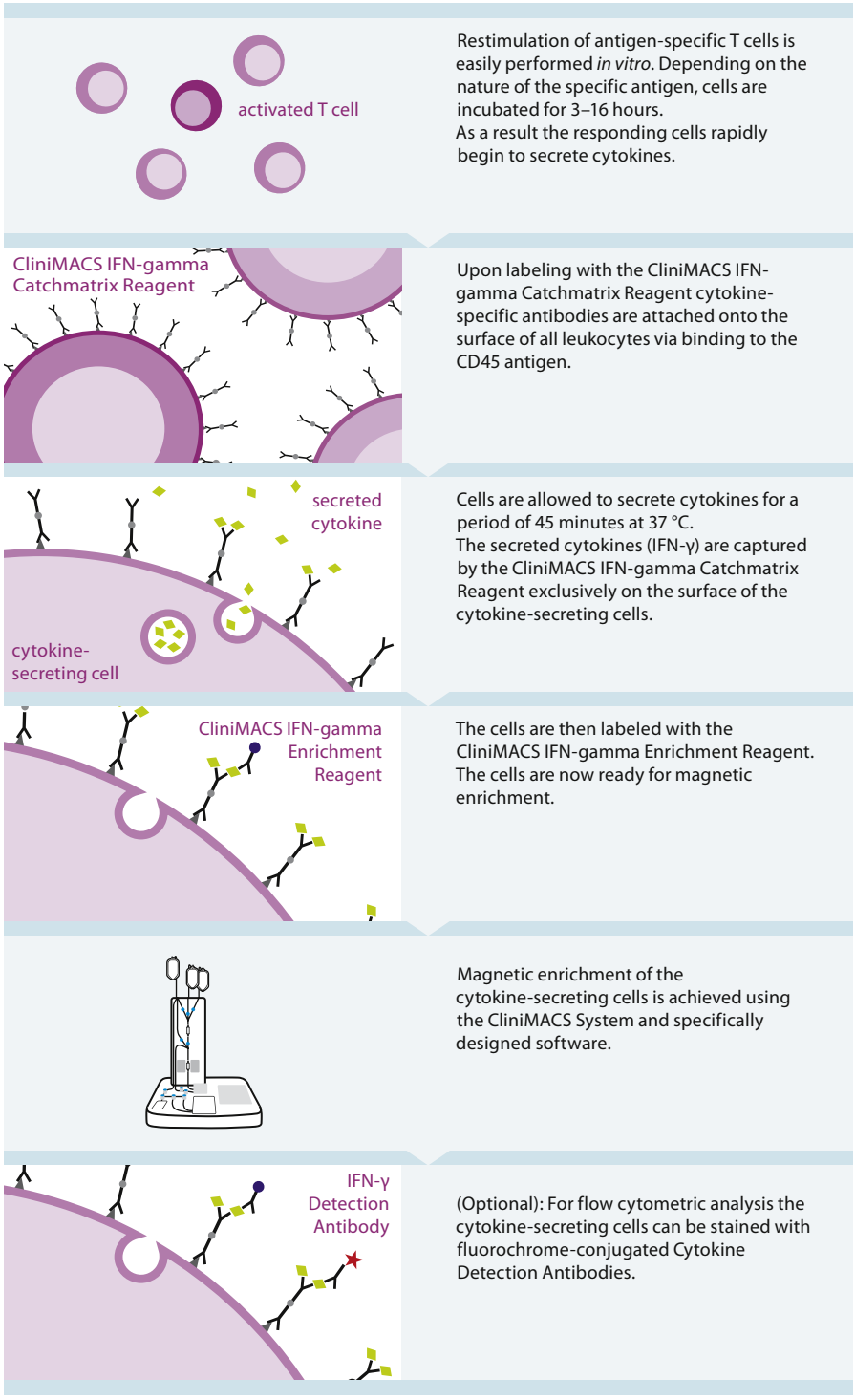



**Figure 1:** Principle of the CliniMACS® Cytokine Capture System (IFN-gamma).

## CliniMACS® Natural killer cell enrichment

Natural killer (NK) cells are known to be first in the line of defense against viral infections and solid tumors. On both malignant and virally infected cells a multiplicity of so called "danger signals" can be up-regulated. These signals can be specifically recognized by NK cells, enabling these cells to become activated and eventually lyse the potentially harmful target cell. It is the balance between stimulating and inhibiting signals which determines whether or not the NK cells will lyse their target cells[1]. More recently, NK cells have been specifically associated with the induction of graft versus leukemia (GVL) effects in hematopoietic malignant diseases in murine models and some retrospective analyses in the human[2–4]. Based on these data, clinical studies[5–7] were initiated to investigate the safety and feasibility of this approach in a haploidentical transplant setting for hematologic malignant disorders. The NK cells were enriched from leukapheresis products[8,9] and given as donor lymphocyte infusions (DLI) at various time points post transplant. One important reason NK-DLI has been used instead of an unmanipulated DLI was the observation that NK cells may induce a GVL effect without inducing graft versus host disease (GVHD); the latter being a serious complication of unmanipulated DLIs in general.
It has been theorized that a KIR-mismatch situation in the GVH direction may enable NK cells to lyse malignant target cells in order to exert GVL effects. This effect may be used to revert impending mixed chimerism or relapse in the above mentioned setting. Safety and feasibility of this approach was recently reviewed.[10]

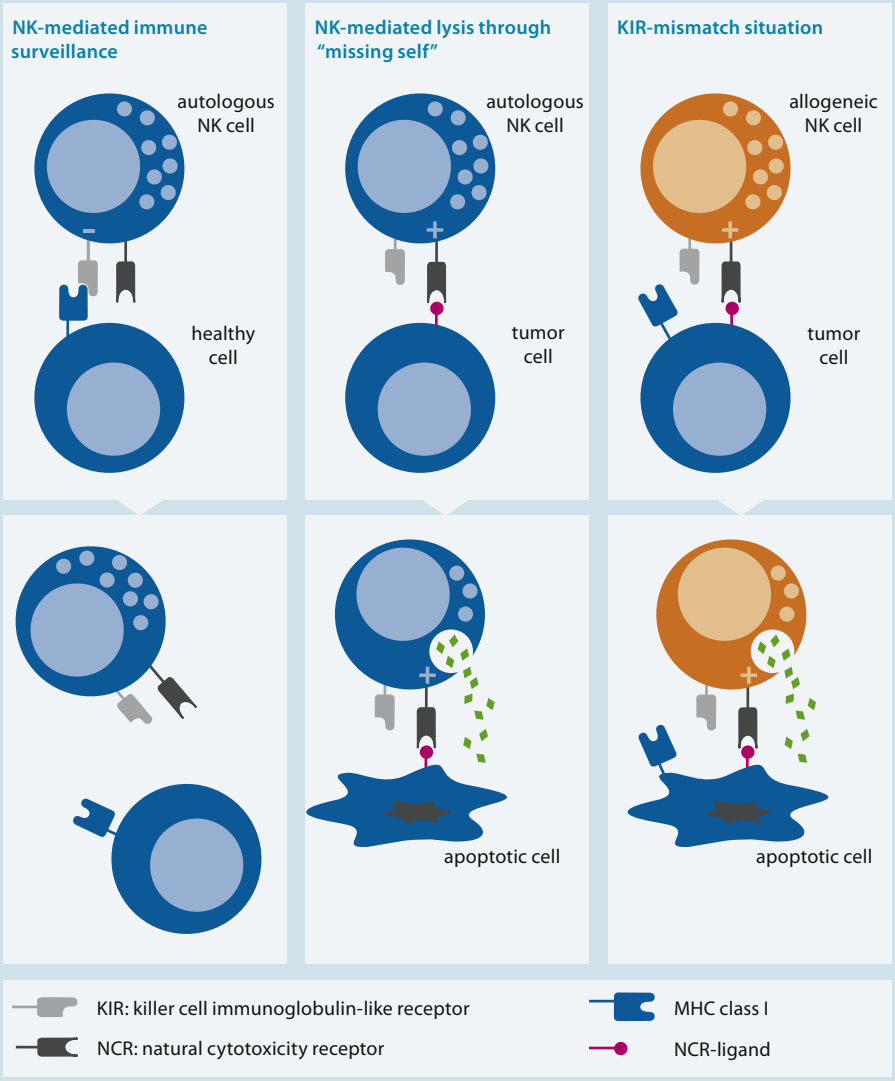



**Figure 1:** Defense mechanisms of natural killer cells.

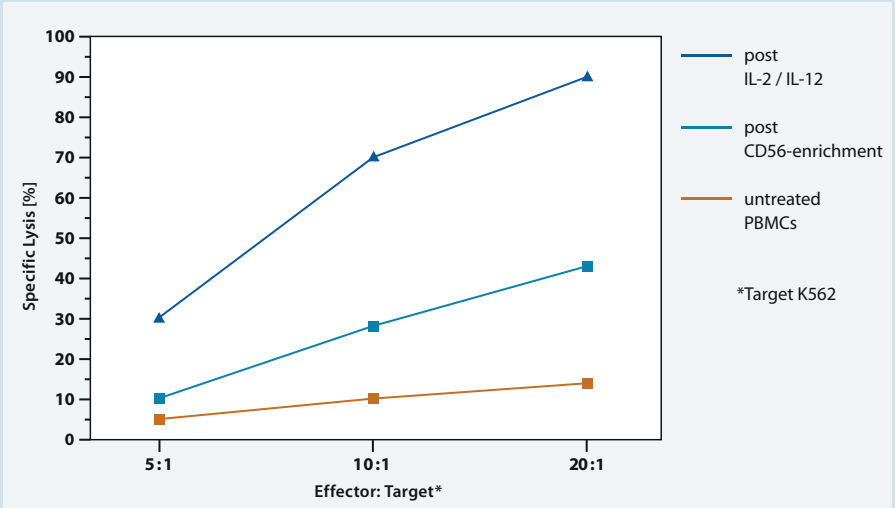



**Figure 2:** Activation of $CD56^+CD3^-$ NK cells upon treatment with IL-2 / IL-12. (Courtesy of Dr. Uharek, Berlin, Germany.)

**References:**
1. Kärre (2002) Science 295: 2029–2031.
2. Ruggeri *et al.* (2002) Science 295: 2097–2100.
3. Giebel *et al.* (2003) Blood 102: 814–819.
4. Elmaagacli *et al.* (2004) Onkologie 27, Suppl. 3: 0194.
5. Uharek *et al.* (2003) Onkologie 26, Suppl. 5: V374.
6. Passweg *et al.* (2003) Onkologie 26, Suppl. 5: P482.
7. Passweg *et al.* (2004) Leukemia 18 (11): 1835–1838.
8. Iyengar *et al.* (2003) Cytotherapy 5(6): 479–484.
9. Duwendag *et al.* (2004) 20th International NK cell Workshop, Noordwijkerhout, NL.
10. Passweg *et al.* (2005) BMT 35:637–643.

## CliniMACS® CD56 Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD56 Reagent** | CE | $10\times10^9$ $CD56^+$ cells from $40\times10^9$ total cells | Europe, US [1)] | **271-01** |
| **CliniMACS CD3/CD56 Reagent Combination** | CE-marked components | $15\times10^9$ $CD3^+$ cells and $10\times10^9$ $CD56^+$ cells from $40\times10^9$ total cells | Europe | **704-01** |
| **CliniMACS CD3/CD56 Complete Kit** | CE-marked components | $15\times10^9$ $CD3^+$ cells and $10\times10^9$ $CD56^+$ cells from $40\times10^9$ total cells | Europe | **740-04** |
| **CliniMACS CD56 MicroBeads** | For research use only, not for use in humans | $10\times10^9$ $CD56^+$ cells from $40\times10^9$ total cells | US, CAN, AUS | **194-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD56 antigen is expressed on essentially all human NK cells, and its density on the cell membrane is increased after activation. The antigen is also present on a unique subset of $CD3^+$ T cells (NKT cells) that mediate non-MHC-restricted cytotoxicity and on some neural tissues and tumors.

The CliniMACS® CD56 Products consist of superparamagnetic iron dextran particles directly conjugated to CD56 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of $10\times10^9$ $CD56^+$ cells from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS® CD56 Products were developed for the enrichment of NK and NKT cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.
In order to generate highly purified $CD56^+CD3^-$ NK cells, the CliniMACS CD56 Reagent is used in combination with the CliniMACS CD3 Reagent. In this approach, the cellular product is first depleted of $CD3^+$ cells and then further enriched for CD56.[1,2]

### Referenced literature

NK cells have been used in haploidentical PBSC transplantation settings as donor lymphocyte infusions (DLIs) to explore the prevention of GVHD and early relapse of hematological malignant diseases (e.g. AML, CML).

Use of NK-DLIs for stabilizing an impending decreasing donor chimerism in a haploidentical transplantation setting has also been published.[3–11]

**References**

1. Duwendag *et al.* (2004) 20th International NK Cell Workshop, Noordwijkerhout, NL.
2. Iyengar *et al.* (2003) Cytotherapy, 5(6): 479–484.
3. Uharek *et al.* (2002) Onkologie, 25, Suppl. 4: P844.
4. Uharek *et al.* (2003) Onkologie, 26, Suppl. 5: V374.
5. Passweg *et al.* (2003) Onkologie, 26, Suppl. 5: P482.
6. Leung *et al.* (2004) J. Immunol., 172: 644–650.
7. Maillard *et al.* (2004) 8th International Symposium on DC, Brugge,Belgium.
8. Giebel *et al.* (2003) Blood, 102: 814–819.
9. Elmaagacli *et al.* (2004) Onkologie 27, Suppl. 3: 0194.
10. Ruggeri *et al.* (2002) Science, 295: 2097–2100.
11. Farag *et al.* (2002) Blood, 100(6): 1935–1947.

# NK cells

**Kit components** (not available in the US)

**CliniMACS CD3/CD56 Reagent Combination (704-01):**

- 1 vial CliniMACS CD3 Reagent
- 1 vial CliniMACS CD56 Reagent

**CliniMACS CD3/CD56 Complete Kit (740-04):**

- 1 vial CliniMACS CD3 Reagent
- 1 vial CliniMACS CD56 Reagent
- 1 CliniMACS Tubing Set
- 1 CliniMACS Depletion Tubing Set
- 2 units CliniMACS PBS/ EDTA Buffer 3×1 L

## Related CliniMACS® Products

| | |
|---|---|
| CliniMACS CD3 MicroBeads | 176-01 |
| CliniMACS CD3 Reagent | 273-01 |
| CliniMACS CD3/CD19 Reagent Combination[1)] | 704-00 |

1) Not available in the US.

## Related MACS® Products

| | |
|---|---|
| CD3-FITC, human | 130-080-401 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

## Single-step NK and NKT cell enrichment procedure

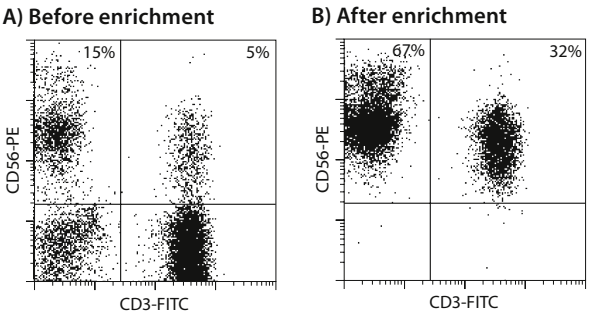



**Figure 1:** Flow cytometric analysis of CD56-enriched cells using the CliniMACS CD56 System.

## Two-step NK cell enrichment procedure

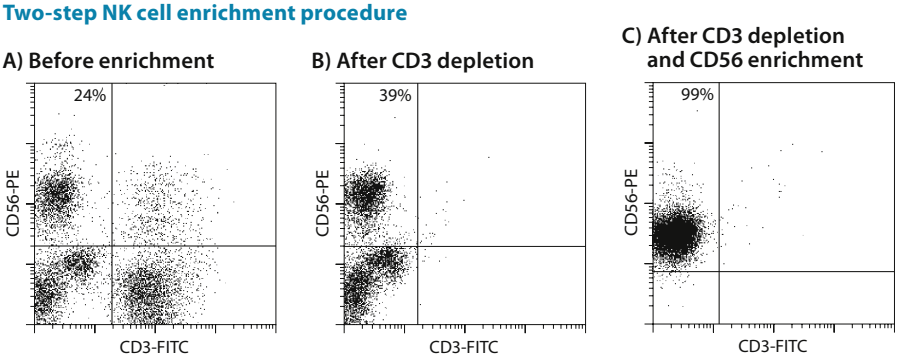



**Figure 2:** Flow cytometric analysis of CD3-depleted cells (B) followed by the analysis of CD56-enriched cells (C) using the CliniMACS CD3/CD56 System.

## CliniMACS® CD19 Cell Depletion

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD19 Reagent** | CE | $5\times10^9$ $CD19^+$ cells from $40\times10^9$ total cells | Europe, US[1)] | **179-01** |
| **CliniMACS CD19 MicroBeads** | For research use only, not for use in humans | $5\times10^9$ $CD19^+$ cells from $40\times10^9$ total cells | US, CAN, AUS | **193-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

As a B cell lineage marker, CD19 is expressed from the early pro-B cell stage to the B cell lymphoblast stage; however, CD19 is down-regulated as B cells mature to plasma cells. The CD19 antigen is also expressed on most malignant B cells and on a subset of follicular dendritic cells.

The CliniMACS® CD19 Products consist of superparamagnetic iron dextran particles directly conjugated to CD19 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $5\times10^9$ $CD19^+$ cells from up to $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS® CD19 Products were developed for depletion of $CD19^+$ B cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.
The depletion of $CD19^+$ cells can be performed to remove unwanted malignant or potentially EBV-infected B cells from cellular products.[1]

**References**

1. Barfield *et al.* (2004) Cytotherapy 6: 1–6.

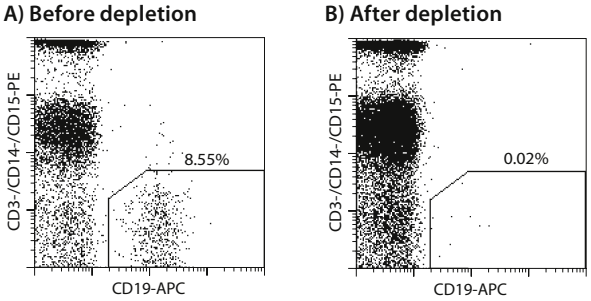



**Figure 1:** Flow cytometric analysis of CD19–depleted B cells from leukapheresis product using the CliniMACS CD19 System.

### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS CD3/CD19 Reagent Combination[1)] | 704-00 |
| CliniMACS CD1c (BDCA-1)-Biotin | 277-01 |

1) Not available in the US.

### Related MACS® Products

| | |
|---|---|
| CD20-FITC, human | 130-091-108 |
| CD3-PE, human | 130-091-374 |
| CD14-PE, human | 130-091-242 |
| CD15-PE, human | 130-091-375 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

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## CliniMACS® Dendritic cell enrichment

Dendritic cells (DCs) have great potential as cellular vaccines for various diseases. Most clinical studies using DCs focus on malignant diseases such as solid tumors or hematologic malignancies. However, novel indications such as viral infections, solid organ transplantation, and autoimmune diseases are also being investigated.

DCs generated from monocytes after CD14 enrichment (MoDCs) have been used in many of these clinical trials and are well characterized.[1–5] *In vitro* experiments have demonstrated that MoDCs and DCs derived from $CD34^+$ precursor cells are able to present antigens and efficiently induce a specific immune response dominated by effector T cells. However, in clinical studies using DCs, clinical responses have been lacking in most patients treated.

It is thought that other components of the immune system including NK cells, myeloid or plasmacytoid blood DCs (PDCs), as well as regulatory T cells may be necessary for a clinical response. Recent findings support a role for regulatory T cells in limiting the tumor-specific immune response induced by DCs.[6] It has been demonstrated that CD1c (BDCA-1)-positive myeloid DCs display a strong costimulatory and cross-presenting capacity.[7]

Plasmacytoid dendritic cells (PDCs) are the most potent Type I IFN-producing cells identified so far.[8] Interferon-alpha-2a is used as pharmaceutical drug in indications such as malignant melanoma and other malignancies. Thus, the local application of PDCs could become a promising tool in enhanced vaccine strategies.

Recent developments will soon enable the use of blood myeloid DCs, which are CD1c (BDCA-1)-positive, or the use of CD304 (BDCA-4)-positive PDCs. The possibility to enrich both cell types will allow for new enhanced DC vaccine strategies. Because these DC subsets are derived directly from blood, no long culturing period – as for MoDC generation – is needed.

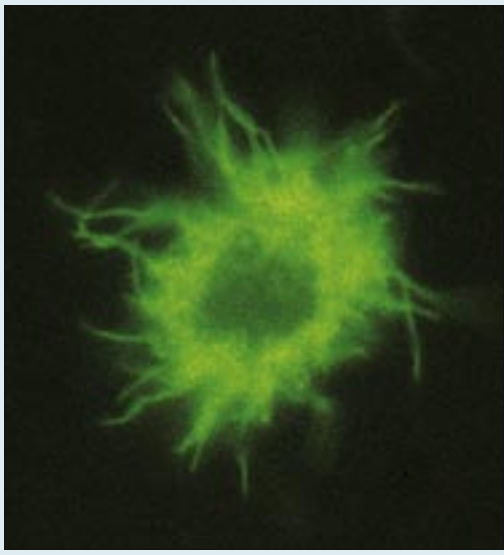

**Figure 1:** Mature blood dendritic cell stained with HLA-DR-FITC.

**References:**

1. Dietz *et al.* (2004) Cytotherapy 6(6): 563–570.
2. Curti *et al.* (2004) Leukemia & Lymphoma 45(7): 1419–1428.
3. Meyer-Wentrup et al. (2003) J. Hematother. & Stem Cell Res. 12: 289–299.
4. Sorg *et al.* (2003) J. Immunol. 26(4): 374–383.
5. Motta *et al.* (2003) Br. J. Haematol. 121: 240–250.
6. Prasad *et al.* (2005) J. Immunol. 174: 90–98.
7. Schnurr *et al.* (2005) Blood 105: 2465–2472.
8. Dzionek *et al.* (2002) Hum. Immunol. 63: 1133–1148.

# Dendritic cells

## CliniMACS® CD14 Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD14 Reagent** | CE | $4\times10^9$ $CD14^+$ cells from $20\times10^9$ total cells | Europe, US [1)] | **272-01** |
| **CliniMACS CD14 Complete Kit** | CE-marked components | $4\times10^9$ $CD14^+$ cells from $20\times10^9$ total cells | Europe | **281-01** |
| **CliniMACS CD14 MicroBeads** | For research use only, not for use in humans | $4\times10^9$ $CD14^+$ cells from $20\times10^9$ total cells | US, CAN, AUS | **191-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD14 antigen belongs to the LPS receptor complex and monocytes strongly express the antigen.

The CliniMACS® CD14 Products consist of superparamagnetic iron dextran particles directly conjugated to CD14 antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $4\times10^9$ $CD14^+$ monocytes in $20\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS CD14 Products were developed for the enrichment of $CD14^+$ cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.
The enriched cells can be used for the subsequent generation of human monocyte-derived dendritic cells (MoDCs).[1]

**A) Before enrichment** **B) After enrichment**

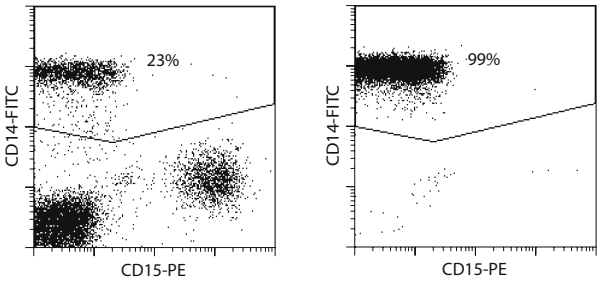


**Figure 1:** Flow cytometric analysis of CD14–enriched cells using the CliniMACS CD14 System.

### Referenced literature

MoDCs are currently being used in clinical trials which mainly target malignant diseases such as solid tumors and hematologic malignancies.[2–8]


**References**

1. Campbell *et al.* (2005) Methods in Molecular Medicine 109 (5): 55–69.
2. Babatz *et al.* (2003) J. Hematother. Stem Cell Res. 12 (5): 515–523.
3. Motta *et al.* (2003) Br. J. Hematol. 121 (2): 240–250.
4. Meyer-Wentrup *et al.* (2003) J. Hematother. Stem Cell Res. 12 (3): 289–299.
5. Sorg *et al.* (2003) J. Immunother. 26 (4): 374–383.
6. Padley *et al.* (2001) J. Hematother. Stem Cell Res. 10: 427–429.
7. Dietz *et al.* (2000) J. Hematother. Stem Cell Res. 9 (1): 95–101.
8. Curti *et al.* (2004) Leukemia & Lymphoma 45 (7): 1419–1428.


### Kit components (not available in the US)

**CliniMACS CD14 Complete Kit (281-01):**

- 1 vial CliniMACS CD14 Reagent
- 1 CliniMACS Tubing Set
- 3 × 1 L of CliniMACS PBS/EDTA Buffer

### Related MACS® Products

| | |
|---|---|
| CD14-FITC, human | 130-080-701 |
| CD15-FITC, human | 130-081-101 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

## CliniMACS® CD1c (BDCA-1) Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | | Order no. |
|---|---|---|---|---|---|
| **CliniMACS CD1c (BDCA-1)-Biotin** | CE | $0.2 \times 10^9$ CD1c (BDCA-1)$^+$ cells from $40 \times 10^9$ total cells | Europe, US[1)] | ***NEW*** | **277-01** |
| **CliniMACS CD1c (BDCA-1)/CD19 Complete Kit** | CE-marked components | $0.2 \times 10^9$ CD1c (BDCA-1)$^+$ cells from $40 \times 10^9$ total cells | Europe | ***NEW*** | **740-03** |
| **CliniMACS CD1c (BDCA-1)-Biotin for Research Use** | For research use only, not for use in humans | $0.2 \times 10^9$ CD1c (BDCA-1)$^+$ cells from $40 \times 10^9$ total cells | US, CAN, AUS | | **255-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CD1c (BDCA-1) antigen is expressed on dendritic cells which are CD11c$^{high}$CD123$^{low}$ and represent a major subset of myeloid dendritic cells in human peripheral blood. Also, the antigen is expressed on a subpopulation of CD19$^+$ B cells.

The CliniMACS® CD1c (BDCA-1)-Biotin Products consist of biotin directly conjugated to CD1c (BDCA-1) antibodies.

One vial contains 5 mL sterile, non-pyrogenic solution suitable for labeling of up to $0.2 \times 10^9$ CD1c (BDCA-1)$^+$ cells from up to $40 \times 10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS CD1c (BDCA-1)-Biotin Products were developed for the enrichment of CD1c (BDCA-1)$^+$ myeloid dendritic cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.
After labeling of target cells with the CliniMACS CD1c (BDCA-1)-Biotin, the CliniMACS Anti-Biotin Reagent is used for the magnetic enrichment of CD1c (BDCA-1)$^+$ cells from the cellular product.
A CD19$^+$ B cell depletion is recommended prior to the enrichment of CD1c (BDCA-1)$^+$ cells.

### Flow cytometric analysis of CD1c (BDCA-1)$^+$ cell enrichment

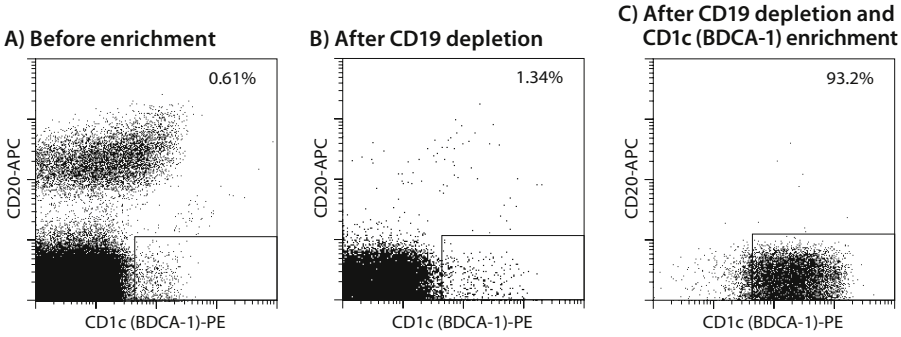


**Figure 1:** Flow cytometric analysis of CD19-depleted cells (B) followed by the analysis of CD1c (BDCA-1)-enriched cells (C) using the CliniMACS CD19– and CliniMACS CD1c (BDCA-1)–Biotin System in combination.

### Kit components (not available in the US)

**CliniMACS CD1c (BDCA-1)/CD19 Complete Kit (740-03):**

- 1 vial CliniMACS CD1c (Anti-BDCA-1)-Biotin
- 1 vial CliniMACS CD19 Reagent
- 1 vial CliniMACS Anti-Biotin Reagent
- 1 CliniMACS Tubing Set
- 1 CliniMACS Tubing Set LS
- 3 units 3×1L CliniMACS PBS/EDTA Buffer


**References**

1. Dzionek A. *et al.* (2000) J. Immunol. 165: 6037–6046.
2. Dzionek A. *et al.* (2002) Hum Immunol. 63 (12): 1133–1148.
3. Piechaczek C *et al.* (2002) 7th International Symposium on Dendritic Cells, Bamberg, Germany: P197.
4. Schnurr M. *et al.* (2005) Blood 105(6): 2465-2472.
5. Davis I.D. *et al.* (2005) Proc. Amer. Assoc. Cancer Res. 46: Abstr. no. 3466.


### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS Anti-Biotin MicroBeads | 192-01 |
| CliniMACS Anti-Biotin Reagent | 173-01 |
| CliniMACS CD19 MicroBeads | 193-01 |
| CliniMACS CD19 Reagent | 179-01 |

### Related MACS® Products

| | |
|---|---|
| Blood Dendritic Cell Enumeration Kit, human | 130-091-324 |
| CD1c (BDCA-1)-PE, human | 130-090-508 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

# Dendritic cells

## CliniMACS® CD304 (BDCA-4) Cell Enrichment

| Product | Regulatory status | Capacity (max.) | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS CD304 (BDCA-4) MicroBeads** | For research use only, not for use in humans | $0.2\times10^9$ CD304 (BDCA-4)$^+$ cells from $40\times10^9$ total cells | Worldwide | **291-01** |

For availability in your country please contact your local representative.

### Description

In peripheral blood, CD304 (BDCA-4, Neuropilin-1) is expressed on human plasmacytoid (lymphoid) dendritic cells, which are characterized as being CD303 (BDCA-2)$^+$, CD4$^+$, Lin$^-$, CD11c$^-$, CD123$^{bright}$, CD45RA$^+$, CD2$^-$. These cells do not express myeloid lineage markers such as CD13 or CD33[1,2].

The CliniMACS® CD304 (BDCA-4) MicroBeads consist of superparamagnetic iron dextran particles directly conjugated to CD304 (BDCA-4) antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of up to $0.2\times10^9$ CD304 (BDCA-4)$^+$ cells out of $40\times10^9$ total cells.

Please inquire about recommended device and accessories.

### Applications

CliniMACS® CD304 (BDCA-4) MicroBeads were developed for enrichment of CD304 (BDCA-4)$^+$ plasmacytoid dendritic cells from human heterogeneous hematologic cell populations in combination with the CliniMACS® System.


**References**

1. Dzionek *et al.* (2000) J. of Immunology 165: 6037–6046. [898]
2. Dzionek *et al.* (2002) Hum Immunol. 63 (12): 1133–1148. [2423]


**A) Before enrichment** **B) After enrichment**

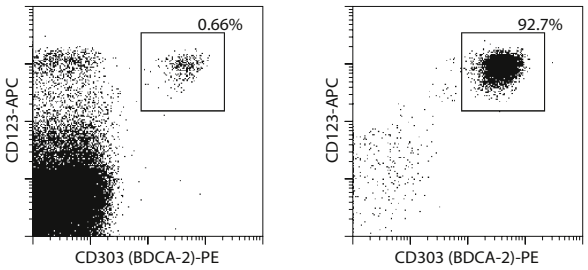


**Figure 1:** Flow cytometric analysis of CD304 (BDCA-4)–enriched cells from leukapheresis harvest using the CliniMACS CD304 (BDCA-4) System.

### Related MACS® Products

| | |
|---|---|
| CD303 (BDCA-2)-FITC, human | 130-090-510 |
| CD303 (BDCA-2)-PE, human | 130-090-511 |
| CD123-APC, human | 130-090-901 |
| CD45-FITC, human | 130-080-202 |
| CD45-PE, human | 130-080-201 |
| Blood Dendritic Cell Enumeration Kit, human | 130-091-324 |

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

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# Flexible labeling system

## CliniMACS® Anti-Biotin

| Product | Regulatory status | Capacity | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS Anti-Biotin Reagent** | CE | $40\times10^9$ total cells | Europe, US[1)] | **173-01** |
| **CliniMACS Anti-Biotin MicroBeads** | For research use only, not for use in humans | $40\times10^9$ total cells | US, CAN, AUS | **192-01** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CliniMACS® Anti-Biotin Products consist of superparamagnetic iron dextran particles directly conjugated to Biotin-specific antibodies.

One vial contains 7.5 mL sterile, non-pyrogenic solution suitable for magnetic labeling of target cells from up to $40\times10^9$ total cells. Please inquire about recommended device and accessories.

### Applications

The CliniMACS® Anti-Biotin Products were developed for the enrichment or depletion of target cells labeled with a biotinylated primary antibody or ligand.

#### Related CliniMACS® Products

| | |
|---|---|
| CliniMACS CD1c (BDCA-1)-Biotin | 277-01 |

#### Related MACS® Products

| | |
|---|---|
| Anti-Biotin-FITC | 130-090-857 |
| Anti-Biotin-PE | 130-090-756 |
| Anti-Biotin-APC | 130-090-856 |

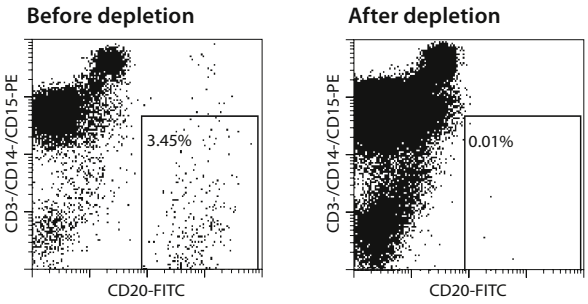



**Figure 1:** Flow cytometric analysis of CD19-depleted cells using the CliniMACS Anti-Biotin System in combination with CD19-biotinylated antibody.

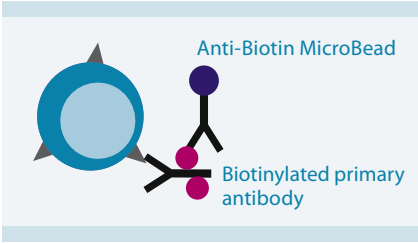



**Figure 2:** Labeling principle using CliniMACS Anti-Biotin Products.

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

## CliniMACS® Biotinylation Kit 500

| Product | Regulatory status | Capacity | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS Biotinylation Kit 500**[1)] | CE | Biotinylation of 500 µg monoclonal antibody | Europe, US[2)] ***NEW*** | **701-06** |
| **CliniMACS Biotinylation Kit 500 for Research Use** | For research use only, not for use in humans | Biotinylation of 500 µg monoclonal antibody | US, CAN, AUS | **257-01** |

For availability in your country please contact your local representative.

1) Outside Europe the CliniMACS® Biotinylation Kit 500 is for research use only.

2) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description/Applications

The CliniMACS® Biotinylation Kit 500 Products have been developed for the biotinylation of monoclonal antibodies for further magnetic cell enrichment from human heterogenerous hematologic cell populations using the CliniMACS System.

One kit is sufficient for biotinylating 500 µg monoclonal antibody.

Please check in advance whether the antibody is suitable for biotinylation, magnetic labeling, and cell separation using the CliniMACS® System.

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

CliniMACS® MicroBeads are for research use only and not for use in humans.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research only and not for therapeutic or diagnostic use.

# CliniMACS® Buffers

## CliniMACS® PBS/EDTA Buffer

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS PBS/EDTA Buffer** | 3×1L plastic bags | CE | Europe, CAN, AUS, US [1] | **700-25** |

For availability in your country please contact your local representative.

1) In the USA, the CliniMACS® System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).

### Description

The CliniMACS® PBS/EDTA Buffer consists of phosphate buffered saline, pH 7.2, supplemented with 1 mM EDTA.
The buffer is supplied in 1 L plastic bags as a sterile, non-pyrogenic solution.

### Application

CliniMACS PBS/EDTA Buffer was developed for cell preparation and separation of magnetically labeled cells with the CliniMACS System. CliniMACS PBS/EDTA Buffer is not intended for direct infusion into humans.

The CliniMACS® System components: Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS System components are available as CE-marked medical devices. In the USA, the CliniMACS System components including the CliniMACS® Reagents are available for use only under an approved Investigational New Drug (IND) application or Investigational Device Exemption (IDE).
CliniMACS® MicroBeads are for research use only and not for use in humans.

**Figure 1:** CliniMACS PBS/EDTA Buffer.

## CliniMACS® PBS/EDTA Buffer for Research Use

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **CliniMACS PBS/EDTA Buffer for Research Use** | 3×1L plastic bags | For research use only, not for use in humans [1] | US | **705-25** |

For availability in your country please contact your local representative.

1) Manufactured under an ISO 9001 certified quality system.

### Description

The CliniMACS® PBS/EDTA Buffer consists of phosphate buffered saline, pH 7.2, supplemented with 1 mM EDTA.
The buffer is supplied in 1 L plastic bags as a sterile, non-pyrogenic solution.

### Application

CliniMACS PBS/EDTA Buffer was developed for cell preparation and separation of magnetically labeled cells with the CliniMACS® System.

**Figure 1:** CliniMACS PBS/EDTA Buffer for research use.

## Cell culture products

The technical features of Miltenyi Biotec cell culture bags make them valuable tools for investigators interesting in culturing cells.

The bags are gas permeable, transparent for microscopy and allow for a closed culture system resulting in reduced risk of contamination.
The bags are individually packed, sterile and tested for endotoxins.

They come in single-tube format or with six needleless access connectors fitting standard laboratory requirement.

The single-tube can be used for sterile docking (according to the instructions for use of the tube welding device).

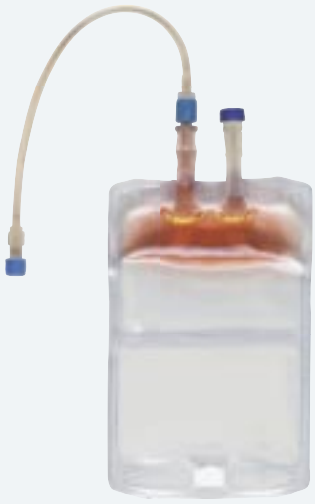
Transfer devices with a male luer lock connector (e.g. tubing or syringe) can be attached directly to the needleless access connectors.

Cell Differentiation Bags are available for three different culture volumes: 100 mL, 250 mL and 500 mL.

Cell Expansion Bags are compartimentalized with easy to open seals for expandable culture volumes as cell numbers increase during culture period. There is no need for changing culture vessel.

The three compartments allow for expandable volumes from 8 mL up to 100 mL.

1.



2.

3.

**Cell Expansion Bag (tube) with incremental culture volumes:** As culture volume increases, seals can easily be opened to give larger culture volumes. No transfer to other bags is necessary.

# Accessories

## Cell Expansion Bags

| Product | Content | Regulatory status | Capacity | Availability | | Order no. |
|---|---|---|---|---|---|---|
| **Cell Expansion Bag (tube)** | 5 Bags | CE[1)] | up to 100 mL | Europe | | **200-074-301** |
| **Cell Expansion Bag (6 ports)** | 5 Bags | CE[1)] | up to 100 mL | Europe | | **200-074-302** |
| **Cell Expansion Bag (tube)** | 5 Bags | For research use only[2)] | up to 100 mL | US, CAN, AUS | ***NEW*** | **130-074-351** |
| **Cell Expansion Bag (6 ports)** | 5 Bags | For research use only [2)] | up to 100 mL | US, CAN, AUS | ***NEW*** | **130-074-352** |

For availability in your country please contact your local representative.

1) The Cell Expansion Bags are manufactured by Miltenyi Biotec GmbH and controlled under an ISO 13485 certified quality system. These products are available in Europe as CE-marked medical devices.

2) Manufactured by Miltenyi Biotec GmbH under an ISO 9001 certified quality system.

### Description

Cell Expansion Bags are gas-permeable and transparent for microscopy.

They have three compartments to allow for expandable volumes of up to 100 mL.
The bag are individually packed, sterile and tested for endotoxins.

### Applications

Cell Expansion Bags are intended for the *in vitro* cultivation and expansion of human cells from heterogeneous haematologic cell populations (e.g. for the expansion of antigen-specific T cells).

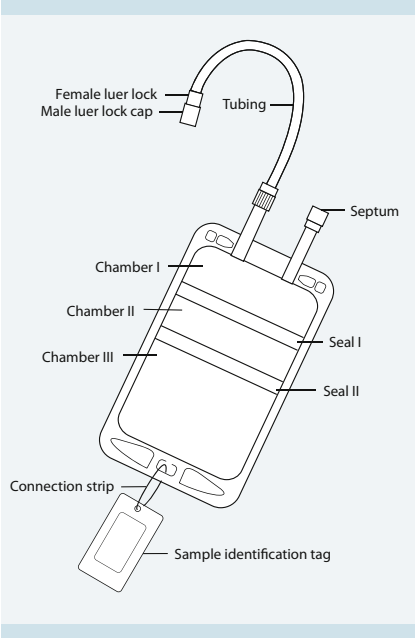



**Figure 1:** Cell Expansion Bag (tube) with two seals for expandable culture volumes.

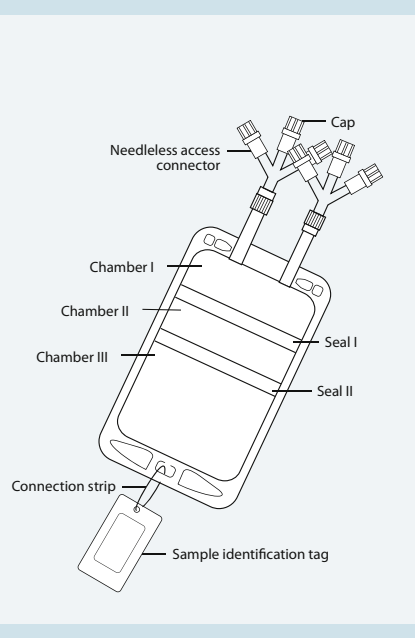



**Figure 2:** Cell Expansion Bag (6 ports) with two seals for expandable culture volumes and six needleless access connectors.

## Cell Differentiation Bags

| Product | Content | Regulatory status | Capacity | Availability | | Order no. |
|---|---|---|---|---|---|---|
| **Cell Differentiation Bag (tube) – 100** | 5 Bags | CE[1)] | 100 mL | Europe | | **200-074-101** |
| **Cell Differentiation Bag (tube) – 250** | 5 Bags | CE[1)] | 250 mL | Europe | | **200-074-102** |
| **Cell Differentiation Bag (tube) – 500** | 2 Bags | CE[1)] | 500 mL | Europe | | **200-074-103** |
| **Cell Differentiation Bag (6 ports) – 100** | 5 Bags | CE[1)] | 100 mL | Europe | | **200-074-201** |
| **Cell Differentiation Bag (6 ports) – 250** | 5 Bags | CE[1)] | 250 mL | Europe | | **200-074-202** |
| **Cell Differentiation Bag (6 ports) – 500** | 2 Bags | CE[1)] | 500 mL | Europe | | **200-074-203** |
| **Cell Differentiation Bag (tube) – 100** | 5 Bags | For research use only[2)] | 100 mL | US, CAN, AUS | ***NEW*** | **130-074-151** |
| **Cell Differentiation Bag (tube) – 250** | 5 Bags | For research use only[2)] | 250 mL | US, CAN, AUS | ***NEW*** | **130-074-152** |
| **Cell Differentiation Bag (tube) – 500** | 2 Bags | For research use only[2)] | 500 mL | US, CAN, AUS | ***NEW*** | **130-074-153** |
| **Cell Differentiation Bag (6 ports) – 100** | 5 Bags | For research use only[2)] | 100 mL | US, CAN, AUS | ***NEW*** | **130-074-251** |
| **Cell Differentiation Bag (6 ports) – 250** | 5 Bags | For research use only[2)] | 250 mL | US, CAN, AUS | ***NEW*** | **130-074-252** |
| **Cell Differentiation Bag (6 ports) – 500** | 2 Bags | For research use only[2)] | 500 mL | US, CAN, AUS | ***NEW*** | **130-074-253** |

For availability in your country please contact your local representative.

1) The Cell Differentiation Bags are manufactured and controlled under an ISO 13485 certified quality system. These products are available in Europe as CE-marked medical devices.

2) Manufactured by Miltenyi Biotec GmbH under an ISO 9001 certified quality system.

### Description

Cell Differentiation Bags are gas-permeable and transparent for microscopy.

They are available for three different culture volumes: 100 mL, 250 mL and 500 mL.

The bag are individually packed, sterile and tested for endotoxins.

### Applications

Cell Differentiation Bags are intended for the *in vitro* cultivation and expansion of cells from heterogeneous haematologic cell populations (e.g. for the generation of dendritic cells from CD14-enriched monocytes).

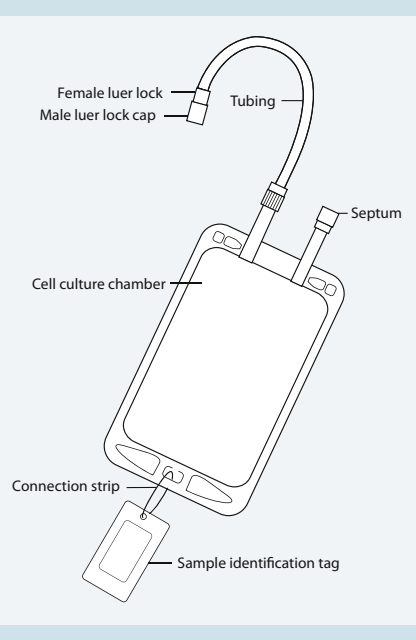



**Figure 1:** Cell Differentiation Bag (tube).

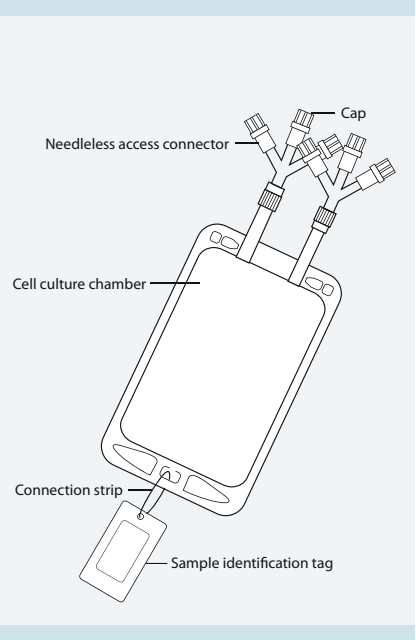



**Figure 2:** Cell Differentiation Bag (6 ports) with six needleless access connectors.

# Accessories

## Pre-System Filter

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Pre-System Filter** | 5 Filters | CE | Europe | **181-01** |

For availability in your country please contact your local representative.

**Description**

Pre-System Filter for cell separation (Blood transfusion filter, 40 micron pore width).
A Pre-System Filter should be used with all CliniMACS® Tubing Sets in order to retain cell aggregates.

Sterilized, non-pyrogenic fluid pathway, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Pre-System Filter.

## Luer/Spike Interconnector

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Luer/Spike Interconnector** | 5 Interconnectors | CE | Europe | **187-01** |

For availability in your country please contact your local representative.

**Description**

Adapter with spike and female luer connector, suitable for the attachment of transfer bags to these CliniMACS® Tubing Sets.

Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Luer/Spike Interconnector.

## Sampling Site Coupler

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Sampling Site Coupler** | 5 Couplers | CE | Europe | **189-01** |

For availability in your country please contact your local representative.

**Description**

Injection port, suitable for cell labeling procedures (e.g. for taking samples).
Sampling Site Coupler is suitable for centrifugation (connected to transfer bags).

Sterilized, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Sampling Site Coupler.

# Accessories

## Transfer Set Coupler/Needle

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Transfer Set Coupler/Needle** | 5 Transfer Sets | CE | Europe | **185-01** |

For availability in your country please contact your local representative.

**Description**
Plasma transfer set with coupler and puncture needle.

This transfer set can be used for connecting the CliniMACS® PBS/EDTA Buffer bag to the cell preparation bag.

Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Transfer Set Coupler/Needle.

## Transfer Set Coupler/Coupler

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Transfer Set Coupler/Coupler** | 5 Transfer Sets | CE | Europe | **186-01** |

For availability in your country please contact your local representative.

**Description**
Plasma transfer set with two couplers.

This transfer set can be used for connecting the CliniMACS® PBS/EDTA Buffer bag to the cell preparation bag or to connect two buffer bags.

Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Transfer Set Coupler/Coupler.

## Transfer Set Needle/Needle

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Transfer Set Needle/Needle** | 5 Transfer Sets | CE | Europe | **188-01** |

For availability in your country please contact your local representative.

**Description**
Plasma transfer set with two needles.

This transfer set can be used for connecting the CliniMACS® PBS/EDTA Buffer Bag to the Cell Preparation Bag.

Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Transfer Set Needle/Needle.

# Accessories

## Transfer Bags 150 mL, 600 mL, and 1000 mL

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Transfer Bag 150 mL** | 5 Bags | CE | Europe | **183-01** |
| **Transfer Bag 600 mL** | 5 Bags | CE | Europe | **190-01** |
| **Transfer Bag 1000 mL** | 5 Bags | CE | Europe | **180-01** |

For availability in your country please contact your local representative.

### Description

**Transfer Bag 150 mL**
Suitable for collecting the positive fraction during a CliniMACS® Separation (in combination with a Luer/Spike Interconnector).
Sterilized, non-pyrogenic, single-packed.

**Transfer Bag 600 mL**
Suitable for cell labeling procedures.
Sterilized, non-pyrogenic, single-packed.

**Transfer Bag 1000 mL**
Suitable for collecting fractions during a CliniMACS® Separation (in combination with a Luer/Spike Interconnector).
Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Transfer Bag 150 mL.

## Transfer Bag 600 mL with 8 couplers

| Product | Content | Regulatory status | Availability | Order no. |
|---|---|---|---|---|
| **Transfer Bag 600 mL with 8 couplers** | 5 Bags | CE | Europe | **184-01** |

For availability in your country please contact your local representative.

### Description

The Transfer Bag with eight couplers ("Octopus Bag") is suitable for cell labeling procedures.

This Transfer Bag enables the operator to perform the sample preparation procedure in a closed system.

Sterilized, non-pyrogenic, single-packed.

Please inquire about recommended device and accessories.

**Figure 1:** The Transfer Bag 600 mL with 8 couplers ("Octopus bag").

# Distributors: products for clinical use

| | | | | |
|---|---|---|---|---|
| **Argentina** | Lab Systems S.A. | Quesada 5916<br>CP 1431 Buenos Aires<br>Ciudad Autónoma de<br>Buenos Aires , Argentina | Phone +54 11 4572 8458<br>Fax +54 11 4572 8458 | direccion@lab-systems.com.ar<br>www.lab-systems.com.ar |
| **Australia** | Miltenyi Biotec<br>Australia Pty. Ltd. | Unit 16 A<br>2 Eden Park Drive<br>North Ryde, NSW 2113, Australia | Phone +61 02 8877 7400<br>Fax +61 02 9889 5044 | macs@miltenyibiotec.com.au<br>www.miltenyibiotec.com |
| **Austria** | Miltenyi Biotec GmbH | Friedrich-Ebert-Straße 68<br>51429 Bergisch Gladbach<br>Germany | Phone +49 2204 8306-0<br>Fax +49 2204 85197 | macs@miltenyibiotec.de<br>www.miltenyibiotec.com |
| **Bahrain** | Al Yamama | Al Saif Medical Centre<br>Ibn Khaldoun Street<br>Amman, Jordan | Phone +962 6 4655 166<br>Fax +962 6 4655 167 | modhafar@alyamamagroup.com<br>www.alyamamagroup.com |
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| **Belgium** | Miltenyi Biotec B.V. | Postbus 85183<br>3508 AD Utrecht<br>The Netherlands | Phone (Belgium) 0800 94016<br>Fax (Belgium) 0800 99626 | macs@miltenyibiotec.nl<br>www.miltenyibiotec.com |
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| **China** | Miltenyi Biotec Trading<br>(Shanghai) Co., Ltd.,<br>Shanghai Office | Rm. 2301, No. 319 Xianxia Rd.<br>Fareast International Plaza A<br>Shanghai 200051, P. R. China | Phone +86 21 6235 1005<br>Fax +86 21 6235 0953 | macs@miltenyibiotec.com.cn<br>www.miltenyibiotec.com |
| | Miltenyi Biotec Trading<br>(Shanghai) Co., Ltd.,<br>Beijing Office | Unit 916, Silver Tower, #2<br>Dong San Huan North Road<br>Chao Yang District<br>Beijing 100027, P. R. China | Phone +86 10 6410 7101<br>Fax +86 10 6410 7102 | macs@miltenyibiotec.com.cn<br>www.miltenyibiotec.com |
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| **Cyprus** | Epsilon & Epsilon<br>Medical S.A. | Apollon Tower, 15 A3<br>64 L. Riankour str.<br>11523 Athens, Greece | Phone +30 210 6996 191<br>Fax +30 210 6920 210 | info@eemed.gr<br>www.eemed.gr |
| **Czech Republic** | BIOHEM spol. s.r.o. | Zlátovska 2211<br>911 01 Trenčín, Slovakia | Phone +421 32 6524 998<br>Fax +421 32 6525 792 | biohem@biohem.sk<br>www.biohem.sk |
| **Ecuador** | Frisonex | C. La Tierra #388/E8-11B y<br>Av. de los Shyris<br>17-17-1413 Casilla, Ecuador | Phone +593 22 267 554<br>Fax +593 22 433 550 | frisonex@frisonex.com |
| **Egypt** | Al Yamama | Al Saif Medical Centre<br>Ibn Khaldoun Street<br>Amman, Jordan | Phone +962 6 4655 166<br>Fax +962 6 4655 167 | modhafar@alyamamagroup.com<br>www.alyamamagroup.com |





In the United States CliniMACS products for clinical use
are available only under an approved Investigational Device Exemption (IDE).

# Distributors: products for clinical use

| | | | | |
|---|---|---|---|---|
| **Estonia** | AS Oriola | Department of Laboratory Supplies & Equipment<br>Kungla Street 2<br>76505 Saue, Estonia | Phone +372 65 15 159<br>Fax +372 65 15 111 | kaari.saarma@oriola.com<br>www.oriola.ee |
| **France** | Miltenyi Biotec SAS | 10 rue Mercoeur<br>75011 Paris, France | Phone +33 1 56 98 16 16<br>Fax +33 1 56 98 16 17 | macs@miltenyibiotec.fr<br>www.miltenyibiotec.com |
| **Germany** | Miltenyi Biotec GmbH | Friedrich-Ebert-Straße 68<br>51429 Bergisch Gladbach<br>Germany | Phone +49 2204 8306-0<br>Fax +49 2204 85197 | macs@miltenyibiotec.de<br>www.miltenyibiotec.com |
| **Greece** | Epsilon & Epsilon Medical S.A. | Apollon Tower, 15 A3<br>64 L. Riankour str.<br>11523 Athens, Greece | Phone +30 210 6996 191<br>Fax +30 210 6920 210 | info@eemed.gr<br>www.eemed.gr |
| **Hong Kong** | Miltenyi Biotec Trading (Shanghai) Co., Ltd., Shanghai Office | Rm. 2301, No. 319 Xianxia Rd.<br>Fareast International Plaza A<br>Shanghai 200051, P. R. China | Phone +86 21 6235 1005<br>Fax +86 21 6235 0953 | macs@miltenyibiotec.com.cn<br>www.miltenyibiotec.com |
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| **India** | Medicons | GH-8/505<br>Paschim Vihar<br>New Delhi-87, India | Phone +91 11 6543 8094<br>Fax +91 11 2528 7644 | medicons@mediconsinc.com<br>www.mediconsinc.com |
| **Indonesia** | PT. TRANSMEDIC INDONESIA | Graha Atrium Lt. 6 Suite 6.02A<br>Jalan Senen Raya No. 135<br>Jakarta Pusat 10410, Indonesia | Phone +62 21 3509 544<br>Fax +62 21 3509 545 | www.transmedic.com.sg<br>doni@transmedic-ind.com |
| **Israel** | Y.A. Almog Diagnostic & Medical Equipment Ltd. | North industrial area 4<br>60850 Shoham, Israel | Phone +972 3 977 33 90<br>Fax +972 3 977 33 91 | info@almog.co.il<br>www.almog.co.il |
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CliniMACS® Reagents, Tubing Sets, Instruments and PBS/EDTA Buffer are manufactured and controlled under an ISO 13485 certified quality system. In Europe, the CliniMACS® System and Reagents are available as CE-marked medical devices.

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