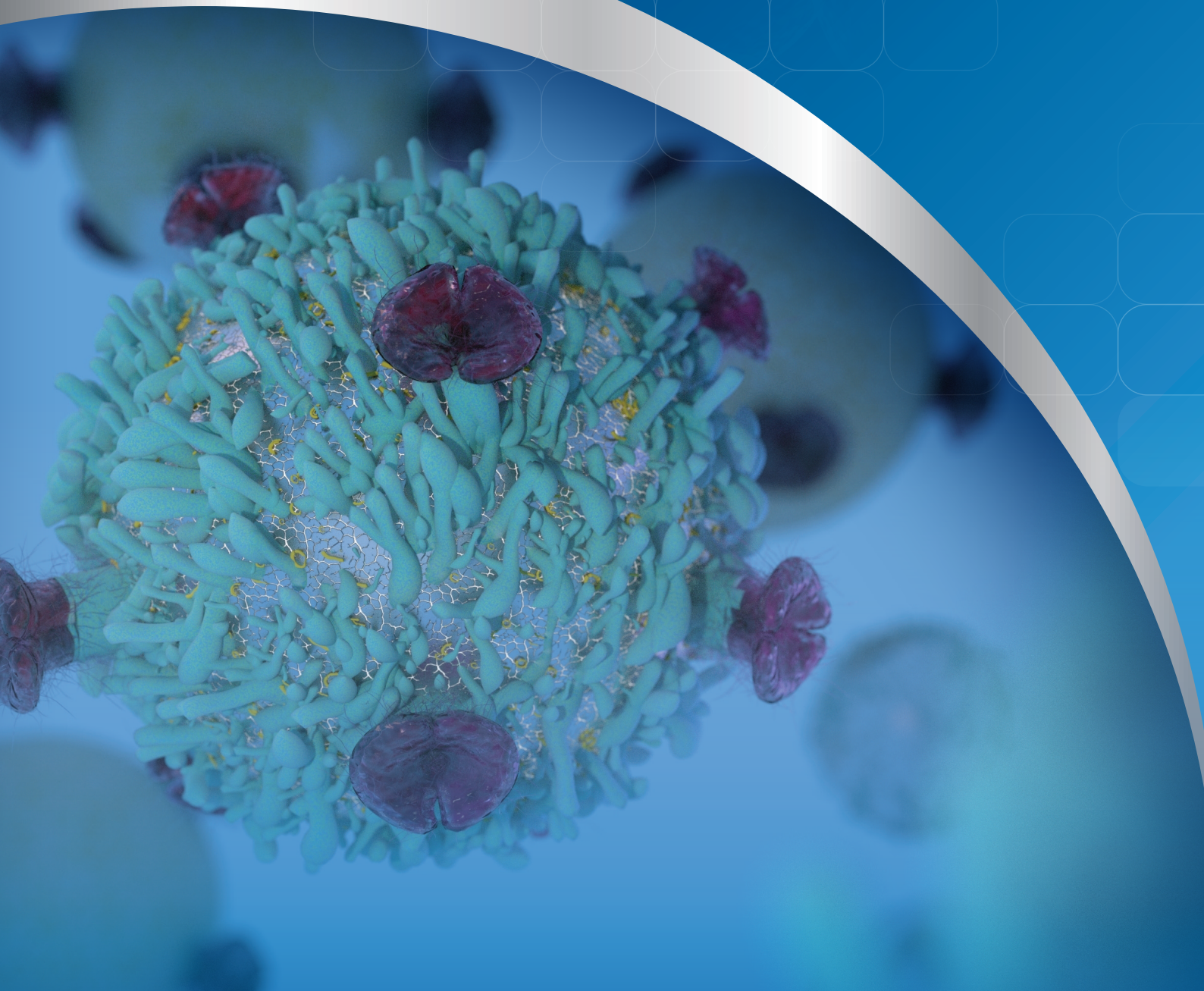
ESCO HEALTHCARE

"Discovery to Delivery"

Esco PuriCradle™

Streamlining Cell Therapy Workflow: Keeping Cells Viable in Every Spin



Esco PuriCradle™

Streamlining Cell Therapy Workflow: Keeping Cells Viable in Every Spin

PuriCradle™ is Esco's innovative solution designed to transition from traditional open centrifuge tubes—requiring operation in a Grade A biosafety cabinet (BSC) within a Grade B cleanroom—to a single-use, column-free, beadless, closed centrifugation cup. It operates within the cGMP-compliant Esco Infinity™ Centrifuge, enabling use in a Grade C or D cleanroom environment*.

It enables hassle-free mononuclear cell isolation from whole blood to PBMCs using density gradient media and/or antibody kits, eliminating the need for columns, magnetic beads, or separators. This ensures consistent target cell isolation while enabling further enrichment of specific immune cells for use as GMP starting material, supporting subsequent cell expansion, genetic modification, or direct concentration into the final cell therapy product.

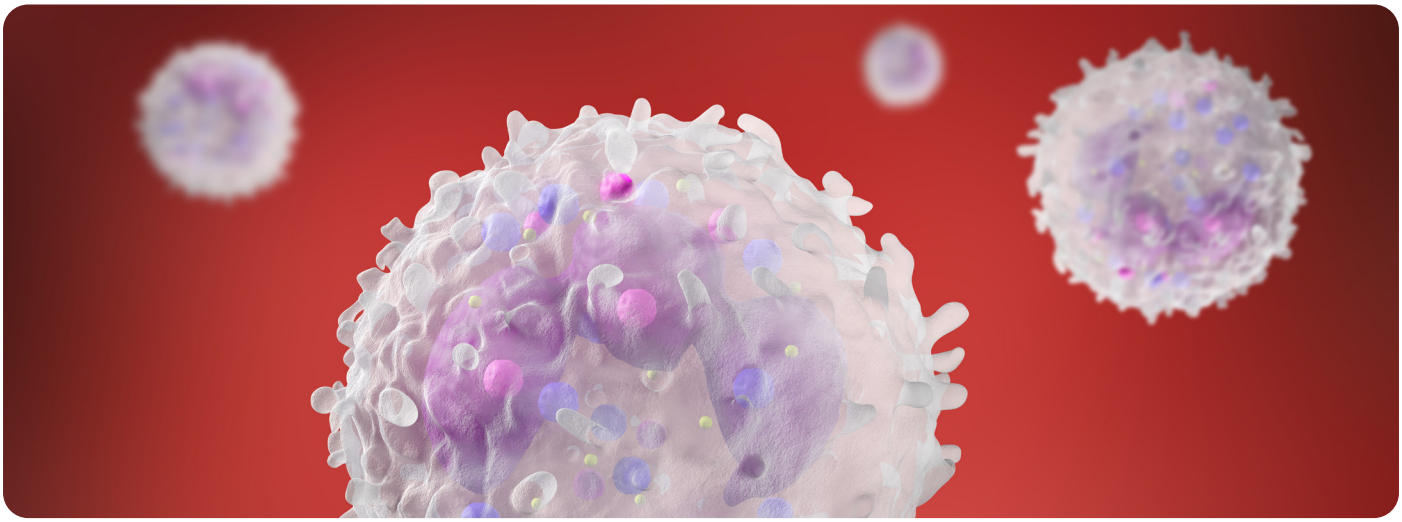
PuriCradle™ facilitates the isolation of starting material for cell and gene therapies (also known as genetically modified cell therapies) directly from whole blood, reducing reliance on costly apheresis or leukapheresis machines. This enables point-of-care cell processing and therapy, making advanced treatments more accessible**.

Post cell expansion, it supports cell washing and formulation before the addition of cryopreservation media for long-term storage. It also enables efficient removal of cryoprotectants prior to administering the final cell therapy product.

PuriCradle™ is available as a standalone with cGMP Esco Infinity™ Centrifuge or can be integrated into a cell processing workstation or isolator, ensuring seamless adaptation to diverse GMP workflows.

**The suitability of a Grade C or D cleanroom environment is subject to risk assessment and compliance with country-specific regulations, internal quality management systems, and clinical development stage requirements.*

***In certain countries, such as Singapore, leukapheresis can only be performed in hospitals. Additionally, in many regions, not all medical centers have access to a full transplant team trained in leukapheresis/apheresis machine operation or the necessary capital expenditure (CapEx) to acquire such systems.*



Why Choose Density Gradient-based PuriCradle™?

Many cell isolation methods rely on **magnetic beads or column-based technologies** to separate specific immune cells. Magnetic beads are tiny particles (micrometer-sized) coated with materials that can bind to specific cell surface markers. These beads contain iron oxide, making them responsive to a magnetic field. On the other hand, column-based work in combination with magnetic beads to retain labeled cells in a column while washing away non-target cells

Unlike magnetic bead-based or column-based separation methods, PuriCradle™ offers a cost-effective, efficient, and cGMP-compatible approach for PBMC and mononuclear cell isolation. Key advantages include:

Closed-System Processing – Reduces contamination risk, allowing operation in a Grade C or D cleanroom instead of a high-cost Grade A/B environment.

No Magnetic Beads or Columns Required – Unlike cell isolation based on magnetic labeling, which rely on beads coated with antibodies to target specific cell types, PuriCradle™ uses density gradient media followed by centrifugation, providing high recovery without the need for bead washing.

Higher Sample Throughput & Cost Savings – Magnetic bead separation is often expensive, requiring additional consumables and specialized handling. Density gradient separation eliminates this cost while still enabling efficient mononuclear cell isolation from whole blood.

Scalability & Flexibility – Well-suited for clinical and research applications, with easy integration into automated GMP workflows and compatibility with various sample sizes.

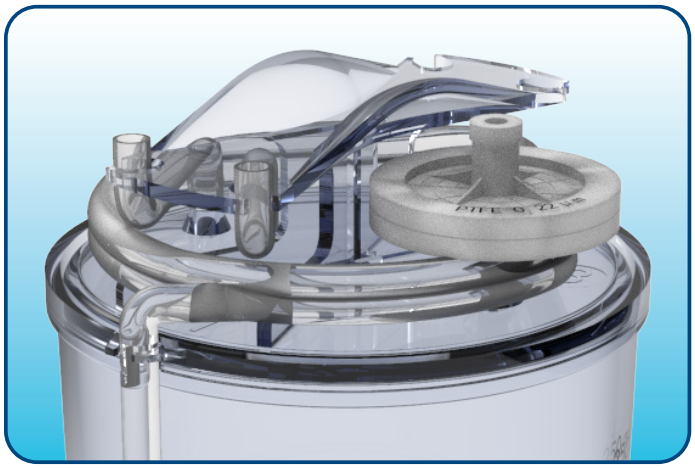
Minimal Sample Manipulation – Reduces contamination risk and cell loss by eliminating multiple washing and processing steps required for bead-based separations.

Features

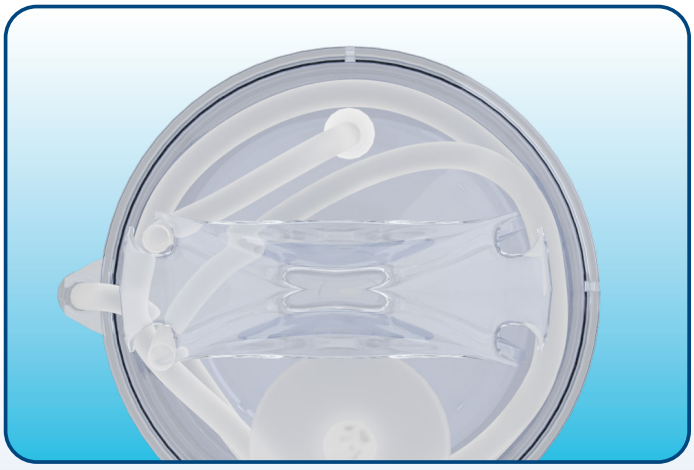
Can be utilized across open and closed system options

Equipped with 0.22µm filter, ensuring no pressure differential is achieved

Upper and lower chambers for easier isolation of target cells



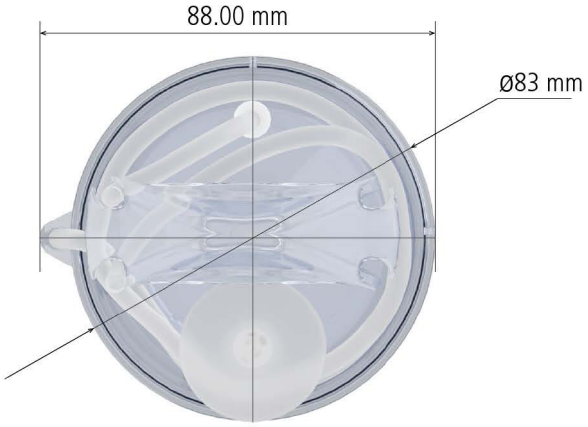
Top butterfly clamp design guarantees secure tubing fixation, preventing detachment even under centrifugation



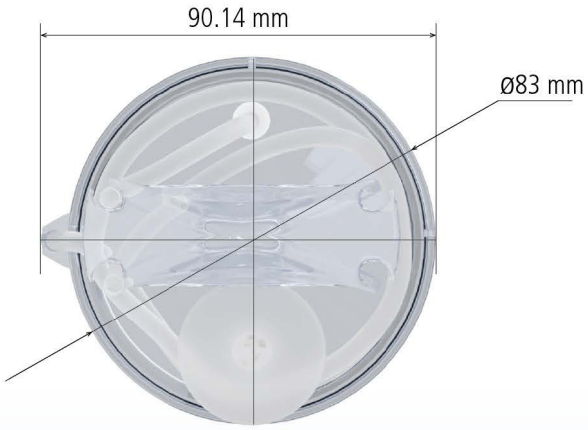
Weldable polyvinyl chloride (PVC) tubings with 5.5mm outer diameter and a 4mm inner diameter

Spinning blood in PuriCradle™ Separation cup with a layered solution (density gradient centrifugation) allows for the separation and collection of PBMCs. This method keeps the cells sterile and yields a large number of viable cells.

Separation Cup



Washing Cup



Applications

1. Mononuclear Cell Isolation

- Peripheral blood mononuclear cells from whole blood, bone marrow

2. Cell Enrichment for Specific Target Cells

- **T Lymphocytes / T Cells** - are a type of white blood cells that play a key role in the immune system, particularly in the adaptive immune response. Subtypes include: helper T cells, cytotoxic T cells and regulatory T cells.
- **Dendritic Cells** - are antigen-presenting cells (APCs) that are essential for initiating and regulating the adaptive immune response. They capture and process antigens, then present them on their surface to T cells, thereby activating them.
- **Natural Killer Cells (NK Cells)** - are a type of lymphocyte that is part of the innate immune system. They provide rapid responses to viral infections and tumor formation. NK cells kill infected or transformed (cancerous) cells by detecting abnormal levels of major histocompatibility complex (MHC) molecules and recognizing stress signals on infected cells.
- **Natural Killer T Cells (NKT cells)** - are a hybrid between T cells and NK cells, sharing properties of both. They recognize lipid antigens presented by the CD1d molecule, which is distinct from the usual MHC molecule involved in antigen presentation.
- **Gamma Delta T Cells (GDT Cells)** - are a subset of T cells that have a unique T cell receptor (TCR) made of gamma and delta chains instead of the more common alpha and beta chains. These T cells recognize a broader range of antigens, including non-peptide antigens, and play a critical role in both the innate and adaptive immune responses.
- **Cytokine-Induced Killer Cells (CIK Cells)** - are a subset of T cells that are expanded in vitro (outside the body) in the presence of cytokines like interleukin-2 (IL-2) and interferon-gamma (IFN-.) to enhance their cytotoxic activity.

  These cells are capable of killing tumor cells and infected cells.

3. Cell Washing

- Cell washing prior to addition of cryopreservation
- Removal of cryopreservation media before infusion

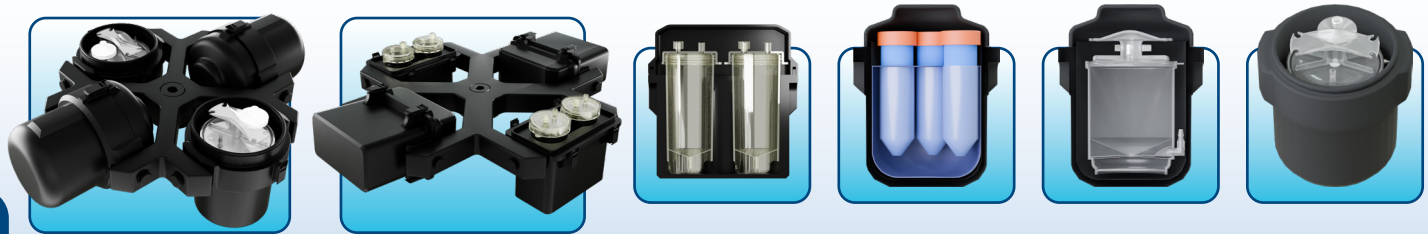
Esco Infinity™ Range Centrifuge

Esco's cGMP-compliant centrifuge is meticulously engineered for both open and closed processing especially for CAR-T cell therapy applications. Its compact design saves space and its low noise performance is preferred in most laboratory setting.

Features

- Benchtop design and Siemens HMI/PLC, compliant with 21 CFR part 11 standards that offers intuitive operation and effortless navigation
- Engineered with Siemens technology for motor and aerosol tight seals
- Swing type rotor with 4x round buckets for biocontainment.
- Designed with aerosol-tight buckets provide an additional layer of protection
- With features that facilitate pressure testing
- With advanced temperature control capabilities
- With programmable / controlled acceleration and deceleration speeds
- Tailored to seamlessly integrate with Esco PuriCradle™ cups, centrifuge tubes (15, 50 ml), and Nanchac™ * separation device.

**Nanchac™ is a proprietary, patented cell separation device developed and owned by Duogenic StemCells Corp., with Nanchac™ being a trademark of the company.*



Cell Processing Isolator (CPI) Integration

The Cell Processing Isolator (CPI) integrated with Infinity™ range centrifuge enables seamless operation throughout the entire cell therapy process, from initial cell collection to final product preparation. It facilitates the isolation of products or processes while ensuring the necessary sterile or aseptic conditions required for cell therapy applications.

With the Esco CPI, procedures such as cell density gradient separation, washing, centrifugation, cell activation, harvesting, and preparation of the final product can be efficiently carried out. Moreover, it offers comprehensive protection for personnel, the product, and the environment, ensuring optimal safety and efficacy throughout the cGMP manufacturing process.

Features

- Easily customizable, depending on client's requirements
- Designed for cGMP Manufacturing of Cell, Tissue, and Gene Therapy Products (CTGTP)
- Modular and adaptable solutions for cell and gene therapy, tissue engineering, seed banking, and cell processing
- Integrates Esco PuriCradle™ cell centrifuge, separation, and washing cups
- Option of docking/undocking capabilites for CO_2 incubator or bioreactor (e.g. static bags/WAVE/Tide)
- Applicable for both autologous and allogeneic cell therapy applications

Esco Infinity Cell Processing Workstation

The Esco Infinity Cell Processing Workstation is designed based on Esco's certified biological safety cabinets. Integrated with Infinity™ range centrifuge, this can support the entire cell therapy workflow. It offers unmatched convenience and safety, ideal for laboratory facilities, featuring an ULPA filtration system with 10x the efficiency of HEPA filters. In addition, the technology is equipped with energy-efficient DC ECM that allows up to 70% energy savings versus AC motor.

Features

- Incorporates Siemens HMI/PLC technology
- Includes a shaking incubator for cell culture applications
- With viable and non-viable particle counter which offers monitoring capabilities for both living and non-living particles
- Option for docking/undocking feature of CO_2 incubator/bioreactor (e.g. static bags/WAVE/Tide)

Custom Adapter Solutions

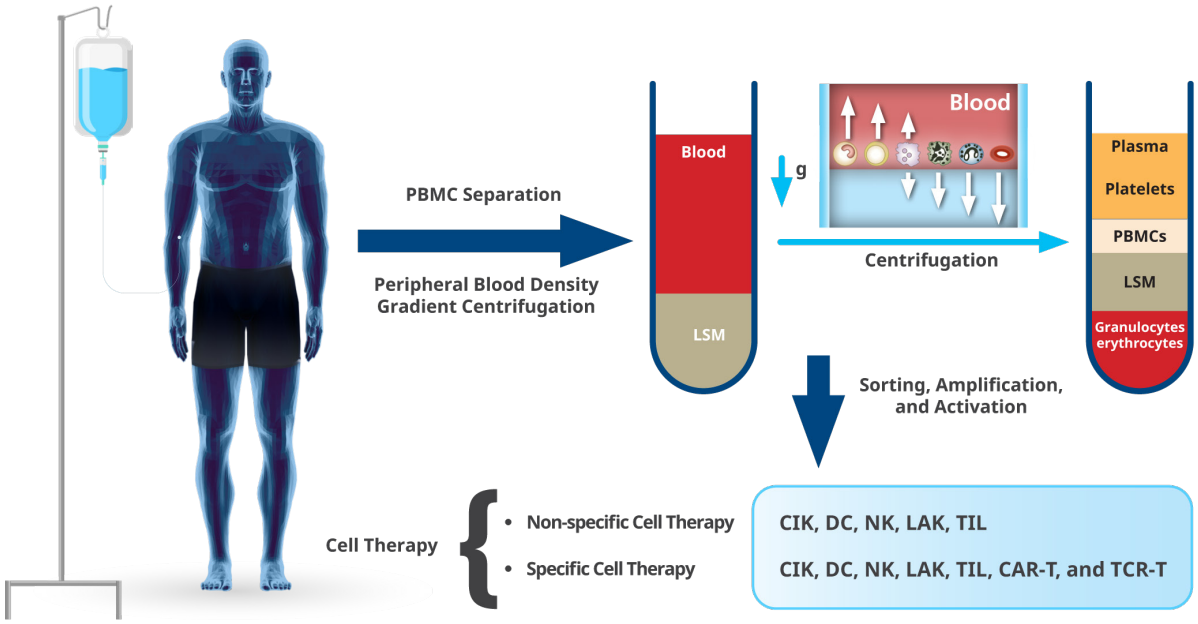
These tools are meticulously engineered to ensure precise compatibility with Esco PuriCradle™ cups, catering particularly to clients utilizing centrifuges outside the Esco Infinity™ range.

Starting Cell Source

This table presents a comparative analysis between the two primary cell sources used in the manufacturing process of CAR-T Cell Therapy.

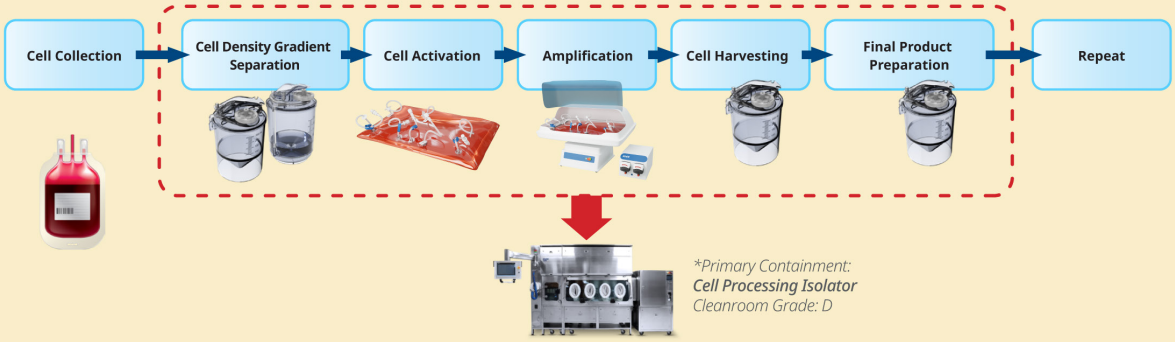
FEATURES	PBMCs	LEUKAPHERESIS
VOLUME	Lower volume/small quantity of highly potent CAR-X cells can be obtained App. 60 ml* ** in a regular 450ml blood donation (buffy coat)*	Larger volume can be obtained as it follows a selective collection process. App. 100 ml* ** depending on absolute lymphocyte count and total blood volume to process per patient.*
VASCULAR ACCESS	Requires standard phlebotomy procedures	Requires standard phlebotomy procedures but may also involve accessing large veins (e.g. internal jugular) for specialized collection tools such as central venous catheters.
INVASIVENESS AND COMPLEXITY	Less invasive procedure	Quite invasive and complex procedure
AVAILABILITY	More readily available as it can be obtained from routine blood donations	Requires scheduling and specialized equipment, making it less immediately available.
PLATELET/RBC CONTAMINATION	Potentially higher risk of platelet and RBC contamination due to standard phlebotomy procedures	Reduced RBC and platelet contamination due to selective collection via leukapheresis.
MATERIAL HANDLING	Easier to handle and process due to the smaller volume of blood collected.	Requires more complex handling and processing, including the use of apheresis machines for cell isolation/separation.
DONOR ATTRITION	Less invasive procedure, potentially leading to higher donor retention rates.	Quite invasive procedure which may result in donor attritions, especially if the donors find the process uncomfortable or inconvenient.
EXPERTISE REQUIREMENT	Requires highly skilled phlebotomist	Requires highly skilled phlebotomist and proficient in operating apheresis machines.
FACILITY REQUIREMENT	Requires facilities equipped for standard blood draw procedures and suitable for smaller-scale manufacturing processes, hence may not require highly specialized facilities.	Facilities need specialized equipment for leukapheresis procedures and typically performed in specialized centers with apheresis machines and trained personnel.
ADVERSE EVENTS	Mild, infrequent adverse reactions	Potentially more frequent, slightly severe adverse reactions
HEALTHCARE SERVICES	Out-patient setting which can lower overall cost	In-patient setting which may contribute to higher overall cost

Cell Therapy Workflow

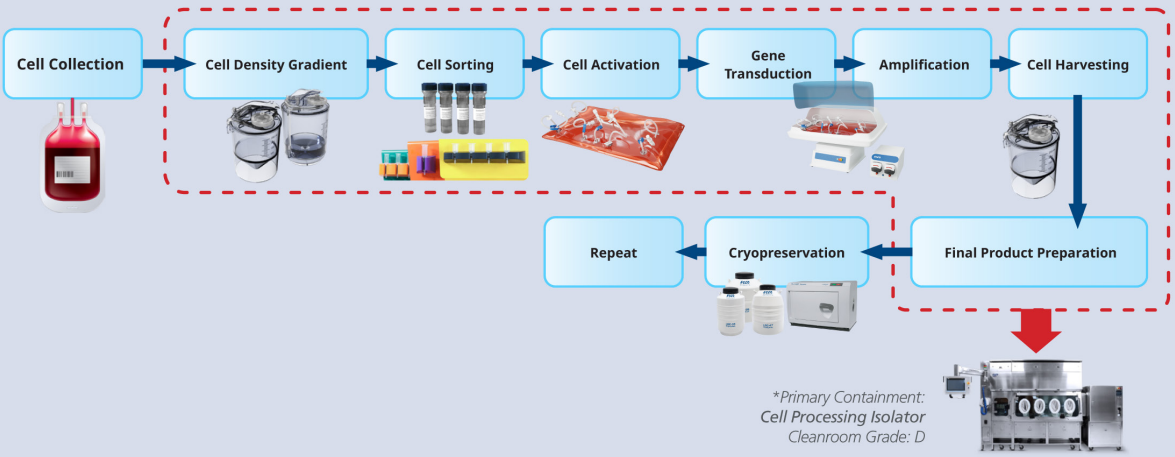


Cell Centrifuge, Separation, and Washing Cup Closed System Applications: Immune Cell Therapy Products

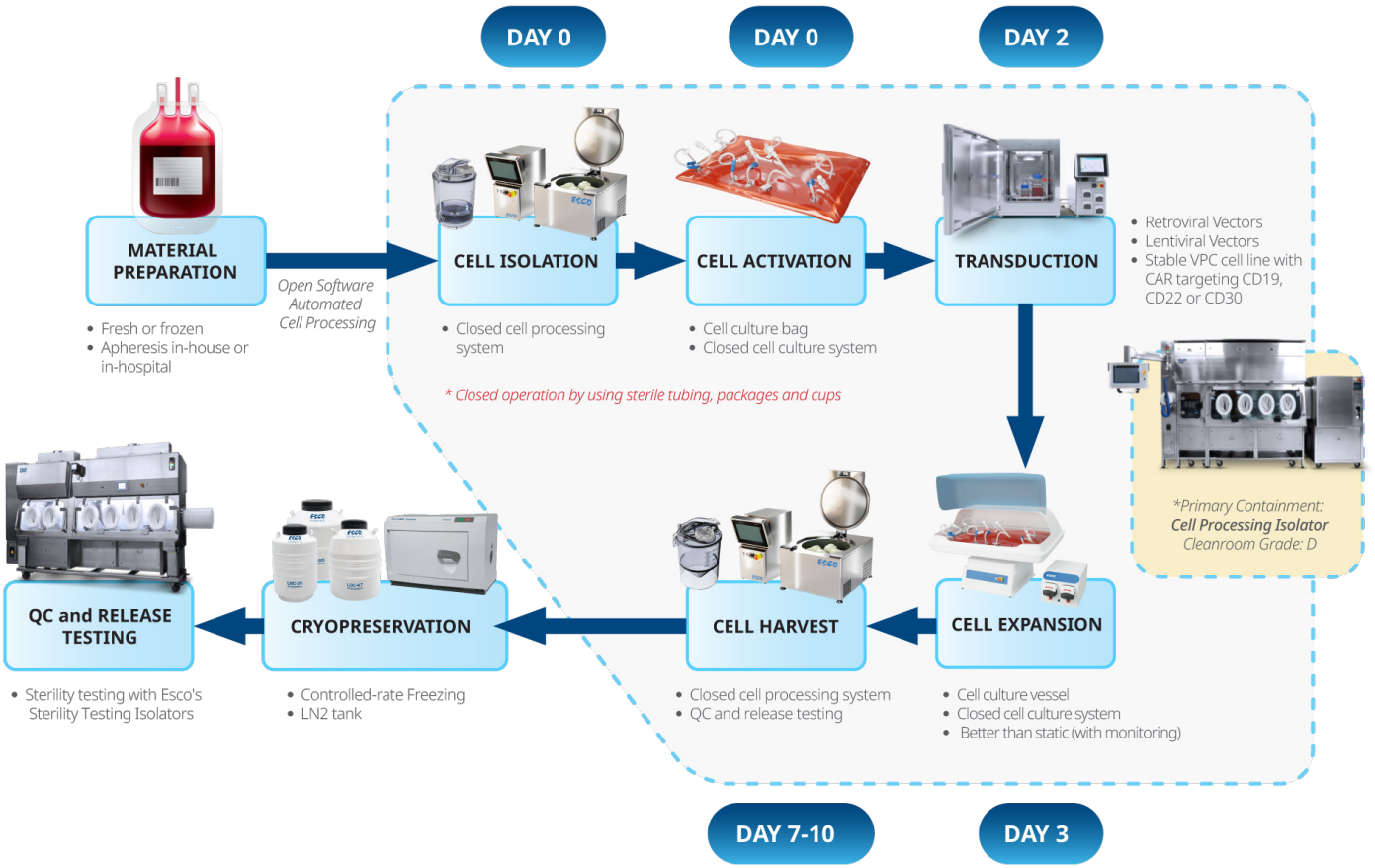
Cell Therapy Workflow (Without Genetic Modification)



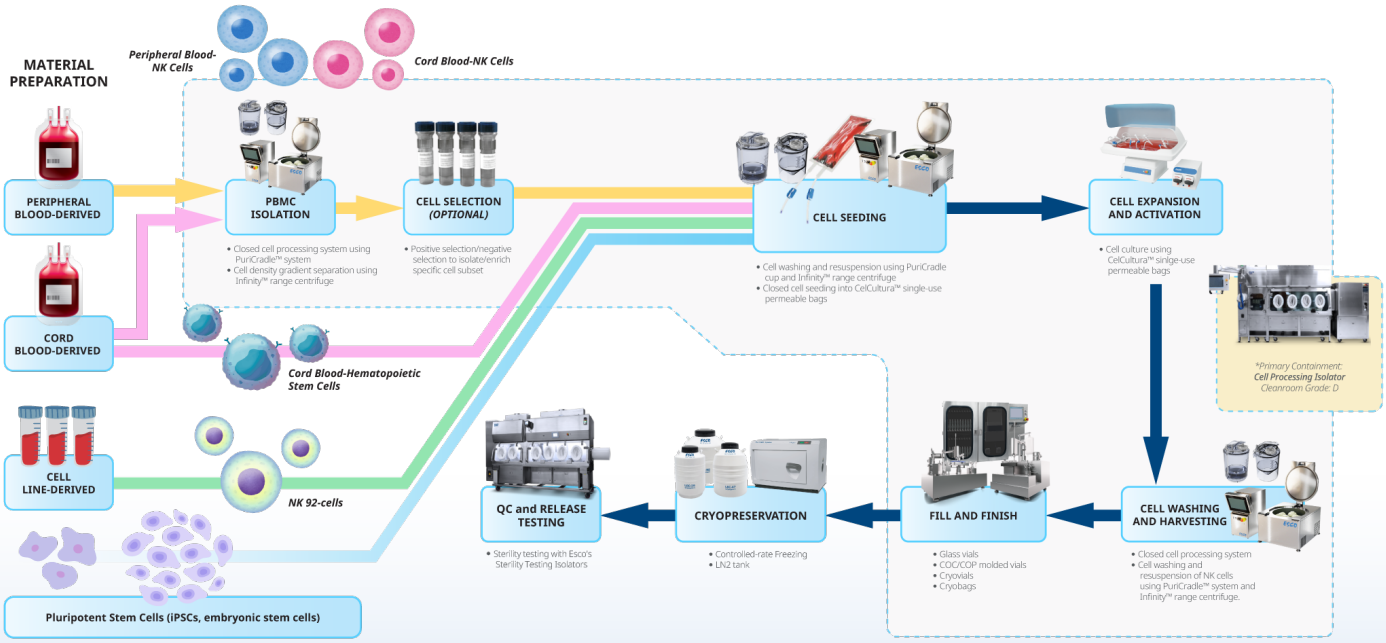
Genetically-modified Cell Therapy Workflow



Esco Aster's cGMP CAR-X Cell Therapy Manufacturing Process



Esco Aster's NK Cell Therapy Workflow



Ordering Information

Item Code	Description
2220009	Infinity, Benchtop Refrigerated Centrifuge (With Siemens HMI/PLC)
5220002	1 x Rotor Swing for PuriCradle Cups
5220003	1 x Rotor Swing for NanChac Tubes
5220004	1 x 250 ml x 4 Closed Buckets for PuriCradle
5220005	1 x 500 ml x 4 Closed Buckets for NanChac
5220006	1 x 500 ml x 4 Standard Bucket
5220010	1 x 250 ml x 4 Standard Bucket
5220011	5 x 50 ml x 4 Standard Bucket
5220012	10 x 15 ml x 4 Standard Bucket
5220007	PuriCradle Separation Cup
5220008	PuriCradle Washing Cup
5220009	PuriCradle Custom Adapters
5220013	NanChac Cell Separation Tubes

References:

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2. *Sauls, R. S., McCausland, C., & Taylor, B. N. (2023b, May 1). Histology, T-Cell lymphocyte. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK535433/*
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5. *Van Kaer, L. (2010). Natural killer T cells in health and disease. Frontiers in Bioscience-Scholar, S3(1), 236–251. https://doi.org/10.2741/s148*
6. *Zanna, M. Y., Yasmin, A. R., Omar, A. R., Arshad, S. S., Mariatulqabtiah, A. R., Nur-Fazila, S. H., & Mahiza, M. I. N. (2021). Review of dendritic cells, their role in clinical immunology, and distribution in various animal species. International Journal of Molecular Sciences, 22(15), 8044. https://doi.org/10.3390/ijms22158044*

ESCO LIFESCIENCES GROUP NETWORK
42 Locations in 21 Countries All Over the World

Air Shower
Aseptic Containment Isolator (ACTI)
Ceiling Laminar Airflow Units
Cleanroom Transfer Hatch
Containment Barrier Isolator (CBI)
Downflow Booth (DFB)
Dynamic Floor Laminar Hatch
Dynamic Pass Box
Evidence Drying Cabinet
Garment Storage Cabinet
General Processing Platform Isolator (GPPI)
Laminar Flow Horizontal Trolley
Laminar Flow Straddle Units, Single and Double
Laminar Flow Vertical Trolley
Pass Box
Soft Wall Cleanroom
Sputum Booth
Ventilated Balance Enclosure (VBE)
Weighing and Dispensing Containment Isolator (WDCI)

Since 1978, Esco has emerged as a leader in the development of controlled environment, laboratory and pharmaceutical equipment solutions. Products sold in more than 100 countries include biological safety cabinets, fume hoods, ductless fume hoods, laminar flow clean benches, animal containment workstations, cytotoxic cabinets, hospital pharmacy isolators, and PCR cabinets and instrumentation. With the most extensive product line in the industry, Esco has passed more tests, in more languages, for more certifications, throughout more countries than any biosafety cabinet manufacturer in the world. Esco remains dedicated to delivering innovative solutions for the clinical, life science, research and industrial laboratory community.

ESCO HEALTHCARE "Discovery to Delivery"

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