

# Meet our Cell Therapy Solutions to Support Therapeutic Success

Grifols Bio Supplies offers a specialized portfolio of human-derived materials to support T-cell and gene therapy manufacturing, with a focus on two key areas: Cell Sourcing and Cell Culture.

## CELL SOURCING



### LEUKOPAKS

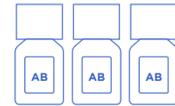
- Dual sourcing from US and EU centers
- High mononuclear cell yield
- Proven safety
  - Viral testing according to FDA or EMA regulations for all donors
  - Leukopak donors are qualified individuals with prior plasma donation experience, adding an extra layer of safety process
  - Back up donor scheduling to ensure on-time availability and delivery
- Research and GMP grades available
- **Formats available**
  - Fresh
  - Split
  - Cryopreserved
- **Documentation provided**
  - CoA, donor demographics

## CELL CULTURE



### HUMAN SERUM ALBUMIN

- Manufactured from plasma sourced from our US-based FDA- and EMA-approved plasmapheresis centers
- Our production strictly adheres to cGMP, IQPP (Plasma Protein Therapeutic Association) standards
- Therapeutic Grade Quality: Licensed medical product (USP and EP) for non-therapeutical use
- High purity: ≥96%
- **Formats available (100 mL)**
  - Bottles: 20% and 25% HSA solution
  - Bags: 25% HSA solution
- **Documentation provided**
  - CoA, BSE/TSE statement, processing overview document, supporting documentation and dossiers to support IND/MA process



### MALE AB SERUM

- Collected in FDA- and/or EMA-approved centers
- Manufactured in ISO-certified, cGMP-compliant facilities
- Proven safety
  - Gamma-irradiated and heat-inactivated options
  - Tested for viral markers, mycoplasma, endotoxins and more
  - Available in large lot sizes for better reproducibility
- **Formats available**
  - 100 mL bottles
  - 500 mL bottles
- **Documentation provided**
  - CoO, CoA, viral inactivation study, safety data sheet, processing overview document

# From Pharma to Pharma. From Science to Solutions



## Quality and Safety

### BUILT FOR EXCELLENCE. TRUSTED FOR PERFORMANCE

- Top class installations and technology
- Manufacturing process governed by strict GMP protocols and compliance with FDA and EMA standards
- Viral marker testing performed on every donation
- Full control from donation to delivery ensuring quality traceability throughout the supply chain
- Regulatory expertise



## A leading worldwide donor network

### TWO CONTINENTS. ONE MISSION

- Extensive global donor networking located across US and EU
- Donors of all genders, blood groups, ages, and backgrounds
- Our donors are rigorously pre-screened, well-characterized to meet highly specific research and manufacturing criteria
- Our leukopaks are collected exclusively from our existing, deeply profiled plasma donors



## Strong supply capability

### SCALABLE CELL THERAPY MANUFACTURING

- Robust, global supply infrastructure that meets demands of time-critical workflows
- More than 400 apheresis centers
- A total of 14+ million annual plasma donations
- Manufacturing facilities in EU and USA

## RELEVANT BIBLIOGRAPHY FOR AMs:

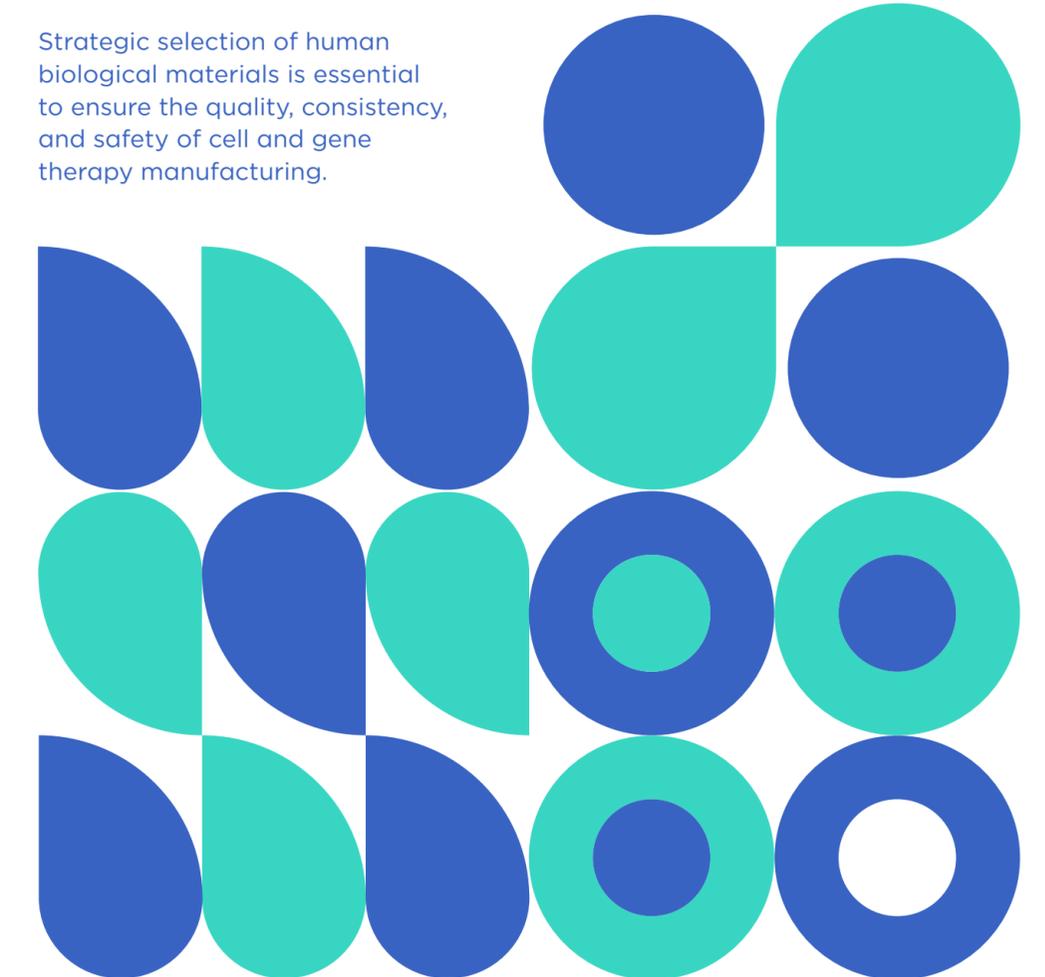
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# Human Biological Materials for Cell and Gene Therapy Manufacturing: CAR-T

**BioSupplies**  
Biological material solutions  
**Cell Therapy**

Strategic selection of human biological materials is essential to ensure the quality, consistency, and safety of cell and gene therapy manufacturing.



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## Human biological materials used in cell and gene therapies (CGT)<sup>1,2</sup>



Leukopaks

### STARTING MATERIALS

Are the initial biological materials used at the beginning of the manufacturing process to create cell-based medicinal products such as leukopaks



HSA

AB

### RAW/ANCILLARY MATERIALS (AMs)<sup>3,8</sup>

Are substances used during the manufacturing process that come into contact with cells or tissues but are not intended to be present in the final product, such as human serum albumin (HSA) and male AB serum (AB)



HSA

### EXCIPIENTS<sup>9,12</sup>

Are substances included in the final formulation alongside the active pharmaceutical ingredient (API), such as therapeutical grade human serum albumin (HSA)

## The importance of the selection of the human raw materials in CGT manufacturing<sup>13</sup>

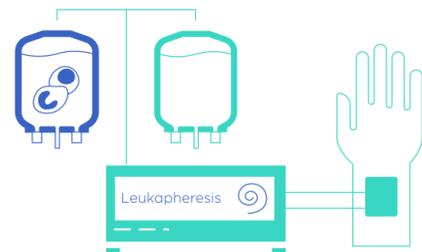
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### COLLECTION

The collection of white blood cells, including T cells, from patient's blood is a procedure called leukapheresis. The blood is passed through a machine that separates the components and collects the desired white blood cells. This process provides a concentrated source of white blood cells, **Leukopaks**, needed to manufacture these treatments.



**Leukopaks serves as a cell sourcing material to develop autologous cell therapy processes and for allogeneic therapies**

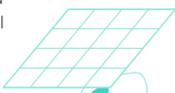
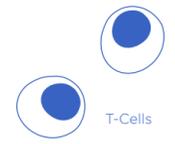


**Important:** A deep understanding of the regulatory landscape of ancillary materials (AMs) is essential

3

### ACTIVATION

T-cell activation is where mature T cells express antigen-specific receptors to recognize antigens, enter the cell cycle, secrete cytokines, and initiate immune functions. In CAR-T therapy manufacturing, this activation step prepares cells for genetic material introduction via transduction or non-viral methods.



2

### ISOLATION

In this step the needed white cells are separated from a mixed cell population. Methods like positive and negative selection precisely target specific white cells (eg, T cells, tumor-infiltrating lymphocytes, natural killer cells) for manufacturing and therapeutic use.



**HSA is used as an ancillary material as part of the isolation buffer preventing cell clumping**



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### VIRAL TRANSDUCTION

After T-cell activation, these cells are genetically modified to express the chimeric antigen receptor (CAR) using lentiviral or adeno-associated viral vectors. This modification enables T cells to target and attack specific cancer cells, enhancing CAR-T-cell therapy effectiveness.

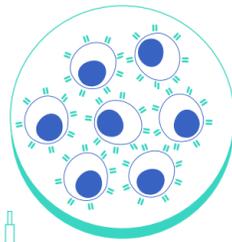


**Documentation of the AMs to meet regulatory requirements:**  
CoO: certificate of origin, CoA: certificate of analysis, Viral inactivation study, SDS: specification sheets, Processing overview document, Dossier from drug master file

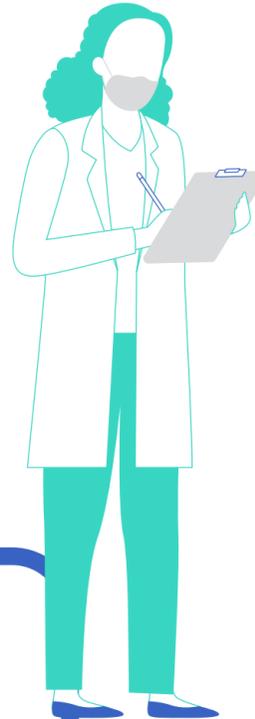
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### EXPANSION

T-cell expansion in CAR-T therapy increases the number of genetically modified T cells (ex vivo). This step ensures enough CAR-positive T cells are reintroduced into the patient, enhancing the therapy's potential to target and destroy cancer cells.



**HSA and human male AB serum are widely used as a supplement in cell culture media. HSA as a nutrient source and reservoir of essential nutrients and human male AB serum offers a balanced mix of growth factors, hormones... Derived exclusively from male donors with AB blood type, it minimizes immunological risks and ensures high consistency across applications**

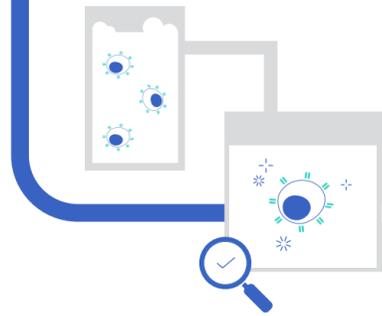


Human male AB serum is considered a low-risk material when sourced from a well-characterized material produced under an established quality system

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### DRUG FORMULATION AND CRYOPRESERVATION

Now CAR T-cells are ready to be prepared as the final product for patient infusion. This preparation may involve extra steps such as cryopreservation, formulation in a particular infusion solution, or further adjustments depending on the specific CAR-T therapy and manufacturing process.



### HARVEST

Harvest phase includes: washing, concentration, removal of impurities and in-process quality control (viability, purity and potency assays). These steps ensure the safety and effectiveness of CAR-T cell therapies for patients.

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**HSA is used as an ancillary material as part of the isolation buffer preventing cell clumping**



**HSA is used as an excipient in the:**  
**Final Formulation:** Provides an excellent shield against toxins and reactive oxygen species reducing stress-induced damage and stabilizes the cell suspension, ensuring viability until administration  
**Cryopreservation and Post-Thaw Functionality:** Coats the surface of the cells, ensuring safekeeping during the freezing and thawing processes