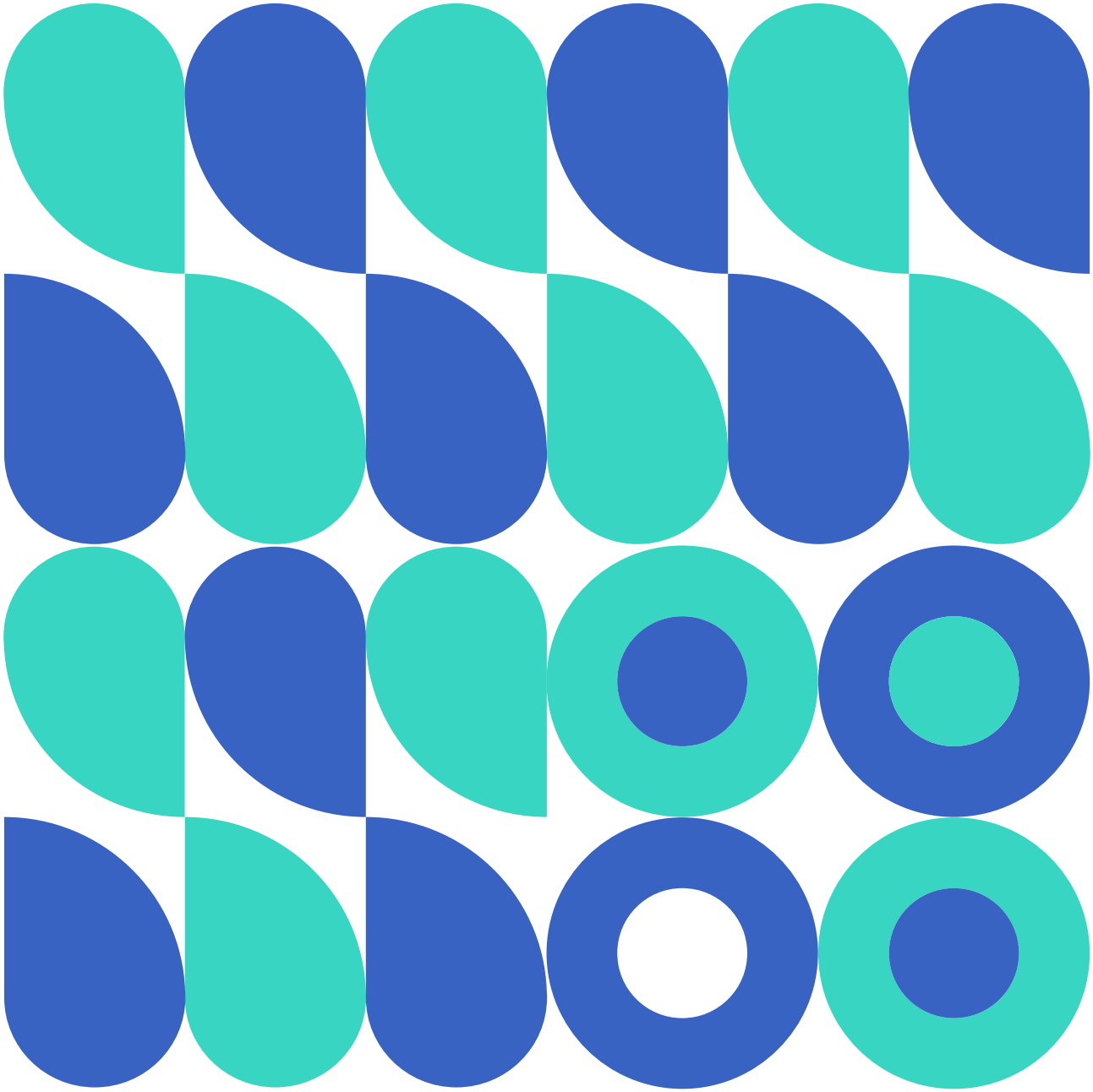
Raw materials for cell therapy manufacture

BioSupplies
Biological material solutions

Cell Therapy



GRIFOLS

The product presented here is not for therapeutic use

Raw materials in CAR-T manufacture

Figure 1 shows a general overview of the 4 main steps of cell therapy CAR-T manufacture. Within each main step, there are multiple smaller steps which require an array of raw materials.

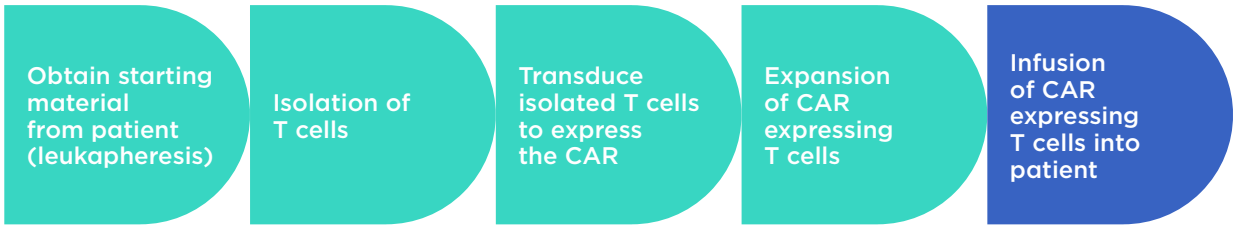


Figure 1.- Overview of CAR-T manufacture

The starting point of any CAR-T therapy manufacture is the starting cell preparation. Starting cellular material typically comes in the form of a mixed cell population such as peripheral blood mononuclear cells (PBMCs) derived from a leukapheresis. From the mixed cell population, individual cell populations need to be isolated. Isolated cells are then transduced with the artificial CAR and expanded, ready for inclusion on the final product. Each of these stages requires multiple raw materials whose quality and safety are vital. Figure 2 shows the most common stages/points at which the Grifols BioSupplies raw materials are used in cell therapy workflows.

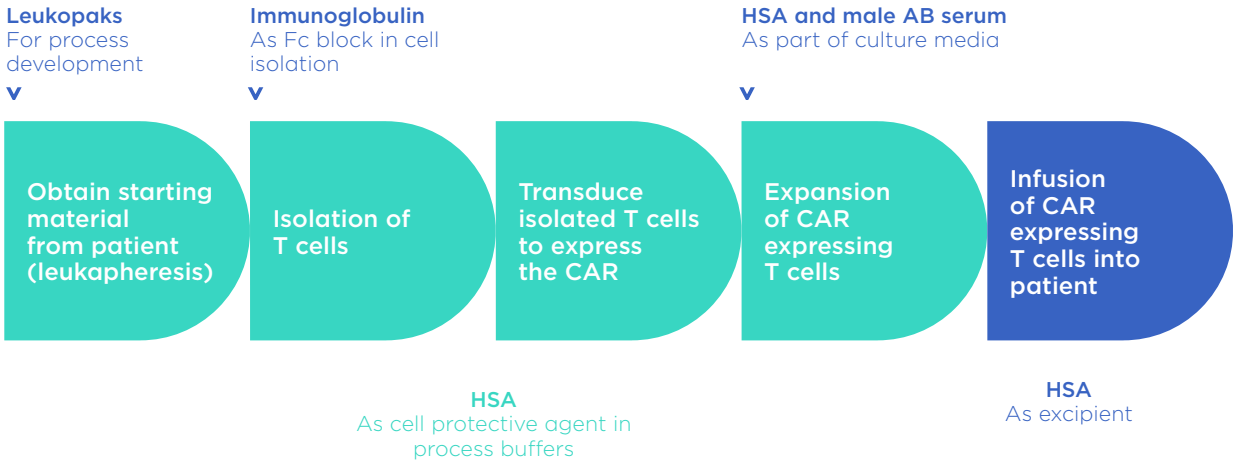
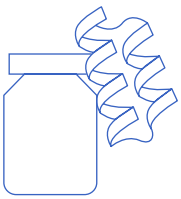


Figure 2.- Common uses of Grifols raw materials in CAR-T manufacture

Human Serum Albumin



The CAR-T manufacturing process includes multiple rounds of buffer changes and resuspensions. To avoid cell death, cells must be maintained in an appropriate buffer. Several published studies report the use of HSA in the washing/resuspension buffer.[1-3] The purpose of the HSA within the washing/resuspension buffer is to prevent cell death. HSA can contribute to cell survival in multiple ways including pH balance, maintaining osmotic pressure and free radical scavenging.

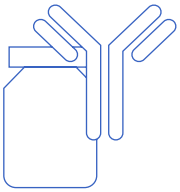
In addition to the use of HSA in cell processing buffers, HSA can also be present in the final infusible solution. To minimise regulatory challenges, it is advisable to use a therapeutic grade of human serum albumin.

GRIFOLS HUMAN SERUM ALBUMIN

Our human serum albumin (HSA) is manufactured from plasma from our FDA- and EMA-approved plasmapheresis centers based in the USA, and complies with the current good manufacturing practice (cGMP), the International Quality Plasma Program (IQPP) of the Plasma Protein Therapeutic Association (PPTA) and the fulfilling of additional requirements set by Grifols.

- Production processes and facilities are certified according to the US FDA and EU regulations
- Grifols HSA is pasteurized and is delivered as a high purity solution
- Grifols Human Albumin is licensed according to both requirements of the United States Pharmacopoeia (USP) and the European Pharmacopoeia (EP)

Immunoglobulin



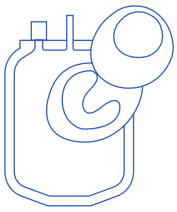
Cell isolation is typically achieved through positive or negative selection using antibodies bound to magnetic beads. As with all antibody-based cell isolation, Fc blocking helps to achieve the best results. Studies have reported using Grifols immunoglobulin in selecting a CD45RA depleted CD3+ T cell population.[2]

GRIFOLS IMMUNOGLOBULINS

Grifols immunoglobulin is manufactured from plasma originated from our own US and EU plasmapheresis centers, complies with cGMPs, IQPP of the PPTA and the fulfilling of additional requirements set by Grifols.

- Production processes and facilities are certified according to the US FDA and EU regulations
- Grifols immunoglobulins are licensed according to both USP and EP requirements

Leukopaks



Leukopaks are useful for process development in CAR-T manufacture. Use of leukopaks allows manufacturers to optimise production processes using highly concentrated cells derived from characterized donors.

LEUKOPAKS

Leukopak is a blood-derived product generated from apheresis, rich in mononuclear leukocytes (ie, lymphocytes and monocytes). It is used by researchers and manufacturers as a starting material in the field of cell therapy. Grifols Bio Supplies offers both:

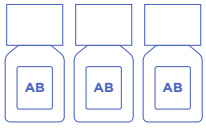
- Leukopaks obtained in Germany collected under GMP conditions
- Research Use Only (RUO) leukopaks obtained in the USA

Collection services:*

- Viral testing and measurement of cell concentration for every donation
- Option to perform immunophenotyping (CD3, CD4, CD8, CD14, CD19, CD56)
- Donations from donors of all gender, blood groups, age, race and other characteristics are available
- Backup donor scheduled for every donation
- Recall donors

*Availability subject to certain regions. For more information on donor collection services, please contact us.

Male AB Serum



Male AB serum is a common supplement in CAR-T cell culture media and provides a mix of hormones, growth and attachment factors, buffering agents, and other nutritional components.

HUMAN MALE AB PLASMA-DERIVED SERUM

Human Male AB Plasma-Derived Serum is manufactured following a cGMP process. Human Male AB Plasma-Derived Serum is manufactured using plasma from FDA-licensed centers within the US. Each plasma unit is tested and found negative for all viral markers using FDA-approved methods. Testing is performed at CLIA and FDA-approved labs (HIV-1/HCV/HBV/Parvo B19/HAV NAT, Anti HIV 1 + 2, Anti HCV, HBsAg and Syphilis -Additional testing available upon request.

- 0.1 µm sterile-filtered
- Custom donor pools available
- Heat inactivation and gamma irradiation available upon request

1. Blaeschke F, Stenger D, Kaeuferle T, Willier S, Lotfi R, Kaiser A, et al. Induction of a central memory and stem cell memory phenotype in functionally active CD4+ and CD8+ CAR T cells produced in an automated good manufacturing practice system for the treatment of CD19+ acute lymphoblastic leukemia. *Cancer Immunol Immunother.* 2018;67(7):1053-1066.
2. Kim-Hoehamer Y, Riberdy J, Zheng F, Park J, Shang N, Métais J, et al. Development of a cGMP-compliant process to manufacture donor-derived, CD45RA-depleted memory CD19-CAR T cells. *Gene Ther.* 2023;30(3-4):222-231.
3. Lock D, Mockel-Tenbrinck N, Drechsel K, Barth C, Mauer D, Schaser T, et al. Automated manufacturing of potent CD20-directed chimeric antigen receptor T cells for clinical use. *Hum Gene Ther.* 2017;28(10):914-925.

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