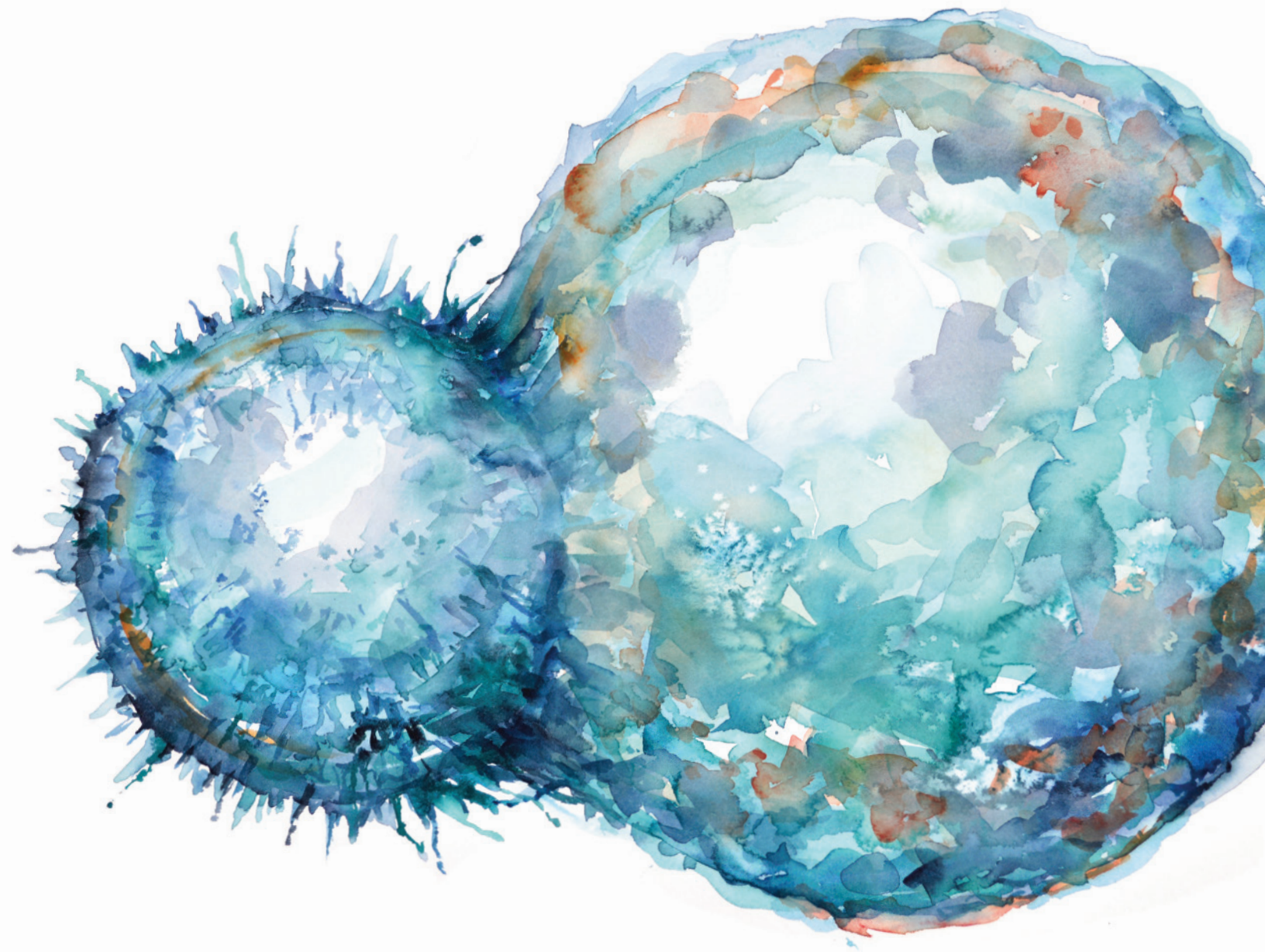
HemaCare®

Understanding and Managing GMP and RUO Starting Materials

GMP AND RUO STARTING MATERIAL FOR CELL AND GENE THERAPY:
QUALITY SYSTEMS DEFINE THE DIFFERENCE



Supporting Cell and Gene Therapy

Cell and gene therapy products, also referred to as Advanced Therapy Medicinal Products (ATMPs), are a family of medicinal products employing allogeneic or autologous human cellular materials, cancer immunotherapies, or genetic materials used to modify the biological properties of cells for treatment of a variety of therapeutic conditions. As with other medicinal products, cell and gene therapy products must be manufactured according to strict quality standards defined by the Food and Drug Administration (FDA) and European Medicines Agency (EMA). To ensure the highest quality and consistency of starting materials, cell collection, processing, and isolation procedures must follow a comprehensive quality oversight system.

GMP-compliant Starting Material and Cells

Cellular starting material quality is directly proportional to therapeutic product quality. The quantity and functionality of target cells in each apheresis unit will ultimately govern downstream potency. Because all cellular starting materials are intrinsically variable, exceptionally trained staff with the expertise necessary to fine tune specific collection parameters, while leveraging a donor program with access to an extensive registry of reliable and recallable healthy donors is essential. To ensure consistency, apheresis instrumentation, mobilization methods, and separation techniques must be optimized and staff training, reagents, supplies, and equipment must have comprehensive quality system oversight.

High-quality research use only (RUO) products provide the flexibility to support early drug discovery and pre-clinical evaluations. However, all successful pre-clinical candidates will eventually need to abide by good manufacturing practices (GMP) regulations, and be processed within a GMP-qualified cleanroom environment before translation to the clinic.

What is GMP?

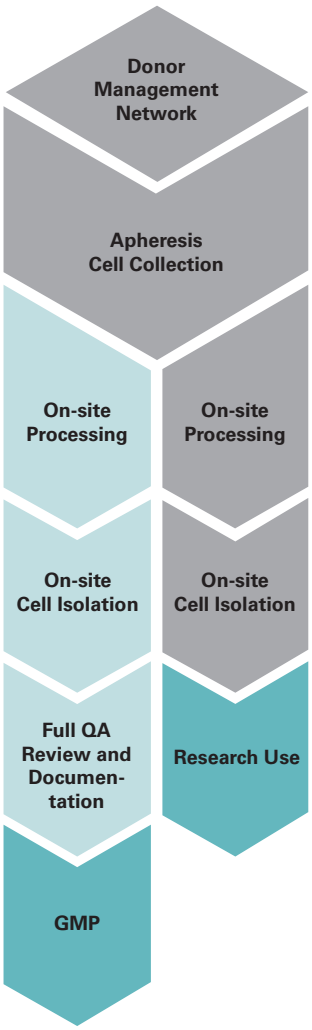
GMP is a system that ensures cellular material is consistently collected and processed following the guidelines set by government regulatory agencies, such as the FDA and EMA, who are responsible for ensuring the quality, efficacy, and safety of pharmaceutical products. In order to guarantee a safe, pure, and effective product, manufacturers must ensure that the production process is validated and thoroughly documented and that the final product is free from contamination and meets established quality standards. This is achieved through the implementation and maintenance of a robust quality management system. Since GMP compliance requires stringent documentation, client consultations can help determine compliance requirements on a per project basis.

Defining the Difference - RUO vs. GMP compliant

Cell and gene therapy starting material designations are determined by the extent of quality assurance documentation required for each product. At HemaCare, we believe the difference between a RUO or GMP-compliant product should never be one of quality or performance. Rather, it is the extensive quality review and documentation surrounding the product that makes it GMP compliant. Building off of the high-quality standards already employed with HemaCare's RUO products, we adopted a comprehensive quality system for our GMP-compliant products that follow the current GMP guidelines that encompass the systems below:

- Qualification of donors
- Qualification of vendors, equipment, and materials
- Equipment and calibration maintenance program
- Development, validation, and maintenance of procedures
- Comprehensive staff training and qualification
- Controlled documents and records management
- Management of deviations and CAPAs
- Monitoring quality indicators for continual process improvement
- Temperature and environmental monitoring program
- Customer complaints
- Internal assessment program and routine external inspections

All GMP-compliant cellular materials are subject to rigorous quality system oversight and meet all regulatory standards required by law.



RUO Cellular Material

- Basic research, drug discovery, pre-clinical development and optimization
- Flexibility for method and process development
- Labeled "Not for Human Use"
- Available products:
  - Peripheral blood
  - Mobilized peripheral blood
  - Bone marrow
  - Cord blood

GMP-compliant Cellular Material

- Collection in GMP-compliant, FDA-registered donor center
- Processing and isolation performed in cleanroom environment
- Intended for further manufacturing to support clinical and commercial use
- Stringent specifications and full quality-assured documentation
- Products:
  - Fresh and cryopreserved leukopaks from peripheral blood
  - Fresh and cryopreserved primary cells and cell fractions – *coming soon*
  - Bone marrow aspirate – *coming soon*

Scalability and Innovation

To meet the increasing demand of the cell and gene therapy industry, HemaCare's expertly designed facility increases our donor capacity, provides advanced GMP capabilities, and greatly improves process workflow.

Cleanroom Units	4 rooms ▹ 1 with isolator ▹ 3 with BSCs
Cleanroom Class	2 Class B 2 Class C (closed processing)

Cleanroom suites include:
▹ Secured access controls
▹ Separate ingress and egress
▹ Individual HVAC systems
▹ Separate designated flow materials and personnel
▹ Validated gowning and material flow procedures
▹ Planned expansion area

Our new state-of-the-art facility is FDA registered, AABB accredited, and licensed by the State of California.

With increased capacity and the planned scalability, HemaCare is committed to the industry and our clients as they grow and transition from product development to clinical and commercial production.

HemaCare's Comprehensive Solutions for Cellular Therapy

Donor Recruitment	Cell Processing and Isolation	Cold Chain Logistics
▹ Recruitment from HemaCare's robust pool of well-characterized, reliable and recallable donors	▹ Apheresis material shipped fresh, same day or cryopreserved	▹ Cryopreservation of starting cellular material and isolated cells
▹ Pre-screening of donors to meet customized specifications	▹ Cells of interest can be purified by density gradient or isolated by immunomagnetic sorting procedures	▹ Packaging and shipment customized to meet client specifications ensuring receipt of highest quality starting material
▹ Customized targeted donor recruitment campaigns	▹ Testing services on unprocessed leukapheresis material or isolated cells (i.e. sterility, endotoxin, mycoplasma)	▹ Batch release performed prior to shipment with short-term sample storage also available in our biorepository

Committed to Your Success

HemaCare is a global leader and trusted brand in the customization of human-derived biological products and services – with many successful collaborations including all three of the FDA-approved cellular immunotherapies currently on the market. Whether your current or future needs are RUO or GMP-compliant cellular material, HemaCare's process development services, combined with a flexible production environment, optimized process flow, GMP-compliant environment, and robust quality system enables HemaCare to address your current and future starting material needs.

Contact HemaCare at (877) 397-3087 to inquire about RUO or GMP-compliant cellular material for your cell-based project.

HemaCare Corporation
8500 Balboa Boulevard, Suite 130, Northridge, CA 91325
(877) 310-0717 | bioresearchproducts@hemacare.com | www.hemacare.com