

Human Blood-Derived Raw Material: Enabling Controlled, Consistent Collection

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Abstract

Human cells are critical raw materials for manufacturing cell therapy products, but often introduce significant variability. Rigorous operational controls and quality systems, however, enable optimal collection of high-quality, consistent cellular material. HemaCare, a long-standing supplier of human-derived blood components, controls apheresis procedures and collection sites under a formal quality system, with GMP-compliant, validated procedures and equipment, and GTP-compliant donor screening and tracking.

HemaCare performed 69,658 cellular apheresis collections in the last five years, including patient and normal-donor PBMCs, G-CSF-mobilized PBPCs and plateletpheresis products, for research, clinical trials, and commercial products.

Expanded capabilities include disease-state and normal-donor bone marrow, umbilical cord blood, and cord tissue collection, immunomagnetic cell selection, cryopreservation, and analysis by flow cytometry.

HemaCare unmobilized apheresis products showed consistently high MNC purity, with 93.8% of products containing $\geq 75\%$ MNC, and an average of $85.2\% \text{ MNC} \pm 6.6\%$ (mean $\pm 1 \text{ SD}$).

Red blood cell contamination was low, with hematocrit averaging $1.8\% \pm 0.8\%$.

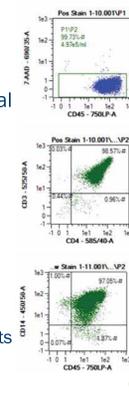
Approximately 85% of HemaCare donors have donated apheresis products 5 or more times, and this repeat-donor pool also contributes to product consistency, as MNC content of individual donor apheresis products had an average coefficient of variation of 3.5%, compared to a CV of 7.7% for all apheresis products.

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About HemaCare BioResearch Products

HemaCare is a leading provider of apheresis products, human blood cells, apheresis collection services, and therapeutic apheresis services

- Apheresis collections and blood-derived products for preclinical research, clinical studies from Phase I to Phase IV, and commercial applications
- Supports applications in immunotherapy, cell therapy, assay development, and medical devices
 - Apheresis PBMC
 - G-CSF-mobilized PBSC
 - Bone marrow
 - Cord blood
 - Peripheral blood
 - Plasma, serum
 - Cell subpopulations
 - CD34⁺
 - CD3⁺, CD4⁺, CD8⁺
 - CD19⁺, CD56⁺, others
 - Healthy-donor and disease-state products
 - Fresh and cryopreserved products



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The HemaCare Advantage

HemaCare is committed to providing our customers with experienced, personalized, responsive, cost effective, and value added services.

Research Products and Cellular Therapy Services

- Donor pool is already pedigreed and will continue to be expanded
- Extensive donor registry with ability to request repeat donor collections
- Predictable, reliable, and validated collection procedures
- Optimized Standard Operating Procedures leading to high degree of standardization and control
- Ability to collect based on specific, customizable protocols
- High-yield, consistent cell collections
- Validated, automated cell counts and five-part WBC differentials
- Established distribution redundancies leading to the ability to ship via FedEx, UPS, World Courier, and various local couriers
- Access to our scientific/technical support 24/7/365

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Human Cells: Standardizing Living Biological Raw Material Through Quality Processes

- Human blood-derived cells are critical raw material for cell therapy, tissue-engineered products, and ex vivo gene therapy products
- Quality and consistency of cellular raw material is a major determinant of final product characteristics
- Controlling cell collection minimizes variability and increases likelihood of success in research and manufacturing
- Training and experience are critical
- Quality systems standardize and control operations

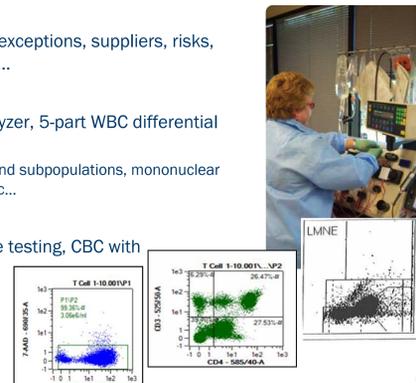
Controlled collection procedures yield optimal, consistent products



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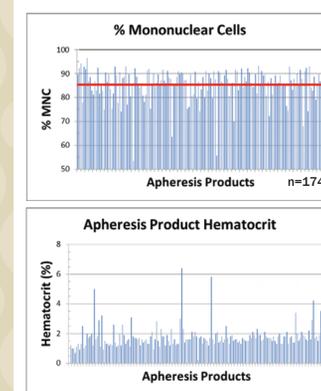
Quality Indicators

- Tracking and trending
 - Donor reactions, deviations, exceptions, suppliers, risks, equipment performance, etc...
- Product QC analysis
 - Automated cell counter/analyzer, 5-part WBC differential (Horiba Pentra analyzer)
 - Nucleated cell (WBC) content and subpopulations, mononuclear cell %, HCT, product volume, etc...
- Donor Testing
 - Screening, Infectious disease testing, CBC with 5-part WBC differential
- Internal and external audits



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Selected Apheresis Product Quality Indicators MNC Purity/Content, RBC Contamination



MNC Purity
Mean $85.2\% \pm 6.6\%$ (mean $\pm 1 \text{ SD}$)
93.8% of products $\geq 75\%$ MNC

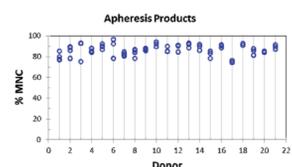
MNC Content
 $10.6 \pm 3.8 \times 10^9$ (mean $\pm 1 \text{ SD}$)

RBC Contamination
Hematocrit $1.8\% \pm 0.8\%$ (mean $\pm 1 \text{ SD}$)
91.3% of products $\leq 2.5\%$ hematocrit

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Donors – The Critical Source

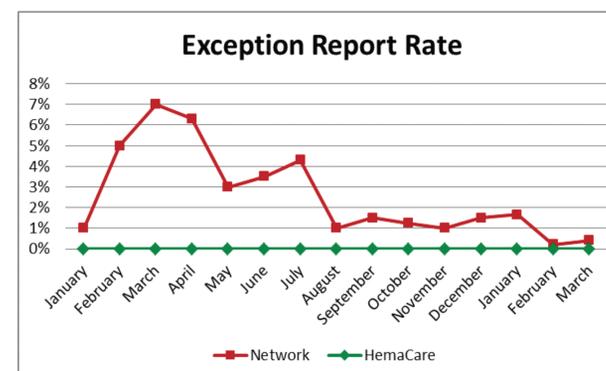
- All donors are qualified per regulations and protocol requirement, with IRB-approved informed consent
- Pedigreed, well-characterized apheresis donor population
 - 85% of HemaCare donors have donated ≥ 5 times/year
 - Facilitates recruitment of donors with specific characteristics required by investigator
 - Medical history, HLA type, other laboratory test results, age, gender, ethnicity, etc...
 - Repeat donors further minimize variability



- Mean 3.5% CV for products per donor
- Mean 7.7% CV for all products
- n=21 donors, 3-5 products/donor

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External Quality Indicators Dendreon Supplier Scorecard



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External Quality Indicators

100%
Right First Time Award

This is awarded to:
HemaCare Blood Donor Center
For its commitment to 100% correct collections

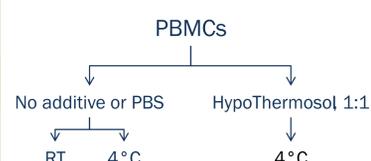
Year Awarded : 2011



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Non-Cryopreserved PBMC Storage

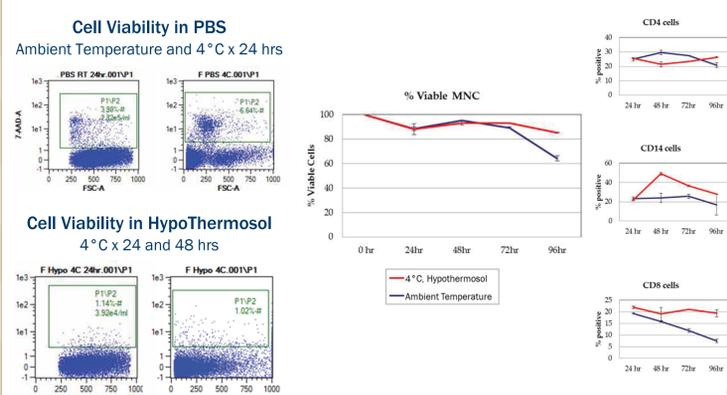
- For many applications, PBMC apheresis products must be used or cryopreserved within 24-48 hours post-collection. Storage in HypoThermosol® (BioLife Solutions) has been shown to increase stability of a variety of cell types, and could extend shelf-life of apheresis PBMCs.
- HemaCare has begun testing stability of MNCs and cell subpopulations stored in HypoThermosol for up to 96 hr without cryopreservation.



Test at t = 0, 24 hr, 48 hr, 96 hr
Cell count with differential
Total WBC and MNC content
% Viable cells (7-AAD)
% Viable MNC recovery
Viable CD4⁺, CD8⁺, CD14⁺, CD19⁺ cell frequency

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Non-Cryopreserved PBMC Storage Pilot Data



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Summary

- Collecting blood-based cellular products in a manner that minimizes variability brings a higher degree of reproducibility to the research project or manufacturing effort
- Quality-based controls such as standardized SOPs, staff training and competency assessments, equipment management, and monitoring of quality indicators reduce this variability
- Availability of repeat donors from a pedigreed donor base enhances the quality and value of this critical, living biological material
- Use of cGMP, serum-free, protein-free biopreservation media such as HypoThermosol shows great promise to enable worldwide shipment of fresh cellular products isolated from apheresis collection, extending shelf-life of cell therapy products, and delaying need for cryopreservation

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