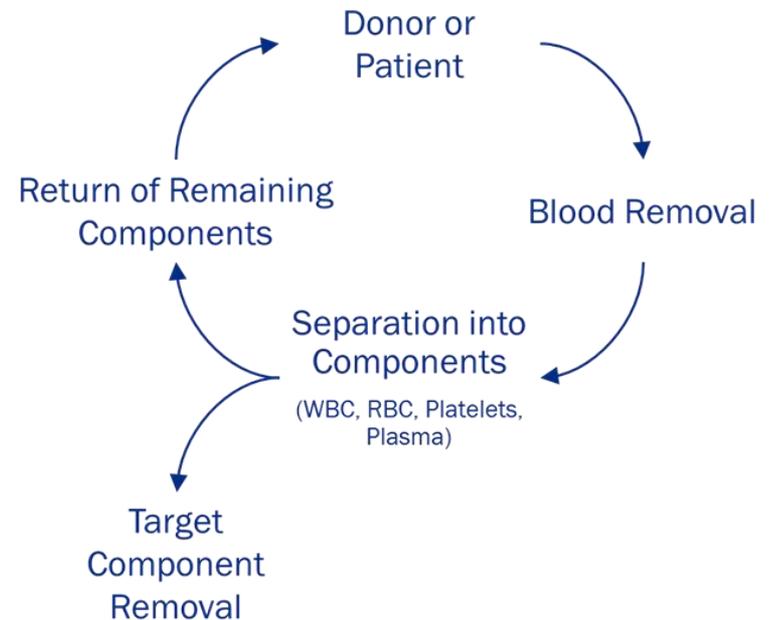


Apheresis Collections for Cell and Gene Therapy Manufacturing

Scott R. Burger, MD
Advanced Cell & Gene Therapy

Apheresis

- Apheresis is the process by which blood is removed from an individual, separated into components, one of which components is retained by the apheresis instrument, and the remainder returned.
- Leukapheresis
 - Collection of WBCs – particularly mononuclear cells (MNCs)
 - Unmobilized leukapheresis
 - Cytokine-mobilized leukapheresis



Leukapheresis in Cell and Gene Therapy Manufacturing

- Leukapheresis is the first step in many cell therapy and *ex vivo* gene therapy manufacturing processes
 - Lymphocytes \Rightarrow CAR-T cells, NK cells, activated T-cells, etc.
 - Monocytes \Rightarrow dendritic cells
 - PBPCs for transplant, *ex vivo* expansion, etc.
- High-quality raw materials are necessary for a high-quality final product

Apheresis Devices for MNC Collection

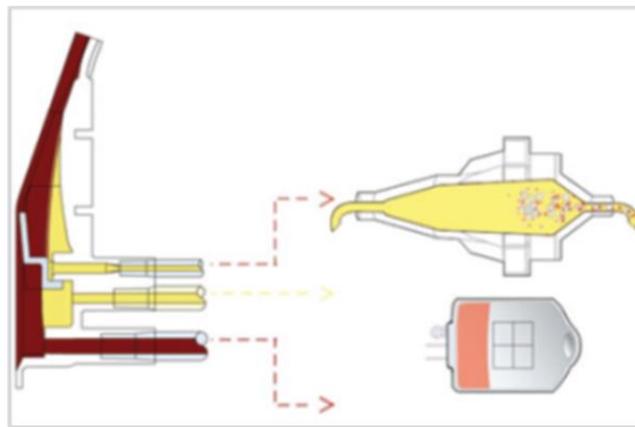
- Spectra and Spectra Optia (Terumo BCT) and Amicus (Fresenius Kabi)
- All three machines use continuous flow centrifugation.
- Both the Spectra Optia and Amicus are highly automated; the Spectra is more manually controlled.



Spectra



Spectra Optia



Amicus

High-Quality Cellular Raw Material is Essential for Cell Therapy Manufacturing

- Controlled, consistent manufacturing processes yield controlled, consistent products
- Leukapheresis, the process by which human blood-derived cellular raw material is collected, requires the rigorous process control as for any manufacturing unit operation
- High-quality raw materials are necessary for a high-quality final product

Ensuring Leukapheresis Process and Product Quality

- Leukapheresis collections under an appropriate Quality system
 - Donor screening and qualification per GTPs
 - Document, qualify/validate procedures and equipment (IQ, OQ, PQ)
 - Qualify vendors, supplies, and apheresis sites
 - Establish quality agreements for critical vendors
 - Monitor equipment and environment
 - Staff training and qualification
 - Documentation and records management
 - Management of exceptions and deviations, CAPA
 - Internal and external inspections
 - Tracking and trending quality indicators

Quality Indicators

- Donor reactions, deviations, exceptions
- QC testing characteristics: products and donors
- Donor
 - Pre-procedure CBC, other screening tests
- Product
 - Total WBC and MNC
 - Volume
 - Purity
 - % MNC
 - Hematocrit or RBC concentration
 - Platelet concentration
 - Immunophenotype, if needed

Summary

- Leukapheresis collection quality is a major determinant of cell therapy manufacturing process success and final product quality.
- Collection under the oversight of a quality system, and compliance with GTPs and GMPs are essential to ensure well-controlled, consistent collection of high-quality leukapheresis products.
- Leukapheresis is the first step in many cell therapy manufacturing processes -- well begun is half done.