# Chemistry, Manufacturing and Control

# Sponsor

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# proposed use

The drug is an allogeneic TCRa/b and CD19 depleted stem cell transplant from a related donor to treat relapsed Juvenile Myelomonocytic Leukemia (JMML) post-allogeneic stem cell transplant.

# Product description

# phase of study

This is an emergency IND for the treatment of a single patient.

# cross-referenced INDs, IDEs

Letters of Authorization have been provided from Miltenyi Biotec for the following Master Files that are provided as an appendix.

* BB MF 10732 CliniMACS Anti-Biotin (FLS)
* BB MF 11441 CliniMACS PBS/EDTA Buffer
* BB MF 12011 CliniMACS CD19 Reagent
* BB MF 12251 CliniMACS Depletion Tubing Set (DTS)
* BB MF 15678 CliniMACS TCR alpha/beta Reagent

# product manufacturing and characterization

**Overview of Manufacturing Responsibilities**

The TCRa/b and CD19 depletion of the mobilized apheresis collection is performed according to the Miltenyi Biotec CliniMACS procedures.

Product Manufacturing

Cell Therapy Laboratory

Indiana University Hospital

550 University Blvd

Indianapolis, IN 46202

**CTL Manager:** Dave Schwering, MT(AMT), CABP

**Transfusion Medicine Director:** Elaine Skipworth, MBA, MT(ASCP)HP

Flow Cytometry testing for TCR a/b and CD19/CD20 expression

Indiana University Cell Immunotherapy and Transduction Facility (CIT)

Cell and Gene Therapy Manufacturing

Indiana University Hospital

550 University Blvd

Room 3453A

Indianapolis, IN 46202

**CIT Manager:** Christina Vaughan, MS, CABP

**CIT/CGTM Director:** Emily Hopewell, PhD, CABP(H)

Apheresis PBMC collections are performed at the following FACT accredited facility:

Transfusion Medicine - Apheresis

Indiana University Hospital

550 University Blvd

Indianapolis, IN 46202

**Transfusion Medicine Director:** Elaine Skipworth, MBA, MT(ASCP)HP

Clinical products are distributed for infusion by the following FACT accredited facility:

Transfusion Medicine – Cell Therapy Laboratory

Indiana University Hospital

550 University Blvd

Indianapolis, IN 46202

**Transfusion Medicine Director:** Elaine Skipworth, MBA, MT(ASCP)HP

Patients are infused at the following facility:

Riley Hospital for Children - Indiana University

705 Riley Hospital Dr

Indianapolis, IN 46202

## Product Manufacturing – Components

### **Cells**

Allogeneic peripheral blood stem cells will be obtained using leukapheresis according to standard procedure. The starting material will be transported to the Cell Therapy Laboratory at 15 – 25oC in a temperature controlled and monitored container. The final product will be cryopreserved per standard procedure until patient is ready for infusion.

* 1. Allogeneic Cell Components
* Cell Source: Allogeneic hematopoietic progenitor cells
* Method of Collection: Apheresis
* Donor Screening: Donor screening will occur according to 21 CFR § 1271
* Donor Testing: Donor testing will occur according to 21 CFR § 1271
  1. Cell Bank System – no cell banking will be used in the manufacture of this product

1. **Reagents**

**Table 7.1 Tabulation of Critical Reagents and Supplies Used in Manufacturing**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Supply / Reagent** | **Concentration** | **Manufacturing Step** | **Preferred Vendor /Supplier** | **Source (human, porcine, bovine,** | **Quality (Clinical, Research, etc.)** |
| CliniMACS™ PBS/EDTA Buffer | N/A | Washing and depletion | Miltenyi | N/A | LOA provided |
| CliniMACS™ Anti-Biotin Reagent | N/A | Depletion | Miltenyi | N/A | LOA provided |
| CliniMACS™ TCR a/b Reagent Kit | N/A | Depletion | Miltenyi | N/A | LOA provided |
| CliniMACS™ CD19 Reagent | N/A | Depletion | Miltenyi | N/A | LOA provided |
| CliniMACS™ DepletionTubing Set | N/A | Depletion | Miltenyi | N/A | LOA provided |
| Blood Transfusion Filter | N/A | Depletion | Pall | N/A | Clinical |
| Immune Globulin | 10% | Depletion | Takeda | Human | Clinical, USP |
| Human Serum Albumin | 5% | Wash, depletion, cryopreservation, infusion | Grifols | Human | Clinical, USP |
| Normal Saline | 0.9% | Cryopreservation | Baxter | N/A | Clinical, USP |
| 50 mL syringe | N/A | Depletion and/or cryopreservation | BD | N/A | Clinical |
| 10 mL syringe | N/A | Depletion and/or cryopreservation | BD | N/A | Clinical |
| 3 mL syringe | N/A | Depletion and/or cryopreservation | BD |  | Clinical |
| Transfer bag | N/A | Washing | Fresenius Kabi | N/A | Clinical |
| Plasma Transfer Set, two spikes | N/A | Washing | Fresenius Kabi | N/A | Clinical |
| Infusion Filter | N/A | Depletion and/or cryopreservation | Baxter | N/A | Clinical |
| Sterile Tube Welding Wafers | N/A | Washing, depletion | Terumo | N/A | Clinical |
| Sampling site coupler | N/A | Depletion and/or cryopreservation | Charter Medical | N/A | Clinical |
| Needle Free Spike | N/A | Depletion and/or cryopreservation | Origen | N/A | Clinical |
| 16G Needles | N/A | Depletion and/or cryopreservation | BD | N/A | Clinical |
| Bags for cryopreservation | N/A | Cryopreservation | Origen | N/A | Clinical |
| DMSO | 10% | Cryopreservation | Mylan | N/A | Clinical, USP |

All supplies and reagents listed in this table have a corresponding example Certificate of Analysis or equivalent provided in the appendix. These documents are provided as examples. Supplies and reagents that are expired are not used.

**Supply Management**

All reagents that have the potential to impact the purity, potency, quality, or safety of the product are qualified based on the use of the material and its risk to the product according to standard operation procedure. Supplies and reagents are controlled through receipt and quarantined until approved for use. Released supplies are labeled and physically segregated from quarantined items. Lot numbers of all materials and supplies used for a production are documented as part of the production record to facilitate look-backs in the event of a deviation and/or recall.

## Product Manufacturing – Procedures

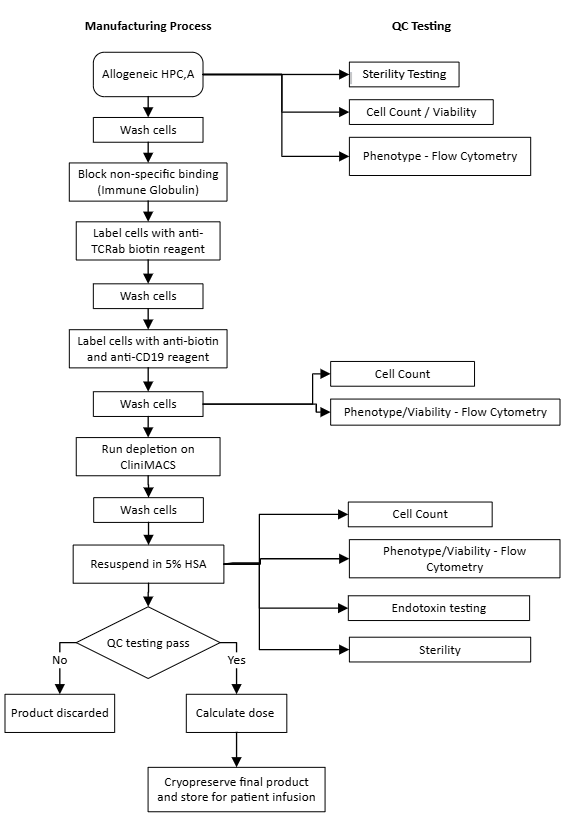
**Overview**

Hematopoietic progenitor cells are collected from a suitable and qualified related donor using apheresis. A maximum of 24 x 10^9 TCRa/b cells and 10 x 10^9 CD19 can be depleted using this process. Any additional cells may be cryopreserved for additional processing if required.

***Depletion of CD19+ and TCRa/b+ Cells***

The apheresis product is collected from the mobilized donor and transferred to the Cell Therapy Laboratory for depletion according to existing transportation procedures. Cells are washed and labeled with antibodies to TCRa/b and CD19, washed again and then depletion is performed on the CliniMACS™. The tubing set is applied to the instrument as directed by the program and the prepared labeled cells are connected to the tubing set as directed by the program. The depletion process runs automatically.

**Figure 7.1 Process for depletion of TCRa/b and CD19 cells (see next page)**



The target cells will be resuspended in 5% HSA v/v. The product will be tested for sterility, endotoxin, viability and identity. The final dose will be cryopreserved in 5% HSA and 10% DMSO. Results from the Endotoxin test, viability, and identity must meet release criteria for the product to be administered. The microbial culture results will not be available prior to release of the product.

**Irradiation**

No irradiation will be used for this process.

**Process Timing & Intermediate Storage**

Collection to infusion should take less than 48 hours if the dose is provided fresh. After the release testing is completed, numbers from the cell count and phenotype will be used to prepare the dose.

Once the dose is prepared, the cells are cryopreserved and stored in the vapor phase of liquid nitrogen until release for approximately one week. Cells are transported from the Cell Therapy Laboratory to the patient bedside and transport takes place in qualified dry shipper. The final product is thawed at the patient bedside.

**Final Formulation**

The patient will receive a target dose of 10 x 10^6 CD34 cells/kg body weight (minimum of 2 x 10^6 CD34 cells/kg body weight). Patients will receive ≤5 EU/kg body weight/hour.

The target CD3+ cell dose will be ≤1.0 x 10^5 cells/kg body weight, with a maximum allowed of <5.0 x 10^5 TCRa/b cells/kg body weight if the CD34+ cell number is <5.0 x 10^6 cells/kg.

The target CD19+ cell dose will be ≤1.0 x 10^5 cells/kg body weight. Rituximab will be given on Day -1 200mg/m^2 IV x 1 dose.

The required dose will be removed from the harvested product and suspended in 5% v/v HSA and cryopreserved after the addition of DMSO. The final product is labeled according to ISBT128 labeling. The final product will not be released until the Certificate of Analysis is completed and approved by the Technical team and the Quality Assurance team. Once approved for release, the CTL will transport patient products to the Riley Hospital for Children for infusion according to their standard procedures.

**Formulation/Infusion Buffer**

The infusion buffer consists of 0.9% saline with 5% v/v HSA and 10% DMSO.

**Excipients**

Excipients in the final product include 0.9% saline, 5% v/v HSA, and 10% DMSO.

**Cell Density/Concentration in the Final Product**

The cell density of the final product will vary based on the total dose required for the patient weight.

**Table 7.2 Storage Method Prior to Use** Cells will be stored using a variety of methods depending on the stage of the process.

|  |  |  |
| --- | --- | --- |
| **Step** | **Storage conditions** | **Timing** |
| Receipt of starting material | 15 – 25oC in a monitored environment | <18 hours |
| After processing | 15 – 25oC in a monitored environment | <3 hours |
| At final harvest | 2 - 8oC in a monitored environment | <4 hours |
| After dose preparation | ≤-150oC in a monitored environment | Dependent on patient conditioning; approximately 1 week |
| At infusion | Ambient temperature | <30 minutes |

# PRODUCT TESTING

## In-Process Testing and Criteria

**Table 7.3 Tabulation of Tests**

|  |  |  |  |
| --- | --- | --- | --- |
| **Test** | **Manufacturing Step** | **Test Method** | **Criteria** |
| Sterility | Starting material, final harvest | Internal Qualified Method | Negative; final product results not available prior to administration |
| Purity (Endotoxin) | Final harvest | Endosafe® nexgen-PTS | Less than 5 EU / kg body weight / hour |
| Identity | Starting material | Flow cytometry, TCRαβ/CD45/CD19  CD34/CD45/7-AAD | For depletion antibody labeling information |
| Identity | Pre-column assessment | Flow cytometry,  CD3/CD16/CD56/CD45  CD20/CD45/CD3  TCRgd/TCRab/CD3/7-AAD  CD45/CD34/7-AAD | For internal information only |
| Cell dose and identity | Final harvest | Flow cytometry\* | CD45/CD34/7-AAD; 2.0 x 10^5 – 10.0 x 10^5 CD34+/kg  CD45/CD20/CD3; ≤1.0 x 10^5 CD20+/kg and ≤1.0 x 10^5 CD3+/kg |
| Purity (other contaminants) | Final harvest | Flow cytometry | CD3/CD16/CD56/CD45; information only |
| Others (cell viability) | Starting material, Final harvest | Flow cytometry, 7-AAD | Report result; Final harvest ≥70% viable CD34+ cells |

\*Refer to Final Formulation section for steps allowed if CD19 and CD3 numbers are higher than recommended.

# 

# FINAL PRODUCT RELEASE CRITERIA/SPECIFICATIONS

**Table 7.4 Final product release criteria and specifications**

|  |  |  |  |
| --- | --- | --- | --- |
| **Test** | **Method** | **Criteria** | **Results Available prior to Release** |
| Sterility | Internal Qualified Method | Negative | No |
| Purity (Endotoxin) | Endosafe nexgen-PTS | < 5 EU/ kg body weight / hour | Yes |
| Identity | Flow cytometry | CD45/CD34/7-AAD; 2.0 x 10^5 – 10.0 x 10^5 CD34+/kg  CD45/CD20/CD3; ≤1.0 x 10^5 CD20+/kg and ≤1.0 x 10^5 CD3+/kg | Yes |
| Cell viability | Flow cytometry | ≥70% viable CD34+ cells | Yes |

**Description of Test Methods**

**Microbiological Testing**

***Sterility Testing (Bacterial and Fungal Testing)***

Samples will be removed as described in the manufacturing workflow. Samples will be inoculated in thioglycolate broth for bacterial cultures and a sterile tube for fungal cultures and submitted to the IU Health Clinical Microbiology Laboratory for culture. Bacterial cultures are incubated for 7 days. Samples tested for fungal contaminants are incubated for 14 days. In the event of a positive sterility culture discovered after administration, the CTL Medical Director and the Principal Investigator will be notified immediately to determine the appropriate treatment plan.

***Gram Stain***

Samples will be stained to assess the presence of gross bacterial contaminants according to standard operating procedure. In the event of a potential positive result, a sample will be sent to the IU Health Microbiology laboratory for confirmation.

**Identity Testing**

***Phenotype by flow cytometry***

Samples from the final harvest will be tested by flow cytometry. The cells will be assessed for viability and phenotype according to the matrix below.

**Table 7.5 Flow cytometry timing and panel**

|  |  |
| --- | --- |
| Part of Process | Tube Number |
| Day of Collection | Tubes 1 and 5 |
| Pre-Processing | Tubes 1 and 5 |
| Post Platelet Depletion | Tube 1 |
| Pre-Column | Tubes 2, 3, 4, 5 |
| Target/Non-Target | Tubes 2, 3, 4, 5 |

**Table 7.6 Flow cytometry phenotyping**

|  |
| --- |
| Markers Being Testing in Each Tube |
| Tube 1: TCRαβ/CD45/CD19 |
| Tube 2: CD3/CD16+56/CD45 |
| Tube 3: CD20/CD45/CD3 |
| Tube 4:TCRγδ/TCRαβ/CD3/7-AAD |
| Tube 5: CD45/CD34/7-AAD |

**Purity Testing**

***Endotoxin***

An aliquot of the final product will be tested for Endotoxin using the Endosafe® nexgen-PTS.

***Viability***

Viability of the starting material will be determined using 7-AAD via flow cytometry.

**CD19/TCRa/b Depletion Experience**

Two engineering runs have been performed using this process to show a decrease in a/b CD3+ cells and CD19+ cells. Mobilized normal donor cells collected by apheresis were purchased from a commercial vendor and received fresh. The results of these runs are provided in the table below.

**Table 7.7 Results from CD19+ and TCRa/b+ depletion.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Run 1 (2024-OCT-11) | | | Run 2 (2024-OCT-31) | | |
| Test | Pre-Depletion | Post-Depletion | Log Depletion | Pre-Depletion | Post-Depletion | Log Depletion |
| ab CD3+ | 1.33x10^10 | 1.36x10^8 | 2 | 3.43x10^10 | 4.50x10^7 | 3 |
| gd CD3+ | 2.74x10^9 | 1.69x10^10 | N/A | 2.90x10^9 | 1.94x10^10 | N/A |
| CD34+ | 8.15x10^8 | 5.56x10^8 | N/A | 3.44x10^8 | 3.13x10^8 | N/A |
| CD20+ | 2.91x10^9 | 6.25x10^ | 1 | 2.28x10^9 | 1.84x10^7 | 2 |
| Post-Processing Viability | 96.4% | | | 89.9% | | |

# product stability

There is substantial data to support product stability of non-enriched mobilized hematopoietic progenitor cells. Consolidated data from a stability audit for these cells is provided in Table 7.8.

**Table 7.8 Stability Data for Cryopreserved Hematopoietic Progenitor Cells**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Auto or Allo** | **Thaw Date** | **Storage Time (yrs)** | **Viability** | **Viable CD34+ Recovery (%)** | **Mean # Colonies CFU** | **TNC Recovery (%)** |
|
| Auto | 08.21.2019 | 16 | 75 | 100 | 56 | 93 |
| Auto | 08.21.2019 | 10 | 88 | 98 | 206 | 86 |
| Auto | 08.21.2019 | 10 | 83 | 100 | 18 | 87 |
| Auto | 08.21.2019 | 13 | 83 | 94 | 99 | 94 |
| Allo | 08.21.2019 | 7 | 77 | 100 | 19 | 92 |
| Allo | 01.07.2020 | 9 | 77 | 100 | 29 | 73 |
| Auto | 01.08.2020 | 8 | 75 | 100 | 12 | 77 |
| Auto | 01.07.2020 | 11 | 76 | 100 | 107 | 66 |
| Auto | 01.08.2020 | 10 | 64 | 100 | 43 | 52 |
| Auto | 01.07.2020 | 8 | 70 | 77 | 14 | 56 |
| Allo | 4/9/2021 | 10 | 68 | 100 | 8 | 104 |
| Auto | 4/9/2021 | 15 | 86 | 100 | 14 | 98 |
| Auto | 4/9/2021 | 15 | 83 | 100 | 306 | 88 |
| Auto | 10/26/2021 | 15 | 80 | 100 | 59 | 75 |
| Auto | 10/26/2021 | 18 | 84 | 100 | 62 | 83 |
| Auto | 3/10/2022 | 12 | 92 | 100 | 152 | 81 |
| Auto | 3/10/2022 | 20 | 87 | 100 | 205 | 86 |
| Allo | 3/10/2022 | 9 | 88 | 100 | 18 | 98 |
| Auto | 9/13/2022 | 13 | 71 | 100 | 2 | 101 |
| Auto | 9/13/2022 | 7 | 88 | 100 | 85 | 80 |

One CD34-enriched product was cryopreserved and thawed for infusion in the past year. The product was cryopreserved on 12/7/2024 and thawed and infused on 12/21/2023. That product had a post-thaw viability of 72%. This product will be cryopreserved for approximately one week. Results are calculated based on reported populations determined by flow cytometry.

The viability of this product will be determined using cells remaining in the product bag after the infusion is completed. This analysis will be a post-thaw cell characterization including the cell number and viability to support the stability of the cells from TCR alpha/beta and CD19 depletion. This data will be submitted as a future amendment to the study.

## OTHER ISSUES

## Product Tracking

All products that are received by the IU Health Cell Therapy Laboratory are tracked from the time of receipt to the point of final product distribution, administration or destruction, as in the case of an unacceptable product, deemed as such by the Transfusion Medicine Director, Medical Director and the Principal Investigator following processing. Loss of chain-of-custody (COC)/chain-of-identity (COI) would have a direct impact on clinical study subjects. COC/COI checks are incorporated throughout the process and before final product administration.

## Labeling and Containers

All labeling is compliant with FDA regulations and ISBT 128 Standards. Label adhesives and ink remain attached, affixed, and legible through all intended environments to include LN2 temperatures, 4°C, room temperature, water bath, friction, and exposure to disinfectants. Label adhesives will be placed on product containers to prevent the risk of chemical leaching into the cell product (i.e. Not placed directly on cell bag plastic containing cells, affixed over a manufacturer label, or not product containing section is acceptable) and to allow adequate visualization of the product contents.

Products are labeled at the site of collection according to ISBT 128 standards including: unique product identification number, the date and time collected, donor identification, name of component, and name and volume of additives. Prior to transfer of the product to the processing facility, the collection label is checked for accuracy by collection staff and processing personnel.

The assigned unique product ID number is permanently attached to all the processing documents and placed in the product batch record. During manufacture, in-process partial labels are used to contain at minimum, the component name, unique product number and donor identification. Labels are verified by a minimum of two trained staff. In addition to partial labels, Products will be labeled with Product Tie Tag prior to distribution for patient administration.

**Figure 7.2 Example of final product label**



## Container Closure & Integrity

The product will be dispensed in a qualified cryopreserved product bag. The product will be cryopreserved and will be transported to the patient bedside in a qualified dry shipper that will hold the required temperature (<150oC) for at least 5 days. The product bag will be removed from the dry shipper and thawed in a qualified water bath at 37oC according to standard procedures. The pediatric BMT unit is located at Riley Children’s Hospital, 705 Riley Hospital Drive, Indianapolis, IN and the cells will be coming from Indiana University Hospital, 550 N University Drive, Indianapolis, IN. This is approximately a 10 minute walk between locations and is the standard procedure for transplant for all pediatric BMT patients treated at Riley Children’s Hospital.

The thawed product will be released to the infusion nurse for the recipient under the supervision of the attending provider per standard operating procedure. The nursing staff will infuse the cells according to established guidelines for hematopoietic progenitor cell products. Briefly, the thawed bag will be spiked with an infusion set and infused via gravity without filtration. There will be no additional manipulation of the cells between thawing and administration.

## 

## Environmental Impact

Under the provisions of 21 CFR§25.31(e), the sponsor-investigator requests that an exclusion be granted from the requirements for environmental assessment. The investigational new drug is intended for use in clinical studies on research in which waste will be controlled; in addition, the amount of waste expected to enter the environment may reasonably be expected to be nontoxic.

## Cell Processing Facility

The Cellular Therapy Laboratory (CTL) is a 1300 sq.ft secure processing area dedicated to the manipulation and storage of cell-based products for treatment of patients on clinical trials and established clinical treatment (Figure 7.3). The CTL is a part of the IU Health Department of Pathology and has overarching general procedures and designated Quality Assurance personnel. The processing facility is located on the third floor of University Hospital, 550 North University Boulevard, Indianapolis, IN 46202. The CTL is a FACT Accredited Processing Facility. Services are provided in compliance with FDA 21CFR §211 cGMP (current Good Manufacturing Practice) as appropriate for early phase trials..

The CTL operates as a multi-use facility designed to eliminate or minimize contamination and/or cross-contamination of materials and cellular products through process controls and functionally closed system manipulations. The facility is equipped with and continuously monitored by the Rees Scientific Centron System with alert and action limits. Facility parameters monitored include temperature, and humidity. Critical equipment, including incubators, refrigerators and freezers are also monitored.  Trained on-call CTL staff members respond to all alarm conditions.

The CTL is a part of the IU Health Department of Pathology. the IU Health Department of Pathology follows a unified Quality Management Plan. The operations of the CTL are defined by approved procedures and all staff are trained on procedures. All procedures are maintained and version controlled within PolicyTech. MediaLab is in place for management of records and personnel training. Procedures are in place to help maintain control of the facility, personnel, and processes. A partial list of these documents is provided below.

**Figure 7.3 Floor plan of the Cell Therapy Laboratory**

A floor plan of a medical center

Description automatically generated

**Table 7.9 List of relevant procedures**

|  |
| --- |
| Title |
| [Supply Inventory](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151289) |
| [Sterility Testing](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151288) |
| [Refrigerator, Freezer and REES Scientific e-Centron Environmental Monitoring System](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151287) |
| [Process Improvement](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151286) |
| [Procedure: Viable Particle Testing](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151285) |
| [Procedure: Validation of Standard Operating Procedures, Forms, Labels and Job Aids](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151284) |
| [Procedure: Validation and Qualification](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=160795) |
| [Procedure: Recalls and Market Withdrawals of Materials](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=161509) |
| [Procedure: Product Storage, Inventory Tracking and Disposal](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151276) |
| [Procedure: Product Quarantine Storage and Warning Labels](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151229) |
| [Procedure: Product Cryopreservation](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151275) |
| [Procedure: Product and Reagent Labeling](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151274) |
| [Procedure: Preparation and Control of Standard Operating Procedures and Forms](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151273) |
| [Procedure: Platelet Reduction of Cellular Therapy Products](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151228) |
| [Procedure: PDF Logger Kit Validation and Operation](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151227) |
| [Procedure: Operation of the Sebra OMNI Sealer](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151226) |
| [Procedure: Operation of CryoMed® Controlled Rate Freezers](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151225) |
| [Procedure: Notification of the Food and Drug Administration and Other Accrediting Agencies](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151184) |
| [Procedure: Nonconformity of Products/Materials and Dose Limitations](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151183) |
| [Procedure: Management of Product Recalls](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151257) |
| [Procedure: Management and Operation of VeriCor Cool Cube Transport Coolers](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151223) |
| [Procedure: LN2 Shipper and VeriCor Cool Cube Transport Cooler Quality Control](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151222) |
| [Procedure: ISBT Label Reprint](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151220) |
| [Procedure: ISBT 128 Donation Identification Number Label Sets](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151219) |
| [Procedure: Internal Assessments](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=181911) |
| [Procedure: Infusion of Cryopreserved Products](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=150960) |
| [Procedure: Infectious Disease Marker Testing](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=150958) |
| [Procedure: Hood Quality Control and Disinfection](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151218) |
| [Procedure: Equipment Management](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151211) |
| [Procedure: Environmental Services Cleaning/Disinfection in Cellular Therapy Lab](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151055) |
| [Procedure: Environmental Monitoring](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=153490) |
| [Procedure: Environmental Disinfection in Cellular Therapy Lab](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151210) |
| [Procedure: Director Designation and Responsibilities: Cellular Therapy Processing Facility](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151207) |
| [Procedure: Data Entry and Electronic Records](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151241) |
| [Procedure: Computer Downtime](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151053) |
| [Procedure: Change Control Management and Risk Assessment](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151052) |
| [Procedure: Cellular Therapy Product Terminology](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151201) |
| [Procedure: Cellular Therapy Product Release](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151200) |
| [Procedure: Cellular Therapy Laboratory Document and Record Management](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151240) |
| [Procedure: Cellular Therapy Lab Supplier Qualification](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151239) |
| [Procedure: Cellular Therapy Lab Sterile Connecting Device Operation](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151198) |
| [Procedure: Cellular Therapy Lab Security](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151197) |
| [Procedure: Cellular Therapy Lab Research Requests](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=153451) |
| [Procedure: Cellular Therapy Lab Quality Management Plan](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=175691) |
| [Procedure: Cellular Therapy Lab On-Boarding, Training and Competency](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151238) |
| [Procedure: Cellular Therapy Lab Occurrence Management](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=152504) |
| [Procedure: Cellular Therapy Lab Liquid Nitrogen Safety](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=150973) |
| [Procedure: Cellular Therapy Lab Inspection Protocol](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=150972) |
| [Procedure: Cellular Therapy Lab Emergency Plan](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=172557) |
| [Procedure: Calculation Recording](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151192) |
| [Procedure: Aseptic Technique for Cell Processing](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151189) |
| [Procedure Receipt of Cellular Therapy Products](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151232) |
| [Investigation of Cellular Therapy Product Infusion Reactions](https://iuhealth.policytech.com/dotNet/documents/?app=pt&source=unspecified&docid=151172) |