1. Education and promotion

1.1. Healthcare professionals

Explanation	Process Elements	Examples
In order to promote optimal use of cells and tissues (cellular therapy), which are a true national resource, healthcare professions must first be educated as to need.	Develop policies and procedures for education and training of healthcare professionals in optimal use of cells and tissues for administration and how to encourage donors.	• Plan educational activities for healthcare professionals and clinicians in use of cells and tissues for cellular therapy • Liaise with clinical programs treating patients that might benefit from cellular therapy • Collect data to monitor progress in use of the national resource of cell and tissue donation • Collect data to monitor success of educational programs in increasing donations

1.2. Public campaigns

Explanation	Process Elements	Examples
The public must be made aware of the value of cell and tissue donation to overall public health and the importance that such donations be voluntary without expectation for remuneration	Establish campaigns to promote voluntary non- remunerated cell and tissue donation as an act of altruism.	• Ensure policies and procedures indicate voluntary and non-remunerated donation • Hold public educational seminars (e.g. schools, colleges, universities, other professional bodies) • Use social media such as Facebook, YouTube, or Twitter, to create population awareness

2. Program organization

2.1. Identify regulatory requirements

Explanation	Process Elements	Examples
Identify national legal and regulatory authority framework Determine if national LRA framework is in place, if not ensure that program works towards its establishment. Become familiar with relevant laws, regulations, and standards	Entity should meet relevant requirements of National Standards. Include legislative and regulatory framework in processes and procedures to support donation and use of cellular therapy products.	• Prepare for certification by a national or international Accreditation Body • Communicate with relevant national body(ies) to ensure compliance with requirements, inspection and authorization of screening, testing, retrieval, processing, storage, distribution, import and export (e.g. EU

	Designate national authority to establish national registry of donors for cellular therapy products.	directives/regulations, US FDA regulations) • Collect and report donation, processing, distribution, import, export and use activity data as applicable • Share information and data on cellular therapy product donation and use to ensure transparency (e.g. donor registries) • Contribute to establishment of needed national registries or identify and participate in existing registries
Identify international legal and regulatory authority framework When using cellular therapy products from unrelated donors often the optimal donor may be found in another country. It is critical to abide by relevant international laws and regulations.	Be aware of and follow appropriate requirements for cellular therapy products import and export.	• Communicate with international bodies to ensure compliance with requirements • Share information and data on cellular therapy product donation to ensure transparency. (e.g. Share adverse events with international donor registries)

2.2. Program structure

Explanation	**Process Elements**	**Examples**
Facilities using cellular therapy product may utilize different organizational models. Some may include all aspects of collection, processing, and clinical use under a single structure while in other cases distinct entities work through agreements for various functions. In particular collection or processing facilities may provide service to more than one clinical program, a model that might work to conserve resources. Adult and pediatric clinical programs may work together as a joint cellular therapy program.	Facilities that constitute the program should be legally identifiable. The relationship facilities to each other and to the overall program must be defined.	• Prepare appropriate organization charts showing how facilities interact • Establish agreements between program facilities as needed • Separate clinical facilities, such as a pediatric and an adult hospital, working as a combined program must demonstrate common protocols, procedures, quality systems, review of results and evidence of regular interaction

2.3. Program Leadership

Explanation	**Process Elements**	**Examples**

The management structure of facilities involved in cellular therapy must be clearly defined and responsibilities of management identified.	Define management responsibilities for all aspects of the program, including clinical, collection, and processing. Designate directors and medical directors as appropriate, for each facility and for quality management . Designate an overall program leader	• Prepare appropriate organization charts showing how management interacts within the program and with the quality program • Define management job descriptions including responsibilities, authorities, position requirements in regards to education, degrees, experience, skills, training, etc

3. Facility requirements and staffing
   3.1. Clinical
      3.1.1. Clinical treatment facilities
      3.1.2. Clinical requirements for physicians, mid-level practitioners, nurses, consultants

Explanation	**Process Elements**	**Examples**
Clinical Program The clinical program may include multiple sites within a healthcare facility including inpatient and outpatient sites. Requirements to ensure adequate space, design, and location to protect patients from airborne microbial contamination must be specified. The program must also determine if therapy will be administered on an outpatient basis, and how intensive care will be provided. Some program inpatient units also provide intensive care, while in other models intensive care is provided outside of the unit.	Define design requirements for inpatient facilities that minimizes the potential for infection. Define requirements for outpatient facilities. Define requirements for intensive care and after hours emergency care.	• Prepare floor plans of inpatient care area and describe methods in place to minimize spread of infections. (e.g. environmental control use such as HEPA filters, hand washing stations, etc.) • Prepare floor plans of areas used for outpatient treatments and follow-up care including description of methods to minimize spread of infections • Develop procedures to perform outpatient administration of cellular therapy products, if performed • Develop procedures for intensive care and for provision of after hours care that involves BMT clinical program physicians
Clinical Staff and Consultants Various models for staffing clinical facilities are used. Some exclusively use physicians who are dedicated to cellular therapy while other programs use	Identify and define the requirements for physician staffing, use of mid-level practitioners, nursing staff, and consultants with appropriate expertise for program operations.	• Develop a program organization chart showing key personnel and their positions participating in clinical program activities. Minimally include physicians, midlevel practitioners, nursing staff, staff providing social and

physicians cross-trained in cellular therapy for after hours care. Programs may also use mid-level practitioners who may assist physicians with patient care. Recipients of cellular therapy are particularly susceptible to complications during the immediate period after administration requiring identification of specialists to consultant for the most common complications. Additional personnel to work with cellular therapy patients before and after product use for social and psychological issues, dietary issues, radiation delivery, pharmacy issues, physical therapy, among others need to be identified. Limiting such personnel to a designated list allows for these consultants and support staff to gain experience in the unique needs of patients undergoing cellular therapy. Personnel to provide support for data management and quality management are also needed.		psychological support, radiation support (if applicable), dietary support, data management, quality management, and others as applicable • Identify personnel providing non-clinical support services for recipients of cellular therapy • Develop policies defining appropriate level of staffing for the activities performed. (e.g. Define minimal nurse patient ratio for inpatient care) • Identify qualified consultants including: Surgery, pulmonary medicine, intensive care, gastroenterology, nephrology, infectious disease, cardiology, pathology, psychiatry, radiology and radiation oncology, transfusion medicine, neurology, palliative and end of life care

3.2. Collection
3.2.1. Collection facility requirements
3.2.2. Collection staff

Explanation	**Process Elements**	**Examples**
Collection The majority of cellular therapy products in more recent years are collected by apheresis. However, historically bone marrow was the most common HPC source and recent studies have shown that for some indications allogeneic bone marrow may be the preferred cellular therapy product source. Umbilical cord blood is an increasing used source for hematopoietic progenitor cells, but for purposes of this document, HPC, cord blood collection will	Define requirements for marrow and apheresis collection facilities, if used.	• Indicate on facility floor plans locations at which collections or harvests will occur and the relationship of the collection facility to the entire program • Identify space within the facility for controlled storage of collection equipment, supplies and reagents • Designate defined areas at the collection site where products are labeled and stored • Designate space at the collection site, or clinical site for marrow harvests, for

not be addressed. Use of HPC, Apheresis versus HPC, Marrow or HPC, Cord for cellular therapy is a decision of the clinical program. One or all three sources may be used. **Marrow** Marrow collection facilities are nearly always associated with the clinical program and involve clinical program physicians and clinical facility staff. Typically products are collected in the operating room with the donor under local or general anesthesia. **Apheresis** The apheresis collection facility is more variable. Apheresis may be part of the clinical program, may be housed in the same institution as the clinical program but under different management (e.g. transfusion medicine), or may be a contracted facility. For autologous programs, collections may occur at the clinical site in designated locations, or in flexible locations possibility even at the patient's bedside. For healthy donors, collections could be at designated clinical sites or elsewhere based on the apheresis collection model.		confidential donor evaluation (allogeneic) and examination (allogeneic and autologous) • Ensure that there is readily available emergency care for any complications that may occur • Define, monitor, and control environmental conditions that may affect the health and comfort of the donor, and the viability, integrity, contamination, sterility, or cross-contamination of the cellular therapy product
Staff The Clinical program typically bears primary responsibility for determining donor suitability, and eligibility (for allogeneic donors) whether the cellular therapy product is collected from bone marrow or by apheresis. Likewise the clinical program most often oversees	Identify and define requirements for healthcare professionals performing marrow harvests or apheresis collection.	• Develop policies describing qualifications for personnel assigned to perform collections • Ensure staff perform a sufficient number of procedures to maintain competency • Establish a formal relationship with operating room administration and staff for performance of marrow harvests

mobilization for apheresis collections and management of the donor after collection. **Marrow** Clinical program personnel most often staff marrow harvests, but given that marrow collections are most often performed in the hospital operating room (OR), OR staff may also be involved. Responsibilities for maintaining marrow harvest supplies and reagents must be assigned. Validation of marrow harvest procedures most often involve the cell processing laboratory. A typical harvest will include a trained healthcare professional (usually a physician) to aspirate marrow, a clinical program healthcare professional (often a mid-level practitioner) to assist (filter product, track volumes, etc), a circulating OR staff nurse, and a trained healthcare professional administering anesthesia and monitoring the donor. For centers performing relatively few marrow harvests a limited number of staff may be designated for this activity to maintain expertise. **Apheresis** Apheresis collection staff may or may not be managed under the clinical program. Staffing needs and support will vary based on the collection facility model employed. Depending upon program activity, apheresis collection staff may also perform other duties (e.g. perform therapeutic apheresis, perform processing activities) or be dedicated to cellular therapy product	Identify and define requirements for healthcare professionals determining donor suitability and eligibility both prior to and at the time of donation. Identify and define requirements and procedures for donor mobilization (if required) and donor management and follow-up.	• Designate responsibilities for ordering, tracking, monitoring and storage of materials and reagents required for marrow harvest or collection by apheresis • Designate responsibilities for donor mobilization and donor management before and after collection • Designate clinical program staff responsibilities for donor workups, including suitability and eligibility (for allogeneic donors) before and on day of harvest or collection • Establish procedures for the optimal mobilization of donors to be collected by apheresis

collection. Typically one individual would oversee the collection of cells from not more than two donors, and more often a single donor.		

3.3. Laboratory
3.3.1. Processing facility requirements
3.3.2. Processing staff

Explanation	Process Elements	Examples
Facility Requirements The processing facility may be part of the clinical program, may be housed in the same institution as the clinical program but under different management (e.g. transfusion medicine or clinical laboratory) or may be a contracted facility. Regardless of management specification of basic requirements for the physical facility are needed.	Define requirements for the cellular therapy product processing laboratory. Ensure that facility design minimizes potential for contamination and cross-contamination and that space and equipment is adequate for the number of types of procedures performed.	• Indicate on facility floor plans location(s) at which processing will occur and the relationship of the processing facility to the entire program • Require that the facility be accessible only to authorized personnel. • Identify space within the facility for controlled storage of processing supplies and reagents • Designate defined areas in the processing facility where products are received, processed, labeled and stored • Require that laboratory space includes or that the laboratory has ready access to all equipment required for product processing, testing, and storage • Define, monitor, and control environmental conditions that may affect viability, integrity, contamination, sterility, or cross-contamination of the cellular therapy product
Staff Processing facility staff may or may not be managed under the clinical program. Staffing needs and support will vary based on the processing facility model employed. Depending upon program activity processing staff may also perform other duties (e.g. perform collection activities, be shared with the clinical diagnostic or	Identify and define requirements for processing facility staffing.	• Develop a processing facility organization chart showing a listing of key personnel and their positions, to whom they report, and their relationship to the Clinical Program • Minimally the organizational chart should include laboratory management, processing staff, and quality management • Develop policies defining appropriate level of staffing for the activities performed

transfusion service laboratory) or be dedicated to cellular therapy product processing. Staff requirements will be a function of the number and complexity of processing procedures performed.		

4. Quality Management
   - 4.1. Organization and responsible individuals
   - 4.2. Quality Plan

Explanation	Process Elements	Examples
Quality System organization All facilities within the cellular therapy program must participate in a Quality System. Each of the defined areas of Clinical Program, Collection Facility, and Processing Facility may have systems that include facility specific requirements, however systems must be integrated. Models range from a single all encompassing Quality System, to separate distinct (but integrated) systems. The model used largely depends upon cellular therapy program management structure. relevant activities of the Quality System should be well documented and management must be actively involved in reviewing the overall function of the system	Define the scope and individuals responsible for quality management within the cellular therapy program. Indicate how quality management is achieved throughout different parts of the program and indicate reporting structure and responsible individuals that make up the Quality System. Develop a process to ensure management review of Quality System Function.	• Create an organization chart specific for the Quality System to include how personnel interact to implement quality management activities • If more than one Quality System is in place, indicate how they integrate to ensure overall cellular therapy program quality • Set up a schedule of regular meetings to include responsible individuals within the Quality System, management, and participants to review quality activities and indicators • Require that the head of the Quality System present a report of the activities and function of the Quality System minimally annually for management review
Quality Plan Overall structure and requirements of the Quality System must be defined by a Quality Plan. The Quality Plan should describe key elements that fall under the Quality System and should describe or reference how key functional elements are achieved.	Create a Quality Plan that defines all key functional elements comprising the Quality System, and that describes or references other documents describing how key elements are achieved.	• Prepare a Quality Plan for each facility that constitutes the cellular therapy program. Include elements described in sections 4.2 through 4.11.

4.3. Personnel
- 4.3.1. Training
- 4.3.2. Competency
- 4.3.3. Continuing education

Explanation	Process Elements	Examples
Personnel qualifications and responsibilities of personnel involved in the clinical treatment, cell collection, processing and administration should be defined	Determine essential skills, educational requirements, degrees or certifications that are required for each position. Create job descriptions for all key personnel or ensure that such descriptions are present, maintained and include requirements specific for cellular therapy. Maintain personnel records to include hiring records, initial training, competency assessments, corrective actions, and continuing education.	• Prepare job descriptions for all personnel including their responsibilities, authorities, and position requirements (e.g. degrees, skills, experience, training) • Periodically review job descriptions to ensure that they remain current and meet needs of the position • Establish and maintain documentation of personnel's name, signature and initials or identification codes, inclusive dates of employment
Training Once suitable personnel are identified and hired they must undergo initial training before being allowed sole responsibility to perform position duties Various training models may be used and it is up to management to determine what is optimal for their circumstances. Some combination of targeted literature review (reading list), training literature (or video) that is process specific, review of standard operating procedures (essential), observation of the trainer or other trained individuals (essential), being observed by the trainer performing actual procedures (essential), performing mock procedures,	Create a uniform training plan for each position category that includes qualifications for trainers and overall responsibility for determining when an individual is trained. Determine which training method or combination of methods is best for the position. In addition to job specific requirements ensure that initial training includes orientation to the institution as a whole, and as appropriate training in needed general skills.	Develop a uniform training plan that includes requirements for: • Minimal trainer qualifications • Orientation to the institution • Training in general requirements for position such as: Safety training in biohazards, chemical, radiation; Infection control; Computer systems, etc • Training in applicable laws, standards, and regulations • Training methods for specific job functions and responsibilities • Documentation of training • Evaluation of training by trainer and trainee • Identify individuals responsible to giving final approval for personnel to perform

performing a predetermined number of procedures, passing written tests, etc.		independently
Competency After initial training it is important to ensure that personnel remain competent. Competency must be assessed on a regular basis, typically annually. As for initial training, there are various models to assess competency. These may include: review of records of completed procedures, observation by a responsible individual during job performance, review of procedures, written or oral tests, case or scenario discussions, among other methods.	Define responsibility for documenting competency for each position and requirements for review of records by quality management. Create a uniform competency assessment plan for each position category.	Develop a uniform competency assessment plan including requirements for: • Individual responsible for assessing competence • Method of assessment, that may include: Observation checklist, written or oral questioning, review of procedure records • Actions if competency is not demonstrated such as: Procedure review and written test, full retraining, Follow-up corrective actions by repeat competency reassessment • Review of competency assessments by quality management
Continuing Education Requirements for continuing education in topics related to a position category are important to keep personnel informed and current. Education may be internal or external and can include attendance at lectures, seminars, conferences, or workshops. Cellular therapy organizations often sponsor educational webinars that may be viewed in real time or available as downloads after presentation. Check websites for educational materials that may include some or all presentations from annual meetings.	Require a minimal number of hours of relevant continuing educational participation for each position category. Provide opportunities to personnel to participate in these activities.	• Establish a mechanism to document and to provide opportunities for continuing education related to job position

4.4. Define critical processes, policies, and procedures

Explanation	**Process Elements**	**Examples**
An important requirement of the Quality System is to identify what aspects of the operation are “critical”. This may be defined as potential of the process, policy, or procedure to change identity, purity,	Define within the Quality Plan processes, policies, and procedures that are critical. Within a critical process, policy or procedure indicate and define elements	• Quality Plan includes a listing of critical processes, policies, and procedures • Annual competency evaluation target critical job functions • Critical policies and procedures adhere to the

potency, or safety of the cellular therapy product if altered or omitted.	(materials, equipment, personnel, documents or the facility itself) that are critical.	document control system • Critical steps in a processing procedure are required to have confirmation by a second individual • See other examples of use of the term "critical" in this document

4.5. Document control

Explanation	**Process Elements**	**Examples**
There are a large number of documents used in any cellular therapy program. Many of these are critical for the cellular therapy product and for functioning of the program. A robust document control system is required to ensure that documents serve their intended functions.	Listing of all active documents adhering to the system.	• Quality Plan includes a listing of all controlled documents by type, such as procedures, policies, worksheets, labels. • For procedure manuals this constitute a current index of all active procedures and policies
	A procedure to prepare, approve, implement, review, revise, and archive controlled documents.	• Procedure describes required elements for standard operating procedures, standard order forms, product labels • Process ensures that only most recent approved document is available • Review of controlled documents is required on a regular basis, minimally every two years •
	Defined retention period for archived controlled documents.	• Retention period is as defined by applicable local, national or international regulations and standards (e.g. typically 10 or more years) • Record inclusive period of use for archived document versions
	A standard format for controlled policies, procedures, worksheets, forms, and labels.	• Document formats separately defined for controlled policies, procedures, worksheets, forms and labels, although consistently should be maintained when feasible
	A numeric or alphanumeric identifier and title for each controlled document,	• Identifier present on document in a place defined by document template

	including version. A system to prevent accidental or unauthorized changes. Documentation of changes made to a controlled document.	• Identifier, or information near to the identifier indicates current version of the document • Electronic versions of controlled document are protected from changes • Complete history of changes associated with each archived controlled document

4.6. Agreements

Explanation	**Process Elements**	**Examples**
It may not be feasible for a cellular therapy program to perform all services that may impact the cellular therapy product. Such services may be outsourced. In this situation it is important that a written agreement (or contract) be instituted that clearly outlines services to be provided and responsibilities of both entities.	Develop procedures for creating agreements with entities that provide services that may impact the cellular therapy product. Ensure that agreements define minimal requirements.	Procedures for establishment and maintenance of written agreements require: • A clear definition of responsibilities of both parties in regards to services to be provided. • That the contracted entity abides by applicable laws, regulations, and standards in regards to services provided. • Audits by the contracting entity to ensure compliance with the agreement • Approval by authorized individuals at both entities • Review and renewal on a periodic basis

4.7. Audits and assessments

Explanation	**Process Elements**	**Examples**
The best way to determine effectiveness of the Quality System is to perform internal assessments and audits of system elements. Facilities that constitute the program should each evaluate elements of the quality program that apply to them on a regular basis. This is particularly important for the clinical program since process or procedure validation does not	Define requirements for individuals performing audits. Define how audits are performed, presented and reviewed.	• Audits performed by individuals with sufficient expertise to identify problems but who are not solely responsible for the process being audited • Procedures and templates describe elements to be audited, time period to cover, minimum number of records to review, persons responsible for the audit plan, how to perform

strictly apply. The intent is to perform a documented systematic evaluation to determine whether policies and procedures have been properly implemented and followed with resultant quality of the final cellular therapy product and other services provided. This process also involves real time review of activities, such as chart review of collection or processing procedures, or targeted audits or activities such as ensuring that pregnancy assessments were performed during designated time frames before product collection or administration.	Define actions to take in response to an audit. Identify elements to audit and create audit schedules. Create an ongoing process for initial and final review of processing and collection records.	and review the audit, and documentation of final review by affected personnel. (e.g. final audit reports reviewed by staff) • Audits presented to management on a regular basis, but minimally yearly. • Audit results used to recognize problems, detect trends and improvement opportunities in the form of short-term and long-term corrective and preventative actions if necessary. Audits minimally include: • Essential data related to product use • Donor screening and testing prior to collection • Delivered chemotherapy doses compare to protocol and to orders. • Management of products with positive microbial cultures • External audits of facilities performing critical contracted services for compliance to agreements Other suggested elements to audit include: • Quality control records such as temperature or LN2 level checks, alarm records • environmental monitoring records • Equipment maintenance in accordance with schedule • Label elements • Facility cleaning • Present of collection or processing orders • Implement a procedure to require that records of product collection and processing undergo initial review at completion of procedures and

		a final review when all release test procedures are completed. • Audit verifies that all procedure steps completed and that test results are complete and are documented.

4.8. Errors, accidents, biological product deviations, adverse events
4.9. Process improvement plan

Explanation	Process Elements	Examples
Recognition and documentation In order to maintain quality programs must implement a system for vigilance and surveillance of collection, processing and administration associated events that could lead to adverse outcome or impaired patient and donor safety. This system must allow for timely detection, investigation, evaluation, documentation, and reporting of process errors, accidents, biological product deviations and adverse events associated with collection or administration.	Include in the Quality Plan procedures for detection, investigation, evaluation, documentation, and reporting of errors, accidents, biological product deviations, and adverse events (referred to in the collection as "event").	Procedures include clear description of: • Event and event severity requiring reporting, and the required timeframe. • Reportable events include: transmission of infectious disease through product administration failure to meet collection or processing release criteria, improper storage temperatures, adverse administration reactions, transportation problems, etc. • How the event is documented (e.g. forms, templates, electronic), and elements to document (e.g. describe event, actions taken, immediate and long term follow-up, final resolution). • Events reportable to the patient's physician (e.g. microbial contamination, product clots) • Events reportable to authorities (i.e. regulatory agencies, accreditation agencies, registries, etc) • Quality management review
Process improvement Recognition and documentation of quality system problems is a necessary first step but is not sufficient to improve the system. Corrective actions are required in direct association with the event and may require longer-term corrections to prevent or reduce likelihood of similar events in the future. To complete the circle there should	Include procedures for corrective and preventative actions and for follow-up to ensure actions were effective in the Quality Plan.	Procedures include instructions to describe: • Corrective actions taken in direct response to the event. (e.g. In response to lower than expected cell recovery after plasma removal, additional TNC were recovered from plasma and added to the plasma-reduced product) • Investigations to evaluate root cause of the event and to determine need for long-term corrective actions. (e.g. Investigation revealed

be follow-up activities to ensure that corrective actions were effective.		centrifuge power supply was failing, causing preset setting to be too slow. Long-term action was to replace power supply) • final resolution of the event evaluation including follow-up to determine if corrective actions were effective (e.g. new power supply was installed and equipment re-qualified for plasma reduction procedure. Monitoring of 10 products demonstrated acceptable TNC recovery in all cases.)

4.10. Interruption of operations and disaster plans

Explanation	**Process Elements**	**Examples**
Operations of the clinical program, collection, or processing centers could be interrupted for a variety of reasons, including acts of nature (e.g. fire, flood, earthquake, severe storms) or other emergencies including drug shortages or reagent and supply shortage, information technology system failure, nuclear accident, etc. While it is not possible to have detailed plans to fit every possibility it is important to have plans in place to increase likelihood that critical program operations can continue.	Include in the Quality Plan, policies and procedures for actions to take in the event operations are interrupted due to emergency, disasters, shortages, equipment failure, or failure of critical systems.	• Institution-wide emergency and disaster plans are referenced in so far as they apply to the cellular therapy program but issues specific to cellular therapy are addressed in program Quality Plan • Potential for shortages of critical drugs, reagents, or supplies required for program function addressed by identifying substitutes or back-up sources. (e.g. alternative effective preparative regimens should be identified in event of drug shortages. Collection and processing facilities should identify and qualify backups for critical equipment {e.g. biosafety cabinet} and sources for critical supplies {e.g. cryopreservation bags}, or reagents {e.g. ACD})

5. Policies and Procedures

5.1. Creation, Approval, Implementation

5.2. Required procedures

Explanation	**Process Elements**	**Examples**
Creation, Approval, Implementation Written policies and procedures are an absolute requirement for each part of the	Ensure that policies and procedures fall under the document control system.	• Policies and procedures are controlled documents.

cellular therapy program (clinical, collection, processing). Policies and procedures are controlled documents so all elements of the document control system apply. Policies and procedure fall under the Quality System. Policies and procedures are also essential elements of process control. Here we will include elements that are specific for creation, approval, and implementation of policies and procedures.	Define responsibilities for policy and procedure creation.	• Creating and modifying procedures primary responsibility of supervisory or quality personnel but may include staff as appropriate
	Define a consistent format for the body of the document.	In addition to elements required for controlled documents (e.g. title, identifier), procedure body formats commonly include: • Clearly written description of objective • Description of required reagents, supplies, and equipment • Stepwise description of the procedure including diagrams, tables and flowcharts as needed • Acceptable end-points, range of expected results • References to other SOPs or policies required to perform the procedure • Required forms or worksheets to record performance and results • Reference section to appropriate sources
	Define process for policy and procedure approval including responsible individuals.	For example approval includes: • Initial review by staff performing the procedure • Management review and approval (e.g. Facility Director or Medical Director) • Quality review and approval
	Define how new and revised policies and procedures are implemented, including effective dates and documentation of staff review and training and review by management.	For example implementation requires • Completion of all review and approvals for the procedure or policy to be effective • Documented review by staff • Documentation of staff training and competence before performance of the new or revised procedure

		• Policies and procedures should be reviewed minimally every two years by responsible management
Required procedures and policies Procedures and policies should be maintained in a standard operating procedures (SOP) manual. Documents must cover all critical aspects of program operations and management, including the Quality System. The SOP manual must be available to staff at the location where procedures are performed. Importantly policies and procedures must be followed. As a result procedures or policies must be changed in conjunction with changes in practice. A change in practice before procedures are updated is a deviation that must be documented.	Write procedures and policies that cover all critical aspects of program operations. Make readily available to staff SOPs relevant to processes being performed. Document that staff adhere to current SOPs and that SOPs are in agreement with work practice.	Procedures and policies describe in sufficient detail how to perform, and when to perform critical program operations. These include: • Technical procedures for collection (e.g. marrow and apheresis collection procedures), processing (e.g. Cell separation procedures, testing procedures), quality management (e.g. audits, validation, cleaning procedures), labeling procedures (e.g. including label creation, label elements), transportation procedures (e.g. shipping, internal transport), etc. • Process procedures (i.e. may sometime be written as policies) for activities such as donor eligibility determination, donor management, donor selection, product receipt, etc. • SOPs essential to job functions of staff are available. If SOPs manuals are maintained electronically staff would have access to all relevant procedures. Should the electronic system fail, hard copies of relevant documents are available. (e.g. Relevant collection SOP present in OR or at apheresis collection site). • Change control procedures require that SOPs, worksheets, forms, and other relevant documents be changed at the time a practice changes. • Worksheets or checklists or other forms of documentation are used to ensure that current procedures are followed.

		• When a change in practice is required before SOP update, event is documented as an SOP deviation. (e.g. A build of an electronic medical record system in put into effect for ordering quality control cultures of cellular therapy products and the previous system is discontinued. However, the system processes are undergoing modifications with use. Draft SOPs cannot be finalized until all changes are made. A planned deviation would be documented.)

6. Donor Issues

6.1. Donor recruitment

Explanation	**Process Elements**	**Examples**
When patients cannot be their own donors or when suitable related donors cannot be identified, unrelated donors may be considered. Typically unrelated donors are identified through donor registries that work with cellular therapy programs. In some cases a program may not have access to registry donors and become involved in donor recruitment. Entities involved in donor recruitment must comply with relevant international and national laws and regulations.	Recruitment and selection of donors must be performed under direction of individuals who are experienced in donor recruitment and management activities including education, consenting, counseling, confidentiality, and medical screening.	• Recruiters are appropriately qualified and provided with timely and relevant training.

6.2. Donor selection and evaluation

6.2.1. Suitability and eligibility

6.2.2. HLA matching for allogeneic donors

Explanation	**Process Elements**	**Examples**
Safety is of primary concern during the process of donor selection both in the autologous and allogeneic setting. Product safety is of equal importance to prevent transmission of disease. These goals are	Establish a process for donor selection and evaluation that ensures that donation is voluntary, and that the donor has been fully evaluated for suitability (i.e. donation is safe and appropriate) and	Procedures established for donor identification, evaluation, selection, and management that include at a minimum: • Donation is voluntary, without payment or coercion

best achieved by insuring that allogeneic donation is voluntary and that there is a process and written criteria for allogeneic donor selection, evaluation and management by trained medical personnel.	evaluation is performed for potential of the collected product to transmit a communicable disease.	• Donors are fully informed of potential risks to themselves and the intended recipient • Donors undergo physical evaluation for suitability that includes medical screening, and where appropriate, high-risk behavior screening, and testing for communicable disease • The most appropriate donor is selected • Donor confidentiality is maintained
Suitability and eligibility Suitability applies to both autologous and allogeneic donors and requires medical screening and examination to ensure that donors can safely undergo mobilization (if required) and collection procedures. Eligibility in contrast, refers to potential of the donated product to transmit disease to the recipient. Eligibility requires both screening for high-risk behavior and testing for disease exposure or current infection with transmissible agents. Relevant agents may vary based on location. Any abnormal or unexpected finding found during suitability or eligibility determination should be reported to the potential donor with recommendations for follow-up.	Establish a procedure or policy to evaluate donors for suitability by trained medical personnel. Evaluation should include risks for expected medical interventions (e.g. administration of mobilizing agent, anesthesia, insertion of a central venous line) as part of the collection process. Evaluation must foremost protect the health and safety of the donor. Recommendations for follow-up of abnormal results must be provided to the potential donor. Establish policies and procedures to determine donor eligibility by trained medical personnel. Evaluation should include assessment of medical and behavioral history that might put the donor at risk for communicable disease, and testing for evidence of current or past exposure to communicable disease agents according to local laws and regulations or if products are to be imported or exported, according laws and regulations at the location where the product will be used.	Suitability procedures include: • Medical history and examination and testing if appropriate, for comorbidity that might affect the health of the donor during the donation process. This should include: o Relevant infections with virus (see eligibility testing below), bacteria or protozoa o Evaluation of respiratory and cardiac health o Pregnancy assessment for female donors of childbearing potential. Eligibility procedures include: • Confidential screening though use of questionnaires for high-risk behaviors (e.g. IV drug use, incarceration in prison, time in areas endemic for relevant disease agents) • Testing (when available) for agents likely to transmit disease (e.g. HIV 1&2, HBV, HCV, Treponema pallidum, CMV) and others of regional significance such as Malaria, Chagas disease, HTLV 1&2, WNV, etc. • Allogeneic donor testing and screening performed no more than 30 days prior to donation for HPC products • Laboratory and test methods used comply with applicable laws and regulations

HLA Matching HLA matching with the potential recipient is essential for allogeneic donors. Degree of matching required will vary depending upon clinical protocols in use. It is commonly accepted that best results for allogeneic HPC product use are for HLA genotypically identical donors. It is critically important that high quality HLA typing is performed at the appropriate level (e.g. 4 digit allele level by molecular techniques) and that reliable laboratories that are properly credentialed are used. For family member donors typing at high resolution (i.e. 4 digits) may not be required so long as haplotypes are clearly identified. It is up to the program to establish criteria they wish to use. It is recommended that potential donors be provided educational materials describing the donation process (e.g. a pamphlet or brochure) before undergoing HLA typing. This should avoid a potential donor found to be the only HLA match to feel compelled to consent against their will.	Program policies must require that HLA typing be performed in laboratories that meet requirements of regulatory authorities and of any donor registries that might be used for donor selection. HLA typing of recipients and donors must include identification of HLA loci and HLA antigens at each locus, at the resolution of typing considered important for a successful outcome. Policies to ensure accuracy of HLA matching must be in place. Potential related donors must be provided with information regarding the donation processes before undergoing HLA typing.	• Cellular therapy program policies require that laboratories used for recipient and donor HLA typing be appropriately credentialed (e.g. ASHI or EFI accredited), must maintain those credentials, and must use testing reagents that are appropriately licensed • Donor selection policy must identify appropriate search algorithms to identify the best matched related or unrelated allogeneic donor for the recipient. Such algorithms must identify appropriate loci to type and the required allele resolution (e.g. HLA-A, HLA-B, HLA-C, HLA-DRB1 at 4 digit allele resolution for unrelated donors) • Samples from donors and recipients are tested minimally a second time using an independently collected sample to verify original typing results • Educational materials describing the donation processes are provided to all potential family members asked to undergo HLA typing

6.3. Consents and confidentiality
6.4. Donor safety and follow-up

Explanation	**Process Elements**	**Examples**
Consent Both autologous and allogeneic donors need to be informed of risks of donation, including use of mobilizing agents and anesthesia when used. Consent documents must use terms the donor understands and be in a language (or interpreted to a	Fully informed legally valid consent must be obtained from the donor prior to start of the collection process (e.g. before mobilization). Consent must include: risks and benefits of the procedure (including use of mobilizing agents and their side effects, if	• Program policies require that health care professional obtaining consent transmit information in the consent form in an appropriate and clear manner understandable to the donor, answer questions, and confirm that responses were understood • When consents are not in the donor's native

language) with which the donor is fluent. For minors, donors who are mentally incapacitated, or those unable to read and understand consent documents, a donor advocate not responsible for the medical care of the recipient should be appointed.	used), identify tests that will be performed, describe alternative collection methods, ensure medical confidentiality, and include the right to ask questions and to refuse to donate. Consent must be obtained by an appropriately informed licensed health care professional from donors (autologous and allogeneic) or their legal representatives.	language, appropriate interpreters, who are not family members of the donor, are used to ensure understanding. • Consents are obtained if donor blood or other biological material or information is stored and/or used for the purpose of approved research • Donor advocates independent from the cellular therapy team treating the patient are appointed for minors, mentally incapacitated or people who are not able to read and understand the donor information
Confidentiality To ensure confidentiality the identity of unrelated donors must be protected. Even for related donors it is important that information revealed during the identification and selection progress remain confidential. In cases where an ineligible donor may be the only available donor, medical findings that increase risk to the patient may only be revealed with written consent of the donor (see above).	Policies and procedures must be in place to maintain donor confidentiality.	• Policies in place listing conditions under which unrelated donors and recipients might be informed of each other's identity and that require consent of donor and recipient. • Recommended standards and policies as provided by the WMDA and available at the WMDA website • Policy against disclosure of related donor medical information, including HLA compatibility, to the patient without written donor consent.
Safety and follow-up Requirements should also be in place to further ensure donor safety during and after the donation procedure.	Serious adverse events occurring during the donation process must be reported to the cellular therapy program Quality System, the institution internal review board, and to responsible regulatory authorizes as required. Policies should be in place for short and long-term follow-up and care of volunteer donors for conditions related to the donation processes. Policies must be in place to inform the	• Procedures are in place for reporting adverse events associated with donation to the cellular therapy clinical program, appropriate authorities (i.e. regulatory agencies, donor registry) • Policies are in place for follow-up and management of donation-associated adverse events.

	cellular therapy clinical program of post-donation donor health issues that might affect the health of the recipient.	

7. Process Controls

7.1. Process and procedure validation

Explanation	Process Elements	Examples
Validation is an important part of a Quality System especially in relation to cellular therapy product collection and processing. Validation is defined as confirmation by examination and provision of objective evidence that particular requirements can consistently be achieved. However, two other terms, verification and qualification also apply to cellular therapy programs. Verification is defined as confirmation of the accuracy of something or that specified requirements have been fulfilled. Qualification is defined as establishment of confidence that equipment, supplies, and reagents function consistently within established limits. Typically equipment is qualified, while a processing procedure in which equipment is used may be validated or verified. Validation or verification requires qualified equipment and are similar to each other except in degree. A new method using an untried reagent (a modified form of ACD for apheresis collection) would require validation, whereas using a new source for ACD would require verification that expected reagent characteristics are met.	Define when validation, verification, or qualification is required. Develop a procedure and templates for validation/ verification.	Validation, verification, or qualification is required for new or changed: • Processes or procedures- new processing or test method (validation), new reagent source (verification), new lot of a critical reagent (qualification). • Equipment- Qualification should occur: o At Installation (IQ) o During operation (OQ) o During performance (PQ) o OQ and PQ are additionally required after major equipment repair or relocation if not designed to be portable. • Validation protocols are prepared for review and approval including details of required testing and required acceptance criteria • A validation plan is prepared if a process requires more than one series of tests, associated validation protocols are linked to the validation plan • data from validation protocol/ validation plans are collected and analyzed • Validation reports displaying a summary of all data, discussion of results and discussion of any deviation are submitted for review and approval • Validation documents should are filed and retained as per national/international criteria • Implementation includes educational

		measures and creation or amendment of SOPs if necessary
	Develop a procedure and templates for qualification.	Installation Qualification (IQ) • Document that all key aspects of installation follow appropriate codes, approved specifications, design intentions and manufacturer's recommendations • Use in-date calibrated equipment when needed (e.g. NIST tachometer) • Documentation obtained when IQ successfully performed by manufacturer technical personnel • Supervisors held responsible for equipment reviews IQ document before proceeding to OQ Operational Qualification (OQ) • Verify equipment, reagents and process operates consistently as intended throughout all anticipated operating ranges and products requirements • Verify equipment performs as per specification • Provide users with necessary instructions, training and operation restriction and requirement • Determine maintenance and calibration programs are to be performed by manufacturer or users Performance Qualification (PQ) • Repeated tests completed according to a validation protocol, show equipment or process performs as expected in a consistent and reliable manner • Document that end products consistently meet expected criteria • Performance Qualification can be conducted

		as o Prospective PQ –before equipment /process is put into practice (preferred method) o Retrospective PQ- after initiating use of equipment /process.

7.2. Materials Management

Explanation	**Process Elements**	**Examples**
To ensure the quality of cellular therapy products there should be policies and procedures to evaluate the ability of suppliers of critical equipment, supplies, and reagents to provide materials of appropriate quality to meet specified requirements.	Processing and collection facilities should have a materials management system that defines and evaluates suppliers of critical materials to ensure that program needs are met.	Supplier qualification consider a number of factors including: • Quality management program defines criteria for supplies of critical materials and performs audits to ensure those criteria are met (e.g. Visit supplier, Document through written surveys) • Ability to meet use demands of the cellular therapy program (e.g. Review history of service) • Response to customer complaints (e.g. ensure mechanism in place)
	Materials management system must establish acceptable parameters for critical equipment, supplies, and reagents used for collection or processing.	• Critical materials coming into direct contact with the cellular therapy product must be sterile and of appropriate grade for the intended use (e.g. medical or clinical grade material).
	Facilities material management system must confirm that each shipment or lot of materials meet defined requirements at time of receipt and prior to release for use.	• At receipt acceptable materials are confirmed to be undamaged with no evidence of contamination. • Receipt records include supply or reagent type, quantity received, lot number, receipt date, acceptability, and if applicable expiration date (e.g. COA review)

7.3. Product collection and processing
- 7.3.1. Physician orders
- 7.3.2. Prevention of contamination and cross-contamination
- 7.3.3. Product sampling and testing
- 7.3.4. Records, including lot records

Explanation	Process Elements	Examples
Product collection and processing Although under most cellular therapy program models responsibility for determining donor eligibility and suitability belongs to the clinical program, both collection and processing facilities need to have access to results of these determinations in order to ensure that products are not distributed for use without proper labeling (see below), proper storage (especially cryopreserved products), proper shipping requirements (under quarantine if eligibility not determine or if ineligible) and proper release approvals if not all criteria are met.	A summary of records indicating donor eligibility must be available to the collection and processing facility.	• Copies of donor history questionnaires and communicable disease test results along with a statement of donor eligibility from the clinical program provided for processing and collection facility records • Facility uses this information to determine requirements for product labeling, storage, shipping and release for administration • Alternatively collection and processing center have access to a summary of eligibility determination records electronically or through some other readily available means
Physician orders A written (i.e. on paper or electronic) request for collection and processing from the clinical program must be issued before collection or processing begins. The collection order should include timing and goals of collection. The processing order should minimally specify cellular therapy product type, identities of recipient and donor, type of processing to be performed and when processing is to be performed. Requirement for orders is to ensure that personnel have clear communication regarding goals of collection and required processing.	The cellular therapy program must have processes in place to transmit physician orders for product collection and processing. The order for collection must minimally specify when collection (or collection series) is to start and goals (e.g. TNC, CD34+ cell number) for collection. Orders for processing should minimally include the cellular therapy product type, identity of donor and recipient, type of processing, and date of processing.	• Physician orders may be preprinted physical documents or may be available through electronic medical record systems • Orders available to the facilities prior to start of collection and processing • A single order is sufficient for collection of HPC, Apheresis products over a series of days until goals are met or multiple bags may be thawed to deliver ordered cell dose so long as product identifiers are specified
Prevention of contamination and cross-	Aseptic methods must be used during all	Procedures to reduce potential for product

contamination Throughout collection and processing procedures it is critical to control and reduce likelihood of microbial contamination. All critical supplies coming into contact with product must be sterile, and collection and processing procedures must be performed using aseptic methods. Cross-contamination between products must also be prevented. This includes potential cross-contamination with infectious agents and well as mix-ups involving actual product or product records. Contamination and cross contamination risk can additionally be reduced by controlling the environment in which collection and processing occurs. Facilities must be clean and orderly and to the extent possible temperature and humidity controlled to reduce airborne contaminates, particularly fungus.	open steps of product collection and processing. Policies and Procedures must be in place to reduce risk of cross-contamination.	contamination include: • Training staff in proper aseptic practices • Minimize open steps during collection and processing (e.g. use of sterile tube welders in place of bag spikes, closed collection systems) • All steps potentially exposing product to the environment are performed in a biosafety cabinet. • Review of materials used for processing and collection at time of use to confirm sterility and for intact packaging and no evidence of contamination (e.g. discoloring, cloudiness). • Validated sterilization and cleaning methods • Routine culturing of products minimally at the end of processing o Investigation of positive results to identify source. • Environmental control of temperature, humidity, ventilation, air quality, and surface contaminates Procedures to reduce cross-contamination include: • Handling of only a single product and product records, at a time in the work environment • Cleaning of work surfaces between products • Control of storage conditions during and after processing (e.g. Double bagging of products during transport and storage, storing frozen products in metal cassettes to reduce breakage)
Product sampling and testing In addition to donor testing for communicable disease agents, ABO and Rh typing, and HLA other tests performed	Procedures must be in place for removal of samples required for product testing to ensure that sample accuracy represents the product and sample identification relates	Sampling procedures require: • Samples accurately represent product (e.g. Product is well-mixed, sample taken at appropriate step in processing, sample is

using samples from the cellular therapy product is also required. These minimally include total nucleated cell count, viability assessment, sterility testing and CD34+ cell content. Other product parameters may also need to be tested depending upon the extent of processing performed (e.g. Must test T cell content if T cell depletion is performed). It is essential that tests are accurately performed either within the laboratory or using external laboratories.	to the product. Product testing must be performed accurately and may be performed within the collection or processing facility or by external laboratories that are properly certified or accredited for the tests performed.	properly stored prior to testing) • Sample labels should include product identifier • Processing or collection records indicate identity of staff member taking sample, and date and if relevant, time sample was taken. Testing procedures or policies require: • Test methods be validated • Appropriate controls or reference materials are used • A proficiency program is in place • If not performed by the facility, external laboratories are properly certified or accredited
Collection and processing records Records of collection and processing procedures that document each critical step are required. It must be possible to trace back what was done, who did it, and what was used in event that problems with the product are identified or potential role of a product in an adverse reaction to administration occurs. It is important that collection and processing records be completed in real time. Other information may also be part of collection or processing records, such as copies of physician orders, results from donor workups such as eligibility screening and testing, record of administration and results from product testing. Duration for retention of collection and processing records are often set by institutional, regulatory or accreditation agency requirements.	Procedures must be in place to document each significant step of product collection and processing. Records should include identity of responsible individual, date, and if relevant time step was performed. Records must include test results and interpretation of each result where appropriate. Records must include lot numbers, expiration dates and manufacturers of critical reagents and supplies and identification of key equipment used in each procedure. Records must be reviewed by trained individuals prior to product release and	• Worksheets, job aids, checklists, or other means used to document collection and processing procedures • Records divided into significant procedure steps (e.g. Receipt of product into the lab, storage before processing, steps in processing, product release) and include dates, if relevant time, and identity (e.g. usually initials) of individual responsible for that step • Common tests include: cell counts, viability, and CD34+ cell assessment (e.g %CD34, CD34/kg) • Procedures require records of supplies, reagents, and equipment (e.g. assign unique identifiers to key equipment to facilitate this record) used be recorded in each record • Policies and procedures specify record review by management and/or by Quality

	records maintained for a period as required by relevant regulatory authorities.	representatives or their designees (e.g. for fresh products processed and distribute the same day, staff may be designated for this review) prior to product distribution and after all testing is complete

7.4. Equipment use and maintenance

Explanation	**Process Elements**	**Examples**
Equipment plays an important role in final quality of cellular therapy products. There should be policies and procedures to identify, qualify (see QM section above), maintain, monitor and calibrate equipment that is critical to provision of collection, processing and administration activities according to recommendations by manufacturers and by national/international guidelines. The best validated procedures and processes will not produce reliable results unless equipment used is properly maintained and calibrated.	Establish a system by which each piece of equipment can be uniquely identified. Maintain records of all equipment in use identifying manufacturer, name and model number, serial number, location, and date of commission linked to the unique identifier. Define criteria in SOPs and document performance of critical equipment maintenance and calibration (if required). Set up performance schedules. Assign responsibility for performance and review and determine actions required if equipment found to be out of calibration. Ensure that equipment that is overdue for maintenance or out of calibration is not used.	• Procedures for qualification of new equipment (see above in QM section) include assignment of a unique identifier placed on equipment and used to link it to processing and collection records for which it was used and to records of equipment maintenance Procedures in place for maintenance and calibration of critical equipment including: • Required elements and frequency (e.g. before initial use, after major repair, after activities that may affect calibration, in accordance with manufacturer's recommendations) • Maintenance requirement for individual types of equipment specify: what is to be done (e.g. timer check), methods used (e.g. stopwatch), who is to do it (e.g. Staff), what are expected results (e.g. within 10% of time set), and how often it is to be done (e.g. quarterly), by whom records are reviewed (e.g. Quality Management). • Clear indication that equipment maintenance and calibration are in date and the date by which the next maintenance is due displayed on or near to equipment • Label equipment that is overdue for maintenance or calibration or that fails to meet requirements as not in use • Specify actions to take if equipment is out of

		calibration in regards to: o Validity of test result o Product quality o Effect on donor or patient safety o Documentation and review of findings

7.5. Therapy Administration
- 7.5.1. Preparative regimens
- 7.5.2. Patient consent
- 7.5.3. Physician orders
- 7.5.4. Product administration
- 7.5.5. Patient safety

Explanation	Process Elements	Examples
Therapy Administration/Preparative regimens The clinical cellular therapy program must also have policies and procedures in place for administration of cellular therapy. Such documents should include requirements for patient informed consent (e.g. For autologous patients consent for administration should be separate from consent obtained at collection), a description of preparative regimens, issuing orders for administration, methods to ensure patient safety, and written procedures describing methods for product administration. See the Quality System section for requirements for outcome analysis after administration.	Develop treatment options and protocols (including preparative regimens) tailored for the types of patients treated (e.g. leukemia, lymphoma, multiple myeloma). Such protocols must consider results as published in the literature. Novel protocols should be done as research with proper approvals and with informed consent from the patient.	• The clinical program has defined standard of care protocols suitable for the types of patients treated based on clinical evidence (e.g. Peer reviewed literature available online using PubMed or clinical trials.gov) • Novel protocols are performed as clinical trials with approval of appropriate institutional review boards
Patient Consent Whether standard of care or research informed consent must be obtained from the patient prior to initiation of preparative regimens. Consents must follow the format required by the institution.	A process to obtain informed consent prior to initiation of treatment leading to cellular therapy product administration must be in place. Such consents must describe benefits and risks of the procedure. See section on donor consents for other requirements.	• Standard templates for obtaining patient consent prior to initial of preparative regimens are in place and include a clear description of the procedures and a description of benefits and risks • Consents become part of the patient medical record

Physician orders Orders must include the preparative regimen in addition to orders for release and administration of the cellular therapy product. Administration orders must be part of the patient medical record and must be available to the processing facility. Administration orders must specify the products to be infused since several products may be stored for a given patient (e.g. multiple collection days for autologous patients, an autologous patient with remaining product now undergoing allogeneic cellular therapy).	Preparative orders must include safe administration of chemotherapy and radiation therapy as appropriate. Treatment orders must specify required doses (e.g. per kg or meter squared) and dose schedules (e.g. daily, or other), and route of administration (e.g. IV, oral). Written (includes electronic) orders for product administration from the patient's physician must be part of the patient medical record and available to the facility releasing product for administration. Order identifies products to be infused.	• Preprinted orders or electronic order templates for given preparative regimens used, and such orders reviewed by the responsible physician • Confirmation by responsible individuals of identity and doses of chemotherapy at preparation in the pharmacy and at administration are performed • Confirmation against orders for radiation therapy is required • Administration orders are part of patient medical record and are available to facility releasing product for administration (e.g. typically the processing facility, but may be released directly from collection) • Orders specify products to be infused (e.g. product and bag identifiers, or all available)
Product administration/Patient safety There must be procedures in place for administration of cellular therapy products that include all product types in use by the program. Many aspects of product administration will be the same for all products, but some will differ based on volume infused, ABO compatibility, and whether the product is fresh or thawed. Procedures must include monitoring of the patient during and after administration for adverse reactions.	Policies for safe administration of cellular therapy products must be written. Such policies must include steps to confirm patient and product identity, proper handling of product before (e.g. stored and transported at proper temperatures, expiration not exceeded) and during administration, duration of administration, and precautions during administration in event of adverse reactions.	Requirements at administration include documentation of: • Product identity (e.g. product unique identifiers and proper name, preferably ISBT 128) and patient identity (e.g. Medical record number, date of birth) confirmed by minimally two trained personnel to match the order for administration • Product expiration date and time (e.g. required for fresh products and for products after thaw) • Following of handling instructions issued from the facility distributing the product (e.g. circular of information) including for all products forbidding use of leukoreduction blood filters, blood pumps, administration into medication lines, etc • Rate of infusion and use of blood filters (not leukoreduction filters) specified based on

		product type (e.g. greater potential for aggregates in marrow products or thawed products justify filter use), volume (e.g. slower rate for larger volumes), and if fresh or thawed (e.g. thawed products should be infused more rapidly to maintain viability, diluted or washed thawed products may be infusion over a longer period that product thawed without further processing)
	Programs must have policies and procedures for determining appropriate volume and dose of red blood cells, plasma, cyroprotectants, and other additives that should be infused.	• Policies and procedures for administration of ABO incompatible (major and minor) establish limits of incompatible red blood cells (e.g. 20-30 mL for an adult) or plasma (e.g. reduce to <50 mL) that should be infused • Policies require processing to remove red blood cells and/or plasma, or if not possible (e.g. No good methods for removing RBCs from apheresis products), establish minimal acceptable doses per infusion (e.g. spread infusion over more than one day). • When using cord blood that is not RBC reduced, require post thaw dilution or wash techniques to dilute or remove RBCs
	A system must be in place to prevent, evaluate, and treat severe adverse events or reactions associated with product administration. Procedures must include responsibilities for reporting to appropriate regulatory authorities.	• Monitor vital signs (e.g. pulse, blood pressure), prior to, during, and following (e.g. at least 1 h) therapy administration. • Observe patients for symptoms of serious adverse reactions (e.g. changes in vital signs, chest or flank pain, difficulties breathing) and treat appropriately • Document severe adverse reactions and report for appropriate follow-up using Quality System elements in place for investigation and reporting

		• In event of reactions discontinue, or slow the rate of product infusion, administer treatments appropriate to the reaction (e.g. medications to lower blood pressure)

8. Coding and Labeling
   - 8.1. Naming systems & product identification
   - 8.2. Labeling operations
   - 8.3. Label Content

Explanation	Process Elements	Examples
Coding and labeling Labels are required on cellular therapy products from time of collection to time of administration. Labels include not only information directly affixed to the product container, but also information that is attached (usually through tie tags), and information that accompanies the product. Regulatory authorities as well as accreditation bodies often have very precise requirements for product label content. Facilities must abide by the most stringent requirements that apply to them. In all cases label information must enable correct identification of product and intended recipient (if known), and must communicate information about the product that is relevant for product handling and clinical management of the intended recipient. Since labels are controlled documents requirements for controlled documents apply. In addition to label content and requirements common to all controlled documents, cellular therapy programs must have procedures in place for the labeling process itself that maximize likelihood that label content is	Collection and Processing facilities must have policies and procedures for product labeling that clearly defines the labeling process and well as label content at all relevant phases (e.g. Collection is typically responsible only for product label at collection). Procedures must describe product naming and identification system used, labeling operations including need for confirmation checks, and required content in regards to both product information and appropriate use of warning statements.	Coding and labeling systems are in place and require: • A standardized naming system in accord with applicable regulations and standards (e.g. ISBT 128 proper names, modifiers, and attributes) • Defined and documented procedures for product labeling • Assignment of unique product identifiers that can be tracked from donation to administration and traced from administration to donor • Label content appropriate for all stages of processing, including: Collection, In process labels, labels at completion of processing, labels at administration • Labels are validated to ensure they can withstand all expected conditions of product handling and storage (e.g. Remain affixed or attached, information does not smear or become illegible, critical information is eye readable

complete and correct.		
Naming System & product identification Historically a variety of terms have been used for the same type of cellular therapy product, for example a mobilized product collected by apheresis has been referred to as peripheral blood stem cells (PBSC), peripheral blood progenitor cells (PBPC), blood stem cells or just plain stem cells, among other names. A standardize naming system and corresponding abbreviations clarifies more precisely the product being referred to. Major accreditation organizations have supported applying the ISBT 128 information system used for blood products to apply to cellular therapy products. Unless different names are required by regulatory authorizes not supporting this standard it is highly recommended that programs adopt the ISBT 128 information system. ISBT 128 also defines a unique donation (i.e. product) identification code that identifies institution, year the product was collected and a 6 digit unique identifier for the product. The unique facility identification number (FIN) is assigned by ICCBBA and maintained in a central database. Likewise product classes, (e.g. HPA, Apheresis) and attributes (e.g. anticoagulants, additives, volume, storage temperature, manipulations, modifications) are assigned codes that are likewise centrally stored. Through use of barcodes on the labels, information regarding the product can be accurately identified worldwide.	Labeling policies and procedure must use a standard terminology for cellular therapy products, and attribute groups, like additives and modification present. Standard names should be used on affixed labels, tie tags added to labels, documentation accompanying the product and any standard forms used by the program. It is recommended that controlled documents use the same standard naming system. A unique product identifier through which products can be tracked to the recipient and traced to the donor is also required. More than one identifier can be assigned if collection and processing are by different facilities so long as records maintain both identifiers. The identifier should include identity of the facility assigning it. Product identifiers should be used to link samples and processing records to product.	Procedures for cellular therapy product labeling require a standard naming system for: • Product class (i.e. product proper name). For example HPC, Apheresis; with the abbreviation HPC(A). • Product modification (e.g. Cryopreserved, Thawed). • Product attributes including core conditions (e.g. anticoagulant, volume, storage conditions) and modifications (e.g. Plasma reduced) • See www.iccbba.org for additional information. • Procedures describe how product identifiers are assigned and how they are associated with the facility assigning them (e.g. ISBT 128 identification scheme used which include FIN number), and how they can be used to identify donation and administration information (e.g. records link current identifier to previous one) • Products, product records, and samples obtained from the product contain the same identifier

Labeling operations Labeling operations must be conducted in a manner that prevents mislabeling or misidentification of the cellular therapy product. Key elements include label design, receipt and approval, storage to prevent mix-ups, version control, destruction of obsolete labels, and application of the label to the product. Labeling operations may use pre-printed labels, labels printed on demand or some combination.	Policies and procedures must be in place to describe how labeling operations are conducted from design to application. Checks must be put in place to ensure that pre-printed or print-on-demand labels contain required information and that the correct label is chosen. Individuals responsible for label approval must be identified. Requirements must be in place to minimize likelihood of mislabeling.	Labeling operations to prevent errors at label creation include: • Review and approval of pre-printed labels prior to use • Storing pre-printed labels for different products in a manner to prevent mix-ups, including removal of all obsolete labels • Confirming print-on-demand labels against an approved template for accuracy Labeling operations to minimize errors at application include: • Apply collection labels before removing product from the proximity of donor • Double check labels for accuracy minimally, at initial application, upon receipt into processing facility, after completion of processing, prior to thawing, prior to administration • Apply new labels after product transfer before bags are disconnected • Complete all data fields on labels or mark as not applicable
Label content Label content at each stage from collection to final administration should be defined. Facilities must be familiar with requirements from relevant authorities in regards to label content and conform to those requirements. When options for specific label content to be affixed (i.e. actually on the product container), attached (i.e. securely connected), or accompany (i.e. in accompanying records) the product understand that content minimally needing to accompany the product can be affixed or attached. Likewise content minimally	Collection and processing facilities must define for each product and for each stage of product (collection, after processing, at infusion) how required information will appear (affixed, attached, accompanying) based on regulatory requirements in effect at their facility. Affixed label content must minimally include product identifier, product proper name, product modifiers, and intended recipient name and identifier if applicable. Facilities must define label content at each stage of the product (collection, after	• Processing facility procedures require that products at infusion contain label information affixed (AF), attached (AT), or accompanying (AC) the product including: o Product identifier-AF o Proper name of product-AF (e.g. HPC, Apheresis) o Product modification -AF (e.g. Thawed/Washed) o Product attributes-AC (e.g. Plasma reduced, DMSO) o Recipient name and identifier-AT (e.g. medical record number) o Identity and address of collection and

needing to be attached can also be affixed. In addition to information required on product labels, labeling elements required for product shipping containers must also be defined. Shipping label content may be dictated by regulations at the site of origin or destination, standards, or by the shipping carrier. It is the responsibility of the facility to identify and abide by applicable requirements.	processing, at infusion). Content must be in compliance with regulatory requirements in effect at their facility. Facilities shipping or receiving products from external sites must identify and define requirements for labeling shipping containers.	processing facility-AC o Date and time collection ended-AC o Product volume-AT o Concentration of anticoagulant and additives-AT (e.g. Heparin + ACD) o Donor identifier (e.g. if related donor, donor name and medical record number) o Recommended storage temperature (e.g. 2-8 C if thawed apheresis product) o Appropriate biohazard and warning labels as required by regulatory authorities. o Statement "For use by intended recipient only" (if allogeneic, or "For autologous use only", if autologous.-AT o Statement to "Properly identify intended recipient and product" for all products.-AT o Statements to avoid leuko-reduction filters and not to irradiate-AT o Date of distribution-AC

9. Product release/distribution
   - 9.1. Release criteria
   - 9.2. Exceptional release, urgent medical care
   - 9.3. Accompanying documents

Explanation	**Process Elements**	**Examples**
Product release/distribution Once a cellular therapy product leaves control of the collection or processing facility it is considered to have been distributed. The collection and processing facility is responsible for establishing criteria to allow release of products for distribution. Procedures for product distribution must also include actions required if a product does not meet release criteria, and must specify what documents	Establish policies and procedures determining criteria for cellular therapy product distribution by collection and/or processing facilities. Such procedures should include criteria for product release for administration. Ensure procedures include documentation that should accompany products at distribution and actions for products not meeting predetermined release criteria.	• Cellular therapy programs may determine that it is more efficient to release all products for administration through the processing facility

must accompany the product. Typically collection facilities release products to the processing facility for processing, potentially storage, and further distribution for administration. However, when processing is not required, some cellular therapy programs choose to allow products not requiring processing to be distributed directly from the collection facility. In such cases, all requirements for release for infusion must be in place in the collection facility.		
Release criteria There are criteria for product release that apply to all cellular therapy products and others that may depend up product type and the processing that was performed. A review of collection or processing records (including storage records) is universally required as is a check of product and container integrity and that samples for all required product testing have been removed. However, final results of a required test may not always be available so should not be considered a release criteria. For example sterility cultures typically require 1-2 weeks before results are known so cannot be a release criteria for fresh products. For allogeneic products release criteria should include a review of donor eligibility requirements with all testing and screening complete.	Policies and procedures must be written to define criteria for product distribution from the collection and processing facilities. Release criteria must minimally include: Examination of the product for evidence of contamination (e.g. discoloration, cloudiness) and of the product container integrity (e.g. must be intact), review of label requirements, review of transport or shipping records, review of collection or processing and storage records, and for allogeneic donors a review of donor eligibility determination.	Release criteria for a fresh allogeneic cellular therapy product from the processing facility for infusion include: • Visual examination of the cellular therapy product shows no evidence of contamination (e.g. expected color, not turbid) and that the primary container is intact • Product is labeled and contains all information required for product at infusion including a product identifier (See label requirements) • Product was transported and stored under specified conditions (e.g. In validated transport cooler at refrigerator temperature from collection to processing) • Processing records are complete, accurate, and in accord with SOPs • Records demonstrate ability to track from donor to recipient and trace from recipient to donor • Review of donor eligibility determination to include: o Donor tests performed within required time (e.g. 30 days) using laboratory and methods approved by regulatory

		authorities o Medical screening summary record shows no increased risk or medical evidence of communicable disease (e.g. may be a signed statement by clinical or collection program of eligibility) • TNC results in product records, samples obtained and submitted for sterility cultures and assessment of viability and CD34+ cells (e.g. May require CD34 results for release)
Exceptional release, urgent medical care Given the nature of cellular therapy, a given product may be life saving if it is from the only or a limited number of suitable donors (e.g. due to need for HLA matching), or if it is the only product available at a time product administration is urgently required (e.g. Patient is aplastic and other suitable products are not on hand). If such a product is found to not meet release criteria (see above) it may be the judgment of the clinician that administration is in the best interest of the patient. Program policies and procedures should have a process for determining when such a product should be used and identify responsible individuals from whom approval must be obtained.	Collection and processing facilities must have policies and procedures for exceptional release of products not meeting established release criteria. Minimally responsibility for approving release of products not meeting technical requirements should be the processing facility director, whereas factors that might affect the health or safety of the recipient require medical director release. In both cases the physician responsible for the care of the patient must be notified. When an allogeneic ineligible donor is used, the clinical program must document the rational for use of the donor and must document informed consent of the donor and the recipient.	Procedures for release of products that fail to meet established release criteria include: • Approval by Processing Laboratory Director for issues that do not affect health or safety of the donor (e.g. record review showed deviations from SOP but product parameters as expected) along with notification of the attending physician • Approval by Medical Director for issues that do affect health or safety of the recipient (e.g. Donor fails to meet all eligibility requirements) • Requirement that events leading to failure to meet release criteria are investigated as biological product deviations, with appropriate corrective actions and follow-up • Documentation in the medical record for use of an ineligible or unsuitable donor describing the rational for use (e.g. no other suitable donor), nature of ineligibility (e.g. positive test or screening), and confirmation that informed consent was obtained from donor and recipient
Accompanying Documents Certain documents may be required to accompany the cellular therapy product at	Specifications for information required to accompany the cellular therapy product must be described by policy or procedure.	A summary of records by which donor eligibility is determined include: • Donor tests results and interpretation

time of distribution. These would include documents containing information that is not affixed or attached to the product, and for allogeneic products includes a summary of records used to determine donor eligibility. Not all documents need to physically accompany the product, rather may be available electronically. Specific requirements for documents that must accompany a cellular therapy product may be dictated by regulatory authorities.	Such requirements must summarize records used to determine eligibility of allogeneic donors.	performed within required time (e.g. 30 days) • Confirmation that testing was performed by a laboratory and using methods approved by regulatory authorities • Documentation that medical screening showed no increased risk or medical evidence of communicable disease (e.g. may be a signed statement by clinical or collection program of eligibility) • Identification of the establishment making eligibility determination
	Specification for information required to accompany allogeneic cellular therapy product if product is distributed prior to completion of donor eligibility determination	For donors released under urgent medical need documents include: • Reason for ineligibility • List of any incomplete testing or screening • Results of screening and testing that has been performed • Statement that product may only be used before eligibility determination is complete under urgent medical need • Documentation that physician using the product notified of incomplete results when they are completed.
	Specifications for information required to accompany all cellular therapy products	Other accompanying information may include: • Instructions for product use to prevent introduction, transmission or spread of communicable disease (e.g. Circular of information) • Instruction for reporting serious adverse reactions to the distributing facility • Required label information not affixed or attached to the product

10. Product storage
    10.1. Temperature and duration

10.2. Safety and security
10.3. Monitoring and alarms
10.4. Inventory control

Explanation	Process Elements	Examples
Product storage After collection products often require storage before they are distributed. For autologous products storage most often required cryopreservation to preserve viability. For fresh products (including those to be later cryopreserved) most often refrigeration is the optimal storage temperature but that may vary depending upon processing requirements (e.g. marrow may be best processed for RBC depletion at room temperatures). Storage by the collection facility is uncommon but may occur, especially if products are to be shipped prior to processing or use. Cellular therapy programs must define conditions of storage for the types of products used, including storage temperature and duration and must have procedures and processes to ensure product safety and security during storage. Temperature monitoring and use of alarms may be required to ensure conditions are meant, and for storage of cryopreserved products, an inventory control system is critical.	Facilities must define in policies and procedures requirements for product storage, including temperature and duration of storage, safety and security of products during storage, determine needs for temperature monitoring and alarm systems, and have a method to control the inventory of stored products.	Procedures for product storage include: • Temperature and duration • Methods to ensure safety and security during storage • Monitoring of storage temperatures using local and remote monitoring and alarms • An inventory control system to locate products in long-term storage
Temperature and duration Optimally cellular therapy products should be processed and administered, or processed and stored as soon after collection as is feasible. Most often there is a delay due to work schedules or need for transport or shipping as would be required for products from unrelated donors. For	Optimal conditions of storage to preserve viability and function, including temperature and storage duration must be established for each type of fresh and frozen cellular therapy product stored at the facility.	Determination of optimal temperature storage for each type of fresh cellular therapy product consider: • Cellular composition of the product (e.g. products containing granulocytes such as whole marrow, may be best preserved at room temperature to prevent granulocyte

most product types and processing procedures optimal preservation of product viability is achieved with storage under refrigeration (1-8 C). This can be achieved using mechanical refrigerators or using thermally insulated containers and ice packs. Studies in the literature have indicated that products can be stored in the cold for up to 72 h with relatively little loss in CD34+ cell viability or function. However, programs need to determine optimal conditions locally. Frozen products are optimally stored at the coldest temperatures feasible. Best are liquid or vapor phase Liquid Nitrogen (LN2) storage freezers. However, such freezers require a reliable source of LN2, but have been shown to maintain product viability for 20 years or more. Vapor phase is generally preferred since the risk of cross-contamination during storage is reduced and such freezers are safer for personnel to use. In the absence of LN2 mechanical freezers capable of maintaining temperatures of -80 C to -120 C are available, however, are more susceptible to failure and less likely to maintain constant temperatures that maximize storage duration. If long-term product storage is not needed, mechanical freezers may be the best choice.	Once established limits of temperature and storage duration must be specified in relevant policies and procedures.	aggregation that can affect processing, mononuclear cell enriched apheresis products in contrast are best preserved at refrigerator temperatures) • Required processing (e.g. If no marrow processing is required, storage at refrigerator temperature may be optimal) Determination of optimal duration of storage for each type of fresh cellular therapy product consider: • The cellular composition of the product (e.g. granulocytes die more rapidly than progenitor cells) • temperature of storage (e.g. products stored in the cold maintain viability longer than products stored at warmer temperatures • Typical time required for products to be transported (e.g. longer storage duration may be required if products are obtained from distant collection sites, facilities need to determine the degree of acceptable loss of stem cell function) • Cryopreserved products are optimally stored at the lowest achievable temperatures. Storage temperatures shown to be effective in order of known duration of storage are: o -196 °C Liquid phase LN2 o -150 °C Vapor phase LN2 o -120 °C Ultra low mechanical freezer o - 80 °C Mechanical freezer
Monitoring and alarms Equipment used for product storage, including refrigerators and freezers should be monitored to ensure that optimal storage	The facility responsible for storage of the cellular therapy product must have a system to monitor storage conditions, including temperature and if LN2 storage	• Temperature or LN2 level monitoring systems are continuous, and record conditions at periodic intervals (e.g. every 4 hours)

temperatures and maintained. There should be a central alarm system to alert personnel when temperature limits are reached. For refrigerators it is as important that temperatures do not get too cold as it is that they are too warm, since inadvertent freezing of a fresh cellular therapy product would likely cause great harm. If LN2 storage tanks are used, it is important that the level of LN2 be monitored as well as the temperature since a loss of LN2 can results in a very rapid rise in temperature. A system should be in place to ensure that critical personnel can be alerted on a 24 hour basis when storage devices are out of specified ranges.	devices are used the level of LN2 in the device. The system must include audible alarms capable of 24 hour notification of staff should designated ranges be exceeded (i.e. too warm or too cold for refrigerators, too warm for freezers).	• Alarm systems sound at site of storage device and if staff is not available 24 hours, system must alert staff when excursions occur (e.g. System may contact staff by telephone) • Establish procedures for transfer of products to alternative storage devices in event of device failure
Inventory control system For cryopreserved products it is important that products be readily located in storage devices. Minimally such an inventory control system should record location of product, including identity of storage device and location within the device in the processing records. As inventory increases and more storage devices are added an electronic system should be considered.	A system to control inventory of stored cellular therapy products is required. Minimally such a system should include the cellular therapy product name, unique identifier, recipient name or identifier (if known), identification of the storage device and location of product within the device. The system must also clearly indicate when products are removed from the device, date of removal and reason for removal.	• Processing records of cellular therapy product cryopreservation include the information specified even if all of the information is not located in one place (e.g. Patient identifier may be elsewhere in the record). • Most important record is location of product and ability to determine if product is still present • An electronic inventory control system is more useful, and such a system should not only allow rapid location of the desired cellular therapy product, but should also identify what products are present in a given storage device

11. Product transportation, shipping, and receipt
    11.1. Within program facilities
    11.2. Between facilities

Explanation	**Process Elements**	**Examples**
Product transportation, shipping and	The cellular therapy program must have	Policies and procedures for transportation and

receipt Cellular therapy products are often transported from one location to another within the facility, including from site of collection to processing, and from processing to site of administration. Requirements for conditions of transportation must be defined as must requirements when the product is received at the site to which it was transported. Generally transport within the cellular therapy program is under control of program personnel requiring conditions that may differ for products transported to more distant sites. When the product leaves control of program personnel it is considered to have been shipped and requirements may differ. Shipped products that cross international borders are subject to governmental regulations by authorities in the country of origin and the country of receipt. It is important for programs to be aware of requirements for exportation and importation to ensure safe transport of the cellular therapy product.	procedures and policies in place for transportation, shipping, and if relevant, importation and exportation of cellular therapy products.	shipping includes: • Requirements for external shipping containers (e.g. labeling, temperature ranges) • Requirements for maintaining product safety (e.g. double bagging) • Accompanying documents must be defined (e.g. contact information) • Procedures at time products leave the facility (e.g. documentation of responsible individuals, dates and time of departure, product condition at departure) • Procedures at receipt of transported products (e.g. responsible individual, dates and times of receipt, product condition at receipt)
Transport with program facilities Under control of program personnel. Typically from collection to processing, and from processing to the site of administration. A validated outer container should be used, temperature monitoring likely not required.	Procedures must be in place for transport of fresh cellular therapy products from the site of collection to the processing laboratory and fresh or frozen products from the processing laboratory to the site of administration.	Procedures for transporting cellular therapy products under control of program personnel includes: • Use of a external transport container validated to maintain the desired transport temperature (e.g. internal ice packs not in direct contact with product) and to protect integrity of the product and safety of personnel during transport • Primary container for fresh product placed in sealed secondary container to prevent leakage (e.g. Zip locked bag)

		• Documentation at pickup and at receipt by two individuals of date and time, responsible individuals, condition of product and product samples (e.g. visual inspection for evidence of contamination and product integrity), product label information, presence of required accompanying documents (e.g. Summary of records used to determine eligibility for allogeneic donors)
Shipping between facilities Not under control of program personnel or requires transport over public roads. Note that even if program personnel are in control of the product if transport requires use of public roads, requirements for shipping should apply. Shipping typically involves a courier or courier service.	Procedures must be in place for shipping fresh or frozen cellular therapy products over public roads Abide by international laws and regulations applicable to import and export of cellular therapy products.	Procedure steps for shipping fresh cellular therapy products not under control of program personnel or transported on public roads includes those required for transported fresh products in addition to: • Labeling requirements for external shipping container minimally including: o Distribution date and time (with zone) o Statements to warn against radiation exposure (e.g. “Do Not Irradiate”) o Statements to identify the contents as biological material (e.g. Medical Specimen”, “Human Cells for Administration”) o Instructions for handling of the shipper (e.g. “Do Not Tip”, “Handle with Care”) o Name, address, and contact information for the shipping and receiving facilities o Other labeling as required by regulatory authorities (e.g. “For Autologous Use Only”, if autologous) • Documents inside the outer shipping container including all information contained on the external label in addition to appropriate biohazard and warning statements • Minimizing time for transport to that determined to be safe for the product being

		shipped • Using a qualified courier to escort products shipped for patients who have undergone high-dose therapy • Ensure compliance with all regulatory requirements for importing or exporting cellular therapy products Procedures for shipping cryopreserved products include those for shipping fresh products in addition to: • Ensuring that the outer shipping container conforms to applicable regulations for the mode of transportation or shipping (e.g. Courier company requirements, requirements for biological materials) • Continuous monitoring and periodic recording of temperature inside the external shipping container in the environment containing the cellular therapy product (e.g. use a data logging thermometer) and the results shared by both the sending and receiving facility

12. Product disposal

Explanation	**Process Elements**	**Examples**
There are occasions when cellular therapy products that are collected cannot be used. The most common reasons are death of the recipient, no further need for the product, or disposal of unused products may be a requirement of agreements with donor registries. Facilities must have a process to control product disposal that prevents inadvertent destruction while allowing the facility to operate with efficiency. For example data have shown that products	Establish policies and procedures for discard or transfer of cellular therapy products that are no longer needed for administration. Ensure that patients and donors are aware of discard policies at the time of product collection.	Policies for discard or transfer of cellular therapy products include: • Agreements with intended recipient, or donor, of cellular therapy products prior to donation specifying length of storage and circumstances for product disposal. (e.g. Define a maximum storage time, such as 5 years, indicate that products will be discard at the time the designated recipient dies) • Require documentation of intended recipient death or documentation from the physician of

collected from patients with Multiple Myeloma are of higher quality than a repeat collection after failure of initial cellular therapy. Since repeat cellular therapy is beneficial in Myeloma treatment, many centers collect sufficient cells for two uses when only a single administration is planned. Over time the storage capacity of the facility may be exceeded hindering the ability to treat current and future patients. Thus a policy for product discard when it is not longer needed is required.		the intended recipient that a product is not longer needed prior to disposal • If agreed upon time limits have been exceeded and the intended recipient is alive, offer the option to transfer product to another facility for storage • Require facility Medical Director approval before discarding or transferring any product • If no agreement was in place at time of collection facilities must make a documented effort to communicate with the patient and with appropriate medical personnel (e.g. Had or has responsibility for care of the recipient) prior to disposal or transfer • Discard or transfer must be documented and must be performed in compliance with applicable laws and regulations

13. Data Management, registry reporting, outcomes assessment

Explanation	**Process Elements**	**Examples**
Data Management, Registry reporting, Outcomes assessment Management of data related to cellular therapy is an important element of good clinical care and investigation. Outcome analysis is a requirement of the Quality System for the clinical program, and to measure outcomes data from each patient must be collected. Programs contributing to transplant registries (e.g. CIBMTR, EBMT, APBMT) are familiar with data reporting elements required by these registries. Such forms are excellent starting points for programs to determine what data elements should be collected and assessed. Data management should be part	A process should be in place for collection of data sufficient for evaluation of cellular therapy administration outcome. Data collection should include minimal elements required by registries such as CIBMTR or EBMT.	A process for data management is established and minimally incudes: • Collection of data from each use of cellular therapy products to include that minimally required by established transplant registries (e.g. CIBMTR) • Regular assessment of cellular therapy administration outcomes including overall survival and non-relapse mortality at day 100 and 1 year, and time to engraftment of neutrophils and platelets

of every program from the beginning, since it is easier to capture information in real time rather than retrospectively.		

14. Records
    14.1. General requirements for all records
    14.2. Electronic records

Explanation	Process Elements	Examples
General requirements for all records Records provide documented evidence that activities have been performed or results have been achieved. Cellular therapy programs must include a management system that ensures accurate creation, security, integrity, and preservation of all critical records. Given the medical nature of the information such records contain, it is critical that the records management system ensure confidentiality as required by applicable laws and regulations. Requirements for document control have already been discussed and many of the elements described there apply to all records	The record management system must facilitate record review prior to cellular therapy product distribution and must permit record review in conjunction with follow-up evaluations or investigations. Records must be made in conjuncture with the activity performed, must indicated by whom they were made, when (if relevant), and must be accurate, legible, and indelible.	• A summary of records used by the clinical program to determine eligibility of allogeneic donors made available to the collection facility, to the processing facility, and at the time of distribution (e.g. eligibility determination summary records may be made available electronically, or may physically accompany products) • Collection and processing records completed as part of the procedures including identity of who performed each step with date and time (if relevant) (e.g. use worksheets or job aids in paper or electronic form that capture initials or signatures for each step and capture date and time when relevant) • Record information is legible (e.g. Using smear-proof ink, typed or captured electronically) • Corrections to records identifiable and the original information maintained (e.g. use single line strike outs to indicate corrected entries, record date and identity of individual making correction) • All records reviewed for completeness and accuracy by a designated individual (e.g. Management or quality program review, with documentation)

	Records must allow tracking of the cellular therapy products from donor to recipient and tracing from recipient to donor. Records must be confidential (when relevant), secure, and retrievable for the duration of storage.	• Records of donor evaluations, collection, processing, and administration include unique product identifier (s) to allow tracking and tracing • Only authorized personnel have access to records containing confidential donor or recipient information (e.g. Records in secure file cabinets, limited access to areas containing records, electronic records password protected) • Equipment is maintained to make legible archived records (e.g. old forms of storage such as floppy disks require a working disk drive, or old records are transferred to more current forms of storage)
Electronic Records Cellular therapy programs commonly use electronic means to make or store records. Some records are only maintained electronically (in lieu of paper), and are used to make decisions, perform calculations, and to create or store information used in critical procedures. In such cases these electronic record systems require procedures parallel in some cases with general record requirements above to ensure their accuracy, integrity, identity, and confidentiality.	When a record is exclusively made and maintained electronically a process must be in place to ensure such records are available, accurate, intact, can be identified, and maintain confidentially. This process must also be applied when the electronic makes decisions or performs critical calculations.	The process to ensure that electronic records systems are accurate, intact, retrievable, and maintains confidentiality includes: • Limited access to only authorized program personnel (e.g. password protection) • Ability to store and accurately retrieve records for the required period of retention (e.g. Record locking to prevent later changes, backups to prevent data loss) • Ensures that product and patient or donor identifiers are unique (e.g. checks to prevent duplicate entries using the existing identifier) • Backup systems that can be used in the event electronic access is lost (e.g. Paper copies that can be used when system is unavailable) • Remote system backups to prevent record loss in event of a disaster • SOP or other written instructions for system use (e.g. available in hard copy or electronically)

		• Requires review and acceptance of data before record is accepted • Record to identify individuals making or modifying the record (e.g. Individual user login) • Documentation of system development, version, validation, installation, and training. • Checks of data integrity (e.g. Built in checks for validity such as required fields or fields with present limits)