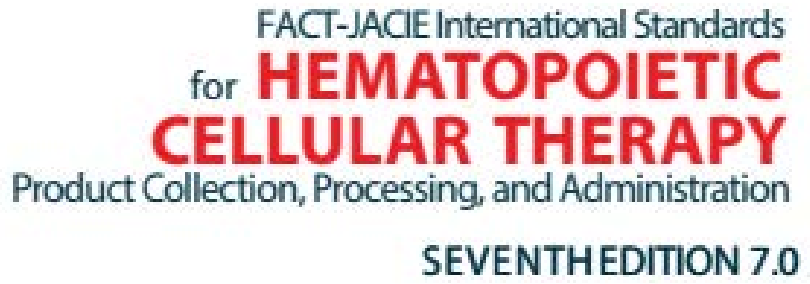
JACIE Quality Management Standards 7th edition



RENZA MONTELEONE
Quality Manager Inspector
Country: Italy

PARTS

A

- TERMINOLOGY, TENETS, ABBREVIATIONS, AND DEFINITIONS

B

- CLINICAL PROGRAM STANDARDS

CM/C

- COLLECTION FACILITY STANDARDS

D

- PROCESSING FACILITY STANDARDS

PART B CLINICAL	PART CM MARROW	PART C APHERESIS	PART D PROCESSING
B1 General	CM1 General	C1 General	D1 General
B2 Clinical Unit	CM2 Marrow Collection Facility	C2 Apheresis Collection Facility	D2 Processing Facility
B3 Personnel	CM3 Personnel	C3 Personnel	D3 Personnel
B4 Quality Management	CM4 Quality Management	C4 Quality Management	D4 Quality Management
B5 Policies and Standard Operating Procedures	CM5 Policies and Standard Operating Procedures	C5 Policies and Standard Operating Procedures	D5 Policies and Standard Operating Procedures
B6 Allogeneic and Autologous Donor Selection, Evaluation, and Management	CM6 Allogeneic and Autologous Donor Evaluation and Management	C6 Allogeneic and Autologous Donor Evaluation and Management	D6 Equipment, Supplies, and Reagents
B7 Recipient Care	CM7 Coding and Labeling of Cellular Therapy Products	C7 Coding and Labeling of Cellular Therapy Products	D7 Coding and Labeling of Cellular Therapy Products
	CM8 Process Controls	C8 Process Controls	D8 Process Controls
	CM9 Cellular Therapy Product Storage	C9 Cellular Therapy Product Storage	D9 Cellular Therapy Product Storage
	CM10 Cellular Therapy Product Transportation and Shipping	C10 Cellular Therapy Product Transportation and Shipping	D10 Cellular Therapy Product Transportation and Shipping
B8 Clinical Research			D11 Distribution and Receipt
B9 Data Management			D12 Disposal
B10 Records	CM11 Records	C11 Records	D13 Records
	CM12 Direct Distribution to Clinical Program	C12 Direct Distribution to Clinical Program	

ROLE OF QM INSPECTOR IN THE INSPECTION TEAM

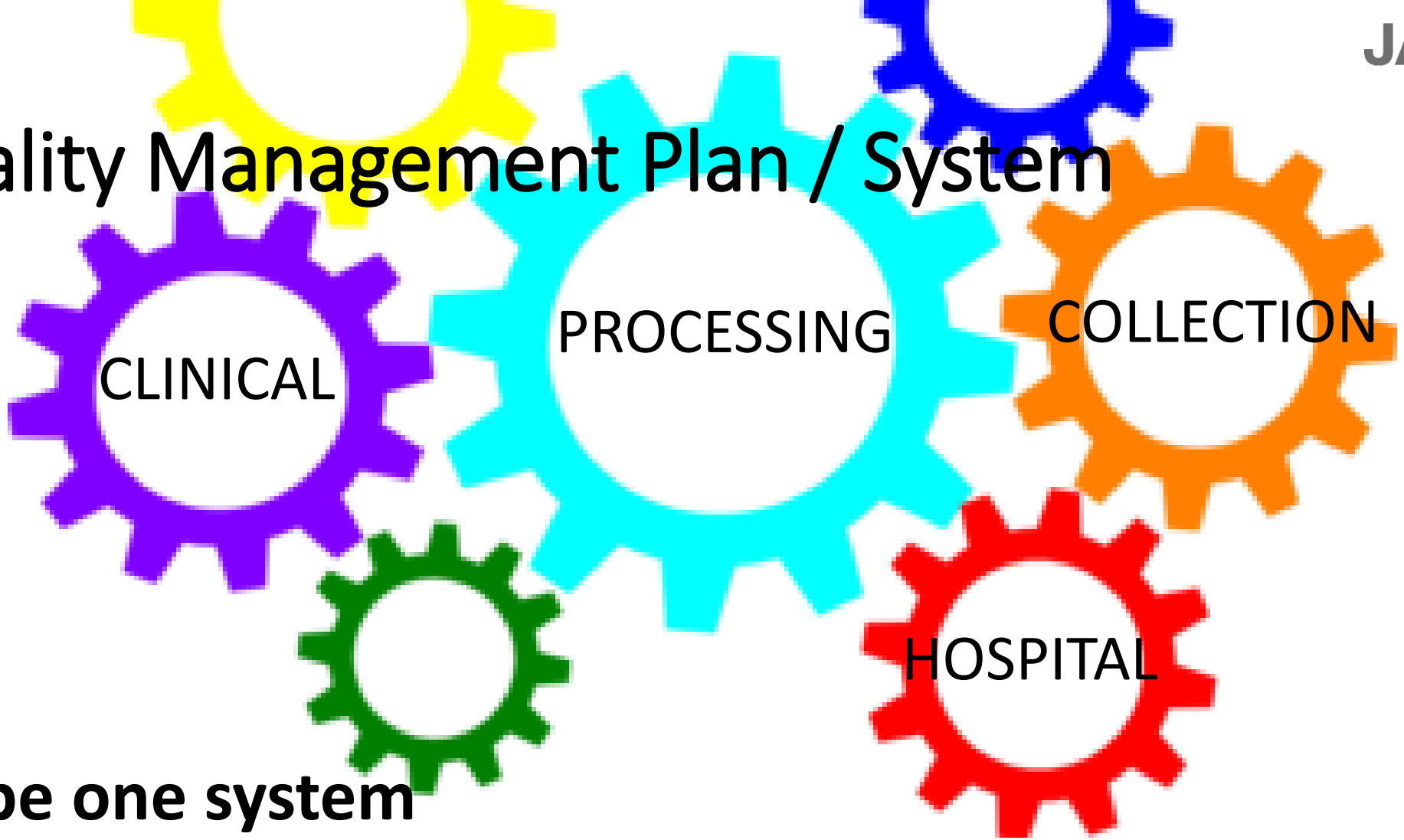
Part B/CM/C/D 4 QM <u>excluding</u>:

- **Outcome analysis**
- **Tracking & traceability/labelling requirements**
- **Qualification**
- **Validation**

NOTE: This 4 subsections will be assessed by the clinical, collection and/or processing inspectors

Parts B/CM/C/D 5 Polices & Procedures

Quality Management Plan / System



- **Can be one system**
- **Can be different systems *BUT* they must have an interface/Link**

QUALITY MANAGEMENT

KEY WORDS

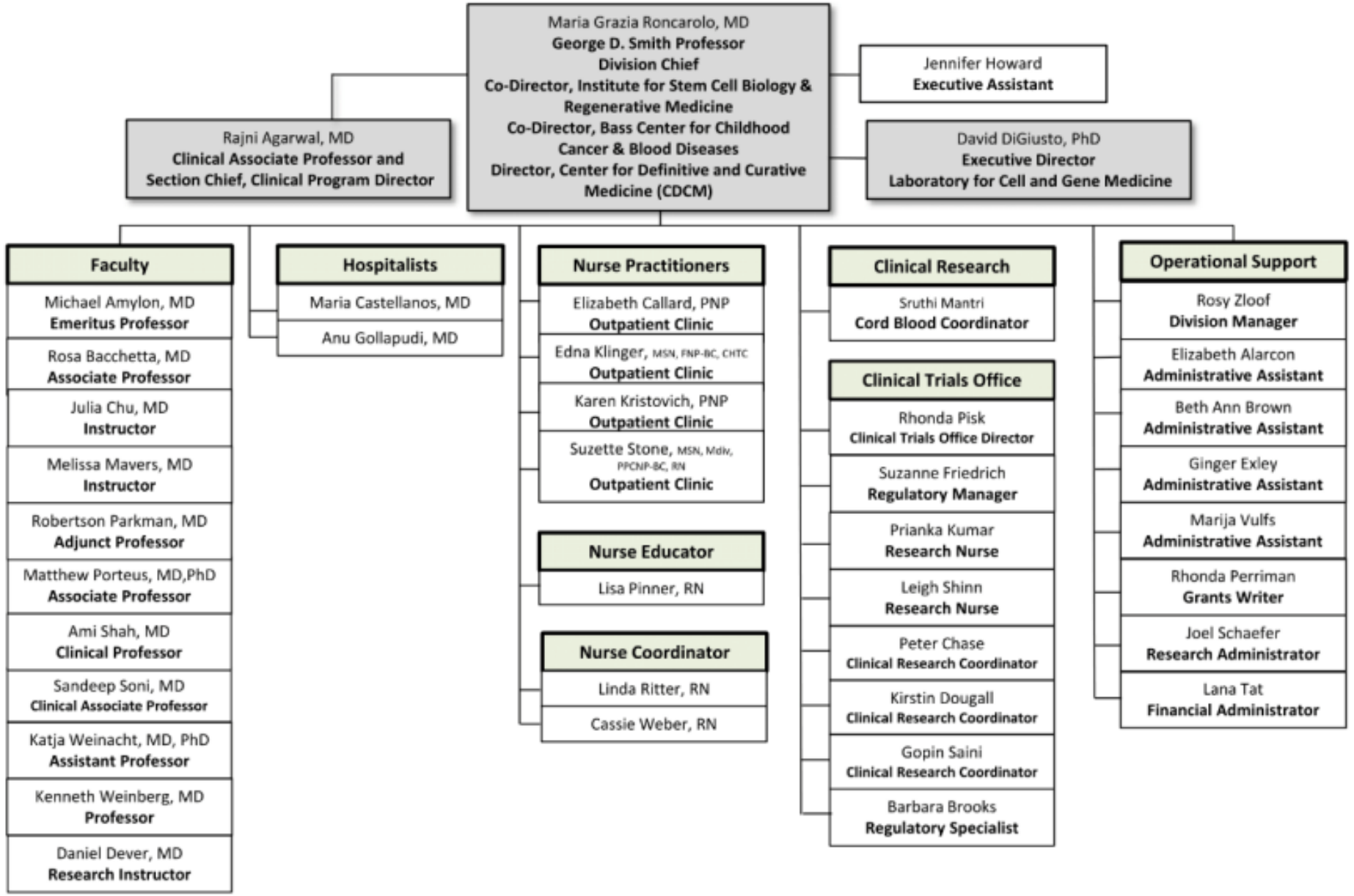
- **TRACEABLE**
- **TRACK DOWN**

WORK ACCORDING TO WRITTEN SOP

REGISTER EVERY STEP OF THE ACTIVITY

- **KEEP UNDER CONTROL THE PROCESSES**
- **REVIEW**
- **IMPROVEMENT**

Division of Pediatric Stem Cell Transplantation and Regenerative Medicine



Stanford MEDICINE | Stanford Children's Health | Lucile Packard Children's Hospital Stanford

Responsibilities

- The **Director** or designee shall have authority over and **responsibility** for ensuring that the **Quality Management Program** is effectively established and maintained.
- The Director shall **annually review** the effectiveness of the Quality Management Program.

Reporting

- The [Facility] Director or designee shall **review and report to staff quality management activities**, at a minimum, **quarterly**.

Staff requirements & training

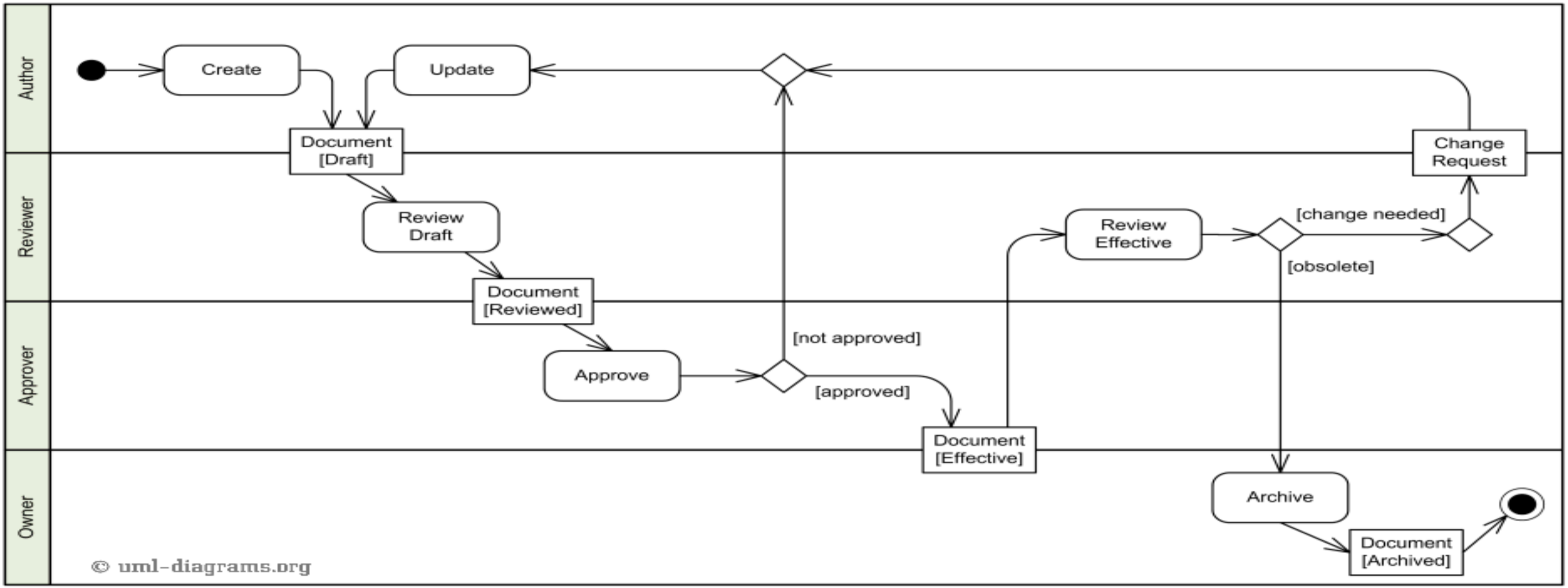
The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements for each key position in the [Facility]. Personnel requirements shall include at a minimum:

- **A current job description for all staff.**
- **A system to document the following for all staff:**
- **Initial qualifications.**
- **New employee orientation.**
- **Initial training and retraining when appropriate for all procedures performed.**
- **Competency for each critical function performed.**
- **Continued competency at least annually.**
- **Continuing education.**

Document Management

- The Quality Management Plan shall include, or summarize and reference, a comprehensive system for document control and management.

Documents: process from draft to implementation



Documents considered critical:

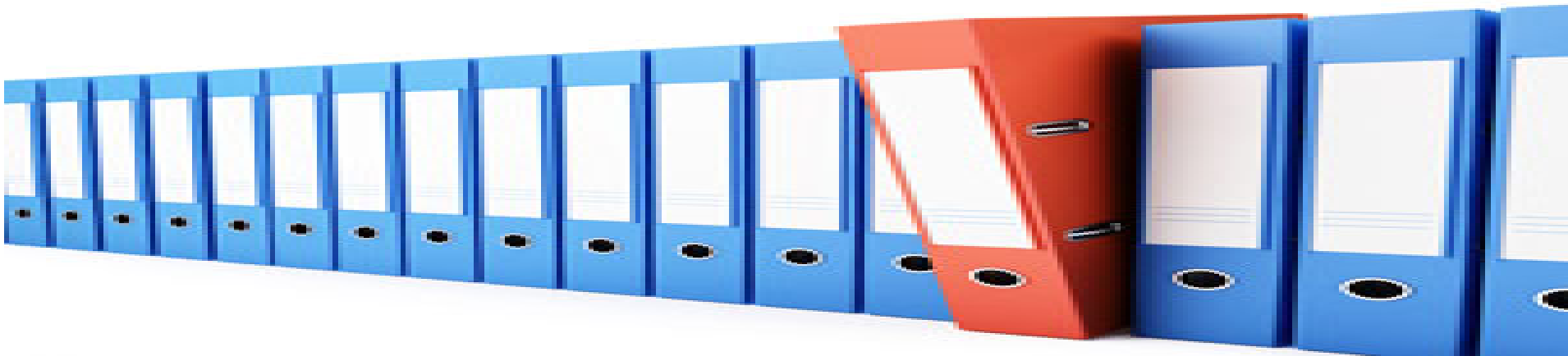
- Policies, protocols, and Standard Operating Procedures
- Worksheets
- Forms
- Labels

The document control policy shall include:

- A **standardized format** for critical documents.
- Assignment of a numeric or alphanumeric **identifier** and a title
- A system for **document approval**, including the approval **date, signature** of approving individual(s), and the **effective date**.
- A system to **protect controlled documents** from accidental or unauthorized modification.
- **Review** of controlled documents **every two (2) years** at a minimum.
- A system for **document change**
- **Archival** of controlled documents
- A system for the **retraction of obsolete documents** to prevent unintended use.

Archival / replacement

- Archived policies and procedures, the inclusive dates of use, and their historical sequence shall be maintained for a **minimum of ten (10) years** from archival or according to governmental or institutional policy, whichever is longer.
- System for **retraction of obsolete documents** to prevent unintended use.



Agreements - SLA

- The Quality Management Plan shall include, or summarize and reference, policies and procedures for establishment and maintenance of written agreements with third parties whose services impact the clinical care of the recipient and/or donor.
- SLA third-party facility performing any step in collection, processing, or testing
- SLA dated and review on regular basis

Clinical: Benchmarking

- The [Facility] should achieve one-year survival outcome within or above the expected range when compared to national or international outcome data.

Audits: The Who & Why

WHO?

- Audits shall be conducted on a **regular basis** by an **individual with sufficient expertise** to identify problems, **but who is not solely responsible for the process being audited**.

WHY?

- Used **to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions** when necessary, and **follow up on the effectiveness** of these actions in a timely manner.

Audits

Audits→ audit plan, assessment and audit results, actions taken, and follow-up assessments and audits

- Adherence to policies and procedures

Accuracy of clinical data.	Safety endpoints and immune effector cellular therapy toxicity management.	Accuracy of the data contained in the MED-A forms	Donor screening and testing.
Verification of chemotherapy drug administered against the written order.	Management of cellular therapy products with positive microbial culture results.	Written agreements with external facilities	Prescription ordering system against the protocol.
	Interim donor assessment	Donor eligibility determination prior to start of the collection procedure.	

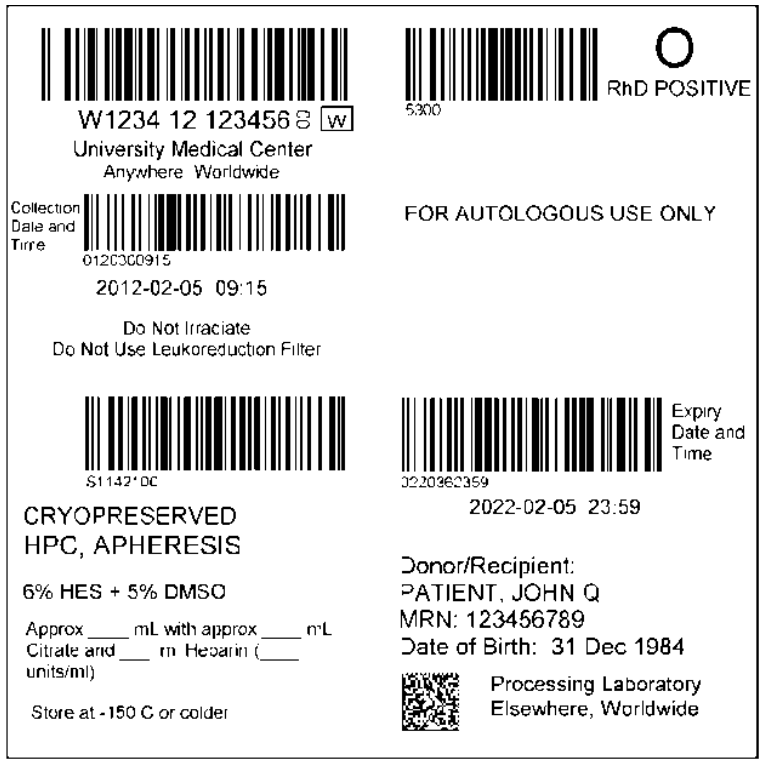
Positive Microbiological Cultures

- Policies and procedures on **positive microbiological cultures**

- Policies and procedures **for errors, accidents, biological product deviations, serious adverse events and complaints**
  - Detection
  - Investigation: root cause
  - Documentation
  - Reporting: to competent authorities, accrediting agencies, Ethic committees,...
  - Correcting and preventing actions

Product Tracking & Tracing

- Policies and procedures for cellular therapy **product tracking and tracing** from the donor to the recipient or final disposition



Contingency plans

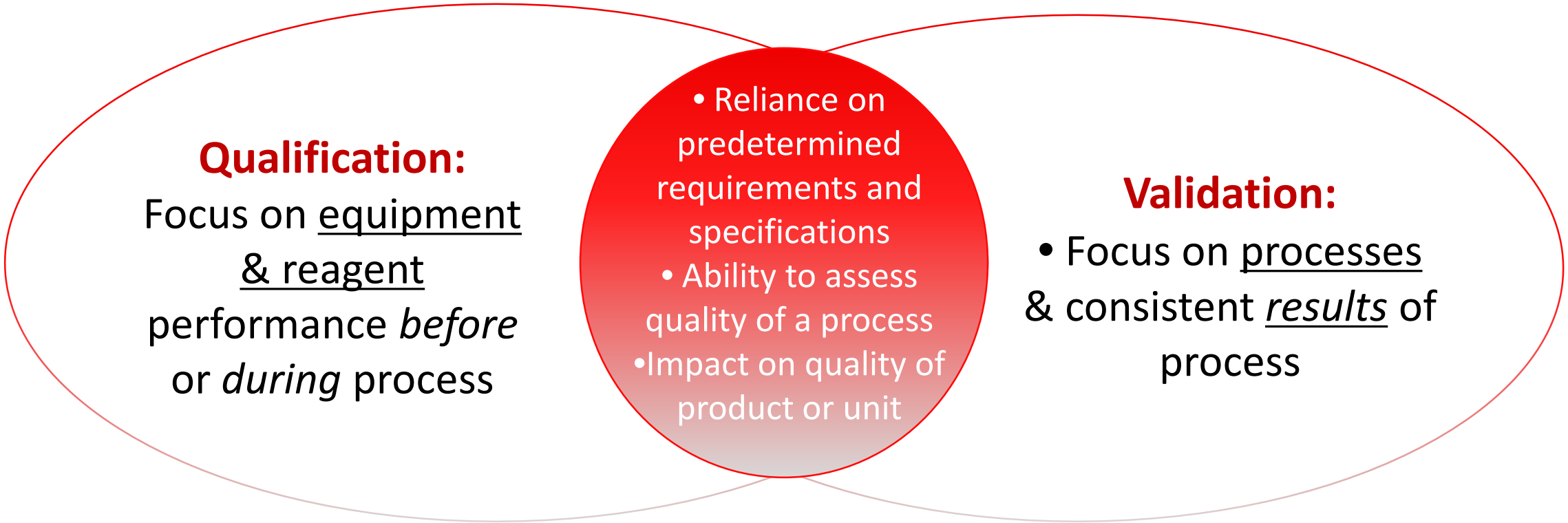
- Policies in the event the Transplant Program's (Clinical/Collection/Processing) operations are interrupted = Contingency plan

Validation/Qualification

- The Quality Management Plan shall include, or summarize and reference, policies and procedures for qualification of supplies and validation and/or verification of the procedure for marrow collection to achieve the expected end-points, including viability of cells and cellular therapy product characteristics.

Qualification & Validation: What is the difference?

(or, more importantly, what is the same?)

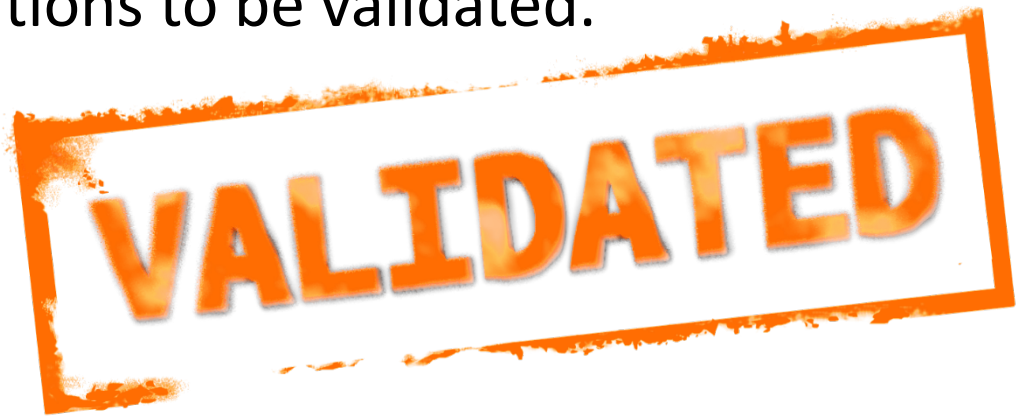


Qualification required of:

- critical manufacturers
- vendors
- equipment
- supplies
- reagents
- facilities
- services

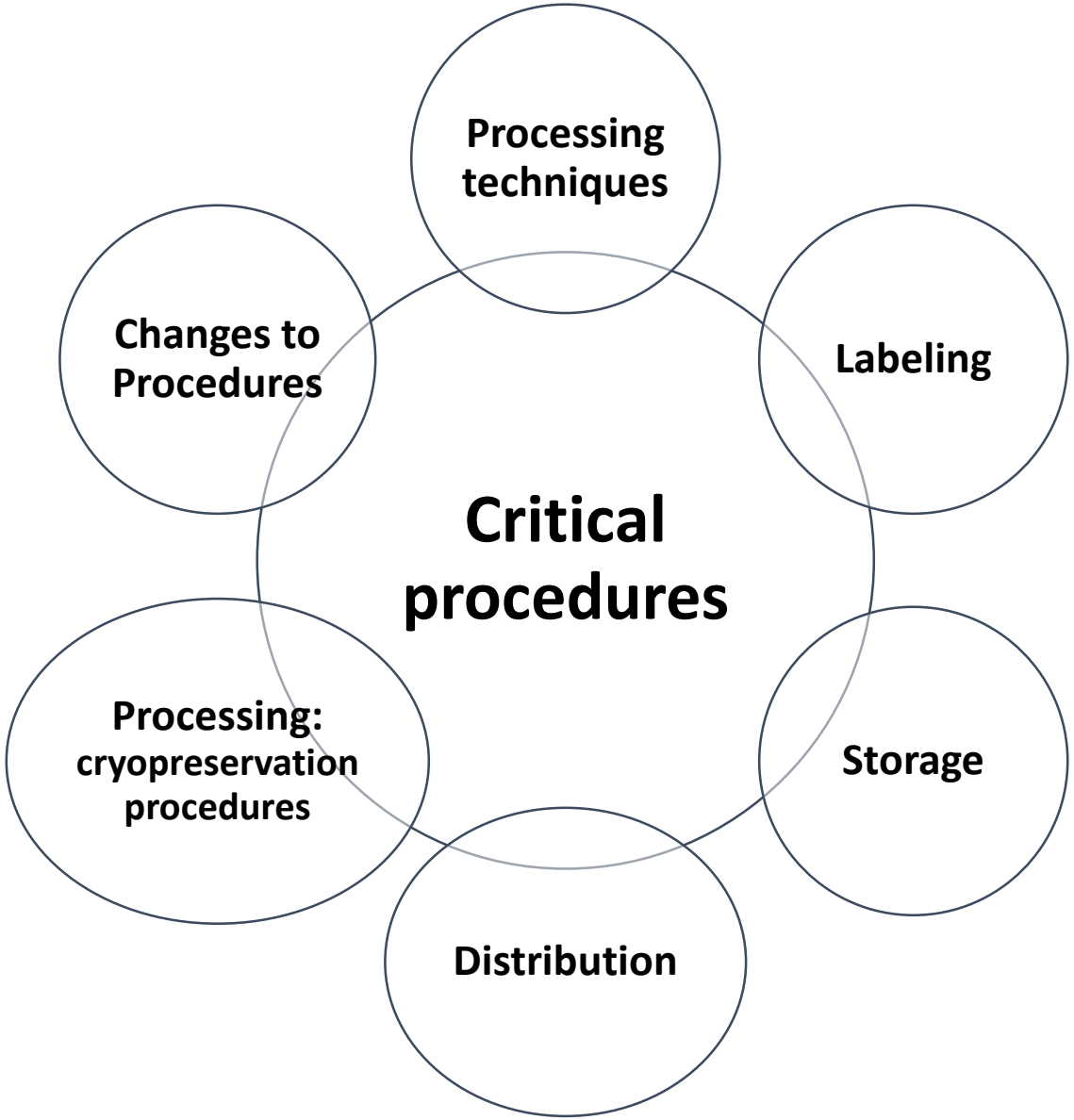
Each validation plan shall include:

- An approved **validation plan**, including conditions to be validated.
- Acceptance **criteria**.
- **Data collection**.
- **Evaluation** of data.
- **Summary of results**.



- **Review and approval** of the validation plan, results, and conclusion by the [Facility] Director or designee and the Quality Manager or designee.
- Changes to a process shall include **evaluation of risk** to confirm that they do not create an adverse impact anywhere in the operation and shall be validated or verified as appropriate.

Validation: What to validate?



Critical procedures shall include at least the following:

Clinical	Collection	Processing
BM collection procedures	collection procedures	processing techniques,
		cryopreservation procedures
	testing	testing
labelling (BM)	labeling	labeling
Storage (BM)	storage	storage
Distribution (BM)	distribution	distribution

Validation: Change to a process

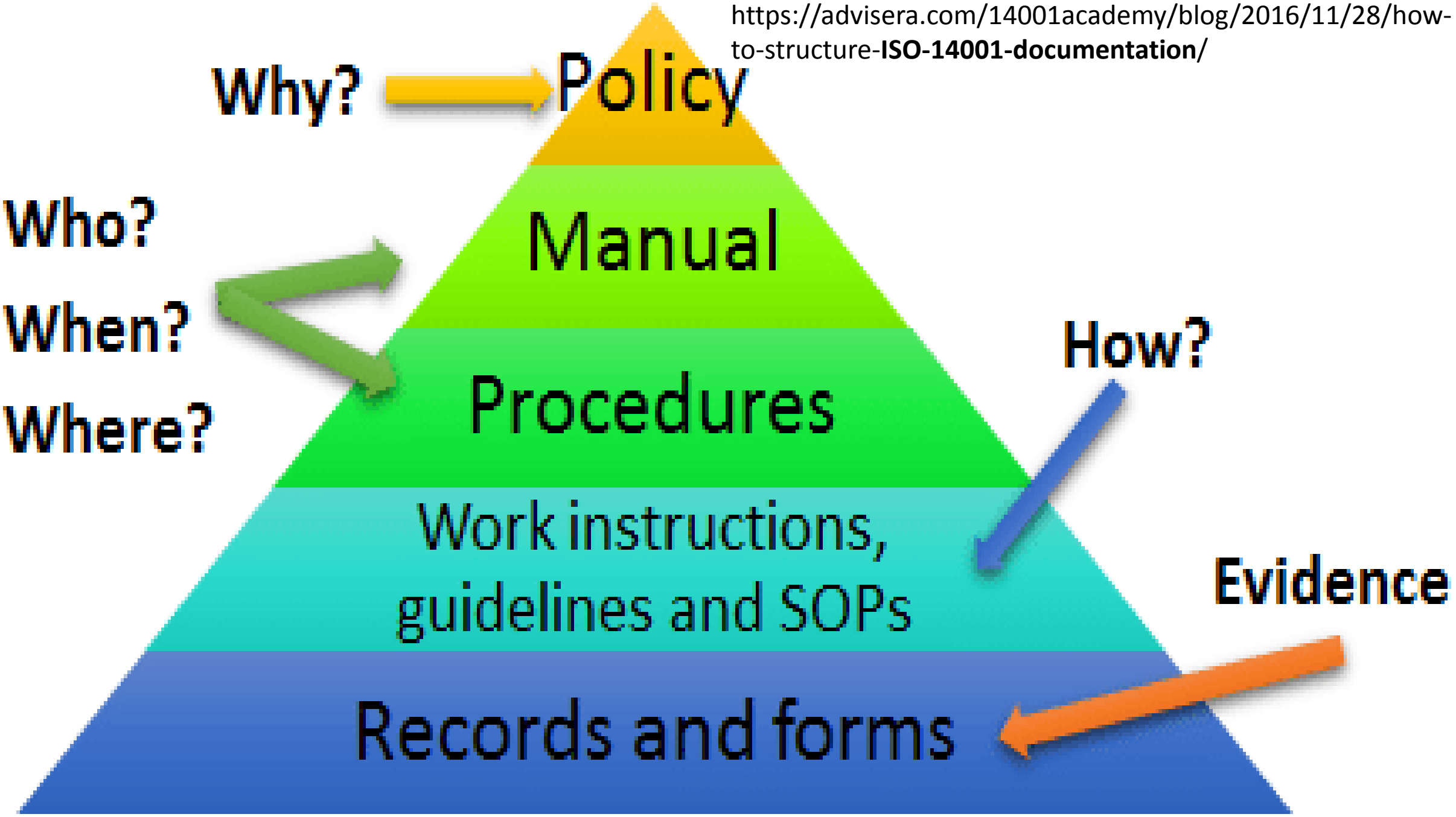
RISK ANALYSIS

Changes to a process shall include **evaluation of risk** to confirm that they do not create an adverse impact anywhere in the operation and shall be validated or verified as appropriate

Risk Consequence x Probability		Probability			
		Unlikely	Not very likely	Possible	Probable
Consequence	Very Serious	Hazardous	Hazardous	Very Hazardous	Very Hazardous
	Serious	Moderately Hazardous	Hazardous	Hazardous	Very Hazardous
	Mild	Moderately Hazardous	Hazardous	Hazardous	Hazardous
	Insignificant	Not Hazardous	Not Hazardous	Moderately Hazardous	Hazardous

POLICIES & PROCEDURES

https://advisera.com/14001academy/blog/2016/11/28/how-to-structure-**ISO-14001-documentation/**



B/CM/CD 5 Lists of required SOPs

B5.1.1	Recipient evaluation, selection, and treatment.						
B5.1.2	Donor and recipient confidentiality.	CM5.1.1	Donor and recipient confidentiality.	C5.1.1	Donor and recipient confidentiality.	D5.1.1	Donor and recipient confidentiality.
B5.1.3	Donor and recipient consent.	CM5.1.2	Donor consent.	C5.1.2	Donor consent.		
B5.1.4	Donor screening, testing, eligibility determination, selection, and ma	CM5.1.3	Donor screening, testing, eligibility determination,	C5	Donor screening, testing ility determination, ment.		
						D5.1.2	apy product receipt.
						D5.1.3	ocessing and process control.
B5.1.5	Management of c e central v access.			4	Management of don o requi tral venou access.		
B5.1.6	Administration of eparat imen.						
		CM5.1	Cellular th pro ion.	5.1.5	Cellular therapy p collectior		
B5.1.7	Administration of	CM5.1.5	istr of blo cts.	C5.1.6	n c d products.		
B5.1.8	Administration of ellular y products, including products under exce l release.						
B5.1.9	Administration of ABO-incompatible products to include a description of the indication for and processing methods to be used for red cell or plasma reduction.					D5.1.4	Processing of ABO-incompatible cellular therapy products to include a description of the indication for and processing methods to be used for red cell and plasma depletion.
B5.1.10	Management of cytokine release syndrome and central nervous system toxicities.						
		CM5.1.6	Prevention -ups and cross-contamination.	C5.1.7	Prevention of mix-ups and cross ation.	D5.1.5	Prevention of mix-ups and cross-contamination.
		CM5.1.7	Labeling (in ding assoc forms a ples).	C5.1.8	Labeling (incl associated f d samples).	D5.1.6	Labeling (including associated forms and samples).
B5.1.11	Duration and conditions of cellular therapy product storage and indications for disposal.					D5.1.7	Cryopreservation and thawing.
		CM5.1.8	Cellular th product n da	C5	Cellula apy proc pira ates.	D5.1.8	Cellular therapy product expiration dates.
		CM5.1.9	Cellular th product stor	C5.1.10	Cellula y pr orag	D5.1.9	Cellular therapy product storage to include alternative storage if the primary storage device fails.
		CM5.1.10	Release and exceptional release.	C5.1.11	Release and exceptional release.	D5.1.10	Release and exceptional release.
		CM5.1.11	Transportation and shipping, including methods and conditions to be used for distribution to external facilities.	C5.1.12	Transportation and shipping, including methods and conditions to be used for distribution to external facilities.	D5.1.11	Transportation and shipping, including methods and conditions within the Processing Facility and to and from external facilities.
						D5.1.12	Cellular therapy product recall, to include a description of responsibilities and actions to be taken, and notification of appropriate regulatory agencies.
							erapy product disposal.
		CM5.1.12	Critical equipment, reagent, and supply eme udin cor s i ven lure	C5.1.13	al reagent an y manageme	D5	Critica nt and supply management.
				5.1	oment operation, e, a nitoring ding corrective actions i ve ilure.	D5.1	ope aintenance, and monitoring g correcti in the event of failure.
				C5.1	ls of equipm reag		ecalls of equi t , and reagents.
				C5.1.16	ing and sanita es including identification of the individuals responsible for the activities.	17	Cleaning and sa edures including identification of the individuals responsible for the activities.
						D5.1.18	Environmental control to include a description of the environmental monitoring plan.
B5.1.12	Hygiene and use of personal protective equipment and attire.	CM5.1.13	Hygiene and use of personal protective equipment and attire.	C5.1.17	Hygiene and use of personal protective equipment and attire.	D5.1.19	Hygiene and use of personal protective equipment and attire.
B5.1.13	Disposal of medical and biohazard waste.			C5.1.18	Disposal of medical and biohazard waste.	D5.1.20	Disposal of medical and biohazard waste.
B5.1.14	Cellular therapy emergency and disaster plan	CM5.1.14	Cellular therapy emergency and disaster plan related	C5.1.19	Cellular therapy emergency and disaster plan	D5.1.21	Cellular therapy emergency and disaster plan

B5.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual procedure shall include:

B5.3.1 A clearly written description of the objectives.

B5.3.2 A description of equipment and supplies used.

B5.3.3 Acceptable end-points and the range of expected results.

B5.3.4 A stepwise description of the procedure.

B5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

B5.3.6 Age-specific issues where relevant.

B5.3.7 A reference section listing appropriate literature.

B5.3.8 Documented approval of each procedure by the Clinical Program Director or designated physician prior to implementation and every two years thereafter.

B5.3.9 Documented approval of each procedural modification by the Clinical Program Director or designated physician prior to implementation.

B5.3.10 Reference to a current version of orders, worksheets, reports, labels, and forms.

your “partner” during the inspection

- Work as **TEAM**…
- **Plan**...plan…plan….
- **Know** very well what you are going to do
- Respect your “**responsabilities**” but also be open to collaborate, flexible…
- Try to create a “comfortable” **enviroment**
- Be “perceptive” to “*leggere tra le righe*” (need translation!!!)
- Work as **TEAM**…

ANY QUESTIONS