World Marrow Donor Association: Quality Manual Template for Registries

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Outline

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2.	**Personnel** Describe how employees (and volunteers) who perform specific functions are adequately qualified and trained to perform their jobs competently - including hiring/qualification requirements, use of job descriptions, training/education programs, initial and ongoing assessment of competency, how staff training records are documented and maintained, and the process for periodic performance assessments.
3.	**Work Environment, Equipment and Safety** Describe the organisation's facility/physical plant and provisions for cleanliness, security, personal safety, maintenance and calibration of essential equipment, environmental controls, disaster plan, and emergency management.
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5.	**Documents and Records Management** Describe how the registry manages and controls essential documents such as policies, standard operating procedures, and manuals of operations - how documents are created, revised, reviewed on a periodic basis, consistently formatted, approved, distributed, implemented, version-controlled, stored, kept secure and confidential, archived, and the timelines for record retention.
6.	**Risk analysis and Problem Management** Outline how problems including, but not limited to, donor testing issues, donor screening, donor adverse events, product labelling, product transport, product integrity, deviations to standards or procedures, and breaches of confidentiality are handled by the registry - include how problems are detected, reported (including importance of an organisational culture that is not punitive regarding reporting of problems), investigated, assessed for risk, corrected, tracked, and trended. Include reference to WMDA's S(P)EAR reporting system, as well as possible need to report serious and unexpected events to other regulatory bodies and competent authorities.

7.	**Suppliers and Services Management** Describe the registry's process to select and qualify suppliers that provide critical materials or services (e.g., granulocyte colony-stimulating factor administration; infectious disease testing services; product transport containers) to ensure they meet requirements. Also describe how contracts/agreements are formed with suppliers, how their performance is monitored on an ongoing basis, and how the inventory of supplies is controlled.
8.	**Information Management** Describe how the registry assures controlled access to electronic data; maintains data security, data integrity, completes routine backup of data; and provides data recovery.
9.	**Monitoring and Review** Outline methods used by the registry to systematically review and monitor registry functions; may include oversight activities, review teams/meetings, quality indicators, inspections, audits, and process improvement initiatives.

Introduction

Pursuit of certification, qualification and/or accreditation with the World Marrow Donor Association (WMDA) is an important and rewarding endeavour on a registry's journey to excellence. Accreditation by WMDA demonstrates your registry's commitment to meet internationally accepted standards to ensure safe and effective management of volunteer donors, delivery of high-quality services and products that ultimately save patients' lives, and efforts to continually improve efficiency of operations.

This Quality Manual template is meant to help your registry identify and document a formal plan to meet basic quality management requirements set forth by regulatory and voluntary accreditation entities. The Quality Manual contributes and refers to well-functioning internal operations and processes. The Quality Manual is also meant to be a "living" document - a guide that is easy to access, easy to read, and easy to understand by all registry members and employees.

Quality plan requirements most often include management of essential functions in the areas of personnel, work environment, key processes, documents and records, problem resolution, suppliers and services, access and security of information, as well as ongoing monitoring and review. Within the manual, we suggest you include references to the relevant standard operating procedures (SOPs) of your registry's quality management system, rather than include the full procedures themselves. In essence, the manual should be a source guide that connects and references all available documentation without including extensive details of the individual processes.

Meaningful quality management also requires ongoing and dynamic collaboration between all registry employees, volunteers, and work units to maintain a positive environment that values continual improvement in support of WMDA's mission. In other words, quality is everybody's responsibility.

Best wishes in your pursuit of WMDA accreditation!
Ensuring Quality Pillar of WMDA

1 General Organisation Information

WHAT? This section provides a brief summary of the registry.
WHY is this important? It is important for the registry to have a clear and defined organisational structure. This provides the basis for the overall implementation of the quality management program and ensures that the structure reflects the needs of the registry, affiliations and customers.

1.1 Corporate Policy

The corporate policy lays down the registry's guiding principles, strategy, and policies. It includes the formulated objectives, decisions, actions and control systems that affect the registry as a whole and it draws attention to the common standards and values that form the basis for all fields of registry work (WMDA 2020 Standard 2.10.1). A strategic plan is helpful to identify future goals (WMDA 2020 Standard 2.10.4). The corporate policy is defined by the organisation's executive management and is generally valid for all employees.

- Explain the strategy of the registry and the future plans.

1.2 History

The registry's history can be briefly outlined to present the founding history and the past development. The historical perspective might serve as an example of registry performance and can be a good indication of how the registry will develop in the future.

- Include a brief summary of the registry's history.

1.3 General Organisation of the Registry

The general organisation information includes the registry's organisational structure and the basis of operation. Mentioning the registry's name and permanent address (WMDA 2020 Standard 2.09) has merely a descriptive nature; proving the registry's identity as legal entity including the registration number, however, is an important element of the general information, as pointed out in the WMDA 2020 Standard 2.01. Subsidiaries and cooperating affiliates, such as laboratories, donor centres, cord blood banks, transplant centres and collection centres, which are functionally part of the registry's performance have to comply with WMDA Standards. The responsibility for examining the compliance with WMDA Standards of all affiliations rests with the registry and requires conscientious documentation (WMDA 2020 Standards 1.06-1.08).
The organisational structure of the registry should be displayed in a simple and straightforward way, such that the leadership and the departments are clearly depicted. Identify the authorised official(s) who must authorise all official documents (WMDA 2020 Standard 2.02).

- Provide the general registry information: name, permanent address, proof of legal status, subsidiaries, and affiliations.
- Define areas of responsibility and give the structure of the registry.
- Identify the senior leadership of the registry.

1.4 Quality Management

1.4.1 Quality management program

In general, service and customer-oriented quality management programs have significant impact on both internal and external aspects of registry work. Internally, quality management interweaves with all registry functions and levels of management, pursuing the objectives of continuous process and service improvement (WMDA 2020 Standard 2.10), as well as compliance with applicable regulations. It is advisable consequently to appoint a person responsible for the quality management program (WMDA Standard 2.02, 2.10). A critical success factor for an effective implementation of quality management is the commitment to quality by the registry's management. Thereby, key aspects to be addressed in a quality management program can be summarized in a high-level quality statement (WMDA 2020 Standard 2.10.1).
From an external point of view, effective quality management strengthens the registry's perception to customers and affiliates, especially when accreditation is achieved.

- Appoint a person who is responsible for the quality management program and the accreditation process.
- Develop a high-level quality statement.
- Write down the registry's management commitment to quality listing adequate resources to support all aspects of the quality management program.

1.4.2 Key regulatory and voluntary accreditation requirements

The decision-making of the registry should be based on relevant measures and regulations. This regards internal decisions that have to be made in accordance with registry objectives as well as efforts that need to meet key regulatory requirements by national and international authorities such as European Union (EU) and the US Food and Drug Administration (FDA). Requirements of voluntary accreditation organisations (e.g., WMDA, FACT-JACIE) provide additional information and guidance (WMDA 2020 Standards 1.05, 1.09 and 2.02).

- Name the authorised official who is responsible for ensuring the registry's compliance with working standards.
- Describe the method with which the registry controls and manages the compliance with working standards of the respective authorities.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020)
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, B4: *Quality Management*
3. US FDA 21 Code of Federal Regulations, Part 1271.160: *Establishment and maintenance of a quality program*.
4. ISO 9001: 2015, Chapters 1-4.
5. European Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on *setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells*, Articles 16 and 24.
6. European Commission Directive 2006/86/EC of 24 October 2006 *implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells,* Article 3 and Annex 1.

2 Personnel

WHAT? The focus of section two relates to the management of personnel from a quality system perspective. This section looks at various elements that should be considered including:

- Creation of job descriptions;
- Establishment of systems and processes that support personnel;
- Development of training programs; and
- Creation of training documentation.

WHY is this important? The provision of safe, high-quality products and services is an essential quality systems' strategy. Addressing personnel as part of the quality system encourages registries to ensure their processes are defined, understood and in control. This ensures that the products and services provided by the registry meet predefined needs of the customer. Processes to support personnel help to form the foundation of every quality system. A shortage of personnel or having untrained personnel increases the risk of errors and accidents. The key to a successful, quality focused organization is to ensure that personnel have the right knowledge and skills to perform tasks and make good decisions.

2.1 General Considerations

It is important to note that the term 'personnel' refers not only to full-time employees but also includes part-time employees, volunteers and contracted personnel participating in registry activities. Therefore, when considering processes involved in the management of personnel, the broader view of personnel should be considered.

- Provide an organisation chart of all departments, staffing volume and key persons.

2.2 Qualifications

The organisation must ensure that its structure is adequate to meet the requirements of the function it performs. This means that there needs to be a *sufficient number* of *trained* personnel to carry out the operations of the organisation (WMDA 2020 Standard 2.08). A shortage or a lack of trained personnel can increase the risk of errors and accidents. Planning processes that anticipate future and ongoing organisational needs help determine resource requirements. As well, assurance that personnel are qualified for the tasks assigned supports availability of resources needed in the future (WMDA 2020 Standard 2.07). Qualifications are identified on the basis of job responsibilities and the associated tasks assigned.

- Describe how your registry assesses the adequacy of workforce size to meet operational needs.
- Describe how your registry assesses the qualifications of personnel.

2.3 Job Descriptions

Job descriptions should be included as part of the quality system as they anchor much of the other activities to support personnel. Job descriptions outline major duties/tasks and responsibilities assigned. They are descriptive and concise so that personnel clearly understand the role they perform and expectations of that role.
Job descriptions identify the necessary pre-requisites that the candidate must hold in order to be considered qualified. Pre-requisite qualifications take into consideration education, experience, training and certifications. Personnel selected for specific roles must meet expectations identified to perform duties associated with the procurement, manufacturing and distribution activities.

Job descriptions should also define reporting relationships, and the relationships between roles. This provides the incumbent with a clear understanding of how his/her role interacts with others. Job descriptions also define who is accountable for the activities conducted in each group within the registry.

- Describe how your registry defines and manages the roles, responsibilities, qualifications, and accountabilities for each personnel position.

2.4 Training Systems

The World Marrow Donor Association's *International Standards for Unrelated Hematopoietic Stem Cell Donor Registries* require that personnel be trained and knowledgeable about the duties they perform (WMDA 2020 Standards 2.03-2.05, 2.07). Training must be conducted, and records of training activities maintained. As such, the remainder of this section focuses on training systems within registries. This is important in a quality system as research confirms that organisations that invest in the training of personnel, consistently demonstrate higher output.

Development of a training system should include the provision of training resources, facilities and budget to execute training for registry personnel (WMDA 2020 Standard 2.07). As with all functions, training resources can be technical or subject matter experts; however, they should also be qualified to execute training. Each registry must develop procedures which form the basis of *some* of the training activities in the organisation. These procedures should define training responsibilities, timelines for review of training programs and frequency of assessing personnel to their role. Quality representatives should be included in the review and evaluation of the training program and management must actively support the training system in order for it to remain effective.

2.4.1 Assessment of Training Needs

To ensure that training activities meet performance requirements within a quality system, a training needs assessment is included as part of the training process. A needs assessment determines knowledge and skill requirements in order to address the gap between current and desired performance. It includes general training requirements to more specialised training as identified in the job description.

2.4.2 Training Design

The complexity of the learning required to close the gap should be considered. The design of training in a quality system takes into consideration this complexity as not all training activities need to be conducted in the same fashion. Minor/simple learning can be achieved through a variety of means including discussion and reading whereas complex learning should include a more thorough training approach. In the case of complex learning that impacts safety, quality, identity, purity and potency (abbreviated "SQuIPP"), competency assessments should be included in the training design. This ensures that the right thing is done in the right way, every time.

In a quality system, training material is designed only after the performance gap has been assessed. Training must cover how to perform the task to close the gap but also the consequences of improper performance and the ensuing impact on quality and product effectiveness. Training that is designed from a quality perspective should include the following:

- A clear overview of the purpose of the training;
- Objectives for the training;
- Identification of the target audience;

- An outline of how training delivery will occur;
- An estimate of the length of time to complete training;
- An overview of the pre-requisites for training;
- A list of learning resources required for training;
- An overview of how learners will be assessed for competency; and,
- Measures to ensure that the training design was effective in achieving learning objectives.

2.4.3 Competency Assessment

Competency assessments should be developed to ensure that the learner is able to demonstrate mastery of the required change in skill, knowledge or attitude. Competency assessments allow for standardised assessment of the learner. Strategies that support the assessment for competency include but are not limited to written scenarios/tests or simulation/direct observation of performance. Competency should be assessed both upfront and on an ongoing basis. Training for volunteers and contracted workers can be less than that for full time personnel if the volunteers and contracted workers have training to the specific tasks they perform and have direct supervision.

2.4.4 Training Delivery

Training is always required at the start of employment with a registry; however, it should be conducted on an ongoing basis throughout the lifecycle of the employee. Training should only be delivered by those qualified to train. Critical aspects of every role should be assessed periodically to ensure that personnel remain competent. Personnel should not work independently until training for tasks has been completed. Training should be reviewed by management.

- Describe your registry's system for managing training, including assessment of training needs; how training is designed/developed; how competency of personnel to perform their assigned tasks is assessed; and how training is delivered.

2.5 Documentation of Training

As part of the design of the training system, it is important to consider how training activities are captured (WMDA 2020 Standard 2.07). There are several aspects to documentation that need to be considered: a system to capture training requirements for each role; documentation of the results found during the needs assessment; the training material designed to meet the performance gap; and the actual documentation that is completed once training has been delivered and personnel have met training requirements.

2.5.1 Training Matrix

Registries must have a means of clearly capturing training requirements for each role. This ensures that training requirements are consistently met by all those performing registry roles. Most often this is achieved through a training matrix.
The training matrix should include mandated training (e.g., regulatory training, safety training, and orientation to the organisation) as well as job specific training and quality training. The level of training required should also be indicated (e.g., exposure (read the document), competency (demonstrate requisite knowledge or a critical skill), and proficiency (demonstrate the ability to achieve pre-determined results). It is the responsibility of management to ensure that the matrix is current and accurately reflects the training needs for each role. As such, the training matrix should be reviewed on a periodic basis.

Training Matrix Example:

TRAINING MATRIX

LEGEND
/ = Performance Measurement
E = Exposure to Information
N/A = Not applicable for Job Title

COURSE/DOCUMENT NAME AND NUMBER	Director	Program Manager	Case Manager	Search Analyst	Data and Reporting Administrator	Activations Administrator – Donor Management	Activations Administrator – Can and International activations	Activations Administrator- Extended, CT & work up
1.1 Introduction	E	E	E	E	E	E	E	E
1.2 Extended HLA Typing - Canadian Registrants	N/A	E	N/A	E	N/A	E	/	E
1.3 Extended HLA Typing - International Registrants	N/A	E	N/A	E	N/A	E	/	E
1.4 Donor Health Screening (CT)	N/A	E	E	N/A	N/A	E	E	E
1.5 Scheduling Potential Donors for Confirmatory Typing	N/A	E	E	N/A	N/A	E	E	/
2.0 Quality Training: Continuous Learning	E	E	E	E	E	E	E	E
3.0 Donor Medical Suitability Manual	N/A	E	E	N/A	N/A	E	E	E

Approved By:

Manager / Designate **Date**

2.5.2 Training Documentation

Documenting training is a means of maintaining a historical record that training has taken place. Needs assessments should capture identified gaps and training materials should be available to ensure standardisation in delivery and competency requirements. Documentation should also be created for training executed at the time of hire and on an ongoing basis (WMDA 2020 Standard 2.07).
Responsibility for the completion and maintenance of training records should be clearly defined within registry policies. The retention period for the storage of training records should also be defined (WMDA 2020 Standard 5.25). This ensures that training records are stored in a consistent manner. Finally, it is recommended that training records be kept separate from personnel records and only available to authorised personnel.

- Describe how your registry documents role-specific training requirements, and how completion of required training is recorded.

Closing

The World Marrow Donor Association (WMDA) has released recommendations regarding the training of some key registry functions to ensure consistency in the management of recruitment personnel. For example, WMDA developed recommendations for minimum qualifications and training of stem cell donor recruiters that should be used as a guideline for management of recruitment personnel. Recommendations can be found at WMDA Share (https://share.wmda.info/x/EgA0Ew).

References

1. Health Canada, Health Products & Food Branch, Guidance Document for Cell, Tissue and Organ Establishments: *Safety of Human Cells, Tissues and Organs for Transplantation*, Health Canada (Adopted April 6, 2009). Page 88.
2. J. M. Juran, A. B. Godfrey (1998), *Juran's Quality Handbook,* McGraw-Hill, New York.
3. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020)
4. CAN/CSA-ISO 9001, Quality Management Systems Requirements: Quality Management Systems - Requirements, Canadian Standards Association (2008). Section: 4.1(b).
5. Pelnik, T.M.,*The Quality System Compendium: GMP Requirements and Industry Practice.* Association for the Advancement of Medical Instrumentation, Arlington, Virginia. (2007), p 62-64.
6. J. D. Roback, B. J. Grossman, C. D. Hillyer, *AABB Technical Manual*, AABB, Bethesda. (2011), p 7-9.
7. European Parliament and the Council of the European Union. (March, 2004). *Directive 2004/03/23, Setting Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells*. Article 152(4)(a) 27.
8. US FDA 21 Code of Federal Regulations, Part 1271: *Human Cells, Tissues and Cellular and Tissue-related Productions*, (last revised April 1, 2013), Part 1271.170 (a) & (b): *Personnel*.
9. J. R. Evans, W.M. Lindsay, *The Management and Control of Quality,* Thomson South-Western, USA, (2005), p 281.
10. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, B4: *Quality Management*
11. 11. A. H. Schmidt, B. Amer, M. Halet, S. Hildebrand, and N. Sacchi for the Quality Assurance Working Group of the World Marrow Donor Association, *Qualifications and training of adult stem cell donor recruiters: recommendations by the World Marrow Donor Association*, Bone Marrow Transplantation (2013), 48, p 148-150.
12. I. Evseeva, K. Coffey, S. Morsch, and V. Parguey for the WMDA Donor Registries Working Group, *Recommendations on the Training of Staff Performing Patient-Donor Search and HLA Matching Activities* (2011).
13. ISO 9001:200815, Chapters 7.

3 Work Environment, Equipment and Safety

What? This section focuses on the facilities, equipment and safety features of the registry. The registry should aim to have a safe environment for its staff, volunteers and visitors taking into account the physical building, the overall work environment and the wider location (WMDA 2020 Standard 2.09.1). Planning should also be made for when the facility may be considered not suitable for use and emergency management plans should include crisis response, disaster recovery and business continuity plans (WMDA Standard 2.10.2).
Why is this important? A registry cannot function without adequate physical working space. It is important to establish when developing a quality system, the processes, procedures and policies required to maintain an environment suitable for the function of the registry, to ensure the safety of personnel, and that consideration has been made in the event of planned and unplanned occurrences that may disrupt normal activity. Consideration of these factors will ensure the continued delivery of high-quality registry services. It is also essential to consider local laws and regulations when developing a quality system that includes the working environment.

3.1 Facility and Work Environment

The registry is required to provide a description of the amount of space available to it (WMDA 2020 Standards 2.09, 2.09.1), including all physical locations associated with the registry. This may include satellite storage rooms or offices in different locations.
Each facility location must have sufficient space so that all work can be carried out in an environment designed to minimize errors, reduce risks to health and safety, and maintain confidentiality.
There should be the ability to review the facility(ies) as the needs of the registry change to ensure they are adequate to perform the designated function.

- Provide a high-level description of your registry's location, facility(ies), and capabilities to meet the provisions identified in section 3.1.
- Document that resources and facilities are provided to a sufficient scale.

3.2 Equipment

The registry must establish procedures to ensure that critical equipment is assigned unique identification; is inventoried; is qualified as acceptable for its intended use through proper installation, verification of functionality, and demonstration that it performs as expected. In addition, procedures regarding maintenance of critical equipment to maintain them in good working order must be evident, to include periodic preventive maintenance and prompt correction of equipment malfunctions (WMDA 2020 Standard 5.03, 5.06). The facility(ies) must have functional communication systems and links to facilitate search and transplant functions, including telephone, fax, and email/internet (WMDA 2020 Standard 5.14).

- Provide a high-level description of how your registry handles critical equipment to ensure and document performance to requirements.
- Provide and document an adequate level of communication equipment and how maintenance is ensured.

3.3 Safety

A registry's program of safety should address potential situations including fire, weather, electrical, biological, chemical, and radiation hazards (WMDA 2020 Standard 2.10.2). The approach to safety should include strategies to prevent, mitigate and treat exposure, in accordance with local/national standards (WMDA 2020 Standard 2.10.3). It is common for facilities to conduct periodic drills for the workforce regarding specific reactions to adverse conditions (e.g., fire drills, bomb threats).

- Describe your organisation's safety plan, in accordance with local/national standards.

3.4 Security

Procedures to maintain the security of personnel and activities and information related to registry activities should be referenced in the quality manual (WMDA 2020 Standards 2.09.1, 3.07, 4.06, 5.02, 5.11, 5.19). This may include the definition of limited access areas, secure entry systems and the procedures to allow for visitors without compromising security.

3.5 Environmental Controls

The registry should ensure that there are procedures in place for the event of changes to the environment. Where possible, an overview of the assessment of factors affecting the environment, including risks, should be stated (WMDA 2020 Standard 2.09.1, 5.06). Examples of factors that may affect the environment include changes in physical location; such as if the registry includes multiple sites, moves premises or expands within a space. More tangible aspects should also be considered, for example room temperature, desk space, lighting and location of equipment. It is good practice in a quality system to have control measures in place which can be commented upon in the quality manual.

3.6 Disaster and Emergency Planning

Policies should be in place to facilitate the continuation of registry services in the event of an emergency or disaster. While it is not possible to plan for all scenarios, a plan that has prepared for an emergency event that affects the facility and its processes is beneficial in a quality manual (WMDA 2020 Standard 2.10.3). The plan should include the identification of an emergency, the preparation of staff the facility and support systems such as IT and communications, contingency measures and recovery from the event (WMDA 2020 Standard 2.10.2). It is anticipated that the registry's business continuity plan and any crisis response and disaster recovery plans are incorporated here.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries, World Marrow Donor Association (WMDA) (version 2020)
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, Part B5: *Policies and Standard Operating Procedures*
3. US FDA 21 Code of Federal Regulations, Part 1271(D): *Current Good Tissue Practice*.
4. J. Pingel, C. Case Jr., B. Amer, R. A. Hornung, A. H. Schmidt for the Quality Assurance Working Group of the World Marrow Donor Association, *WMDA crisis response, business continuity, and disaster recovery guidelines*, Biol Blood Marrow Transplant (2012) 18, p 1785-1789.
5. ISO 9001:2015, Chapters 7.

4 Key Processes

WHAT? This section identifies the registry's key processes and describes how the registry ensures the quality of its operations and services through effective management of its processes.
WHY is this important? A registry must manage its key processes as defined by WMDA Standards, particularly as they relate to working with stem cell donors including maternal donors of cord blood at all stages of their involvement, including:

- Recruitment;
- Informed consent;
- Donor characterization/HLA typing;
- Workup/screening and eligibility, including medical evaluation and infectious disease testing;
- Product collection;
- Post-donation follow-up; and
- Requests for subsequent donations.

Effective management of key processes is essential to promote the quality of registry operations and services to its donors and other key stakeholders.
Effective management of key processes is achieved through process control methods such as standard operating procedures (SOP, i.e., specific work instructions); compliance with requirements of applicable regulations and standards; process validation; process improvement efforts; process change control; and mechanisms to approve and document exceptions or deviations to standard processes (WMDA 2020 Standards 2.10, 2.10.1).

- Identify the key processes of your registry.
- Describe the process control methods used by your registry. They may include the following:

4.1 Standard Operating Procedures (SOP)

Pursuant to WMDA 2020 Standard 2.10.1, the registry must maintain written policies and protocols for all procedures performed in the registry. This must include manual of operations, standard operating procedures, and forms. In addition, the registry must ensure that other entities acting on its behalf follow relevant policies and protocols (WMDA 2020 Standards 1.06-1.08).
A standard operating procedure is commonly defined as: a document that describes in detail the process or chronological steps taken to accomplish a specific task. A procedure is more specific than a policy. The instructions within each SOP should be written in stepwise progression. Each step should be clearly and concisely conveyed to assure the procedure can be applied consistently and replicated by different operators.

- Provide a list of the registry's SOPs.

4.2 Compliance with Requirements of Applicable Laws, Regulations and Standards

Regulatory agencies expect the registry and its affiliated partners to have defined SOPs related to biological product manufacturing requirements, including but not limited to: donor screening; donor testing; product recovery, processing, labelling, storage, packaging, distribution; the safety, quality, identity, purity or potency of the product; potential transmission of a communicable disease or contamination of the product; donor safety, and patient safety.

- Describe how the registry monitors donor management processes for compliance with requirements of cellular therapy regulations and standards, including EU, FDA, WMDA, and FACT-JACIE. Describe compliance with other applicable laws and requirements that govern the registry.

4.3 Process Evaluation and Validation

Process evaluation and validation involves testing the steps of each key process to assess whether the procedure operates effectively and as intended. Process validation is important to assure the procedure or service meets the need of the donor and other relevant stakeholders. Process validation is not a one-time effort; it must be conducted on an ongoing basis to detect variations and inefficiencies that may affect the quality of registry operations.

- Describe how your registry conducts evaluation and validation of its key processes.

4.4 Process Improvement

Upon discovery of inefficiencies or variability in key processes, how does the registry act to improve its processes to better meet the needs and expectations of donors, transplant centres and other stakeholders?

- Describe methods used by the registry to improve key processes (note: may include application of specific process improvement tools such as the Plan-Do-Check-Act cycle, flow chart analysis, lean management techniques, etc.).

4.5 Process Change Control

Process Change Control is a systematic approach to ensure changes to key processes are planned, assessed, approved, and communicated to appropriate stakeholders prior to implementation. Change control involves cross-functional impact analysis, risk assessment (WMDA 2020 Standard 2.10.3), and process verification/validation as needed to ensure that the changes do not create adverse impact or unintended consequences elsewhere within registry operations (WMDA 2020 Standard 5.07).

- Describe how your registry assesses, manages, and communicates changes to its key processes.

One of the most important requirements of Change Control is to maintain end-to-end documentation of all changes made, for audit trail purposes.

- Describe how your registry assesses, manages, and communicates changes to its key processes.
- Describe how your registry maintains documented history of changes.

4.6 Exceptions and Deviations to Key Processes

In general, it is industry practice within the field of cellular therapy to allow deviation from key processes (as defined in policies and procedures) when necessary. The registry should have guidelines in place that outline the criteria for allowing exceptions or deviations, including authorized individuals to review, approve, and document their occurrence.

- Describe how your registry handles, approves and documents exceptions or deviations to its key processes.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020)
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, A3: *Definitions and* B5: *Policies and Standard Operating Procedures*.
3. US FDA 21 Code of Federal Regulations, Part 211: *Current Good Manufacturing Practice for Finished Pharmaceuticals,* Part 1271: *Human Cells, Tissues, and Cellular and Tissue-Based Products*, Part 1271.225: *Process changes,* Part 1271.230: *Process validation.*
4. Standards for Cellular Therapy, 9th Edition, Section 5, 7, AABB,
5. American Society for Quality, website, http://ASQ.org

- Plan-Do-Check-Act cycle: http://asq.org/learn-about-quality/project-planning-tools/overview/pdca-cycle.html;
- Lean: http://asq.org/learn-about-quality/lean/overview/overview.html;
- Flowchart: http://asq.org/learn-about-quality/process-analysis-tools/overview/flowchart.html.

6. European Union Commission Directive (8 February 2006) 2006/17/EC *implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells,* Article 2.
7. ISO 9001:2015, Chapters 4, 8.

5 Documents and Records Management

WHAT? This section describes how the registry manages and controls essential documents such as policies, standard operating procedures, and manuals of operations, and how registry's records are controlled.
WHY is this important? The registry must maintain written policies and protocols for all processes performed in the registry as defined by WMDA and maintain records of its activities (WMDA 2020 Standards 5.10, 2.10.1).
Effective management of documents and records is essential to accomplish the registry's operational and quality goals, ensures that the registry is performing according to a defined set of protocols and demonstrates its ability to accurately record, trace and retain data in all its forms (WMDA 2020 Standards 5.10, 5.11).
Effective management of documents and records control is achieved by defining how documents are created, consistently formatted, approved, revised, reviewed, distributed, implemented, version controlled, stored, kept secure and confidential, and archived. Also, timelines for records retention should be defined (WMDA 2020 Standard 5.25).

5.1 Document Management

A documented procedure shall be established to define the document controls needed.

- Provide a current listing of all critical documents that shall comply with the document control system requirements. This list must include all critical documents that are currently in effect.
- Controlled documents shall include for example: policies and SOPs, forms, labels, educational, promotional, and recruitment materials.

Documents should remain legible and readily identifiable. Controlled documents must include a system for numbering and titling that allows for unambiguous identification of the documents and revisions of documents with the same title.

- Define consistent formats for documents. Use the following features for each document: unique identifier; title; version indicator; registry identification; page number.

Documents should be approved for adequacy prior to issue. There should be a system to approve new or changed documents that identifies the responsible individuals and clearly indicates the effective date that the document must be in place.

- Describe who in the registry can create documents, who is the person authorized to approve them prior to issue and how this process is documented. An approval section may be part of the document (i.e., SOPs), or linked to the controlled document through its identifier.

In order to assure that a task will not be performed by personnel until they are trained, documents should be implemented and distributed to relevant personnel according to an established procedure. This procedure should include written confirmation that relevant personnel have received and read the document.

- Describe how new/revised documents are implemented and distributed for registry and/or registry affiliates use. Signatures to indicate reading and/or training must be maintained for all new and revised SOPs.

Documents should be adequately reviewed and updated for continued relevance and accuracy.

- Define documents' review on a periodic basis and describe how they are updated and re-approved as necessary. Ensure that changes and the current revision status of documents are identified.

Relevant versions of applicable documents should be available at the point of use.

- Establish a master list of all current documents used by the registry. Update the list regularly.

Documents should be retained to ensure security, confidentiality and loss prevention. There shall be a system to ensure that controlled documents cannot undergo accidental or unauthorized modification (WMDA 2020 Standards 5.02, 5.19).

- Describe how all documents are kept protected against unauthorized access, modification or destruction. The procedure should include directions regarding how staff access work instruction and related registry documentation on a daily basis. The document control process may be electronic or paper-based: describe the documentation system in your registry.

Unintended use of obsolete documents should be prevented. Suitable identification should be applied to them if they are retained for any purpose.

- Describe how invalid and obsolete documents are removed. Define how obsolete versions are retained and how suitable identification is applied to such documents.

5.2 Records Management

A record is a special type of document that furnishes objective evidence of activity performed, observation made or a result. According to WMDA 2020 Standard 5.10, the registry must maintain records of its activities. All patient and donor communications and records must be stored to ensure confidentiality and to allow traceability and be maintained for an appropriate period of time (WMDA Standards 5.05, 5.11, 5.25). A documented procedure must be established to define the controls needed for records.
Records should remain legible, readable and readily identifiable, i.e. identify or reference the product, process, person or event they retain.

- Describe how to keep track of changes made to records, to include the date of change and the identity of the person who changed the records.

Records should be adequately stored and retrieved.

- Describe how records are stored (paper or electronically) and where they are archived (physical location, computer folder, etc.). Describe the ability to access and retrieve records within an appropriate timeframe.

Records should be adequately protected.

- Describe how records are protected against deletion or alternation of previously recorded information. Describe how archived records are protected from unauthorized access, modification or destruction. Define methods to ensure confidentiality of information contained within records upon their destruction.

Records should be retained at least as long as dictated by national laws or standards.

- Describe how records are retained according to a specified schedule as defined by the registry and/or regulatory bodies.

Disposition of records is the final stage of record management in which a record is either destroyed or retained and archived.

- Describe how records in your registry are destroyed or archived.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020).
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, B10: *Records*,
3. ISO 9001:2015 Chapter 7.5.
4. European Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on *setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells,* (23), (28), Articles 8, 14.
5. European Commission Directive 2006/86/EC of 24 October 2006 *implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells*, Article 9.

6 Risk Analysis and Problem Management

WHAT? This section describes how a registry assesses risks and handles problems once they have occurred in order to ensure the quality and safety of its operations and services.
WHY is this important? A risk is a positive or negative deviation from the expected. A registry should have a documented risk management plan to mitigate against risks, and processes to manage risks or incidents should they arise (WMDA 2020 Standard 2.10.3). Problem management is the process responsible for managing the lifecycle of all incidents. The registry needs to devote special attention to the quality of the stem cell product and to the donor's health. According to WMDA Standards a registry must document, investigate and take remedial and/or corrective action measures whenever a **SAE** (serious adverse event) or **SAR** (serious adverse reaction) occur due to registry operations that impact the health and safety of donors or patients (WMDA 2020 Standards 8.09, 8.10, 8.10.1, 8.10.2, 9.03)**.** This includes but is not limited to:

- Donor testing issues;
- Donor screening;
- Donor adverse events;
- Product labelling;
- Product transport;
- Product integrity;
- Patient related issues;
- Deviations to standards or procedures; and
- Breaches of confidentiality

Effective risk and problem management is essential to prevent problems and resulting incidents from happening, eliminate recurring incidents, and minimize the impact of incidents that cannot be prevented in order to accomplish the registry's operational and quality goals.
Effective problem management is achieved through a consistent process that ensures risk and problems are detected, logged, reported, investigated, assessed for risk, corrected, tracked, and trended.

6.1 Risk analysis

Risk management is the identification, evaluation, and prioritization of risks followed by application of resources to minimize, monitor, and control the probability or impact of unfortunate events (WMDA 2020 Standard 2.10.3). Risks can come from various sources at any stage of the registry operations and procedures, or events of uncertain or unpredictable root-cause.

- Describe how the registry manage and addresses potential risks in its operations: Define the risk type; Define the activity/source from where the risk comes from; Determine what category the risk falls under; Describe the risk; Define the impact and the probability of occurrence; Establish how the registry will treat the risk and create a predefined list of treatments; Define the acceptable action to treat the risk.

6.2 Problem Detection

The first stage of a problem management process is the identification of a problem. Problems could be detected during the registry ongoing operations and through monitoring and assessment activities including audits and review of records. This stage also includes the initial recording of the problem including all relevant information that is available when the problem occurs. In order to have an efficient problem management

process it is very important to create an organization culture that is not punitive regarding reporting of problems.

- Describe how each problem is recorded and logged and how to allocate and assign the problem case for further investigation. Indicate the authorised person in the registry for problem management.

6.3 Problem Reporting

Pursuant to WMDA Standards, adverse reactions such as medical incidents or unforeseen occurrence that might seriously influence the quality and safety of the stem cell product or donor's health need to be reported to the WMDA sponsored international centralized database (S(P)EAR) (WMDA 2020 Standards 8.10, 8.10.1, 8.10.2, 9.03, 9.04). According to WMDA 2020 Standard 9.04, the registry must comply with governmental regulations including requirements to report such adverse reactions to a regulatory agency. Also, donor health issues post-donation potentially affecting the health of a patient having received an HSC donation from that donor must be reported to the transplant centre (WMDA 2020 Standards 8.10.1, 9.05). The registry must have processes in place that enable the collection centre or the transplant centre to report such issues.

- Describe how the registry reports SAE and SAR for compliance with WMDA Standards and other applicable laws and requirements that govern the registry.

6.4 Problem Investigation and Risk Assessment

Problem investigation involves examination, inquiry and analysis of all available data about the problem. Problem investigation results in deciding whether it is actually a problem, stating the problem in measurable terms, determining the problem owner, getting the root cause of the problem, and deciding whether correction and prevention actions will be required. As part of the problem investigation a risk assessment analysis may be performed in order to determine quantitative or qualitative value of risk related to an actual problem and recognize hazard.

- Describe how your registry performs problem determination and the investigation process. This may include application of root cause analysis and risk assessment methods.

6.5 Problem Correction

Once the problem has been identified and facts concerning the issue collected, analysed and investigated, the registry should take corrective and preventive actions (CAPA). Corrective action is a reaction to any cause/non-conformance. Preventive action is prediction of a problem and trying to avoid the occurrence through self-initiated actions and analysis related with processes/products. Verifying or validating corrective and preventive actions, communicating corrective and preventive action activities to responsible people, providing relevant information for management review and documenting these activities are essential in dealing effectively with product and quality problems, preventing their recurrence, and preventing or minimizing failures. Implementation of a CAPA system is the path towards improvement and effectiveness of quality management systems as required according to WMDA 2020 Standard 2.10.

- Describe how the registry takes actions to eliminate the cause of nonconformities and potential nonconformities to prevent occurrence and recurrence in order to protect patients, donors and other clients.

6.6 Problem Tracking and Trending

The registry should have methods of problems tracking and reporting trends in order to detect areas needing improvement.

- Describe how your registry tracks and identifies trends of problems, nonconformities and complaints.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020).
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, Part B: *Clinical Program Standards*.
3. US FDA 21 Federal Code of Operations, Part 1271.160: *Establishment and maintenance of a quality program* and 1271.320: *Complaint file*.
4. ISO 9001:2015, Chapter 6, 10.
5. European Commission Directive 2006/86/EC of 24 October 2006 *implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells,* Article 3 and Annex 1F.

7 Supplier and Services Management

WHAT? Selecting dependable, high-quality suppliers to provide materials and services to support registry functions is an important process. Registries must be responsible for documenting and ensuring that the materials and services meet established requirements and that the suppliers are fully qualified to allow the registry to satisfactorily perform its key functions.
WHY is this important? A quality management system includes the registry as a national organisation as well as all entities with which the registry enters into cooperation. The WMDA 2020 Standards 1.06-1.08 and 5.28 describe the requirements for cooperation and assign the registry to be in the position of responsibility. The combination of all internal and external services, partners and supplies contributes to the final product quality, donor and patient safety. In order to ensure a consistently high-quality product and donor/patient safety the WMDA Standards must be adhered to carefully when considering potential suppliers and critical materials.

7.1 Pre-Selection Activity

Identifying requirements and specifications for suppliers of materials and services:

A written description of requirements and specifications that are individually defined for each type of material or service will assist the registry in assuring the ongoing quality and maintaining adequate oversight of all suppliers and services. Requirements should include both, business requirements (needs of the registry and its donors and other stakeholders) and requirements set forth according to regulations, accrediting bodies, and other relevant regional/national/international regulations or licenses. Written description of requirements serves to describe the criteria utilised for selection of the suppliers and can be utilised in offering bids for materials or services. The specifications should ensure that the registry will have adequate inventory and capacity to perform its key functions while meeting the WMDA Standards. For example, WMDA 2020 Standard 3.17 describes the requirements for donor testing to meet standards established by local regulation for these types of services.
In addition, determination of the criticality of a potential material or service should be considered. A material or service may be defined as “critical” if it comes in contact with or becomes part of a cellular product during collection, manufacture, storage or transport that could directly affect the safety, quality, identification, potency or purity of the product, the results of laboratory testing, or the safety of the donor and or patient. Generally, suppliers of critical materials or services require more rigorous assessment prior to selection and approval.

- Describe how your registry identifies and documents requirements and specifications for materials and services.

7.2 Initial Review and Qualification

Gather additional relevant information: Initial assessment to determine whether a supplier is qualified typically involves gathering of additional information to determine acceptability, beyond the original list of requirements and specifications. Additional information to be gathered may include facility and contact information, regulatory/accreditation/certification/licensing status, quality system information, financial performance, and other acceptability criteria compiled in consultation with relevant subject matter experts.

- Describe how your registry gathers relevant information regarding prospective suppliers.

Determine method(s) of qualification: Methods to review, assess and qualify suppliers may vary based on criticality, risk, scope or impact of the materials or service on registry functions and donor safety. Methods of qualification may include:

- Qualification by checklist;
- Desk audit of supplier information/data;
- Onsite inspection or audit;
- Retrospective qualification (review of historical performance);
- Reference checking;
- No formal qualification, due to minimal impact/risk of materials or services.

➢ Describe how your registry determines the method(s) to qualify suppliers.

7.3 Supplier Selection and Approval

Once qualification activities are completed, it is important to evaluate and document the results. Selection of a critical supplier should include objective evidence that qualification and acceptability criteria have been met, and that management approves of the selection.

7.4 Forming Supplier Contracts or Agreements

A written contract or agreement helps to ensure that each party has an understanding of the terms and requirements. It can also be utilised to define how critical materials will be accepted or rejected, roles and responsibilities, reporting requirements, and consequences, if performance expectations are not met.

➢ Describe how supplier contracts or agreements are established and managed over time.

7.5 Ongoing Performance Monitoring

It is important to establish and track the performance of suppliers and service providers to document their quality. The interval, level of detail, and quality measures to be tracked will be very different depending on the type of supplier (e.g., HLA typing will be monitored differently than the supplier of donor recruitment brochures). Putting efficient mechanisms in place to monitor performance is also important for identifying any changes in quality that may require corrective action (for example WMDA 2020 Standard 3.18). Deviations/performance issues may result in action ranging from audit to termination of the supplier agreement.

➢ Describe the ways in which your registry monitors supplier performance and how deviations/performance issues are addressed.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020).
2. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, D6: *Equipment, Supplies and Reagents*.
3. US FDA 21 Code of Federal Regulations, Part 1271.150: *Current good tissue practice requirements* and Part 1271. 820.50(a): *Evaluation of suppliers, contractors, and consultants*.
4. Standards for Cellular Therapy, 9th Edition, Section 4.6: *Qualification of Suppliers*, AABB.
5. *Vendor Qualification: Points to Consider*. AABB, 2011.
6. ISO 9001:2015, Chapter 8.4.
7. European Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on *setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells*, (23), (28), Article 24.

8 Information Technology and Information Management

WHAT? This section addresses a registry's use of systems for information management and information technology. In brief, it describes how the registry assures controlled access to electronic data; maintains data security, confidentiality, and integrity; validates software for its intended use; completes routine data backup and allows for data recovery.
WHY is this important? A registry must attend to its information technology and information management practices as defined by WMDA Standards section 5, particularly as they relate to the establishment of systems, procedures, staff training, and supporting documentation. If the registry's information systems are subject to regulatory inspection; therefore, compliance with all national information security, privacy, legal, and regulatory requirements should take precedence in registry decisions and implementation.

8.1 Controlled Access to Electronic Data

Registries should evaluate electronic data classifications and determine appropriate access levels using role-based access to ensure compliance with confidentiality requirements (WMDA 2020 Standard 5.19). Access decisions are derived from information security, privacy, legal, and regulatory requirements. Adherence with codes of conduct related to system and data usage are recommended. In addition, periodic training and annual review and sign off should be required of anyone who has access to sensitive data. All information systems must uniquely identify and appropriately authenticate users or processes acting on behalf of users in accordance with compliance requirements. Appropriate means of system authentication (multiple factors or varying mechanisms) must be selected based on the sensitivity of information processed by an information system.
In addition to identifying and authenticating users at the information system level (i.e., at system logon), identification and authentication mechanisms should be employed at the application level, as required to meet compliance requirements.

- Describe how your registry ensures access to electronic data is limited to authorised individuals.

8.2 System Documentation

The registry must document evidence that the performance of computer systems and software has been tested and validated for their intended use and specifications (WMDA 2020 Standard 5.01). Such documentation must be approved prior to implementation, both for new applications and for modifications to existing applications. In addition, each system in use must have adequate documentation regarding its qualification, maintenance and user operation. If outside entities/third parties are involved in the registry's information management functions, the responsibilities of both the registry and the third party must be documented (WMDA Standards 5.28).

- Describe how your registry maintains documentation regarding specifications, testing, validation, maintenance, and user operation of relevant computer systems and software applications.

8.3 Data Security and Confidentiality

Data security includes compliance with all national information security, privacy, legal, and regulatory requirements. Guidance for creating an environment for securing data can be obtained from ISO 27001 or NIST Special Publication 800-53. Some basic elements of providing data security include secure login authentication, encryption, anti-virus and anti-malware software, and firewall technologies.
Periodic assessment of the security controls of information systems to ensure that controls are sufficient to meet information security and privacy requirements is strongly advised. An internal information security and privacy role or department is recommended with the role of developing and implementing policies, standards, and plans of action designed to address security and privacy data risks in information systems.
The registry must maintain current documentation of the hardware, software/network architecture, and external connections. It must be evident that electronic connectivity and communication between affiliate organisations is built on organised logic and implemented to minimize risks regarding security, vulnerabilities, and exploitation (WMDA 2020 Standards 5.02, 5.03, 5.08).

- Describe how your registry evaluates and upholds the security and confidentiality of data within its information systems.

8.4 Data Integrity

Registry policies, standards and procedures regarding information management should be maintained that dictates how data are entered by internal staff or submitted by third parties, and how the data are saved to registry databases. Data integrity measures and classification should be defined and implemented to ensure the data are evaluated and validated prior to accepting data changes such as patient and donor HLA or demographic information (WMDA 2020 Standards 5.13, 5.15). Ensuring data integrity includes testing and validation of new or modified software and the associated display of information (WMDA 2020 Standards 5.07, 5.08).
Policies, standards and procedures related to resolving discrepant data should be established. It is recommended that audit records are captured to record relevant data changes. Audit records provide monitoring, reconstruction of events, problem identification, analysis, investigation, and reporting of unlawful, unauthorised, or inappropriate activity. Audit tracking allows for verifying an individual's actions on information systems in order to demonstrate compliance with policies, standards and procedures.

- Describe how your registry evaluates and maintains the integrity of data within its information systems.

8.5 Routine Data Backup and Recovery of Data

Maintaining alternate storage of registry data and the ability to recover this information in a timely manner is critical to continuity of registry business operations. The registry must document how backup of all systems and data is performed regularly at reasonable intervals. Backups must be validated by data recovery tests (WMDA 2020 Standard 5.04). Redundant and reliable software and hardware architecture should be used to minimise the probability of failure or data loss and the possible length of a down time (WMDA 2020 Standard 5.03).

- Describe how your registry ensures backup and recovery of data in the event of system disruption.

8.6 Retention of Data Records

Records must be maintained per national laws or standards (WMDA 2020 Standards 5.05, 5.25).

- Describe your registry's policy regarding retention of data records.

References

1. ISO/IEC 27001:2013 *Information technology -- Security techniques -- Information security management systems – Requirements.*
2. National Institute of Standards and Technology (NIST): Special Publication 800-53 Revision 4, *Security and Privacy Controls for Federal Information Systems and Organizations*. 04/30/2013.
3. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020).
4. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, B10: *Records*.
5. US FDA 21 Code of Federal Regulations, Part 1271.160(d): *Computers*.
6. European Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on *the protection of individuals with regard to the processing of personal data and on the free movement of such data.*

9 Monitoring and Review

WHAT? This section outlines methods used by the registry to systematically review and monitor registry operations and the performance of the quality management system.

WHY is this important? Systematic review and monitoring is important to assess and assure conformance to the standards, regulations, policies, and procedures that form the foundation of registry operations and the quality management system. Review and monitoring also serves to illuminate areas of both strength and improvement for the registry.

Monitoring and review methods may include internal audits, external audits, laboratory proficiency testing, outcomes data, quality indicators, and feedback from customers and other stakeholders (e.g., WMDA 2020 Standards 1.06-1.08, 3.18, 4.14).

Information gathered from monitoring and review activities should be periodically analysed. Results should be shared with registry leaders and responsible personnel and included in reports of the quality management system.

Audits represent one of the principal activities of a quality management program. Audits are conducted to ensure that the quality management program is operating effectively and to identify trends and recurring problems in all aspects of facility operation. An audit involves verification activity, such as inspection or examination, of a process or quality system, to ensure compliance to requirements. Compliance is verified by examination of objective evidence. An audit can apply to an entire organisation or to a specific function or process or collaborating entity.

Auditing methods may include direct observation of functional activities and workflow, interviews with personnel, and review of written procedures, reports, and records.

9.1 Internal Audits

Internal audits are a tool to objectively examine and assess operational processes, identify strengths, recognise problems, and correct deficiencies. Internal audits are beneficial because they can provide deep insights regarding compliance to regulations and the performance of the quality management system.

Internal audits may be conducted by designated staff trained in audit techniques. The auditor should be knowledgeable about the functions being audited, but not solely or directly responsible for the audited functions (conflict of interest).

The registry should have procedures in place that describe internal audit tasks related to the frequency and scheduling of audits, establishing the scope and purpose of the audit (i.e., audit plan) including who performs the audit, the standards being audited against, preparative activities, steps in conducting the actual audit, documentation practices, reporting audit findings to leaders and responsible personnel, and timelines for follow up regarding corrective action related to non-conformances.

Internal audits may be prioritised according to the regulatory compliance risk of an area of conformance. The focus of an internal audit may be toward a system in general (such as the overall quality management system), or toward a specific component or targeted area within a process.

The results of internal audits shall be used to recognise problems, detect trends, identify improvement opportunities, and implement corrective actions when necessary.

- Describe how your registry conducts internal audits. Include information regarding the provisions outlined in Section 9.1.

9.2 External Audits

External audits include inspections and surveys conducted by individuals outside of the registry (e.g., regulatory and accrediting bodies). External audits may be announced or unannounced.

The registry should have procedures that describe how external audits will be managed, including designated staff to be notified of the audit, specific responsibilities of staff during the audit, and provisions for the audit team's workspace and access to registry documents and records.

- Describe how your registry manages external audits.

9.3 Laboratory Proficiency Testing

Another important method of external auditing is proficiency testing of laboratories to ensure the adequacy of testing methods, equipment, and competency of testing personnel.

Per WMDA 2020 Standards 3.18 and 4.14, registries must have established approaches to monitor and ensure the accuracy and completeness of the data listed in the donor database, including a system to ensure the quality of HLA typing results.

- Describe how your registry conducts proficiency testing of its affiliated laboratories or which accreditations are required.

9.4 Additional Methods of Monitoring and Review

In addition to audits and proficiency testing, the registry may utilise other methods including but not limited to outcomes reports, quality indicators, review boards, and feedback from customers and stakeholders to monitor and review registry activity and performance of the quality management program.

- Outline additional methods of monitoring and review utilised by the registry.

9.5 Analysis and Communication of Findings and Data

Findings and data collected from audits and other types of monitoring and review should be aggregated, trended and analysed. Action plans derived from monitoring and review activity should include the following: a detailed description of any corrective action(s) to correct non-conformances; a target date for completion of corrective action(s); and follow-up activity or re-audit to verify that the corrective actions were effective.

Finally, results should be shared with registry managers, responsible personnel, affected stakeholders, and included in reports of the quality management system.

- Describe how your registry analyses findings and data collected from audits and other types of monitoring and review and creates action plans to address findings of non-conformance.
- Describe how your registry communicates results with key stakeholders and includes results in reports of the quality management system.

References

1. World Marrow Donor Association WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries (version 2020).
2. US FDA 21 Code of Federal Regulations, Part 1271.160(6)(c): *Audits*.
3. FACT-JACIE International Standards for Cellular Therapy, 7th Edition, B4.8: *Audits*.
4. Standards for Cellular Therapy, 9th Edition, Section 8: *Internal and External Assessments*, AABB.
5. E. M. Areman, K. Loper, Cellular Therapy: Principles, Methods, and Regulations, Chapter 13: *Audits of Cellular Therapy Facilities*, AABB, 2009.
6. ISO 9001:2015, Chapter 10.
7. A. H. Schmidt, J. Pingel, P. Bregy, M. Israeli, B. Bream, WMDA project of the Quality Assurance Working Group: Key performance indicators for registries, WMDA recommendation, available on https://share.wmda.info/x/1YC1EQ

WMDA Quality Manual and WMDA Standards Cross reference Table

WMDA Quality Manual	Related WMDA Standards
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1.3 General organization of the registry	1.05, 1.09, 2.02, 2.10, 2.10.1
1.4 Quality management	
2 Personnel	
2.1 General considerations	
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3.6 Disaster and emergency planning	2.10.2, 2.10.3
4 Key processes	2.10, 2.10.1
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4.2 Compliance with requirements of applicable laws, regulations and standards	

WMDA Quality Manual	Related WMDA Standards
4.3 Process evaluation and validation	
4.4 Process improvement	
4.5 Process Change Control	2.10.3, 5.07
5 Documents and records management	5.10, 5.11,5.25, 2.10.1
5.1 Document management	5.02, 5.19
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6 Risk Assessment and Problem management	2.10.3, 8.09, 8.10, 8.10.1, 8.10.2, 9.03
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6.3 Problem reporting	8.10, 8.10.1, 8.10.2, 9.03, 9.04, 9.05
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8.3 Data security and confidentiality	5.07, 5.08, 5.13, 5.15

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8.4 Data integrity	5.03, 5.04
8.5 Routine Data Backup and recovery of data	5.05, 5.25
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9 Monitoring and review	
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