QUALITY MANUAL

REDOME
INSTITUTO NACIONAL DE CÂNCER

INCA

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Brazilian Registry of Volunteer
Bone Marrow Donors (REDOME)
José Alencar Gomes da Silva
National Cancer Institute (INCA)
MINISTRY OF HEALTH

TABLE OF CONTENTS

Presentation 4
History of REDOME 5
1. SCOPE 6
1.1. IDENTIFICATION DETAILS 6
2. NORMATIVE REFERENCES 7
3. TERMS AND DEFINITIONS 7
3.1. NOMENCLATURE FOR HLA SYSTEM FACTORS 7
4. CONTEXT 7
4.1. REDOME CONTEXT 7
4.2. STAKEHOLDERS 8
4.2.1. Stakeholders - Internal 9
4.2.2. Stakeholders - External 9
4.3. QMS SCOPE 9
4.4. QMS PROCESSES 11
5. LEADERSHIP 14
5.1. LEADERSHIP AND COMMITMENT 14
5.1.1. Generalities 14
5.1.2. Customer Focus 14
5.2. QUALITY POLICY 15
5.3. ROLES, DUTIES AND ORGANIZATIONAL AUTHORITIES 15
6. PLANNING 17
6.1. ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES 17
6.2. QUALITY GOALS 18
6.3. CHANGE PLANNING 18
7. SUPPORT 18
7.1. RESOURCES 18
7.1.1. Generalities 18
7.1.2. Personnel and Skills 19
7.1.2.1. Consultation with Experts 19
7.1.3. Infrastructure 20
7.1.4. Environment for Process Operations 20
7.1.5. Organizational Knowledge 21
7.2. AWARENESS AND COMMUNICATION 21
7.3. DOCUMENTED INFORMATION 21
8. OPERATION 22
8.1. OPERATIONAL PLANNING AND CONTROL 22
8.2. REQUIREMENTS FOR THE PROVISION OF SERVICES 23
8.2.1. Communication with the Customer 23
8.2.2. Requirements Related to the Provision of Services 24

8.2.3. Critical Analysis of Requirements Related to the Provision of Services 25
8.2.4. Changes in the Requirements for the Provision of Services 25
8.3. DESIGN AND DEVELOPMENT OF SERVICES 25
8.4. CONTROLLING PROCESSES, PRODUCTS AND SERVICES PROVIDED EXTERNALLY 26
8.5. PERFORMANCE OF SERVICES 27
8.5.1. Service Performance Control 27
8.5.2. Identification and traceability 28
8.5.3. Property Owned by Customers 29
8.5.4. Preservation 30
8.5.5. Follow-up Activity 30
8.5.6. Change Control 30
8.6. RELEASE OF SERVICES 31
8.7. CONTROL OF NON-COMPLIANT OUTPUTS 31
9. PERFORMANCE EVALUATION 31
9.1. MONITORING, MEASUREMENT, ANALYSIS AND EVALUATION 31
9.1.1. Generalities 31
9.1.2. Customer Satisfaction 32
9.1.3. Analysis and Evaluation 32
9.2. INTERNAL AUDIT 33
9.3. CRITICAL ANALYSIS BY THE COORDINATION BOARD 33
9.3.1. Generalities 33
9.3.2. Critical Analysis Input 33
9.3.3. Critical Analysis Outputs 34
10. IMPROVEMENT 35
10.1. GENERALITIES 35
10.2. NON-COMPLIANCE AND CORRECTIVE ACTION 35
10.3. CONTINUOUS IMPROVEMENT 36
References 37

Presentation

Guided by values such as ethics, transparency, cooperation and innovation, we hereby present our Quality Management System Manual, which aims to establish guidelines for REDOME's actions and promote the quality of its operations. Its scope covers the entire REDOME Quality Management System, defining its structure and content.

Dr. Danielli Oliveira

REDOME Technical Coordinator

History of REDOME

The Brazilian Registry of Volunteer Bone Marrow Donors (REDOME) started its activities back in 1993; since 2000, it has been part of the National Transplant Policy of the General Committee of the National Transplant System (CGSNT) under the Ministry of Health (Laws No. 9,434 and No. 10,211/2001), based on principles such as free donations, beneficence towards recipients and non-maleficence towards living donors, subject to the technical coordination and management of the National Cancer Institute (INCA).

Throughout its history, REDOME has made efforts to keep up with technical and scientific advances, with a view to promoting a significant improvement in transplant results for our patients, who find renewed hopes of leading a full, healthy life in the volunteer donors in our registry.

MISSION: "To promote integrated actions, aimed at providing excellent care to volunteer donors, for the benefit of patients who need cell therapy and bone marrow transplantation."

VISION: "To play our role in the national policy of cell therapy and bone marrow transplantation, cooperating with national and international entities, becoming a global reference in the care and safety of volunteer donors, as well as in supporting innovation and scientific research."

VALUES: Ethics; Genetic and Cultural Diversity; Equity; Respect; Transparency; Humanization; Safety; Cooperation; Innovation.

1. SCOPE

This Quality Manual describes REDOME's Quality Management System (QMS), its organization and general responsibilities. It defines the scope of this QMS and outlines the system documents along its contents. It presents the guidelines, definitions and references required for us to be and remain properly accredited for the quality standard of the services provided.

The REDOME QMS seeks to increase stakeholder satisfaction, continuous improvement and compliance with all applicable regulatory requirements.

Therefore, the scope of the Quality Management System covers all REDOME departments and their processes.

1.1. IDENTIFICATION DETAILS

REDOME:

Name	Brazilian Registry of Volunteer Bone Marrow Donors (REDOME)
Address	Rua do Resende, 128, Centro, Rio de Janeiro / RJ CEP 20.231-091
Telephone	(21) 3207-4700 and 3207-4701
Home page	http://redome.inca.gov.br/

INCA:

Corporate name	MINISTRY OF HEALTH - José Alencar Gomes da Silva National Cancer Institute (INCA)
Address	Praça Cruz Vermelha, 23, Centro, Rio de Janeiro / RJ CEP 20.230-130
Home page	https://www.inca.gov.br/

2. NORMATIVE REFERENCES

This Quality Manual uses the following standards as guidelines:

- ISO 9001:2015 - Quality Management System - Requirements;
- WMDA - World Marrow Donor Association - International Standards for Unrelated Hematopoietic Stem Cell Donor Registries. 2020

3. TERMS AND DEFINITIONS

For the purposes of this Manual, the terms and definitions of ISO 9000:2015 - Quality management systems - Fundamentals and Vocabulary shall apply.

3.1. NOMENCLATURE FOR HLA SYSTEM FACTORS

REDOME uses the nomenclature set forth by the Nomenclature Committee for HLA (Human leukocyte Antigen) System Factors under the WHO (World Health Organization) (WHO Nomenclature Committee for Factors of the HLA System).

4. CONTEXT

4.1. REDOME CONTEXT

The procedures developed by REDOME are discussed and planned in periodic meetings between coordinators, supervisors and advisors. These meetings cover the general framework of REDOME, addressing operational aspects, indicator analysis, strategic planning, project monitoring, contingency planning and data protection.

The following documents provide for REDOME's strategic actions and the regulation and operationalization of all administrative procedures under its general framework:

- 000.5980.000 IT POLICY
- 000.5980.001 FINANCIAL AND BUDGET POLICY
- 000.5980.002 PRIVACY POLICY
- 000.5980.003 COMPATIBLE DONOR SELECTION AND IDENTIFICATION POLICY
- 000.5980.004 COMMUNICATION POLICY
- 000.5980.005 DONOR PROTECTION POLICY
- 000.5980.100 COMMUNICATION WITH THE REDOME NETWORK
- 000.5980.101 DOCUMENTS AND RECORD CONTROL
- 000.5980.102 CONTINGENCY PLAN
- 000.5980.103 ACCREDITATION CONTROL
- 000.5980.104 NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS
- 000.5980.105 CRITICAL ANALYSIS
- 000.5980.106 REDOME STRATEGIC PLANNING

4.2. STAKEHOLDERS

REDOME aims to consistently provide services that meet the expectations and needs of stakeholders, as well as all applicable statutory and regulatory requirements.

REDOME's operational activities are carried out by the staff assigned to the National Cancer Institute (INCA) in Rio de Janeiro; in addition to its own team, REDOME is also supported by various INCA services.

4.2.1. Stakeholders - Internal

- Coordinators, Supervisors, Employees and Technical Teams (REDOME);
- National Cancer Institute (INCA);
- National Transplant System (SNT);
- MINISTRY OF HEALTH.

4.2.2. Stakeholders - External

- Donors;
- Patients;
- Doctors;
- Support Foundations;
- Blood centers;
- Laboratories;
- Students;
- Researchers;
- Non-governmental organization (NGOs) and the like;
- Press;
- Society.

4.3. QMS SCOPE

The scope of REDOME's Quality Management System is developed and applied based on the international standards defined by the World Marrow Donor Association (WMDA, 2020) for unrelated hematopoietic stem cell donor registries, as well as ISO 9001:2015 - Quality Management Systems - Requirements, covering all planning, organization and control activities conducted by REDOME's internal departments:

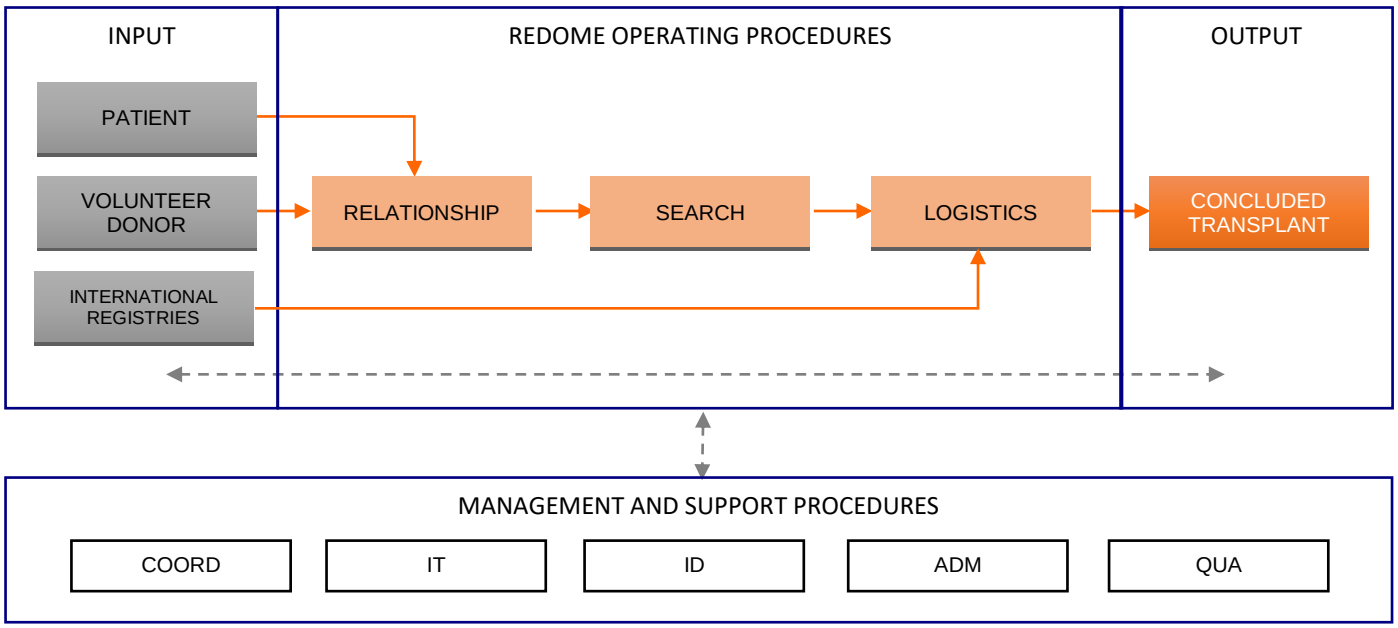
- **Relationship**: Donor care, medical support, post-transplant communication; public relations;

- **Compatible donor selection and identification (Donor Search)**: Selection of unrelated donors or umbilical cord units for transplantation, based on technical criteria for matching;
- **Logistics of donors, samples and cell products for transplantation:** Transporting donors to collection centers, monitoring their clinical evaluation stages for the collection of cells for transplantation (*work up*), importing and shipping cell products for transplantation.

In addition to those above, the following support processes are also represented:

- **Information Technology** (IT): Systems Development, Help Desk and Data Science;
- **Institutional Development** (ID): Finances, New Business and International Relations;
- **Administrative Advice**;
- **Quality Advice**.

The sequence and interactions between these procedures are defined and shown in FIGURE 1.



Key

Service flow

Information flow

COORD – REDOME Technical coordinators

IT – Information Technology

ID – Institutional Development

ADM – Administrative

QUA – Quality

FIGURE 1 – Macro Flow of REDOME Processes.

Source: Internal development.

4.4. QMS PROCESSES

The criteria, methods and information considered necessary to ensure the operability, procedural monitoring, control and effectiveness of all service activities performed within the scope of REDOME, are divided into Institutional Policies (IP), Administrative Standards (AS), Administrative Manuals (AM), and Service Instructions (SI), aiming to:

- Ensure that all teams are fully trained;

- Allow the performance of audits to ensure that Quality Management Systems comply with the specified requirements;
- Ensure that the needs of the stakeholders are met.

REDOME's documentation structure is established in ADMINISTRATIVE STANDARD No. 000.5980.101 - DOCUMENT AND RECORDS CONTROL. A hierarchy divided into levels is obeyed, as shown in FIGURE 2.

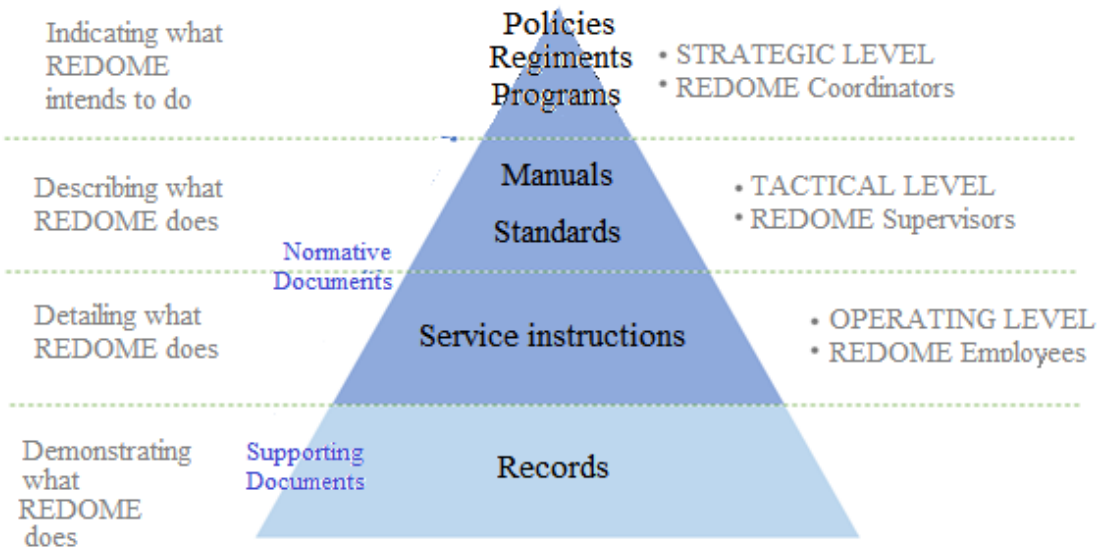


FIGURE 2 - REDOME Documentation Hierarchy.

Source: Prepared based on ISO 9001:2015 and INCA Administrative Standard - Document Development and Maintenance - No. 300.2020.001

- **Institutional Policy – IP**: Document containing REDOME's strategic actions. Its objective is to define general guidelines for planning, organizing, coordinating, executing and assessing every activity and process developed by REDOME. Policies must be consistent with ethical limits, data security and the values shared by REDOME.

- **Internal Regulation – IR**: Internal document that establishes a set of rules to regulate REDOME operations. It must contain the hierarchical levels, respective duties and relationships between the parties involved (*stakeholders*). It must also be in line with the applicable legislation.
- **Program – PR**: Document that establishes actions and initiatives to be developed to address a certain topic or meet an objective.
- **Manual – MA**: Explanatory document that describes, directs and provides guidelines on how things should be done, handled and used. It has an educational nature and can focus on REDOME's internal or external audience, such as professionals from transplant and collection centers, blood centers and laboratories.
- **Administrative Norm – AN / Technical Norm – TN**: Document that provided for the regulation and operation of administrative or technical processes within the general scope of REDOME.
- **Service Instruction – SI**: Document in which REDOME details the internal processes of each sector (“what” is done and “how” is it done). Each SI is intended to standardize different processes and guide all those involved in the internal scope of their execution.
- **Records**: Records can be kept physically or electronically. These aim to present results or provide evidence of different activities, that is, supporting documents intended to objectively demonstrate those activities were performed as established in other REDOME documents (IP; IR; PR; MA; AN; TN; SI). Examples of records include: forms, lists, check lists, scripts, minutes, action plans and reports.

5. LEADERSHIP

5.1. LEADERSHIP AND COMMITMENT

5.1.1. Generalities

The REDOME Coordination Board is committed to the development, implementation and continuous improvement of the QMS; for this purpose, it must ensure:

a) Accountability for the effectiveness and transparency of the QMS;
b) The establishment of quality policies and objectives for the QMS, in line with the framework and the strategic direction of REDOME and INCA;
c) The integration of QMS requirements in REDOME processes;
d) The promotion and use of a procedural approach and risk mindset;
e) The availability of the necessary resources for the QMS;
f) Clear communications about the importance of effective quality management and compliance with QMS requirements;
g) The achievement of the intended results established by the QMS;
h) The engagement and support of the people, in order to contribute to the effectiveness of the QMS;
i) The constant promotion of improvements;
j) The support of other relevant management roles.

5.1.2. Customer Focus

The REDOME Coordination Board is committed to all stakeholders, especially REDOME's volunteer donors, who represent its main “client”.

Leadership and commitment are shown through the description of instructions for each field, with the purpose of standardizing all processes and monitoring their development, through performance indicators and periodic meetings with supervisors, as well as critical analysis meetings.

The REDOME Coordination Board ensures that the relevant statutory and regulatory requirements are understood by the team, and consistently met.

Action plans are prepared, whenever necessary, in order to address risks and opportunities, aiming to promote compliance and provide excellent services to volunteer donors (REDOME Mission).

5.2. QUALITY POLICY

REDOME's Quality Policy is currently being defined. An official definition will be discussed and recorded in the minutes of the corresponding meeting, according to ADMINISTRATIVE STANDARD No. 000.5980.105 - CRITICAL ANALYSIS.

Once it is officially defined, the policy will be documented and disclosed internally through email and training sessions, with a view to ensuring it is understood and applied by employees; also, it will be disclosed externally through the REDOME website, so that it is known by everyone.

This is an outline of REDOME's Quality Policy:

“REDOME aims to promote integrated actions to serve volunteer donors and comply with current legislation, in pursuit of quality, competence, ethics, transparency and cooperation, under principles of continuous improvement.”

5.3. ROLES, DUTIES AND ORGANIZATIONAL AUTHORITIES

The powers and responsibilities of those roles relevant to REDOME processes are assigned through the description of duties stated in the Service Instructions and Administrative Rules. These Instructions were prepared by their sector teams and reviewed by a procedural supervisor, who critically reviewed the document for its adequacy, accuracy and compliance with REDOME's policies and guidelines. All QMS documents were validated and approved by the REDOME Coordination Board.

All REDOME employees were informed via email and/or newsletter about the release of these documents. Policies, manuals and other terms are disclosed through REDOME's platforms, information systems and/or website. When necessary, training sessions are carried out with the concerned parties; training developments and attendance are both recorded for control purposes.

The specification of responsibilities and publication of documents are established in ADMINISTRATIVE STANDARD No. 000.5980.101 - DOCUMENT AND RECORDS CONTROL.

The organizational structure of REDOME is defined according to the following organizational chart (FIGURE 3):

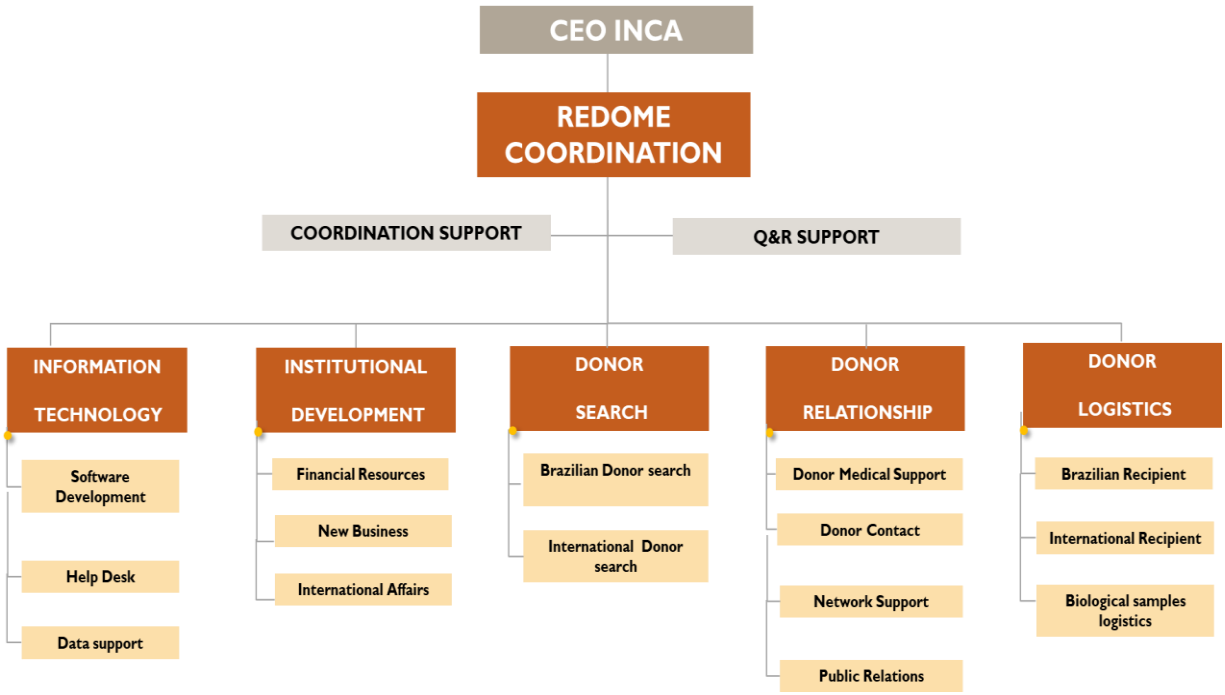


FIGURE 3 - REDOME Organizational Chart.

Source: REDOME Strategic Planning.

6. PLANNING

6.1. ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES

REDOME, through periodic meetings on strategic planning, data protection and quality, seeks to understand the external and internal scenario in which it is inserted; whenever necessary, actions are discussed, planned and taken to minimize risks and seek appropriate opportunities for the potential impact on the compliance of the services provided.

Sectoral indicators are presented and assessed for their performance at periodic supervision meetings with REDOME coordinators and advisors. Each supervisor presents the results obtained in their field, evaluates changes and receives suggestions, which contribute to the achievement of objectives and improvement of results.

Periodic meetings are described in ADMINISTRATIVE STANDARD No. 000.5980.105 - CRITICAL ANALYSIS. Issues identified as contingencies for the performance of REDOME activities are monitored and analyzed by the supervision and coordination teams. Document No. 000.5980.102 - CONTINGENCY PLAN details this procedure.

REDOME also has a Quality Nucleus (QN), composed of a multisectoral team of REDOME employees (at least one from each sector), the objective of which is to plan, implement, organize and monitor REDOME QMS activities. The members of this Quality Nucleus are responsible for multiplying and training other members of their sectoral teams. The QN meets periodically, according to the need or project in progress, and has a person in charge, considered a representative of the coordination board for matters related to the REDOME QMS.

All these actions aim to: ensure that the QMS achieves its results; monitor the actions defined in previous meetings; increase desirable effects; prevent or reduce undesirable effects; and foster improvements.

6.2. QUALITY GOALS

REDOME's quality goals are currently being defined. An official definition will be discussed and recorded in the minutes of the corresponding meeting, according to ADMINISTRATIVE STANDARD No. 000.5980.105 - CRITICAL ANALYSIS.

Once they are officially defined, these goals will be documented and disseminated internally through email and training sessions, in order to ensure that they are understood and applied by employees; also, they will be disclosed externally through the REDOME website, so that they are known by everyone.

This is an outline of REDOME's Quality goals:

- Stakeholder satisfaction - internal and external;
- Continuous improvement of operational and technological processes;
- Transparency with stakeholders.

6.3. CHANGE PLANNING

Changes that may affect REDOME and QMS processes are discussed in advance, with the fields involved, analyzing their impacts, and redefining flows, if necessary.

This considers: the purpose of any changes and their potential consequences; the integrity of the QMS; the availability of resources; and the allocation or reallocation of powers and responsibilities.

7. SUPPORT

7.1. RESOURCES

7.1.1. Generalities

REDOME ensures the provision of the necessary resources for the establishment, implementation, maintenance and continuous improvement of the QMS.

Restricted resources or resources outside REDOME's internal capabilities are procured by INCA, or through support foundations, depending on the nature of the contract.

OUR FINANCIAL AND BUDGET POLICY (Nº 000.5980.001) establishes the principles, limits, responsibilities, timeframes and procedures related to the budgeting and financial management of REDOME.

7.1.2. Personnel and Skills

The REDOME Coordination Board and field supervisors ensure that all employees have the necessary competence, in terms of knowledge and skills, to fulfill all requirements relevant to their positions.

An Administrative Standard is being developed to describe the duties and competencies necessary for the performance of each REDOME position/function, as well as the corresponding academic background, experience and specific knowledge.

REDOME maintains an internal quality consultancy system, focused on the effective implementation of the QMS, process control and training.

7.1.2.1. Consultation with Experts

Considering the complexity of all technical aspects surrounding its procedures, REDOME keeps in touch with academic and research entities, as well as specialized societies, by means of research and collaboration projects and working groups.

Accordingly, whenever it is necessary to clarify possible issues in the field of histocompatibility, the Search team consults the specialist members of ABHI (Brazilian Association of Histocompatibility), whether through email or at the telephone. This consultation is recorded in our dedicated system for search activities, SISMATCH, jointly with the progress of the patient or donor.

Clinical matters related to donors and patients can be discussed with INCA specialists or representatives of SBTMO (Brazilian Society for Bone Marrow Transplantation and Cell Therapy).

7.1.3. Infrastructure

REDOME has the physical infrastructure, information and communication technology necessary to run and manage its work procedures, maintaining the effectiveness of the QMS and the scope of compliance of the services provided, as described below:

- Room in the INCA building, the expansion of which is being planned;
- Computers and Laptops;
- INCA's Institutional email (@inca.gov.br);
- Software / platforms (SISMATCH / REDOMEWEB / REDOMENET / EMDIS);
- Document and non-compliance control software (Qualyteam);
- Project management software (JIRA);
- Its own website (http://redome.inca.gov.br);
- Chatbot (software that exchanges messages simulating a human conversation);
- Corporate cell phones, telephone extensions and Audible Response Unit (electronic assistance).

7.1.4. Environment for Process Operations

REDOME provides and maintains a suitable environment for the conductions of its processes, aiming to ensure compliance in all services provided, through onsite or remote work (teleworking).

REDOME values the following principles: equity, transparency, division of responsibilities and the right to privacy.

Currently, REDOME employees work in a hybrid way, that is, they alternate working days at the office and working remotely (teleworking) throughout the week.

7.1.5. Organizational Knowledge

Knowledge regarding REDOME processes is determined through Service Instructions (SI), Administrative Standards (AS), Administrative Manuals (AM), and Institutional Policies (IP), which describe work flows and activities.

Each supervision follows the regulations incumbent upon it. Whenever new regulations emerge, stakeholders are informed and, if relevant, internal or external training sessions are carried out.

7.2. AWARENESS AND COMMUNICATION

Through communications, lectures and training, REDOME keeps its employees informed about the QMS, strategies, institutional policies, data security and regulations.

REDOME has employees responsible for communication - internal, external, national and international, as well as public relations, focusing on effective communication with all stakeholders.

Our communications are further detailed in the following documents: 000.5980.004 COMMUNICATION POLICY and 000.5980.100 COMMUNICATION WITH THE REDOME NETWORK.

7.3. DOCUMENTED INFORMATION

REDOME defines as documented information, all SI, AN, AM, IP, and other records, whether internal requirements, WMDA or ISO 9001.

The entire process of creating, updating and controlling documents is established in ADMINISTRATIVE STANDARD No. 000.5980.101 -

DOCUMENT AND RECORDS CONTROL, available and accessible to all employees through the online document control system: DOC Qualyteam. All REDOME employees are registered and have access (with password) to this system.

8. OPERATION

8.1. OPERATIONAL PLANNING AND CONTROL

REDOME plans, implements and controls the processes necessary to meet the requirements of its stakeholders, and seeks to achieve compliance with the services provided in a manner consistent with the requirements of the QMS.

REDOME's operational activities are carried out by a team of employees assigned to the National Cancer Institute (INCA) in Rio de Janeiro; these activities, aimed at serving volunteer donors and patients, remain under the direct management of INCA, and can be summarized as follows:

- Maintaining a unified registry containing information of all volunteer donors and patients applying for unrelated hematopoietic stem cell transplantations;
- Selecting and identifying compatible donors for Brazilian patients referred to unrelated hematopoietic stem cell transplantation, which includes requesting laboratory and clinical procedures from international registries;
- Logistics of biological samples and volunteer donors, for the purpose of collecting cell products for transplantation.

The set of Service Instructions (SI) establishes specific conditions for performing REDOME's operational services. Other documented information used by REDOME are: Administrative Norms (AN), Administrative Manuals (AM), and Institutional Policies (IP).

The outputs of these processes are evaluated through the monitoring of indicators, management of non-compliances, controls and sectorial updates of the processes, contingency management and periodic meetings with supervisors and the Quality Center. If any deviation is identified, analyses, action plans and monitoring activities are carried out by the person in charge.

8.2. REQUIREMENTS FOR THE PROVISION OF SERVICES

8.2.1. Communication with the Customer

REDOME's communication management is shared by the Technical Coordination and employees from the different fields involved, who work for the constant improvement of our communication actions, identifying problems and proposing solutions.

REDOME develops and promotes policies, regulations and manuals that enable the instrumentation of different audiences, guaranteeing access to the necessary information for patients and volunteer donors for the purpose of transplantation of unrelated hematopoietic stem cells.

These communication channels are available:

- Website: http://redome.inca.gov.br ;
- Email: redome@inca.gov.br ;
- Chatbot on the website;
- Application (for donors);
- Hotline: (21) 3207-4700. REDOME has a hotline to clarify any doubts, through automated answers, or through human assistance, carried out by a duly trained employee;
- Ombudsman: REDOME provides a channel for sending complaints, doubts or suggestions through the INCA Ombudsman service:
  - Email: ouvidoria.geral@inca.gov.br
  - Telephones: (21) 3207-1399 / 3207-1420/ 3207-1613

- Message form: https://www.inca.gov.br/ouvidoria#formul%C3%A1rio

Our communications are further detailed in these documents: 000.5980.004 COMMUNICATION POLICY and 000.5980.100 COMMUNICATION WITH THE REDOME NETWORK. Document No. 000.5980.102 CONTINGENCY PLAN describes the contingencies for the communication channels made available.

8.2.2. Requirements Related to the Provision of Services

REDOME is part of the National Transplant Policy of the General Committee of the National Transplant System (CGSNT) under the Ministry of Health (Laws No. 9,434 and No. 10,211/2001), based on principles such as free donations, beneficence towards recipients and non-maleficence towards living donors, subject to the technical coordination and management of the National Cancer Institute (INCA).

These are statutory and regulatory requirements applicable to REDOME's activities (full references at the end of this Manual):

- LAW No. 9,434, of February 4, 1997;
- LAW No. 10,211, of March 23, 2001;
- LAW No. 13,709, of August 14, 2018 .
- Ordinance 685 of June 16, 2021;
- Ordinance 1229 of June 15, 2021;
- Consolidation Ordinance No. 4, of September 28, 2017;
- Ordinance No. 2,600, of October 21, 2009.

8.2.3. Critical Analysis of Requirements Related to the Provision of Services

In order to verify the relevance, adequacy and effectiveness of all provided services, as well as the QMS, the REDOME Coordination Board holds periodic meetings with supervisors, and plans to hold biannual meetings for critical analysis.

Operational aspects and requirements related to REDOME's services, indicators and projects are discussed. The decisions and actions defined through this review must be associated with opportunities for improvement, including adjustments to regulatory and WMDA standards, any need for QMS changes, and resource requirements.

REDOME has established and maintains a procedure for its coordinators to carry out critical analyses: ADMINISTRATIVE STANDARD – No. 000.5980.105 CRITICAL ANALYSIS.

8.2.4. Changes in the Requirements for the Provision of Services

When there is any change in the services provided by REDOME, as required by legislation or the competent bodies, stakeholders are informed by email, at meetings, or on the REDOME website, according to the scope of the parties involved.

8.3. DESIGN AND DEVELOPMENT OF SERVICES

REDOME projects are monitored and followed up through a project management tool (JIRA). They are also reviewed, analyzed and evaluated in periodic supervision meetings, and, if relevant, in Critical Analysis meetings (ADMINISTRATIVE STANDARD No. 000.5980.105 - ANALYSIS CRITICAL), in order to support decision-making and ensure the improvement of REDOME's operational, strategic and quality processes.

8.4. CONTROLLING PROCESSES, PRODUCTS AND SERVICES PROVIDED EXTERNALLY

REDOME promotes standardization and guidance throughout its entire network of national and international partners, including bone marrow donor registries from around the world, national and international regulatory organizations (ADMINISTRATIVE STANDARD No. 000.5980.100 - COMMUNICATION WITH THE REDOME NETWORK).

REDOME seeks to guide product and service suppliers on best practices in their relationship with REDOME. The Supplier Relationship Manual (Nº 000.5980.305) contains topics such as receipt and delivery of products and services, responsibility in the provision of services, penalties, confidentiality, supplier evaluation and communication channel.

REDOME has established a procedure to control the accreditation of Histocompatibility and Immunogenetics Laboratories, Transplant Centers and Blood Centers (ADMINISTRATIVE STANDARD No. 000.5980.103 - ACCREDITATION CONTROL).

In order to standardize all services provided and guide its partners, REDOME has the following Manuals:

- 000.5980.300 BLOOD CENTERS MANUAL: the purpose of this manual is to advise blood centers in relation to services, records and requests for the collection of blood samples from Volunteer Bone marrow donors for confirmatory testing (CT), in order to provide guidance on how the requests must be conducted.
- 000.5980.301 HISTOCOMPATIBILITY LABORATORIES MANUAL: The purpose of this manual is to advise histocompatibility laboratories on how to perform the HLA typing of patients and Volunteer Bone marrow donors and sending these results through REDOME's information technology systems.

- 000.5980.302 COLLECTION CENTERS MANUAL: The purpose of this manual is to provide information and guidance on best practices throughout the stages of medical evaluations, laboratory tests, collection of hematopoietic progenitor cells (HPC) for transplantation, transport of biological products and follow-up of volunteer donors after collection.
- 000.5980.303 INTERNATIONAL REGISTRIES MANUAL: The purpose of this manual is to briefly explain the most important aspects of the donor selection and testing process, the collection and logistics of hematopoietic stem cells, our privacy policy and the disclosure of donors registered in REDOME to international registries.
- 000.5980.304 TRANSPLANTATION CENTERS MANUAL: The purpose of this manual is to provide information and guidance on good practices in the stages of filling out the patient register and prescribing the collection of cell products for transplantation, in order to guarantee the best care for patients awaiting an unrelated donor hematopoietic stem cell transplant.
- 000.5980.306 GUIDELINES FOR TRANSPORTING HPC: The purpose of this manual is to guide the proper transportation of Hematopoietic Progenitor Cells (HPC).

8.5. PERFORMANCE OF SERVICES

8.5.1. Service Performance Control

The services performed by REDOME are carried out in accordance with regulatory and statutory requirements, as per topic 8.2.2. herein.

REDOME has adequate infrastructure and people designated and competent to develop the services provided, as described in items 7.1.2 and 7.1.3. above.

REDOME's critical activities are described in Service Instructions (SI), which establish specific conditions for performing REDOME's operational services, as well as process flows, information systems, controls and records used (attached to each SI).

REDOME's internal departments control the performance of services by monitoring indicators. REDOME indicators (both strategic and operational) are reviewed, analyzed and evaluated at periodic supervision meetings and Critical Analysis meetings, in order to support decision-making and ensure the improvement of REDOME's operational, strategic and quality processes.

REDOME has a specific non-compliance management software. If any deviation is identified, analyzes, action plans and monitoring are carried out by the person in charge (ADMINISTRATIVE STANDARD No. 000.5980.104 - NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS).

8.5.2. Identification and traceability

The methods used for the identification and traceability of services are established in the Service Instructions, and are operationalized by the use of information systems: SISMATCH / REDOMEWEB / REDOMENET / QUALYTEAM / JIRA.

Records are tracked through the systems by which they are operated, or in conjunction with other records used (Ex.: Forms and email). The systems themselves keep records of all operations performed on them.

Our IT POLICY (Nº 000.5980.000) establishes a set of procedures and responsibilities concerning the use of IT resources (equipment, systems, applications, software), to be met by all REDOME employees and service providers.

8.5.3. Property Owned by Customers

By “customer property”, we mean all personal data, as well as examination and medical reports. REDOME works to guarantee the privacy of all users of its computerized systems, patients and donors, and makes sure that all information made available within the scope of the process of identifying compatible donors for allogeneic transplantation respects the privacy of patients and donors, in accordance with the General Data Protection Law (LGPD) - LAW No. 13,709, OF AUGUST 14, 2018.

REDOME establishes, in its documents, all principles, responsibilities and procedures to protect and safeguard such information:

- 000.5980.002 PRIVACY POLICY: This document aims to establish the principles, limits, responsibilities, and procedures related to the confidentiality and protection of REDOME data, and is intended for all employees, direct users of the REDOME network (blood centers, histocompatibility and transplant centers), public servants from INCA and the Ministry of Health, donors and patients treated by REDOME, health professionals, and society in general.
- 000.5980.003 COMPATIBLE DONOR SELECTION AND IDENTIFICATION POLICY: This document aims to establish the principles, responsibilities and procedures relating to the selection and identification of compatible donors for the purpose of unrelated hematopoietic stem cell transplantations.
- 000.5980.005 DONOR PROTECTION POLICY: This document aims to establish the principles, responsibilities and procedures

related to the protection of REDOME volunteer donors in the stages of registration, compatibility assessment and collection of hematopoietic progenitor cells (HPC) for unrelated transplants.

8.5.4. Preservation

The handling, identification, storage, transmission and protection of records referring to services provided are duly established, in order to guarantee that their delivery took place in accordance with all requirements.

8.5.5. Follow-up Activity

REDOME guarantees all the necessary support to donors before, during and after the collection of cells for transplantation, according to regulatory and WMDA definitions.

Descriptions of these procedures are contained in the Logistics and Customer Service Instructions, especially in SI: 000.5980.402 RECIPIENT HEALTH INFORMATION AND DISCLOSURE and 000.5980.410 DONOR FOLLOW UP.

8.5.6. Change Control

When necessary, changes are planned (topic 6.3.), communicated to interested parties (topic 8.2.4.), and controlled through action plans generated in periodic supervision meetings or critical analysis held by the Coordination Board (ADMINISTRATIVE STANDARD No. 000.5980.105 - CRITICAL ANALYSIS). When relevant, these changes are controlled through a project management tool (topic 8.3. of this Manual).

8.6. RELEASE OF SERVICES

The SI establish specific conditions for the release of the services provided by REDOME.

Evidence of compliance and traceability is documented in the information systems: SISMATCH / REDOMEWEB / REDOMENET / QUALYTEAM / JIRA.

8.7. CONTROL OF NON-COMPLIANT OUTPUTS

REDOME ensures that all operations that do not comply with the established requirements are identified, controlled and informed to the parties involved. ADMINISTRATIVE STANDARD No. 000.5980.104 - NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS establishes the appropriate treatment for non-compliances observed in the activities that make up the process of providing REDOME services.

REDOME has a specific non-compliance management software (TOOLS Qualyteam), which documents the description of every non-compliance and any action taken in response to it, identifies the authority deciding on this action, and files the evidence of the process.

9. PERFORMANCE EVALUATION

9.1. MONITORING, MEASUREMENT, ANALYSIS AND EVALUATION

9.1.1. Generalities

REDOME carries out the monitoring, measurement, analysis and evaluation of its processes through performance indicators. They are listed in the indicator management map, which states: indicator names, fields, purposes, formulas, data sources, measurement units, periodicity, targets, people in charge, and stakeholders.

Records of REDOME processes are kept, so, in the event planned results are not achieved, adjustments and corrective actions are taken, as appropriate.

When the results of indicators are determined and any inconsistency that can be opened in a Non-Compliance Record (NCR) is identified, the case must be described and analyzed according to ADMINISTRATIVE STANDARD No. 000.5980.104 – NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS, ensuring that actions are taken and implemented.

9.1.2. Customer Satisfaction

Complaints received by the service, logistics and search departments, whenever possible, will be analyzed and resolved at the operational level or, in the most critical cases, by the REDOME Coordination Board. REDOME also monitors donor satisfaction through complaints registered with the INCA Ombudsman. When relevant, a Non-Compliance Record (NCR) is opened, according to ADMINISTRATIVE STANDARD No. 000.5980.104 - NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS.

An Administrative Standard is being developed with a focus on addressing customer complaints and a donor satisfaction survey.

9.1.3. Analysis and Evaluation

REDOME analyzes and assesses data and information collected through monitoring and measurements at the following meetings:

- Periodic meetings between coordinators, supervisors and staff;
- Indicator analysis meetings;
- Strategic planning meetings;

- Project monitoring meetings;
- Data protection meetings and contingency plans.

The results of these analyzes are used to assess: compliance of services provided, donor satisfaction, effectiveness of the implemented planning, effectiveness of actions taken to address risks and opportunities, performance, and the need for improvements in the QMS.

9.2. INTERNAL AUDIT

An Administrative Standard focusing on internal audit is under development. The planning and implementation of this audit program will be defined, including frequency, methods, responsibilities and requirements.

9.3. CRITICAL ANALYSIS BY THE COORDINATION BOARD

9.3.1. Generalities

REDOME's coordinators, supervisors and advisors critically analyze the QMS every six months to ensure its continued adequacy, sufficiency, effectiveness and alignment with REDOME's strategic direction.

The complete critical analysis procedure is described in ADMINISTRATIVE STANDARD No. 000.5980.105 - CRITICAL ANALYSIS.

9.3.2. Critical Analysis Input

Critical analysis is planned and carried out taking into account:

- The status of those actions arising from previous critical analyses;
- Changes in external and internal issues that are relevant;
- Changes in current legislation or WMDA recommendations, and their impact on REDOME's operation;

- Information on the performance and effectiveness of the quality management system;
- Definition of goals, objectives and action plans to improve the quality management system;
- Non-compliances, as well related corrective and preventive actions;
- Indicator monitoring results;
- Results of audits (internal and external) or inspections;
- Adequacy of policies, standards, manuals and instructions for operational processes;
- The sufficiency of financial and human resources;
- The effectiveness of actions taken to address risks and opportunities;
- Opportunities for improvement.

9.3.3. Critical Analysis Outputs

Critical analysis outputs include decisions and actions pertaining to:

- Opportunities for improvement, including adjustments to regulatory standards in current legislation and the WMDA;
- Any need to change the quality management system;
- Need for financial or human resources.

In case it is necessary to open a Non-Compliance Record, this must be duly signaled in the minutes of the corresponding meeting. The procedure for opening this RNC is described in ADMINISTRATIVE STANDARD No. 000.5980.104 - NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS.

Critical analyzes are recorded in meeting minutes and filed by quality advisors.

10. IMPROVEMENT

10.1. GENERALITIES

Opportunities for improvement are discussed, selected and planned in periodic meetings between coordinators, supervisors and advisors, and in critical analysis meetings. The following aspects are addressed in these meetings:

- Operational and service improvements;
- Improvements to meet stakeholder needs and expectations;
- Improvements in operational and strategic indicators;
- Improvements in the QMS;
- Improvements aimed at regulatory standards of current legislation and the WMDA.

Whenever relevant, improvements can be added to the project portfolio for monitoring and control purposes, through a specific software (JIRA).

Improving measures are evidenced in action plans, the minutes of meetings and/or a specific software.

10.2. NON-COMPLIANCE AND CORRECTIVE ACTION

Non-compliances are detected through:

- Feedback from donors, including complaints;
- Feedback from REDOME employees;
- Feedback from REDOME partners, such as International Registries, Blood Centers, Collection Centers and Transplant Centers;
- Monitoring of REDOME's Performance and Operational Indicators;
- Monitoring the work routine of REDOME coordinators and supervisors;

- Audits (internal and external) or inspections;
- REDOME Critical Analysis Meetings;
- The INCA Ombudsman.

Non-compliances are recorded in the TOOLS Qualyteam system. After its registration, a tool is selected to identify the root cause of any non-compliance: Five Whys, Ishikawa Diagram, and others. Then, an action plan to eliminate the cause(s) of non-compliance (actual or potential) is established, taking into account the intensity and potential risks of non-compliance.

The registered non-compliances are followed up until the final solution, that is, until the corrective or preventive actions carried out are evaluated and considered effective.

ADMINISTRATIVE STANDARD No. 000.5980.104 - NON-COMPLIANCE, CORRECTIVE AND PREVENTIVE ACTION RECORDS establishes the appropriate treatment for non-compliances.

10.3. CONTINUOUS IMPROVEMENT

REDOME continually seeks to improve the adequacy, sufficiency and effectiveness of the services provided and the QMS, through periodic meetings, analysis of indicators and data, corrective and preventive actions, and critical analysis.

References

BRAZIL _ Ministry of Health. **Ordinance 685 of June 16, 2021**. Available at: https://bvsms.saude.gov.br/bvs/saudelegis/Saes/2021/prt0685_18_06_2021.html

BRAZIL. Ministry of Health. **Ordinance 1229 of June 15, 2021**. Available at: https://brasilsus.com.br/wp-content/uploads/2021/06/portaria1229.pdf

BRAZIL _ Ministry of Health. **Consolidation Ordinance No. 4**, of September 28, 2017. Available at: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2017/prc0004_03_10_2017.html

BRAZIL. Ministry of Health. **ORDINANCE No. 2,600**, OF OCTOBER 21, 2009. Approves the Technical Regulation of the National Transplant System. DF: 2009. Available at: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2009/prt2600_21_10_2009.html

BRAZIL. Presidential Office. Chief of Staff. **LAW No. 9,434, OF FEBRUARY 4, 1997.** Provides for the removal of organs, tissues and parts of the human body for the purpose of transplantation and treatment and other provisions. DF: 1997. Available at: http://www.planalto.gov.br/ccivil_03/leis/l9434.htm

BRAZIL. Presidential Office. Chief of Staff. **LAW No. 10,211, OF MARCH 23, 2001.** Amends provisions of Law No. 9,434, of February 4, 1997, which "provides for the removal of organs, tissues and parts of the human body for the purpose of transplantation and treatment." DF: 2001. Available in: http://www.planalto.gov.br/ccivil_03/leis/leis_2001/l10211.htm

BRAZIL. Presidential Office. General Secretariat. Undersecretariat for Legal Affairs. **LAW No. 13,709, of August 14, 2018 :** General Personal Data Protection Law (LGPD). 2018. Available at: http://www.planalto.gov.br/ccivil_03/_ato2015-2018/2018/lei/l13709.htm

HLA. Nomenclature for Factors of the HLA System. Available at: http://hla.alleles.org/nomenclature/index.html

ISO. International Organization for Standardization. **ISO 9000:2015**. Geneva Geneva , Switzerland : ISO, 2015. Available at: https://www.iso.org/obp/ui/#iso:std:iso:9000:ed-4:v1:en

_____**ISO 9001:2015**. Geneva, Switzerland: ISO, 2015. Available at: https://www.iso.org/obp/ui/#iso:std:iso:9001:ed-5:v1:en

WMDA. World Marrow Donor Association. **International Standards for Unrelated Hematopoietic Stem Cell Donor Registries** . 2020. Available at: https://wmda.info/wp-content/uploads/2021/01/WMDA-2020-Standards_AM1_Jan2021-1.pdf

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