ARTHA BEAUTY RESEARCH INNOVATION

MA.QA.EN.001 - MANAGEMENT SYSTEM MANUAL FROM ARTHA RESEARCH

Revision 02 - November 2023

1. INTRODUCTION

The Management System Manual formalizes the Quality and Operational Excellence System of **ARTHA RESEARCH** and contains its fundamental elements in order to inform and serve as a basis for taking actions and decisions, aiming to achieve and maintain the quality standard of products and services recommended by the organization. This Manual was prepared following the requirements of **ISO 9001 - Quality Management System version 2015,** describing how the **ARTHA RESEARCH** specifically meets each requirement.

2. THE IMPORTANCE OF ISO 9001

The decision to follow **ISO 9001** is a strategic decision of the organization. **ISO 9001** must go far beyond a certification for the company, it serves to guide processes and ensure **a better customer experience and satisfaction**, since this is the reason for the company to exist and must be the north of all its actions. The standard is not intended to oblige and/or standardize the management systems of all organizations. Note that throughout the texts of the requirements below, the standard always contains the word “shall”, but does not determine “how”. The organization itself should determine “how”.

3. APPROACH BASED ON RISK MANAGEMENT

ISO 9001:2015 brings as a novelty the importance of Risk Management. **Risk is the effect on uncertainty, that is, the positive or negative deviation related to the expected result of a process, project, or any other objective. Thus, risk management is a process that aims to identify, analyze and plan actions in order to avoid unwanted situations or leverage opportunities.** In quality management it is very common to discuss the **“why”** something happened. When we change this perspective and start to apply risk management, the search becomes to identify the **“what ifs?”** of the processes: "**what if that happens? What if it doesn't? What if something goes wrong? What if it works?”** in order to manage them with the possibility of preventing threats to the business and making the most of opportunities.

4. CONTEXT OF THE ORGANIZATION

4.1. UNDERSTANDING THE ORGANIZATION AND ITS BACKGROUND

ARTHA RESEARCH identifies as Internal Issues those issues related to values, culture, training and knowledge, socioeconomic profile, diversity, risk perception of employees and stakeholders involved with the organization, in addition to the processes necessary for conducting Clinical Studies.

As for External Issues, **ARTHA RESEARCH** considers the movement of the business market, the technological and political scenario, public health context, legal issues, globalization and the international, national and regional market.

This exercise of determination/identification of internal and external issues with impacts on the company's business **ARTHA RESEARCH** are reviewed, monitored and analyzed during the Critical Analysis meetings of the Senior Management programs to occur **annually.**

Evidence of the analysis of Internal and External Issues must be verified at the exits of the Critical Analysis meetings of the Senior Management.

The first Critical Review meeting is scheduled for **December 2022.**

4.2. UNDERSTANDING THE NEEDS AND EXPECTATIONS OF STAKEHOLDERS

ARTHA RESEARCH identifies as Interested Parties those described in the table below with their respective requirements.

This stakeholder identification exercise for **ARTHA RESEARCH** is reviewed, monitored and analyzed during Senior Management Critical Analysis meetings programs to occur **annually.**

Evidence of Stakeholder reviews should be verified at the outputs of Senior Management Critical Review meetings.

The first Critical Review meeting is scheduled for **December 2022.**

If new Parts and Requirements are identified, this Manual will be revised in order to keep Table 1 below updated.

Table 1: Mapping of Stakeholders, their Requirements and Risks

No.	Stakeholders	Stakeholder Requirements	Risk
1	Shareholders	Profitability	Lack of Financial Return as expected
2	Clients	Comply with the BPC Requirements and other applicable Clinical Research legislation throughout the Clinical Studies	Deviations listed during the conduct of Clinical Studies
		Comply with applicable legal requirements, including labor, health and safety, environment and ethics issues	Deviations listed during the conduct of Clinical Studies
		Comply with the Specific Requirements of Clinical Studies in accordance with the Study Proposal and Protocol	Deviations listed during the conduct of Clinical Studies
		Development of New Methodologies to accompany the technological development of the market	Loss of Customers to Competition
		Competitive prices on the market	Loss of Customers to Competition
3	Suppliers	Ethics during business transactions, including payment as agreed between the parties	Delay in payments resulting from lack of communication between the parties for a clear definition of conditions and requirements
4	Ethics Committees	Comply with the BPC Requirements and other applicable Clinical Research legislation throughout the Clinical Studies, with respect to Research Participants.	Ethics-related deviations with Research Participants while conducting Clinical Trials and managing Participant data (LGPD)
5	Research Participants	Compliance with applicable legislation, including the requirements for the Protection of your Data according to GDPR.	Deviations related to Data Protection of Participants
		Compliance with the requirements established in the Research Protocol and Consent Terms specific to each Clinical Study	Deviations listed during the conduct of Clinical Studies
6	Regulatory Body	Comply with Applicable Requirements throughout the entire operation, including installations (Easy)	Deviations related to compliance with legal requirements, including access and periodic assessment of legislation applicable to the business.
7	Employees	Comply with legal requirements, including labor requirements	Deviations related to compliance with legal requirements, including access to and periodic assessment of applicable laws.
		Adequate working conditions, including ergonomics, rest, adequate training and a career plan	Employee Turnover
8	Neighborhood	Comply with applicable legal requirements, including issues of health and safety, environment, ethics, among others applicable	Deviations related to compliance with legal requirements, including access to and periodic assessment of applicable laws.

4.3. DETERMINING THE SCOPE OF THE QUALITY MANAGEMENT SYSTEM

The organization determined the limits and applicability of the QMS, as stated in the Management System Policy.

The scope of services of ARTHA RESEARCH includes the Management of Clinical Studies Technical Documents; Preparation, Conduct and Monitoring of Clinical Studies and Consumer Tests; Scientific Consulting; Data Management and Analysis; Preparation of Technical Reports and Training.

All sections of the ISO 9001 standard: 2015 are applicable to the planning and execution of the services of **ARTHA RESEARCH.**

4.4. QMS AND ITS PROCESSES

ARTHA RESEARCH establishes and encourages the process approach advocated by ISO 9001, defining and managing:

- **Process inputs, controls and outputs to ensure that desired results are achieved, and**
- **Interfaces between processes to ensure that system effectiveness is achieved.**

In this context, what we call "Voice of the Customer" is the main guideline for the planning and organization of activities and actions, where customer needs are defined through the **preparation of Specific Clinical Studies Protocols** where items related to monitoring methods, measurements and specific indicators for each project are described, in addition to authorities and responsibilities and risks and opportunities.

The specific responsibilities and the sequence of interaction of the main processes are also described in Operating Procedures (PR) and Work Instructions (IT).

Authorities and Responsibilities are clearly defined both generically and specifically for each Clinical Trial to ensure they are communicated periodically and are clear to all employees and third parties. In addition, business risks and opportunities are identified regularly, following the process-based approach.

5. LEADERSHIP

5.1. LEADERSHIP AND COMMITMENT

The top management of **ARTHA RESEARCH** provides evidence of your commitment to the development, implementation and improvement of our QMS in a very tangible way:

- **Taking responsibility for the effectiveness of the quality management system;**
- **Designating a highly qualified professional as responsible for the QMS;**
- **Establishing a solid Policy** in accordance with the Values, Mission and Vision of the Founders and essential for the establishment of the desired organizational culture.
- **Ensuring that this Policy is understood, implemented and maintained at all levels of the organization through effective communication, training for employee awareness, events for discussions and Branstorming, regular critical analysis, unfolding of individual and collective GOALS AND GOALS and activities evaluation and feedback.**
- **Ensuring that all department leaders** demonstrate their commitment to QMS development and improvement through:
  a) Provision of necessary resources;
  b) Establishment of objectives and goals;
  c) Implementation of the approach/thinking based on risk management;
  d) Involvement and participation of employees and third parties in the management of the QMS;
  e) Management that seeks continuous improvement of its processes.
- **Keeping the proper focus on the customer through the following activities** :
  a) Management of complaints and other customer feedback, with periodic monitoring in order to identify opportunities for improvement;
  b) Through constant contact and building a partnership relationship with customers and third parties;
  c) Constant mapping of risks and opportunities.

5.2. POLICY

The Policy of **ARTHA RESEARCH** indicates the organization's management commitment and focuses on what is important in order to guide employees and other interested parties towards the company's Vision, Mission and Values. Various topics are included in the Policies, such as:

a) Commitment to meet the Legal Requirements and Other Applicable Requirements;

b) Commitment to ensuring Data Protection;

c) Ethics in business and in the execution of services;

d) Quality of Services with a Search for Continuous Improvement;

e) Respect and Protection of the Environment;

f) Respect and Protection of the health and safety of Employees and Third Parties;

g) Repudiation of Gender Inequality, any form of Discrimination, Child and Slave Labor;

h) Ensure Participation and Consultation of employees and third parties;

i) Social Responsibility with the community.

The Policy of **ARTHA RESEARCH** is reviewed at regular intervals, **at least during the Senior Management Critical Analysis exercises held annually,** in order to guarantee its continuous adequacy to the company's strategy and objectives.

We ensure that the Policy is communicated and understood at all levels of the organization through regular training, awareness-raising and auditing activities.

In addition, the policy is also available to Interested Parties on our Website, Social Networks and Strategic Points of our Facilities.

5.3. ORGANIZATIONAL ROLES, RESPONSIBILITIES, AND AUTHORITIES

Authorities and Responsibilities in **ARTHA RESEARCH** are documented and communicated at the stage of hiring each employee through the preparation of complete and detailed profiles for each position / function (***Job Description***). The ***Job Description*** guides the recruitment and selection process in order to ensure that the hiring of new employees is as assertive as possible. In addition, it allows the communication of Role, Responsibility and Authority to be already defined and to be communicated at a first opportunity to employees. In addition, a specific document called ***Matrix of Authorities and Responsibilities*** are prepared by Project/Clinical Study, in order to designate and guide employees in their specific functions in the Projects.

In both documents it is clear the responsibilities and authorities of the employees responsible for:

a) Ensure that the management system complies with the requirements of ISO 9001:2015;
b) Ensuring that processes are being delivered in accordance with the intended outputs;
c) Report QMS performance and improvement opportunities
d) Ensuring that processes are delivering the expected result
e) Promote customer satisfaction
f) Ensure QMS integrity and communicate when system changes occur.

6. PLANNING

6.1. ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES

ARTHA RESEARCH determines the risks and opportunities that need to be addressed to ensure that the QMS can achieve the intended results and lead to improvements, as well as avoid undesirable effects through periodic updating of the ***BCP – Business Continuity Plan. The risks and opportunities mapped are present within the BCP, with the respective Severity and Probability assessments in order to allow their Prioritization.***

According to the priority of each risk/opportunity, preventive actions and contingency actions must be established. The BCP is reviewed at regular intervals, **at least during the Senior Management Critical Analysis exercises held annually,** in order to ensure its proper review.

In addition to the BCP **ARTHA RESEARCH,** assess the Risks and Opportunities of each Project/Clinical Study at risk analysis reunions.

This analysis of specific risks and opportunities for each Clinical Study begins in the Proposal phase, the Feasibility stage, and can be updated during the conduct of the Studies themselves.

Among the advantages of using software for this management of risks/opportunities, we can point out: (a) visibility of risks and priorities; (b) ease of establishing and creating actions for designated employees in order to mitigate risks; (c) share specific assessments with other stakeholders, making the process more efficient and enabling the use of data during critical analysis and for taking action.

6.2. QUALITY GOALS AND PLANNING TO ACHIEVE THEM

ARTHA RESEARCH determines specific Objectives and Goals for each department/process through the use of tools called **BALANCED SCORECARDS.** The use of SCORECARDS brings benefits due to the ease of visualization, allowing for more effective communication. With SCORECARDS it is possible to visualize the performance goals for each **KPI (*Key Performance Indicator*) - Performance Indicator. The goals are organized into bands as follows:**

a) **Expert**

b) **Advanced**

c) **Beginner**

d) **Not accepted**

The division into bands with specific colors allows for the quick identification of problem areas that require immediate action.

Along with the SCORECARD, an orientation guide is kept with the definitions on the construction of each KPI, including the motivation to measure what was established, the calculation memories to guarantee reproducibility, responsible and periodicity of measurement.

All employees must know the respective SCORECARDS applicable to their processes.

SCORECARDS are reviewed at regular intervals, **at least during the Senior Management Critical Analysis exercises held annually,** in order to ensure adequate updating of objectives and goals and allow for new planning and action strategies.

6.3. CHANGE PLANNING

ARTHA RESEARCH pays special attention to change management as it understands that unplanned changes increase the risks involved in the business and can be opportunities for improvement. In this way, constant awareness is carried out with employees and leaders, especially in order to raise awareness of the importance of prior communication of changes.

The organization also implements periodic sessions of ***Standing Talk, Branstorming rounds,*** among other activities that encourage communication between areas and analysis of changes when applicable. Changes considered significant must be robustly analyzed through a specific form, in order to allow for their proper planning, considering the purpose of the change, its potential consequences, the availability of resources and the maintenance of the integrity of the Quality Management System.

7. SUPPORT

7.1. RESOURCES

PEOPLE - **ARTHA RESEARCH** determines and provides the necessary resources for the establishment and maintenance of its Quality Management System and the success of its operations, considering the capacities and restrictions of its internal resources and the need to subcontract third parties as Investigators of its Clinical Studies and other suppliers, planning and executing a robust and judicious management on them.

Further details on the management of Competencies, Skills, Education and Experience of employees are described in the internal procedure **PR.RH.001 – Procedure for Competency Management and Employee Training.**

Details on and management of Third Parties are described in the internal procedure **PR.AD.001 – Procedure for the Management of Suppliers and Purchases.**

INFRASTRUCTURE - **ARTHA RESEARCH** provides an adequate infrastructure for the effective and optimized functioning of its processes, to achieve compliance of its services and to ensure the preservation, integrity and confidentiality of Investigational Products, Data of Research Participants, Collaborators and other interested parties and Documents of Clinical Studies , including Customer property when applicable, ensuring the application of best practices in terms of Information Security. Further details on Information Security are described in the internal procedure **PR.IT.001 – Procedure for IT Management and Information Security.** **Furthermore, ARTHA has a restrict control access, that beginning at the building entry, being monitored 24 hours 7 days a week. The facilities are kept closed with keys, under management of delegated employees. It is the reception responsibility to ensure that only allowed people and external subjects enters Artha, together with Artha's employees.**

ENVIRONMENT - It is the policy of **ARTHA RESEARCH** ensure an appropriate, healthy and happy environment for its employees, establishing various campaigns and activities in the search for feedback and improvements in the environment. It is important to note that Clinical Studies often have specific requirements for temperature and humidity, which are described in the Research Protocols. In addition, an Infrastructure assessment is carried out regularly by the Research Ethics Committee, which assesses the conditions under which the Studies will be carried out.

MONITORING AND MEASUREMENT - **ARTHA RESEARCH** establishes monitoring and measurement processes during several critical points of its processes, among them we can highlight the use of Equipment/Measuring Instruments, which range from Precision Scales to specific equipment used in the conduct of Clinical Studies. All equipment is **properly calibrated** and have specific requirements for **Maintenance and Verification,** with the prior determination of **Acceptance Criteria**. Further details on Equipment are described in the internal procedure **PR.EQ.001 – Equipment Management Procedure.**

ORGANIZATIONAL KNOWLEDGE - **ARTHA RESEARCH** establishes the necessary knowledge for the execution of its activities when it prepares the profile of each position/position (Job Description). In addition, it is the company's policy to encourage training and exchanges between employees, always delegating replacements for each position/function, ensuring that knowledge is multiplied and maintained in the company. It is also ARTHA's policy to ensure that knowledge is converted and transmitted to procedures and videos in order to enable more effective internal training and capacity building. The company encourages ***Updates Rounds*** , such as updating sections on scientific topics as a constant source of knowledge for the team. Further details on the management of Competencies and Training of employees are described in the internal procedure **PR.RH.001 – Procedure for Competency Management and Employee Training.**

7.2. COMPETENCE

ARTHA RESEARCH determines the skills needed for each position/function through the Job Description - profile of each position/position, where the job requirements are described **Education + Experiences + Trainings + Required Skills.**

In this way, new employees are already evaluated during the selection process, comparing their evidence with the necessary requirements for the position/function, in order to guarantee an assertive hiring.

If it is found that the candidate or even employee does not meet the necessary requirements for their position/function, it is necessary to prepare an action plan to direct and guide the candidate/employee to acquire the item that is out of date**. Evidence of Education + Experiences + Trainings + Necessary Skills must be maintained for each employee.** Further details on the management of Competencies, Skills, Education and Experience of employees are described in the internal procedure PR.RH.001 – Procedure for Competency Management and Employee Training.

7.3. AWARENESS RAISING

ARTHA RESEARCH establishes a robust training program for employee awareness, which begins in the induction phase where new employees are trained and evaluated during the first 4 weeks of work. Still in the induction phase, employees are trained in the general items of the Quality System, including Policy, Manual, Objectives and Goals, Procedures and other documents that are fundamental for a basic understanding of the company's management system.

ARTHA guarantees that all employees are aware of how their actions and activities compromise and impact the company's services and the consequences of their actions.

A General Training Matrix is kept up to date with all training, critical analysis and periodicity of refresher training. This matrix is alive and frequently updated.

7.4. COMMUNICATION

ARTHA RESEARCH establishes a program of internal and external communication to Stakeholders as described in Table 2 below.

Table 2: Internal and External Communication to Stakeholders

Stakeholders	Communication			
	what to communicate	How to communicate	who should communicate	When should you communicate
Shareholders	Performance Results	Presentations / Meetings	CEO - Executive Director	Quarterly
Clients	(1) New Methodologies (2) News about ARTHA (3) Commercial Prospecting - Values (4) Values (5) Advances, Documentation and Results of Clinical Studies (6) Satisfaction Surveys	(1) Email, Newsletter, Meetings, Website, Social Media (2) Newsletter and Social Media (3) Virtual and In-person Meetings (4) Email - default proposal (5) Presentations and Reports (6) Form in Google Forms	(1) CEO - Director (2) Recruitment Leader (3) CEO (4) CEO - Director (5) Operational Leader (6) Quality Leader	(1) When applicable (2) At least **1 newsletter per semester** (3) According to the business plan (4) **Within 3 business days of customer order** (5) According to the Research Protocol (6) At the end of each Clinical Study
Suppliers	(1) Needs / Orders (2) ARTHA Internal Requirements 3 Payment Conditions (4) Feedbacks - evaluation results	(1) Email (2) Purchase Order, Contracts (when applicable) and *Due Diligence* (3) Purchase Order and Contracts (when applicable) (4) Email and at the time of second party audits and through the audit report.	(1) Buyer (2) Administrative Leader (3) Administrative Leader (4) Quality Leader	(1) Before purchase/service (2) Before purchase/service (3) Before purchase/service (4) After purchase/service according to the item of supply - **at least 1 time a year** - or after a second party audit (second audit plan).
Ethics Committee	(1) Clinical Studies Submission Dossier (2) Clinical Studies Amendments (3) Interim and Final Clinical Study Report (4) EAG	(1) Email and Brazil Platform (2) Email and Brazil Platform (3) Email and Brazil Platform (4) Email and Brazil Platform	(1) Operational Leader (2) Operational Leader (3) Operational Leader (4) Operational Leader	(1) Before the start of the Clinical Study (2) When applicable (3) At the end of the Clinical Study **or every 6 months from the start of the Study (intermediate)** (4) **Within 7 business days of reporting the event.**

Research Participants	(1) Registration in the database (2) Rights under the LGPD and Consent to Use and Protection of Data (3) Open Research Announcements (4) Scheduling for visits (5) Research Participant Rights under the GCPs and Specific Consent for each Clinical Trial (6) Clinical Study Requirements (7) Medical results and assessments in accordance with the Research Protocol (8) Follow-up during the course of the Study with reminder of visits and requirements to be met (9) Reimbursement (10) Maintenance of data in the ARTHA database according to LGPD (11) Satisfaction Survey and feedback activities	(1) Google Forms link present on Social Media, Website or forwarded through WhatsApp (2) Google Forms link present on Social Media, Website or forwarded via WhatsApp (3) Social Media, Website (4) WhatsApp, Mobile, Email or Website (5) ICF and verbal explanation in a private room (6) ICF and verbal explanation in a private room (7) Verbal (8) WhatsApp, Mobile, Email or Website (9) Pix (10) Google Forms link sent by WhatsApp or Email (11) Google Forms link sent by WhatsApp or Email	(1) Recruitment Team (2) Recruitment Team (3) Recruitment Team (4) Recruitment Team (5) Clinical Team - according to the Matrix of Authorities and Responsibilities (6) Clinical Team - according to the Matrix of Authorities and Responsibilities (7) Investigators (8) Recruitment Team (9) Financial Leader (10) Recruitment Team (11) Recruitment Team	(1) Prior to registration of the Participant in the ARTHA database (2) Prior to registration of the Participant in the ARTHA database (3) When a new survey is opened - until participant recruitment is complete (4) When a new survey is opened - until participant recruitment is complete - before each visit (5) Prior to participant involvement in the Clinical Study (6) Prior to participant involvement in the Clinical Study and throughout the course of the Clinical Study (7) During the course of the Clinical Study (8) During the course of the Clinical Study (9) According to Research Protocol (10) **Every 3 years of the month of registration at the bank** (11) After carrying out the Research considered critical
Regulatory Bodies	certificates of regularity	Specific websites of regulatory bodies / E-mail	Administrative Leader	If applicable.
Employee	(1) Internal Policies, Manuals and Procedures (2) Labor/legal requirements (3) Calendars (4) Training Matrix (5) Evaluation results - feedback (6) Satisfaction survey (7) Critical analyzes and lessons learned (8) Results of internal audits (9) Clinical Study Requirements	(1) Presentations, Training Material and Documents made available in the Qualiex Software (2) HR Documents (3) Excel (4) Excel (5) Individual meetings, Assessment tests (6) Form through Google Forms (7) Presentations - Meetings (8) Presentations - Meetings - Audit Report (9) Clinical Study PREVIEW and KOM Events	(1) Quality and Department Leader (2) ADM/HR Leader (3) ADM/HR Leader (4) Quality Leader (5) Quality and Department Leader (6) Quality Leader (7) Quality Leader and Executive Board (8) Quality Leader (9) Operational and Quality Leader	(1) Induction Program and in accordance with the Training Matrix (2) Induction Program (3) Annually and with each update (4) Monthly (5) Annually (6) Annually (7) Monthly (summarized) / Annually (year result) (8) According to the audit program (9) Before the start of each clinical study.
Neighborhood	(1) Any problem with neighborhood impact (2) Evacuation drills and other safety and environmental campaigns	(1) Meeting with the condominium manager / Flyer / Social Media (2) Flyer	(1) Administrative and Quality Leader (2) Administrative and Quality Leader	(1) When applicable (2) When applicable

7.5. DOCUMENTED INFORMATION

The Quality Management System of **ARTHA RESEARCH** includes documented information required by ISO 9001: 2015 and any documentation required by the company to carry out its activities and to ensure the effectiveness of its QMS.

The QMS documentation includes:

a) Management System Policy
b) Management System Manual
c) OPERATIONAL PROCEDURES
d) Work Instructions
e) Forms and Templates
f) Documents of external origin and others

it's politics from the company encourage alternative, modern and technological forms of documentation, bringing videos and virtual materials whenever possible in order to attract collaborators and be an alternative source of knowledge.

In order to guarantee the efficiency of the documentation management process, ARTHA chose to use the **Qualiex Software > DOCS Module** for all document handling. Among the advantages of using the software, we can mention: (a) version control; (b) unavailability of obsolete versions; (c) automatic header and footer generation; (d) strict permissions control; (e) document validation circle; (f) automatic generation of master lists; (g) read confirmation and (h) print management.

Company policy is NO PRINTING. Management System documents must be accessed solely and exclusively through the software platform. Specific Clinical Studies documents have printing authorization for designated collaborators.

Further details on Document management are described in the internal procedure PR.QA.001 – Documentation and Archiving Management Procedure.

8. OPERATION

8.1. OPERATIONAL PLANNING AND CONTROL

ARTHA RESEARCH determines requirements for the performance of its services and products and criteria for verification of processes and acceptance of results, however, most of the criteria and requirements are established by the clients themselves and are expressed in the Research Protocols of Clinical Studies.

During the preparation of the proposal and the Feasibility stage, a Critical Analysis is carried out with the leadership of the main departments, which analyzes the risks involved in each Project, the methodologies to be applied and the need for resources to be used to ensure the success of the Project and service. to the Customer Requirements defined in the Protocol.

All planning begins in the Feasibility phase, as well as the definition of controls that will be applied, even if the proposal is not converted into a Project.

Once converted into a Project, the Operational Manager together with the Operational leader is responsible for preparing the Clinical Study planning and verifying all necessary requirements including methodologies, application of clinical scales, application of Reproducibility and Repeatability protocols, availability of equipment , new and refresher training, changes in facilities and outsourcing of professionals, if necessary.

8.2. REQUIREMENTS FOR PRODUCTS AND SERVICES

COMMUNICATION WITH THE CUSTOMER - **ARTHA RESEARCH** determines requirements for communicating with the client, as described in Table 2 above. The idea is to fully customize customer service, centralizing communication in order to seek excellence. In addition, technical validations are performed to verify that customer requirements have been met as described in the internal procedure. **PR.PC.005 – Internal Validations.**

- ✓ **At the end of each Clinical Study, an NPS Satisfaction Survey (*Net Promoter Score*) is sent to Clients, using a form on Google Forms. This methodology has the advantage of being just 1 question: "On a scale of 0 to 10, how likely are you to refer our Clinical Research company in the cosmetics area to a collection, relative and friend?". Through the result it is possible to make a series of analyzes and comparisons with other organizations.**

Still in the scenario of communication with the customer, it is important to note that complaints must be treated as Critical Nonconformities, and must be treated immediately as described in the internal procedure PR.QA.002 – Management of Audits, Nonconformities and Action Plans.

Finally, all external customer documentation, including their data, is extremely confidential and must be handled with care. Contingency actions in cases of deviations are established in the ***BCP – Business Continuity Plan.***

DETERMINATION AND CRITICAL ANALYSIS OF REQUIREMENTS - As previously mentioned **ARTHA RESEARCH** determines and critically analyzes the requirements requested by the client and other requirements during the critical analysis phase of the proposal, Feasibility, where a multidisciplinary team meets to analyze the risks and opportunities of each Project. During these analyzes all requirements must be analyzed, including legal requirements and requirements not expressed by the customer. Some critical points below:

- ✓ **Evidence of Feasibility is held internally.**
- ✓ **No Clinical Trial can start without a Commercial Proposal signed by both parties – ARTHA + CLIENT.**
- ✓ **It is also important to note that changes in the scope of service defined between ARTHA and the Clients, after signing the Proposals, must be registered in the respective form: Out of Scope Notification and Approval and/or Protocol Amendment Notification and Approval. No changes or additions may be made without the prior approval of the Sponsor and ARTHA's Senior Management.**
- ✓ **Significant Amendments to the Protocol must be submitted for prior consideration by the Ethics Committee and it must be analyzed whether a new consent form for Research Participants should be applied.**
- ✓ **A review of the legal requirements applicable to the scope of ARTHA's services is carried out quarterly, in order to verify if there has been any update of norms/legislation or even the publication of a new norm/legislation. This activity is under the responsibility of the Quality area, which must provide feedback on the topic during the Feasibility activities.**
- ✓ Further details on proposal management and customer feedback are described in the internal procedure **PR.CO.001 - Commercial Management: Focus on the Client.**

8.3. DESIGN AND DEVELOPMENT OF PRODUCTS AND SERVICES

Inside **ARTHA RESEARCH** there is a Research & Development branch of activity focused on the development of new methodologies to propose new Research Protocols to Clients. Currently, this area is under the responsibility of the Operational leader, although an exclusive department for R&D is planned in the future.

However, it should be noted that ARTHA's scope of services is extremely technical and all Clinical Studies are considered new projects because they are different Investigational Products with different applications and methodologies. Therefore, even in a “standard” Clinical Trials such as Acceptability in Use with Dermatological Assessment for example, it is necessary to apply all the requirements of this item 8.3.

PROJECT PLANNING AND DEVELOPMENT – The planning stages begin in the proposal phase, varying according to the scope of the Project. Planning usually comprises the following steps:

a) Evaluation of the Customer's Order with analysis of risks and opportunities, evaluation of methodologies, clinical scales, recruitment and applicable requirements, analysis of the availability of equipment and facilities, among other items - **Feasibility stage, performed by a multidisciplinary team.**

b) Preparation of a preliminary plan.

c)Preparation of the Commercial Proposal and delivery to the customer within 72 hours - **according to procedure PR.CO.001 - Commercial Management: Customer Focus.**

d) Acceptance of the Proposal by the Client.

e) Determination of the Team involved in the Study, including selection of Investigators - **according to procedure PR.PC.007 – Reproducibility and Repeatability of Clinical Scales, Selection and Training of Investigators.**

f) Preparation of the final Clinical Study Plan, including:

- ✓ **Preparation of Clinical Study documentation;**
- ✓ **Submission of the dossier for ethics evaluation to the CEP (Ethics Committee);**
- ✓ **Dates for team training;**
- ✓ **Dates of Visits;**
- ✓ **Date of sending the Results to the Clients;**
- ✓ **Periods for Internal Validations.**

g) Preparation of Study Documentation and Sponsor Approval.

h) Preparation of TMF (Trial Master File) - **according to procedure PR.PC.001 – TMF management.**

i) Dossier Submission for CEP Evaluation - **according to procedure PR.PC.003 - Regulatory Management: Submission to the CEP/CONEP System.**

j) Clinical Trial Start Meeting – KOM (***Kick off Meeting***), with the entire team involved in the Clinical Study for training.

k)Preparation of Investigative Products - **according to procedure PR.PI.001 – Management of Investigational Products.**

l) Preparation of Facilities

m) Equipment Check - **according to procedure PR.EQ.001 - Equipment Management.**

n) Conducting Visits.

o) Periodic meetings and customer feedback.

p) Documentation validation - **according to procedure PR.PC.005 – Internal Validations.**

q) Data input - **according to procedure PR.QA.004 – Data Entry Management.**

r) Statistical analysis - **as defined in the Research Protocol.**

s)Analysis of Results and preparation of the Final Report - **as defined in the Research Protocol.**

t) Organization of customer deliverables and sharing - **as defined in the Research Protocol.**

u) Customer Approval.

v) Satisfaction survey - **according to procedure PR.CO.001 - Commercial Management: Customer Focus.**

w) Evaluation of the team involved in the Study (when applicable)

x)Archiving of Clinical Study Documentation - **according to procedure PR.QA.001 – Documentation and Archiving Management.**

y) Lessons Learned Meeting.

INPUTS – Inputs may vary according to the scope of the Project. They usually comprise:

- ✓ **Customer request;**
- ✓ **Analysis of legal and other applicable requirements;**
- ✓ **Analysis of the Research Participants Database**
- ✓ **Registration of Participants and Term of Consent for the Use of Data (LGPD)** - **according to MA.QA.002 – ARTHA RESEARCH Data Protection Manual.**
- ✓ **Term of consent of the Participant in the Clinical Study** - **according to procedure PR.PC.002 - Application of TCLE (Free and Informed Consent Term).**

CONTROLS – Controls may vary according to the scope of the Project. They usually comprise:

- ✓ **Internal Validations;**
- ✓ **Double data entry (*double data entry*);**
- ✓ **SCORECARD Panel with specific KPIs by Clinical Studies;**
- ✓ **Adverse Event Management - according to procedure PR.PI.004 – EA Management.**
- ✓ **Deviation Management.**

OUTPUTS – Outputs may vary according to the scope of the Project. They usually comprise:

- ✓ **Final Clinical Study Report;**
- ✓ **Photos of the Participants – protecting their identity;**
- ✓ **Data collected from Participants - protecting their identity;**
- ✓ **Statistical analyses.**

CHANGES – Changes are previously registered and approved by clients and Senior Management through Extra Scope and Research Protocol Amendments forms. Unplanned changes are managed according to item 6.3.

8.4. CONTROL OF PROCESSES, PRODUCTS AND SERVICES PROVIDED EXTERNALLY

ARTHA RESEARCH determines the necessary requirements for externally provided products and services through a robust process of:

(a) Supplier registration with application form ***Due diligence;***

(b) Classification of suppliers according to their Criticality and impact on the company's business;

(c) Definition of evaluation criteria by supply categories;

(d) Selection Assessment;

(e) Communication of Requirements;

(f) Acquisition Evaluation;

(g) Periodic Requalifications;

(h) Second Party Audits;

(i) Feedback to Suppliers.

This entire process aims to establish controls and clear and effective communication with external providers.

In order to guarantee greater control and traceability for this process, ARTHA chose to use the **Qualiex Software > Supply Module** for supplier management.

Further details on supplier management are described in the internal procedure **PR.AD.001 – Management of Suppliers and Purchases.**

Still in this context of external providers, it is important to say that the Investigators assigned to the Clinical Trials can be hired as ARTHA Collaborators or as Critical Providers managed by Clinical Trials. This entire process of selection, training and evaluation of Investigators is extremely critical since the Reproducibility and Repeatability of Clinical Evaluations must be guaranteed, mitigating existing variations between Investigators. In this sense, preliminary validations and refresher training are necessary as described in the internal procedure **PR.PC.007 - Repeatability and Reproducibility of Clinical Scales, Selection and Training of Investigators.**

8.5. PRODUCTION AND SERVICE PROVISION

PRODUCTION CONTROL AND SERVICE PROVISION - **ARTHA RESEARCH** controls Clinical Studies in accordance with customer requirements, Good Clinical Practices, LGPD and other applicable legislation. All controls are determined in the respective Research Protocols and may involve:

- ✓ **Temperature and Humidity Control of the Facilities;**
- ✓ **Traceability of Research Participants;**
- ✓ **Weighing and Labeling of Investigational Products;**
- ✓ **Blinding of Investigational Products;**
- ✓ **Calibration and Verification of Equipment Calibration;**
- ✓ **Monitoring and Measurement of Performance Indicators;**
- ✓ **Internal Validations;**
- ✓ **Data entries by 2 different collaborators;**
- ✓ **Statistical analysis to detect inconsistencies;**
- ✓ **Internal audits, among others.**

IDENTIFICATION, TRACEABILITY AND PRESERVATION - **ARTHA RESEARCH** guarantees the identification and traceability of its products through the use of simple and unique coding, which accompany each customer order from the proposal to the final report of the Clinical Study, as described in the procedures **PR.QA.001 – Documentation and Archiving Management and PR.CO.001 – Commercial Management: Focus on the Client.**

PROPERTIES BELONGING TO CUSTOMERS AND PROVIDERS - **ARTHA RESEARCH** manages all property of customers and external providers through the control of external documents. All these documents are organized and made available within the **Qualiex Software > DOCS Module,** under the responsibility of the Quality area, avoiding the use of obsolete versions, printing and copying of documents. Any deviation related to Third Party Properties, managed by ARTHA, must be reported immediately to the external providers.

POST DELIVERY ACTIVITIES - Within the scope of service of **ARTHA RESEARCH** post-delivery activities are the revisions of the Final Reports arising from requests from Clients / Clinical Trials Sponsors. Revisions are planned and are common, however, the internal validation circle is intended to reduce these reworks as much as possible. In addition, staff should be trained to identify "out of scope" requests that would be reviews arising from new requests by customers.

We can also consider post-delivery activities as those that occur after the end of the Clinical Study, such as managing the retention sample of Investigational products, disposal of Investigational products and documentation management. All these steps are managed in accordance with the respective internal procedures.

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CHANGES – Changes are previously registered and approved by clients and Senior Management through Extra Scope and Research Protocol Amendments forms. Unplanned changes are managed according to item 6.3.

8.6. RELEASE OF PRODUCTS AND SERVICES

The release of products only occurs in **ARTHA RESEARCH** after the end of all internal validation cycles, which include:

- ✓ **Validation of Clinical Study Documents prior to submission for Sponsor approval;**
- ✓ **Validation of the Submission Dossier to the CEP/CONEP System;**
- ✓ **Validation of the TMF (Trial Master File) before the start of the Clinical Study;**
- ✓ **Validation of Clinical Study documentation between visits;**
- ✓ **Validation of Adverse Event (AE) reports;**
- ✓ **Data Entry Validation;**
- ✓ **Validation of the Final Report and other deliverables to the Sponsor;**
- ✓ **Validation of the TMF (Trial Master File) after the Clinical Study.**

Further details are described in the procedure **PR.QA.005 – Internal Validations.**

8.7. CONTROL OF NON-CONFORMING OUTPUTS

All validation steps described above in item 8.6 are essential to ensure that non-conforming items are identified in a timely manner to be corrected. Evidence of corrections made, communication and those responsible are registered within the Qualiex Software > Planos Module, since the dynamics of the process is agile. However, if significant and/or systemic deviations are detected, recurring Non-Conformities must be opened for root cause analysis and a more robust treatment, as described in the procedure **PR.QA.002 – Management of Audits, Non-Conformities and Action Plans.**

It is important to note that within the Clinical Research process, Deviations from the Research Protocol may occur. Deviations are expected and acceptable provided they are communicated to the Sponsor/Customer. For this reason a list of deviations per Clinical Study is maintained and communicated to the Sponsor in the Final Study Report. Significant

deviations must be reported promptly and action to be taken must be verified with Sponsor. These deviations are not converted into NC as they are expected, however it is a good practice to group them into *clusters* and jointly and macro evaluate the deviations that occurred in Clinical Studies during lessons learned meetings as they are a source of improvement opportunities.

9. PERFORMANCE EVALUATION

9.1. MONITORING, MEASUREMENT, ANALYSIS AND EVALUATION

ARTHA RESEARCH determines what should be measured in the following situations:

- **Management system -** Objectives and Goals are defined annually and are broken down into Performance Indicators (KPI), managed through the ***Balanced Scorecard*** as described in item 6.2. Updates of its results are made monthly and disclosed internally to all those involved.
- **Project Performance Indicators -** Scorecard panels are also defined by Project/Clinical Studies according to the criticality of each Study. Simple and low criticality studies do not necessarily need a Scorecard. The results are updated throughout the Clinical Study, with a frequency to be defined and are consolidated and presented during the lessons learned meetings.

The results of both cases are used as Inputs for the monthly management meetings and for the annual Critical Review meetings of Senior Management.

CUSTOMER SATISFACTION - ARTHA RESEARCH monitors the perception of its customers through Satisfaction Surveys in the NPS (Net Promoter Score) format, sent through its own form created within Google Forms, always at the end of the Clinical Studies. Further details are described in the internal procedure **PR.CO.001 - Commercial Management: Customer Focus.** In addition, any feedback received must be used as a source of opportunities for improvement, whether during a visit to the customer or during monitoring, as well as complaints must be managed according to Non-Conformity.

ANALYSIS AND EVALUATION - ARTHA RESEARCH analyzes and evaluates all monitoring and measurement results in order to detect:

a) Topics with more % deviations;
b) Teams with more difficulty performing;
c) Processes that are not adequate and that must be reviewed;
d) % of customer satisfaction and complaints;

e) % of Clinical Studies completed in accordance with the Research Protocol;

f) % of Clinical Studies completed on time

g) % effectiveness of risk analysis

h) % of satisfaction and efficiency with external providers, among other significant items.

The importance of generating this data is to allow management analysis and action taking aimed at the continuous improvement of processes, services and the management system itself.

9.2. INTERNAL AUDIT

ARTHA RESEARCH establishes a program of annual internal audits in order to verify the compliance of processes and the management system against the requirements of:

a) Standard ISO 9001:2015;

b) Good Clinical Practices;

c) General Data Protection Law;

d) Ethics and Compliance

e) Other applicable legal standards and requirements;

f) Internal Requirements described in the ARTHA Management System documentation such as Policies, Manuals, Procedures and Work Instructions;

g) Customer requirements as described in externally sourced documents;

h) Requirements defined in the Research Protocols.

Although annual, if detected as necessary, this audit frequency can be reduced and adjusted for specific areas and processes considered critical.

In this scenario, at least **2 internal collaborators** are kept trained as auditors. These employees are responsible for auditing the company's areas according to the audit program and internal procedure **PR.QA.002 – Management of Audits, Non-Conformities and Action Plans.** Always paying attention to the rule that the auditor cannot audit his own area. Other requirements regarding internal audits must be consulted in the respective procedure.

9.3. CRITICAL ANALYSIS BY TOP MANAGEMENT

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@lschwenck – 28/11/2023	@bnahum – 29/11/2023	@tpontes - 30/11/2023

ARTHA RESEARCH critically analyzes its Management System during the conduct of **Annual Critical Analysis Meetings of Senior Management** under the responsibility of the Quality leader and with the participation of the other leaders of the organization. For this activity, a management presentation is prepared containing all the inputs and evidence necessary for the analysis and Branstorming of the team.

INPUTS - All inputs determined by ISO 9001 must appear during this management review, including, but not limited to:

a) Status Update of outputs from previous Critical Review Meetings (when applicable);

b) Review of Internal and External Issues that impact the ARTHA system;

c) Monitoring and Mediation Results, as described in item 9.1.

d) General Assessment of the Objectives and Goals defined for the Management System;

e) General Assessment of Objectives and Goals defined for Clinical Studies;

f) Results and Global Assessment of Non-Conformities managed in the period;

g) Efficacy Assessment of Actions established to address Non-Conformities;

h) Results and Performance of Audits carried out in the period, including internal, supplier and certification (when applicable);

i) Supplier performance evaluation results;

j) Assessment of available resources in the period;

k) Evaluation of the effectiveness of the risk and opportunity monitoring process;

l) Opportunity management assessment.

OUTPUTS – During the meeting, several analyzes and Branstorming are carried out by the team involved. **A preliminary action plan must be completed throughout the meeting in order to record actions arising from these discussions.** The action plan must contain at least the following information:

a) Opportunities for improvement and changes in ARTHA's management system and processes;

b) Specific Resource Needs;

c) Specific actions of the business areas in order to seek continuous improvement of their processes.

At the end of the meeting, the Quality area must consolidate the action plan, communicate it to everyone present at the meeting via email and attach it to the presentation in order to maintain traceability. At the next Critical Review Meeting this action plan must be reviewed and the effectiveness of your actions must be analyzed.

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10. IMPROVEMENTS

10.1. GENERALITIES

It is the policy of **ARTHA RESEARCH** continuously improve its Management System and its Processes.

For this, ARTHA uses a series of tools and methodologies in order to continuously improve its processes, such as:

- ✓ Internal communication between areas through events ***PREVIEW, KOM, STANDING TALK, Branstorming rounds, campaigns*** , among others;
- ✓ Performance analysis through ***Monthly and annual management meetings*** and ***visual management through BALANCED SCORECARDS.***
- ✓ Leadership participation, supervision and accountability by encouraging ***GEMBA WALK*** (leadership in the field accompanying the processes);
- ✓ processes through ***Stream mapping and VSM (Value Stream Mapping)*** in order to eliminate activities that do not add value to the business.
- ✓ Ongoing customer feedback in order to hear the **"voice of the customer"** through a robust business plan.

10.2. NON-COMPLIANCE AND CORRECTIVE ACTION

ARTHA RESEARCH believes that Non-Conformities are powerful tools for continuous improvement and for this reason it encourages the opening and proper management of NCs through training for awareness, awareness and training of its employees, including training for root cause analysis aimed at unfolding assertive actions for the appropriate dealing with the causes of deviations.

The NCs are analyzed individually and are also grouped in order to allow action to be taken to address clusters of greater significance with respect to deviations.

The entire NC management process is managed as described in the internal procedure **PR.QA.002 – Management of Audits, Non-Conformities and Action Plans.**

Aiming at greater control, visibility and traceability in this Non-Conformity management process, ARTHA chose to use the **Qualiex Software > Occurrences Module.**

10.3. CONTINUOUS IMPROVEMENT

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@lschwenck – 28/11/2023	@bnahum – 29/11/2023	@tpontes - 30/11/2023

As mentioned in item 10.1 **ARTHA RESEARCH** continuously improve its Management System and its Processes through a series of analyses, tools and methodologies. This entire process is conducted by highly qualified professionals who seek constant updates of knowledge in order to apply them in ARTHA's business.

ARTHA RESEARCH brings in its origin and culture the philosophies of **LEAN, OPERATIONAL EXCELLENCE and KAIZEN,** infecting all parties involved in the business to improve daily for themselves, for the collective and for the success of the organization.

11. REVISION HISTORY

Version	Date	Comments	Critical Review Analysis
00	April 2022	Initial release	NA
01	June 2022	Removed ISO 9001 text.	NA
02	November 2023	Removed Qualiex Risk and Metrology Module, and aligned the document removing the executive leader funcitons. Acces control was also added to the section 7.1.	Not significant: confirmation review.

12. ATTACHMENTS

Not Applicable

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