CONCEPTUAL MODEL FOR ADEQUACY OF A QUALITY MANAGEMENT SYSTEM ACCREDITED IN ISO 17025 STANDARD TO THE PRINCIPLES OF GOOD LABORATORY PRACTICES AND RISK ASSESSMENT OF NON-COMPLIANCE – A CASE STUDY

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ABSTRACT

The quality control of the laboratories that serve the pharmaceutical industries aims at guaranteeing the quality of the products and services provided. In recent years, due to the new resolutions of the Brazilian Health Regulatory Agency (ANVISA) related to analytical laboratories, two new standards (RDC 301/2019 and RDC 390/2020) have been issued, and these are focused on good practices, restricting the operation to the laboratories that attend to those requirements. Therefore, the only way for the laboratories to be adequate to the Brazilian legislation is by implementing these standards. Thus, the present work aims at creating a model for a hybrid QMS implementation with GLP assistance in a laboratory accredited by the ABNT NBR ISO: IEC 17025 standard, identifying the risks and proposing respective risk responses. In conclusion, the results of implementing the hybrid system and the associated risks of failure are presented and prioritized using AHP. The process on how to provide the possibility of recognition in the GLP requirements (NIT-DICLA-35) by the evaluating body and the company's internationalization is also demonstrated.
Keywords: GPL, ISO/IEC 17025, Integrated Quality Management System, RDC, AHP

1. INTRODUCTION

In a scenario where the market is increasingly competitive, globalized, and demanding, analytical laboratories, which provide testing services for quality control in pharmaceutical products, face constant challenges. One of them is seeking to meet the qualification requirements to become suitable suppliers to the pharmaceutical industries or even maintain its direct competitors. In recent years, there has been an intense update of the National Health Surveillance Agency (ANVISA) to align them with international regulations better. For this, the organization must comply with the new resolutions related to analytical laboratories (RDC 301/2019 and RDC 390/2020), which require these industries to adopt the general guidelines of Good Laboratory and Manufacturing Practices. The new resolutions (RDC 301/2019 and RDC 390/2020) focus on good practices, restricting the performance to laboratories that meet these requirements, even those that meet the ABNT NBR ISO:IEC 17025 standard, previously a priority criterion. Thus, quality control laboratories need to comply with these resolutions for recognition and qualifications, delivering quality analyzes generating credibility and competitiveness in the market. A specific laboratory of a company located in Rio de Janeiro, which operates in the quality control segment, needs to adapt to these resolutions and in this context. A study was conducted in this company to understand and report, through a literature review and scientific and exploratory research, the requirements for adaptation of a hybrid QMS. The studied analytical laboratory had an implemented quality management system based on ISO 17025. This study was necessary to meet these new requirements of the pharmaceutical market and provide the possibility of recognition in the GLP requirements (NIT-DICLA-35) by the evaluating body and the company's internationalization. This hybrid QMS serves as the basis for the

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implementation of a Pharmaceutical Quality System suitable for the automation of processes aimed at meeting Industry 4.0 and aiming at international regulatory demands.

In this competitive scenario, analytical laboratories, which carry out analyses for quality control of pharmaceutical products, need to meet the qualification requirements to become suitable suppliers for the pharmaceutical industries. The National Health Surveillance Agency – ANVISA, demands these industries adopt the general guidelines of Good Laboratory Practices. This brings a practical problem that needs to be solved: How to serve the pharmaceutical market in a quality control laboratory, or how to comply with the various regulations applicable to an analytical laboratory, including RDC 390/2020, recently published by ANVISA? Failure to comply with the various laws applicable to an analytical laboratory, including RDC 390/2020, recently published by ANVISA, can mainly lead to loss of the market against competitors in line with the legislation, as in the qualification process, the contracting company must guarantee the compliance with the requirements of good laboratory practices by the contracted company.

This study aims to create a conceptual model for the implementation of a hybrid QMS with GLP compliance in an analytical laboratory with QMS implemented based on the ABNT NBR ISO: IEC 17025 standard, in order to meet the new requirements of the pharmaceutical market, aiming at increasing the scope of activities, efficiency and effectiveness of processes, as well as providing the possibility of recognition in the GLP requirements (NIT-DICLA-35) by the evaluating body and the internationalization of the company.

None of the researched previous studies presented information on how to create a conceptual model. Some of these researched papers are listed herein in section 2. The study responds to the following important research questions:

Research Question 1: How to serve the pharmaceutical market in a quality control laboratory?

Research Question 2: How to comply with the various laws applicable to an analytical laboratory, including RDC 390/2020, recently published by ANVISA?

Aiming at responding to the research questions, the authors firstly compared the standards ABNT NBR ISO: IEC 17025:2017 - General requirements for the competence of testing and calibration laboratories, to RDC ANVISA 11/2012 - Good Practice Guidelines for Quality Control Laboratories and RDC ANVISA 301/2019 - General Guidelines for Good Medicine Manufacturing Practices, concerning quality control and NIT-DICLA-035 - Principles of Good Laboratory Practice. Secondly, defined actions to adapt the quality management system based on the ABNT NBR ISO: IEC 17025:2017 standard to the requirements of good practices governed by ANVISA. After defining the actions, the authors implemented a self-assessment process to verify the system's suitability for qualification in REBLAS – Brazilian Network of Analytical Laboratories (ANVISA). Finally, the implemented QMS was assessed regarding compliance with NIT-DICLA-035 - Principles of Good Laboratory Practice, with the objective of recognition by the Cgcre (General Coordination of Accreditation) of INMETRO. The paper is structured as follows: Section 2 describes the methodology and previous studies on the conceptual model for implementing a hybrid QMS with GLP compliance. Section 3 presents the discussion, and section 4 the conclusion. In the end, the list of references used in this paper is provided.

2. DESCRIPTION

2.1 Methodology

The case study was conducted following these steps: The steps that were used in this research are presented below to obtain the parameters for a diagnosis of the organization's management, as well as the survey of motivations, benefits, barriers, and difficulties observed by an organization for the adoption of a QMS as a strategic tool. The first step was an analysis of the theoretical framework and updated scientific literature on the implementation of the principles of good laboratory practices, using the keywords: good laboratory

practices, ISO 17025:2017, RDC 512/2021, RDC 301/2019, RDC 390 /2020 and analytical laboratory. The second step was the data collection, and the third was a review of the standards. The fourth was the conduction of a survey, based on standards, to define the requirements of each standard that would be included in a requirements comparison table. The fifth step was preparing the self-assessment checklist to assess the adequacy of the standards in the sixth step. The seventh step was the definition of missing requirements with prioritization with AHP. The last step was implementing actions to meet missing requirements. Fig. 1 shows the flowchart with these steps.

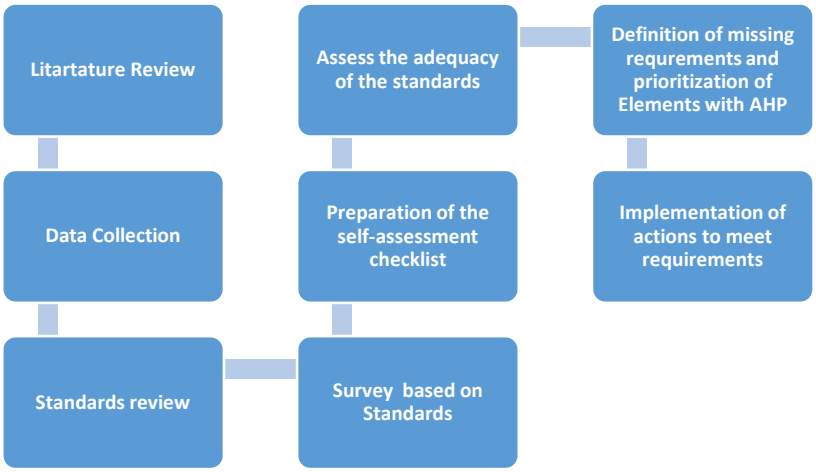

Fig. 1 – Methodology flowchart

2.2 Analytical Laboratories: Brazilian Legislation

The National Health Surveillance Agency (ANVISA) [1] is the regulatory agency for food and medicine in Brazil, being linked to the Ministry of Health (MS). It is responsible for registering and licensing drugs from pharmaceutical laboratories and other companies within the flow of pharmaceutical products in the country. In line with international legislation, ANVISA was accepted in November 2016 as a new regulatory member of the International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. In line with ICH regulations, together with international regulatory agencies such as the U.S. Food and Drug Administration (FDA), European (EMEA, European Medicines Agency), and Canadian (Health Canada) food and drug agency, ANVISA has as mission the protection and promotion of health of the population, by intervening in the health risks arising from the production and use of medicines. There has been an intense update of ANVISA's resolutions in recent years to better align them with international regulations. From 2012 to 2018, the regulation governing the analytical laboratories was RDC 12/2012, which aimed to establish the criteria for qualification of laboratories and their respective tests in REBLAS. RDC 12/2012 required accreditation in one of the following current standards: ABNT NBR ISO/IEC 17025 [2], ABNT NBR ISO/IEC 17043 or recognition according to the Principles of Good Laboratory Practice (GLP) and its complementary documents of the Organization for Economic Cooperation and Development (OECD), or other standards applicable to the accreditation or recognition of laboratories. At the time, the laboratory under study opted for accreditation in the ISO 17025 standard. In 2018, RDC 234/2018 came into force, which provided for the outsourcing of stages of analysis of drug quality control, which defined in Chapter 5 Art. 17 of Annex 1 the requirements that the company should adapt to be qualified for the provision of services, which could be: qualification with REBLAS for contracted tests; compliance with RDC 512/2021; GMP certification, when dealing with a drug or biological product manufacturer; accreditation following the ISO 17025 standard for

contracted tests; or proof of compliance with Good Laboratory Practices, according to internationally recognized guidelines. Thus, the outsourced analytical laboratory to carry out Quality Control activities could choose one of the ways mentioned in Annex 1 to comply with the legislation for qualification by its customers. In this way, the laboratory under study continued to comply with the regulation by complying with accreditation by ISO 17025. RDC 390/2020 was recently published in the Official Gazette of the Union (DOU), which "Establishes criteria, requirements, and procedures for operation, qualification in REBLAS and accreditation of laboratories analytics that perform analyzes on products subject to the sanitary surveillance regime and take other measures." This RDC came into effect in August 2020, with analytical laboratories having until August 2021 to adapt to its requirements.

2.3 Quality Management System applicable to Analytical Laboratories

In order to ensure laboratory quality control, it is essential to adopt management processes that allow those involved to monitor the performance of technical procedures, continually review the methods adopted, and evaluate the results. In a quality management system, all aspects of laboratory operation, including organizational structure, processes, and procedures, must be addressed to ensure [3]. A laboratory performs numerous procedures and processes that need to be precise to guarantee the results' reliability. What is more, these procedures are divided into several steps and performed by different people. Some points are highly critical, such as: carrying out the collection of samples and materials, preparing the samples to be analyzed; discarding the samples; storing and recording the analysis results; report the results to customers [4]. Due to the incredible complexity of this laboratory system, analytical laboratories seek quality systems that can provide services to their customers with the guarantee of quality, confidence, and security in the results [5]. In Brazil, currently, the primary standards used for management and quality assurance for pharmaceutical quality control analytical laboratories are ISO 9001, ISO/IEC 17025, GLP principles, and Anvisa regulations related to good practices - RDC No. 301/2019 and RDC No. 11/2012. requirements

2.4 Good Laboratory Practices

Good Laboratory Practice (GLP) is a quality system relating to the organization and conditions under which laboratory and field studies are planned, performed, monitored, recorded, reported, and archived. The concept of GLP arose along with the concern regarding the validity of results obtained in non-clinical trials. The concepts of BPL mobilized not only the U.S. but the entire world. Due to non-American companies that needed to export or register their products in American lands, they needed to adapt to new practices and disseminate in their countries. In 1978, the GLP principles were developed by the Organization for Economic Cooperation and Development (OECD), using as a reference the principles established by the United States Food and Drug Administration (US-FDA) in 1976 in order to guarantee the quality of the results on the risks associated with chemicals. Becoming formally recommended to be used by countries members in 1981 [6]. The GLP guidelines were written due to the need for better control of the generated data, from planning the studies, documentation of data, and its retention, to the issuance of the final report. It was covering its submission to the competent authorities as well. Such controls would inhibit fraud and contribute to increased care with the study's planning, conduct, and data [7]. The National Health Surveillance Agency (ANVISA) regulates and supervises all areas of health, including the quality control analytical laboratories. Through Resolutions of the Collegiate Board (RDC) No. 11/2012 and 301/2019, ANVISA establishes the current requirements necessary to adopt good laboratory and manufacturing practices. RDC No. 11/2012 filled a regulatory gap, offering guidelines to guide the inspection of analytical laboratories by states and municipalities and the issuance of a Permit or Sanitary License. The standard defines, for example, how the quality policy, infrastructure, environmental conditions, human resources, procedures, and documentation for the laboratories should be, in addition to indicating the need for internal audit, corrective and preventive measures, in order to obtain safe results and traceable (FIOCRUZ, 2021). RDC 301/2019 increased the rigor to the requirements that constitute

the pharmaceutical quality system and the need for the commitment of top management, further developing its proximity to international guidelines. Furthermore, detailing of the requirements is noticeable, making it easier for companies to implement them. The NIT-DICLA-035 standard comprises all stages of a study. First, the study starts with the signature of the study plan (PE), and then the field phase is carried out, then the laboratory phase, and ends the study with the signature of the study report (RE). The Good Laboratory Practice guidelines are geared towards the organization's needs when developing a particular study. These guidelines are notably important concerning the requirements of the technical assessment of the relevance of the proposed methodology. It is also essential concerning the study's objectives, the technical competence of the personnel to carry out the procedures and the content of the report with the details of preparation, execution, and conclusion of the study [8]. Laboratories seeking to operate following Good Laboratory Practices need to follow the requirements of NIT-DICLA-035, where only the basic principles to be followed by any GLP test facility are presented. The standard is included with some other complementary documents are NIT-DICLA 034 – BPL for Field Studies; NIT-DICLA 036 – Study Director Responsibilities; NIT-DICLA 037 – Short Term Studies; NIT-DICLA 038 – Computerized Systems; NIT-DICLA 039 – Sponsor Responsibilities; NIT-DICLA 040 – Suppliers; NIT-DICLA 041 – Quality Assurance and NIT-DICLA 043 – GLP in Multi-Site studies.

2.5 Analytic Hierarchy Process (AHP)

Bhushan and Rai [9] also conducted a noteworthy study about AHP, stating that AHP was developed and extensively studied. It is currently applied for decision-making in several complex scenarios, in which people work together to make decisions and where human perceptions, judgments, and consequences have long-term repercussions. An important study about AHP is the one conducted by Maris et al. [10]. The author stated that multi-criteria programming through Analytic Hierarchy Process is a technique used for decision making in complex environments in which diverse variables or criteria are considered. According to the author, AHP transforms comparisons, often empirical, into numerical values. Wu and Fang [11] proposed a novel approach that combined fuzzy Delphi and Fuzzy AHP for detecting competencies via experts' opinions and questionnaires to create the professional-managerial framework. Cavallo et al. [12] propose applying the Analytic Hierarchy Process for sustainable urban development by focusing on economic, environmental, and social impact. Hnilica et al. [13] studied the use of multiple-criteria decision-making methods for complex assessment of the work environment using AHP. Her contribution defined the need to assess individual pairs of risk factors conscientiously and responsibly in Saaty's matrix. AHP, as an attribute decision-making tool, has become an essential branch of decision-making since then [14]. To Mu and Pereyra-Rojas [15] to analyze the decision utilizing the analytic hierarchy process, one should create a model for the decision, break down the decision into a hierarchy of goals, criteria, and alternatives, derive priorities (weights) for the requirements. The importance of criteria is compared pairwise concerning the aimed objective to derive their weights. This comparison can use data of human choices or judgments as a form of underlying information. Analytic Hierarchy Process (AHP) approach has been used in the management domain to analyze complex situations and make sound decisions [16]. Fayer [17] study described shortcomings in applying the method that usually comes from the decision-maker. The three significant elements of AHP are hierarchy construction, priority analysis, and consistency verification [18]. The Analytic Hierarchy Process remains a popular multi-criteria decision method (Goepel, 2018). The results obtained using the AHP method are influenced by the credibility of information [19]. Thanks to this Method, a reasonable solution can be reached for situations with many solutions in which specific criteria are formed [20]. The consistency of judgments can then be evaluated to ensure a reasonable level of consistency. Kurek et al. [25] described the use of two methodologies: Principal Component Analysis (PCA) and Analytical Hierarchy Process (AHP). An analytical hierarchy process is an effective risk assessment method in which a questionnaire is used to collect experts' responses [21]. For Lin et al. [22], AHP is widely used in group decision-making (GDM). The Analytical Hierarchy Process method is used from the multi-perspective approach [23]. Aghaei et al. [24] claimed that safety risk management is critical for performing in large projects. Sienkiewicz-Małyjurek [26] claims the impact of this risk on the effectiveness of joint activities is still underestimated. The results allow a better understanding of issues of risks. In consequence, they indicate risk symptoms are worth keeping track of to prevent ineffectiveness.

3. DISCUSSION

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The studied company develops technological innovations for products, processes, and services, focusing on the convergence of enabling technologies such as nanotechnology, biotechnology, and communication and information technology. A highly qualified multidisciplinary team with a strong specialization in analytical methods associated with artificial intelligence techniques reduces innovation barriers. It brings academia closer to the market and offers solutions that facilitate decision-making, contributing to the increase in the competitiveness of companies in the global scenario. Its scope of action offers quality control services for APIs, excipients, and medicines, contributing to solid-state monitoring for the Brazilian pharma-chemical and pharmaceutical industries. It currently serves around 70 national pharmaceutical and chemical companies, being the only private company qualified in its scope of operation. In Brazil, currently, the primary standards used for management and quality assurance for pharmaceutical quality control analytical laboratories are ISO 9001, ISO/IEC 17025, GLP principles, and Anvisa regulations related to good practices - RDC No. 301/2019 and RDC No. 11/2012. The comparison between the regulations and standards is shown in Tab.1.

	ISO 9001	**ISO/IEC 17025**	**Principles of BPL**	**Anvisa BPL**	**Anvisa BPF**
Standards to be followed	ABNT NBR ISO 9001:2008	ABNT NBR ISO/IEC 17025:2017	NIT-DICLA-035	RDC nº 11/2012	RDC nº 301/2019
Purpose of the Standard	Quality Management Systems - Requirements	General requirements for competence of testing and calibration laboratories	Principles of Good Laboratory Practice - GLP	Principles and requirements for carrying out analyzes with quality, reliability and safety, in products subject to Sanitary Surveillance	General Good Manufacturing Practice Guidelines for Medicines
Application	Any type of organization	Testing and Calibration Laboratories	Study Laboratories not clinical	Laboratories that perform analysis of products subject to Sanitary Surveillance	Companies that carry out the operations involved in the manufacture of medicines
Quality Assurance	Certification, obtained after an audit carried out by a certifying company, authorized by INMETRO	Accreditation, obtained after an INMETRO audit	Recognition in GLP, obtained after an INMETRO audit	Qualification at REBLAS	Qualification as a supplier to the pharmaceutical industries
Coverage	Management Systm	Technical competence	Technical competence	Technical competence	Technical competence

Tab.1 Comparison between regulations.

The choice of model for quality assurance, standards, and procedures depends on the characteristics of the laboratories and their objectives with this implementation [27]. ABNT NBR ISO 17025, RDC 512/2021, and RDC 301/2019 standards were used to assess the similarities and differences between the two quality management systems mentioned, in addition to a literature search focused on current works with a range of 10 years for the most part. At the end of the verification of the adequacy of the standards, a self-assessment was carried out using the self-assessment checklist. The guidelines recommended both in the RDC's related to Good Laboratory Practices and by ISO/IEC 17025 have as a common objective to guarantee the reliability of the achieved experimental data [28]. In order to understand the main differences in the requirements, a comprehensive matrix was created listing the requirement from the standards.

Tab.2 shows the elements with risk of non-compliance and the requirements to be met to comply with ISO/IEC 17025, RDC 512/2021, RDC 301/2019 or BPL - DIT DICLA 035 to avoid the risk of non-compliance. It is worth highlighting the agreement of some essential requirements. The standards emphasize the importance of the laboratory's defined responsibilities. Employees need to know their role and the importance of being well executed. Together with this, the norms highlight the direct commitment of the leadership. Regardless of the hierarchical level, everyone in the organization must be involved with the management system to achieve the objectives. The requirements also point out that employees need to be trained and trained for the function performed.

Elements with Risk of Non Compliance		**Requirements to be met to comply with from ISO/IEC 17025, RDC 512/2021, RDC 301/2019 or BPL - DIT DICLA 035 to avoid the Risk of Non Compliance**
S1	Organization and Management	Define a study director; Define a quality manager. Define an Archivist Organization and Management Define a quality policy.
S2	Quality System	A Quality Manual or equivalent documentation must be established and must contain a description of the quality management system, including management responsibilities
S3	Personnel	The laboratory must establish a training program appropriate to its current and planned activities
S4	Equipment with Data processing	The laboratory must, concerning computer systems for the input, storage, registration, processing, recovery, update, and data transmission, have: I - computer program (software) documented, verified and validated as to its suitability to use; II-procedure documented and validated to protect
S5	Products and services provided externally	Qualify, through periodic evaluations, suppliers of equipment, materials, reagents, inputs, supplies, and services that affect the quality of the analyses.
S6	Procedure for investigating out-of-specification and out-of-trend results	Procedure for investigating out-of-specification and out-of-trend results Investigation of out-of-spec and out-of-trend results
S7	Data control	Document the master agenda for all study plans, standard operating procedures, and reporting.
S8	File of documents	Define person, procedure, and space to file all documents and test items relevant to the study by defined period.
S9	Biosafety	Have an updated system of biosafety risk management for all activities with agents of risk to human, animal, and environmental health, including waste management, access to personnel who may be exposed to these agents
S10	Materials and reagents	The laboratory must implement adequate procedures for specification, acquisition, receipt, storage, storage, stock control, validity control,

		distribution, and disposal of reagents, supplies, and consumables with the quality required by the analysis, meeting health safety standards human, animal and the Environment. Laboratory reagents, solutions, reference chemicals and culture media must be identified with the date of preparation and opening and the signature of the person who prepared them. The bottles of reagents and solutions must be unambiguously labeled to allow the correct identification, use, storage, observance of the deadline of validity and disposal.

Tab.2 Missing requirement

Experts from the studied company pairwise evaluated the Elements with Risk of Non-Compliance. The weight of each element is shown in the last column of Fig. 3. The Weights were color-coded as pet Tab 3.

Impact Level Score		
Score	Impact Level	Impact
5	High	More than 0,16
4	Elevated	0,12-0,16
3	Moderated	0,08-0,11
2	Low	0,04-0,07
1	Limited	Less than 0,04

Tab. 3: Categories of risk factors

Fig.2 shows the Elements with Risk of Non-Compliance with respective weights, which are color-coded with the impact score level as per Tab.3.

Criteria Comparison Matrix

Elements with Risk of Non Compliance	S1 - Organization and Management	S2 - Quality System	S3 - Personnel	S4 - Equipment with Data processing	S5 - Products and services provided externally	S6 - Procedure for investigating out-of-specification	S7 - Data control	S8 - File of documents	S9 - Biosafety	S10 Materials and reagents	**Normalized Matrix**										**Weights**
S1 - Organization and Management	1	3	5	3	3	5	3	5	5	3	**0,29**	0,48	0,46	0,10	0,15	0,31	0,14	0,19	0,13	0,14	0,24
S2 - Quality System	1/3	1	3	3	5	3	3	5	5	3	0,10	**0,16**	0,28	0,10	0,24	0,18	0,14	0,19	0,13	0,14	0,16
S3 - Personnel	1/5	1/3	1	5	7	3	5	3	3	3	0,06	0,05	**0,09**	0,16	0,34	0,18	0,24	0,11	0,08	0,14	0,15
S4 - Equipment with Data processing	1/3	1/3	1/5	1	1/5	1/5	1/3	1	3	1/5	0,10	0,05	0,02	**0,03**	0,01	0,01	0,02	0,04	0,08	0,01	0,04
S5 - Products and services provided externally	1/3	1/5	1/7	5	1	3	3	3	3	1/3	0,10	0,03	0,01	0,16	**0,05**	0,18	0,14	0,11	0,08	0,02	0,09
S6 - Procedure for investigating out-of-specification	1/5	1/3	1/3	5	1/3	1	5	3	3	5	0,06	0,05	0,03	0,16	0,02	**0,06**	0,24	0,11	0,08	0,23	0,10
S7 - Data control	1/3	1/3	1/5	3	1/3	1/5	1	5	5	3	0,10	0,05	0,02	0,10	0,02	0,01	**0,05**	0,19	0,13	0,14	0,08
S8 - File of documents	1/5	1/5	1/3	1	1/3	1/3	1/5	1	7	3	0,06	0,03	0,03	0,03	0,02	0,02	0,01	**0,04**	0,18	0,14	0,05
S9 - Biosafety	1/5	1/5	1/3	1/3	1/3	1/3	1/5	1/7	1	1/5	0,06	0,03	0,03	0,01	0,02	0,02	0,01	0,01	**0,03**	0,01	0,02
S10 Materials and reagents	1/3	1/3	1/3	5	3	1/5	1/3	1/3	5	1	0,10	0,05	0,03	0,16	0,15	0,01	0,02	0,01	0,13	**0,05**	0,07
TOTAL	3,47	6,27	10,88	31,33	20,53	16,27	21,07	26,48	40,00	21,73											

Fig. 2 – Elements and respective weights

Among the Elements with Risk of Non-Compliance, the element "*S1 - Organization and Management"* was classified as high impact and *"S2 - Quality System and Personnel"* with elevated impact. The elements "S5 - *Products and services provided externally", "S6 - Procedure for investigating out-of-specification," and "S7 - Data control"* were classified as moderate impact. These elements were prioritized in the implementation of the actions to comply with the requirements.

4. CONCLUSION

According to the results presented in section 3, considering the methodological guidelines and analyzing the literature, the conceptual model made it possible to upgrade the QMS based on the ABNT NBR ISO: IEC 17025 standard. It was also possible to meet the new Brazilian regulatory demands based on good practices for qualification in REBLAS – Brazilian Network of Analytical Laboratories (ANVISA).

The target of the study was to create a conceptual model for adequacy of a quality management system accredited in ISO 17025 standard to the principles of good laboratory practices and risk assessment of non-compliance. The model identified the Elements with Risk of Non-Compliance that could affect operational safety and sustainability. The requirements to be met to comply with ISO/IEC 17025, RDC 512/2021, RDC 301/2019, or BPL - DIT DICLA 035 to avoid the Risk of Non-Compliance were defined for all elements. The prioritization of the elements was performed with AHP, and the essential elements to be addressed first were: *S1 - Organization and Management*, which was classified as high impact and, *S2 - Quality System and Personnel* with elevated impact.

This study contributes to the previous findings of other researchers presented in the section literature review since most of them did not cover the proposal of a Conceptual Model and the use of a quantitative approach using AHP and with a focus on defining the elements and requirements be complied with. This paper aimed at completing this gap by proposing and describing a method to apply AHP to prioritize the elements with Risk of Non-Compliance and define adequate requirements that could optimize quality, safety, and sustainability. The study was conducted within the facilities of an analytical laboratory, and the result can be generalized to other laboratories. The implications are relevant since compliance with the requirements can be conducted more safely. By following the proposed model, operational failures and accidents can be prevented.

The proposed methodology revealed some crucial results, thus contributing to previous studies on the subject and may help to overcome some of the challenges faced by quality leaders and other professionals looking for safety and quality in analytical laboratories. The study was conducted based on the experience and knowledge of experts on the subject. As explained in the Introduction Section, some papers have been published addressing compliance with Quality Management System accredited in ISO 17025 in different domains in the latest years. However, no previous study could be found covering a conceptual model for adequacy of a quality management system accredited in ISO 17025 standard to the principles of good laboratory practices. A study about the use of Risk assessment of non-compliance and the use of AHP to identify the elements with Risk of Non-Compliance could not be found either. It is noteworthy here that this paper proposes an optimized approach that could be used in any organization.

In response to the first question: *How to serve the pharmaceutical market in a quality control laboratory?* Aiming to answer this question, the authors sought to understand the Brazilian legislation regarding analytical laboratories. It can be considered that analytical laboratories, which carry out analyses for the quality control of pharmaceutical products, need to meet the requirements of good practices in the laboratory to continue adequate suppliers to the pharmaceutical industries. ANVISA demands these industries to adopt the general guidelines of Good Laboratory Practices and restrict the performance to the laboratories that meet these requirements.

In response to the second question: *How to comply with the various laws applicable to an analytical laboratory, including RDC 390/2020, recently published by ANVISA?* As described in Section 3, a comparison

of all requirements of each standard to adapt the quality management system based on the ABNT NBR ISO standard was performed, the missing requirements identified, and a comprehensive comparison matrix was prepared. Actions to comply with the missing requirements allow the implementation of the hybrid management system as a quality control tool for the scope-related processes. And through the self-assessment checklist, the suitability system for qualification in REBLAS – Brazilian Network of Analytical Laboratories (ANVISA) can be verified.

It can be concluded that the quality system's adequacy based on the ABNT NBR ISO: IEC 17025 standard with GLP compliance provided the studied company with meeting the new requirements of the pharmaceutical market. Thus, it is possible to say that the adequacy of the management system to the principles of good practice provided more outstanding quality and the possibility of recognition in the GLP requirements (NIT-DICLA-35) by the evaluating body and the internationalization of the company.

For further study, the authors recommend continuing this research, with the objective of recognition by the Cgcre (General Coordination of Accreditation) of INMETRO (National Institute of Metrology, Quality, and Technology) meeting the requirements of NIT-DICLA-035 - Principles of Good Laboratory Practice and the implementation of a Pharmaceutical Quality System suitable for automating processes to meet Industry 4.0, aiming at international regulatory demands

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