Self-assessment model for pharmaceutical companies based on Good Manufacturing Practices for pharmaceuticals in Brazil: a multicriteria approach

A S Nunes[1], **M F L Almeida**[1], **D R Louzada**[1]

[1] Graduate Program in Metrology, Pontifical Catholic University of Rio de Janeiro, Rio de Janeiro, 22451-900, Brazil

louzada@puc-rio.br

Abstract. This paper aims to present a self-assessment model for pharmaceutical companies in Brazil that can verify their capacity to meet the requirements established in the Brazilian regulation concerned with Good Manufacturing Practices (GMP) for pharmaceuticals. The methodology comprises (i) literature review and documentary analysis of the central research themes, (ii) definition of the analytical structure based on the Analytic Hierarchy Process (AHP) method, aligned with GMP for pharmaceuticals, (iii) application of the AHP method for assigning weights to the regulatory requirements established in the Resolution of the Collegiate Board 658/2022, published by the National Health Surveillance Agency (Anvisa) in Brazil, (iv) application of the self-assessment instrument addressed to Brazilian pharmaceutical companies and determination of their capacity level to meet each regulatory requirement/item of the RDC 658/2022, and (v) employment of the Importance-Performance Analysis (IPA) method to prioritize regulatory requirements/items that should be improved to comply with the regulation. An innovative self-assessment model based on the GMP for pharmaceuticals stands out as the main result of this study. It can support decision-making processes related to the certification of pharmaceutical firms by Anvisa.

1. Introduction

The pharmaceutical industry plays a critical role in improving global health by developing and manufacturing life-saving pharmaceutical products, and ensuring their quality and safety becomes paramount. With global harmonization of regulatory requirements and quality standards and national and global business consolidations ongoing at a fast pace, pharmaceutical manufacturers, suppliers, contractors, and distributors are impacted by continual change [1-4]. One of the key pillars in maintaining the highest standards of quality adopted by the pharmaceutical industry worldwide is the adoption of Good Manufacturing Practices (GMP) for pharmaceutical products, published by the World Health Organization (WHO) [5] in line with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) [6].

The essence of GMP lies in its role as a crucial component of a quality management system, ensuring the consistent production and control of pharmaceutical products to meet the appropriate quality standards for their intended purpose and as mandated by the marketing authorization. GMP is a comprehensive framework to ensure that pharmaceutical products are consistently produced,

controlled, and distributed, meeting the required quality standards. In recent years, the spotlight on GMP has intensified as the pharmaceutical industry faces evolving challenges, such as the rise in complex therapies, globalization of supply chains, and increasing demand for faster drug development [5,6].

The GMP guidelines have become a beacon of trust and reliability, providing a solid foundation for manufacturers, regulators, and consumers. By adhering to these best practices, pharmaceutical companies can mitigate risks, prevent potential product recalls, and ultimately safeguard public health [3]. In Brazil, GMP for pharmaceuticals were regulated by the Brazilian Health Regulatory Agency (Anvisa) and established in the RDC 658/2022 to ensure that pharmaceutical products are consistently produced and controlled according to quality standards appropriate for their intended use [7].

Brazil stands out in the global pharmaceutical landscape due to the country's continental dimensions and the significant domestic market for medications, currently fluctuating between the 10th and 8th positions [8]. Pharmaceutical markets in emerging countries are improving their global rankings, while developed markets appear in lower positions. At this growth rate, Brazil is estimated to reach 6th by 2026 [8]. For Brazil to achieve the future positioning predicted by the Research Pharmaceutical Industry Association in Brazil (Interfarma, acronym in Portuguese), pharmaceutical companies operating in the country must strive for operational excellence and innovation to offer medications with the highest level of quality, safety, and efficacy for end consumers [8].

In this context and based on the following assumptions (i) GMP guidelines for pharmaceuticals play a fundamental role in the growth perspective of the Brazilian pharmaceutical industry, (ii) the changes proposed by the National Health Surveillance Agency (Anvisa, acronym in Portuguese) for the equivalence of GMP for pharmaceuticals to be adopted in Brazil regarding the international standard will require adjustments and modifications in pharmaceutical companies operating in this country to adhere this regulation, (iii) the pharmaceutical companies operating in this country will seek high levels of excellence and innovation performance to provide consumers with products of the utmost quality, safety, and efficacy to comply with this regulation, (iv) the adherence to rules aligned with PIC/S can expand export opportunities for Brazilian pharmaceutical companies, and (iv) the literature review, covering the period from 2000 to 2023, indicated the need for empirical studies focusing on tools to assist Brazilian pharmaceutical firms in assessing their capacity to comply with regulation established in the RDC 658/2022, the main question to be answered throughout this study is defined as follows:

"How to assess the capacity of pharmaceutical companies regarding compliance with the regulation established in the RDC 658/2022, from the perspective of obtaining the GMP certification to be granted by Anvisa?"

Addressing the above question, this work aims to bridge research gaps by creating and applying a conceptual multicriteria model for pharmaceutical firms based on the RDC 658/2022 structure.

The paper is structured in five sections, including this introduction. Section 2 provides a literature review synthesis, encompassing previous works published between 2000 and 2023 that focused on the central research themes, i.e., harmonization and adoption of GMP of pharmaceutical products worldwide, process maturity models, and decision-making methods applicable to the intended modelling. In Section 3, the research design and methodology are briefly presented. Section 4 introduces a self-assessment model based on the RDC 658/2022 for Brazilian pharmaceutical companies, employing two decision support methods (i) the Analytic Hierarchy Process (AHP) and (ii) the Importance-Performance Analysis (IPA). Section 5 discusses the potential contributions of combining these two decision-making methods to enhance self-assessment efficiency by pharmaceutical firms seeking certification by Anvisa and summarizes the concluding remarks.

2. Literature review

A literature review was conducted focusing on the following themes (i) harmonization and adoption of GMP of pharmaceutical products worldwide, (ii) process maturity models, and (iii) decision-making

methods applicable to the intended modelling. The bibliographic review was complemented with resolutions by Anvisa and regulatory bodies in other countries, to consolidate the theoretical and normative framework of this research [5-7, 9-13].

In the first stage of the literature review, we delve into the essence of GMP for pharmaceutical products [5-7] to examine key principles that underpin the guidelines, their impact on different aspects of pharmaceutical production, and the challenges and opportunities in their implementation.

A second literature search focused on the subject "process maturity models" was performed on peer-reviewed articles indexed in the Scopus database, covering the period between 2010 and 2023. Three references on this subject provided the basis for defining the maturity scale to be included in the conceptual model [14-16].

The third search regarding decision-making methods applicable to the model design was concentrated on two methods previously selected by the authors according to the objectives of the intended modelling. They are (i) the Analytic Hierarchy Process (AHP) method [17] and the Importance-Performance Analysis (IPA) [18,19].

The interest in developing a self-assessment model for the certification of pharmaceutical companies in Brazil, based on the RDC 658/2022, was confirmed by the findings in the literature review [20-28]. These findings indicated the inexistence of empirical studies or methodological approaches and self-assessment models for this purpose, even considering previous editions of GMP for pharmaceuticals. This gap confirmed the opportunity to deepen our knowledge of how to contribute to Brazilian pharmaceutical companies to be able to identify the critical issues and improvement opportunities to be managed in order to obtain the certificate issued by Anvisa, according to the RDC 658/2022, recently published on 30th March 2022.

3. Research design and methodology

In this Section, we present the research design aimed at addressing the questions outlined in Table 1.

Table 1. Research design

Phase	Stage	Research questions [Section]
Motivation	Problem definition and the rationale for the research.	Why should we develop a Self-assessment model for pharmaceutical companies based on Good Manufacturing Practices for pharmaceuticals in Brazil? [Section 1].
Development (What and How?)	State of research on central themes and identification of research gaps and unsolved problems.	What are the significant gaps in the existing knowledge regarding the harmonization and adoption of the GMP for pharmaceuticals in which the current regulation on the GMP for pharmaceuticals in Brazil aligns? [Section 2].
	Definition of the research methodology.	How to assess the capacity of pharmaceutical companies regarding compliance with the guidelines and requirements of GMP for pharmaceuticals in Brazil, according to the RDC 658/2022, from the perspective of obtaining the GMP certification to be granted by Anvisa? [Section 3].
	Development of a self-assessment model for pharmaceutical companies in Brazil based on the RDC 658/2022	What elements should make up the hierarchical analytical structure in line with the guidelines and requirements of the RDC 658/2022? How to define the weights of the requirements of the RDC 658/2022 from the perspective of a given pharmaceutical company to hold the Anvisa certificate? [Section 4]? What structure and scale should compose a self-assessment instrument to be applied with managers and specialists of a given pharmaceutical company to evaluate its capacity to fulfil each requirement/item of RDC 658/2022? [Section 4]? To what extent the use of the Importance-Performance Analysis (IPA) method can help a given pharmaceutical company to identify the requirements that should be prioritized in an action plan, with a view to future certification of the company by Anvisa? [Section 4]?
Analysis of managerial implications (What do the results mean regarding actions?)	Discussion of the results and implications of this research.	What are the primary differentiating factors of the self-assessment model compared to previous studies on the adoption of the GMP of pharmaceuticals in different continents? What are the managerial implications of this research? [Section 5]

The design follows a procedural model inspired by Rocha et al. [29], comprising three phases and five stages. This approach offers a well-defined structure and a carefully planned course of action for our study. The research phases include motivation, development, and validation.

The initial stage comprises problem definition and rationale establishment for the research. Further, the second stage involves a comprehensive review of existing literature on the central research themes, aiming to identify gaps in the literature and unresolved aspects within the specific field of study. The third stage focuses on selecting the research methodology, while the fourth stage revolves around creating a self-assessment model for pharmaceutical companies in Brazil based on RDC 658/2022 [7]. Lastly, the final stage is dedicated to the discussion of research findings and their managerial implications.

Initially, a literature review was conducted focusing on the central research topics, as described in Section 2. The current state of research analysis led to the identification of two research gaps: (i) the first refers to the inexistence of empirical studies or methodological approaches that can contribute to Brazilian pharmaceutical companies to identify the critical issues and improvement opportunities to be managed in order to obtain the certificate issued by Anvisa, according to its compliance to the RDC 658/2022 requirements; (ii) the second gap is concerned with the use multicriteria decision-making methods combined with the Importance-Performance Analysis to help companies to achieve the mentioned objectives.

The research methodology comprised a formal modelling process to develop the referred self-assessment model. The focus on unaddressed research gaps led to selecting of the Analytic Hierarchy Process (AHP) and the IPA methods, considering the context and characteristics and the focused regulation – the RDC 658/2022 and the preliminary review of decision-making methods [30]. Besides, the formal modelling included the definition of a maturity scale to measure the capacity of a given pharmaceutical company to evaluate its capacity concerning the fulfilment of each requirement/item of this Resolution.

Applied to the context of this research, the AHP method comprises three steps: (i) formulation of the evaluation objective and definition of the analytical hierarchical structure according to the requirements and items of the RDC 658/2022; (ii) value judgments about the importance of the Resolution's requirements/items, through pairwise comparisons of these elements at two levels (i.e., requirements and items); (iii) algebraic development to obtain the weights of requirements and items. A detailed description of the AHP method can be found in [17].

This method was chosen to integrate the model because it allows structuring a complex evaluation problem into an analytical hierarchy with levels, which facilitates comparisons between RDC 658/2022 requirements and items. Another justification for this choice is the possibility of analyzing the internal consistency of judgments while assigning weights to the requirements and items of the Resolution. This allows experts to review their opinions if inconsistent results are obtained. In this case, they should provide judgments or preferences for a consistency test using pairwise comparison matrices' consistency ratios (C.R.). The C.R. is calculated by dividing the consistency index by the corresponding random value. For detailed information on the C.R. calculation, please refer to [17].

In parallel to the employment of the AHP method, the research methodology includes the definition of a five-point scale derived from widely adopted process maturity models across various industries identified during the literature review [14-16]. In the context of a particular pharmaceutical company, assessment data should be gathered from its managers and experts and then synthesized to obtain the final assessment results regarding its capacity concerning the fulfilment of each requirement/item of RDC 658/2022.

For this stage, the research methodology included elaborating an assessment instrument based on the structure of the RDC 658/2022 with the referred maturity five-point scale. Experts with formal education or experience in the fields of compliance assessment processes, health surveillance, or pharmaceutical quality systems should conduct a pre-test.

Subsequently, the second decision-making method (IPA) [18-19] was employed in the last stage of the modelling phase. This method has been largely used to identify areas that require improvement in a given system or organization. It helps assess the importance of various factors or criteria and their corresponding performance to identify priorities for action. Integrating the IPA method in the self-assessment model can assist a pharmaceutical company in efficiently elaborating an action plan to enhance its capacity to comply with the requirements/items of the RDC 658/2022.

4. Self-assessment model for Brazilian pharmaceutical firms based on the RDC 658/2022 requirements

Based on the methodology outlined in Section 3, this Section presents the self-assessment model comprising five stages described in subsections 4.1 to 4.5.

4.1. Stage 1: Definition of the weights of the elements of the self-assessment model: using the AHP method

This first stage refers to identifying the constituent elements of the self-assessment model for pharmaceutical companies based on the structure of RDC 658/2022 (Table 2).

Table 2. Elements of the self-assessment model based on the structure of the RDC 658/2022 [7]

Requirements	Items
R1 – Pharmaceutical quality system	R11 - Good Manufacturing Practices (GMP) for pharmaceuticals
	R12 - Quality control
	R13 - Product quality review
	R14 - Quality risk management
R2 – Personnel	R21 - Key personnel
	R22 - Training
	R23 - Personal hygiene
	R24 - Consultants
R3 – Facilities and equipment	R31 - Facilities
	R32 - Production areas
	R33 – Storage area
	R34 - Quality control areas
	R35 – Auxiliary areas
	R36 - Equipment
R4 - Documentation	R41 - Generation and control of documentation
	R42 - Good documentation practices
	R43 - Documentation retention
	R44 – Specifications
	R45 - Manufacturing formula and process instructions
	R46 - Procedures and records
R5 – Production	R51 - Prevention of cross-contamination in production
	R52 - Validation
	R53 – Raw materials
	R54 - Manufacturing operations for intermediates and bulk products
	R55 - Packaging materials
	R56 - Packaging operations
	R57- Finished products
	R58 - Rejected, recovered, and returned materials
	R59 - Shortage of products due to manufacturing restrictions
R6 – Quality control	R61 - Good Manufacturing Practices and quality control
	R62 - Ongoing stability program
	R63- Technical transfer of analytical methods
R7 – Outsourced activities	R71 - Contracting Party
	R72 - Contracted Party
	R73 - Contract
R8 - Complaints and product recall	R81- Personnel and organization
	R82 - Procedures for handling complaint investigations, including possible quality deviations
	R83 - Investigation and Decision-Making
	R84 - Root Cause Analysis and Corrective and Preventive Actions
	R85 - Product Recall and Other Risk Reduction Actions
R9 - Self-Inspection	R91 - Self-Inspection

Figure 1 below represents the analytical hierarchical structure for assessing the capacity of a given pharmaceutical company concerning compliance with the requirements of RDC 658/2022 [7].

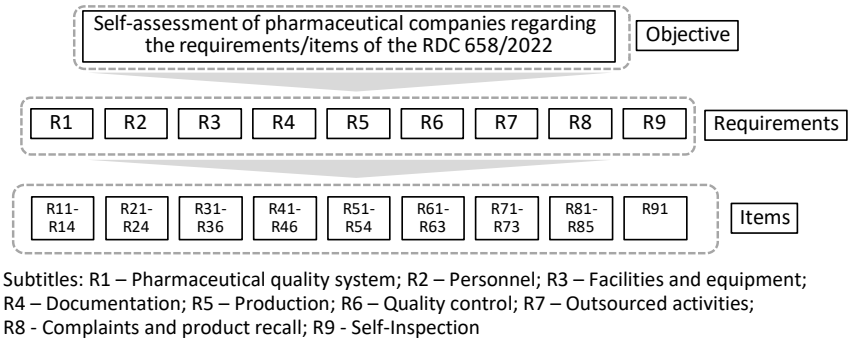

Figure 1. Analytical hierarchical structure for self-assessment of pharmaceutical companies, according to the RDC 658/2022

4.2. Stage 2: Definition of the weights of the elements of the self-assessment model: using the AHP method

This second stage refers to the value judgments made by experts with formal education or experience in compliance assessment processes, health surveillance, or pharmaceutical quality systems. The Saaty scale is used to compare the importance of RDC 658/2022 requirements and the items subordinate to each requirement.

For this purpose, ten forms should be prepared for the experts to fill out, as follows: (i) the first form consists of the nine requirements; (ii) the second form includes the items subordinate to the 'Pharmaceutical Quality System' requirement (R1); (iii) the third form includes the items of the 'Personnel' requirement (R2); (iv) the fourth form includes the items of the 'Facilities and Equipment' requirement (R3); (v) the fifth form includes the items of the 'Documentation' requirement (R4); (vi) the sixth form includes the items of the 'Production' requirement (R5); (vii) the seventh form includes the items of the 'Quality Control' requirement (R6); (viii) the eighth form includes the items of the 'Outsourced Activities' requirement (R7); (ix) the ninth form includes the items of the 'Complaints and Product Recall' requirement (R8). There is only one item for the 'Self-Inspection' requirement (R9), so this single item is not subject to paired comparison using the AHP method.

For pairwise comparisons of requirements and items of the RDC 658/2022, Saaty's nine-point scale should be used (Table 3).

Table 3. Saaty's nine-point scale [17]

Scale	Linguistic scale
1	Equally important
2	Equally to moderately more important
3	Moderately more important
4	Moderately to strongly important
5	Strongly important
6	Strongly to very strongly more important
7	Very strongly more important
8	Very strongly more important to absolutely important
9	Absolutely important

As the distribution of the 41 items among the nine requirements of the RDC 658/2022 is not uniform. Some requirements (e.g., R6 and R7) contain only three items, while others include four items (R1 and R2), six items (R3 and R4), and even nine items (R5).

Therefore, it is necessary to initially normalize the weights obtained using the IPÊ® tool [31] for each requirement so that the normalized weights of all items under a specific requirement add up to 1.0. The objective of this phase is to determine which items, according to the experts' opinions, are most important for each requirement.

For requirements with few items (R6, R7, and R9), the initial normalization already allows discerning the relative importance of their items. However, when many items are under a particular requirement (e.g., R5), the importance becomes dispersed, hindering discrimination. One alternative is to compare the normalized importance degrees with the percentage importance that would be obtained if all items had the same importance (simply dividing 1.0 by the number N of items per requirement), referred to as the equimportant value.

By dividing each item's normalized value by the requirement's equimportante value, we obtain each item's relative importance. In this case, the higher the relative importance is compared to 1.0, the more important the item is in relation to the others under the same requirement of the RDC 658/2022. Conversely, the lower the value compared to 1.0, the less important the item is. Considering the extreme cases, an item with a normalized importance of 0.0 will also have a relative importance of 0.0. On the other hand, a dominant item with a normalized importance of 1.0 will have a relative importance of 1.0/(1.0/N) = N (number of items). In other words, the relative importance of the items will range between 0.0 and N, but they will likely concentrate within the range of 0.5 to 2.5.

4.3. Stage 3: Definition of the scale and the self-assessment instrument for a particular pharmaceutical company

This stage comprises two steps. The first refers to the definition of the scale to be adopted by pharmaceutical companies regarding compliance with the requirements and items of the RDC 658/2022, as mentioned in Section 3. A five-point scale of evolution is proposed for each of the nine requirements and 41 items of the RDC under consideration. The second step involves the development of the assessment instrument, following the hierarchical structure represented schematically in Fig. 1.

The first version of this instrument underwent a pre-test conducted with three experts. The first expert had over ten years of experience in organizational management consulting, including pharmaceutical companies; the second expert was a professional from Anvisa with over eight years of experience in evaluating compliance of pharmaceutical companies; and the third expert was one of the professors from the Graduate Program in Metrology at PUC-Rio. After the evaluation by these experts, some suggestions were incorporated into the final version of the instrument. Table 4 presents the five-level scale integrated into the self-assessment instrument for pharmaceutical companies concerning compliance with the requirements of the RDC 658/2022.

Table 4. Maturity scale integrated into the self-assessment instrument

Maturity Level	Scale	Description
Nothing, informal or *ad hoc*	1	The company's capacity regarding compliance with the requirements of RDC 658/2022 needs to be established, or if it is established, it is done informally, on a case-by-case basis, or ad hoc.
Managed at the basic level	2	The company's capacity regarding compliance with RDC 658/2022 requirements is established at a basic level.
Defined and managed	3	The company's capacity regarding compliance with RDC 658/2022 requirements is established proactively but needs to be systematically and continuously improved.
Systematically managed	4	The company's capacity regarding compliance with the requirements of RDC 658/2022 is established systematically and continuously improved but not yet optimized.
Optimized	5	The company's capacity regarding compliance with RDC 658/2022 requirements is established systematically, continuously improved, and optimized. Management is based on active monitoring, feedback, and learning.

4.4. Stage 4: Evaluation and calculation of the level of capability of the pharmaceutical company to comply with the requirements of the RDC 658/2022

Applying the self-assessment instrument with the manager(s) responsible for the internal evaluation of the pharmaceutical company's compliance with the requirements of the RDC 658/2022 can be conducted in one or more consensus meetings [17] or individually. If the second option is chosen, it is recommended to subsequently employ fuzzy logic to calculate the collective results [32].

This stage should include the following steps: (i) presentation of the self-assessment instrument to the managers responsible for the internal evaluation of the pharmaceutical company's compliance with the requirements of the RDC 658/2022; (ii) individual completion of the self-assessment form by the evaluators followed by a consensus meeting involving the evaluators; and (iii) formatting the data collected in the consensus meeting for further analysis, using the Importance-Performance Analysis (IPA) method. This analysis should be conducted in stage 5 of the model's application.

The self-assessment instrument that is integrated into the proposed model consists of nine sections. The sections of the instrument correspond to the requirements of the RDC 658/2022, and the evaluation of the company's capacity level regarding compliance with a specific requirement should be based on the evaluation of its items, following the hierarchical analytical structure represented in Figure 1. For representing the self-assessment results, it is recommended to construct radar charts, one for each of the nine requirements of the Resolution, as suggested in [33].

4.4. Stage 5: Analysis of the results of the self-assessment and preparation of the report for the pharmaceutical company: using the IPA method

This final stage of the model refers to the analysis of the results obtained in stage 4 and the preparation of the self-assessment report of the pharmaceutical company regarding compliance with the requirements of the RDC 658/2022. The objective of this stage is to chart decision-making zones, which will enable to establish action plans for enhancing the company's capacity to comply with the mentioned requirements/items, as shown in Fig. 2.

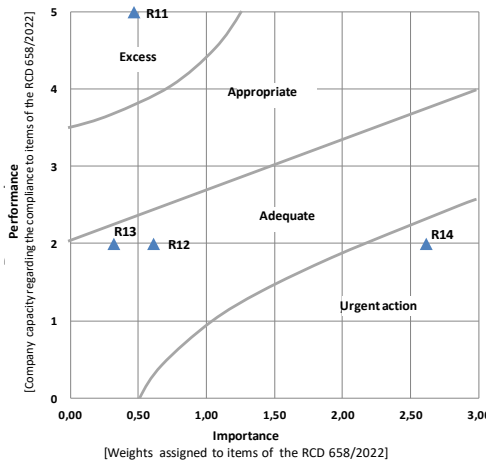

Figure 2. An illustrative example of an IPA matrix for the 'Pharmaceutical quality system' items

Using the Importance-Performance Analysis (IPA) [18,19], a two-dimensional space is generated for each of the nine requirements of the focused Resolution. The horizontal axis represents the importance assigned to each requirement/item of RDC, and the vertical axis represents the company's capacity to comply with each item subordinated to the nine requirements. The respective importance scales are defined by the intervals between the maximum and minimum values of the final weights calculated for the items of each requirement of the RDC 658/2022 (resulting from stage 2 of the model). The IPA matrices, one for each requirement of the focused Resolution, enable managers and

collaborators responsible for the Pharmaceutical Quality Management System of the company to map four zones for proposing actions aimed at achieving higher maturity levels.

As shown in Figure 2, the four decision-making zones are (i) 'Excess zone', corresponding to items of low importance and high performance, where it is necessary to assess whether resources are allocated above what is needed; (ii) 'Adequate zone', in which items have balanced importance and performance in the short and medium term, but this balance is not sustainable in the long term; (iii) 'Improvement zone', with items of intermediate importance and performance; and (iv) 'Urgent action zone', with items of high importance and low performance, which are critical and require urgent initiatives from the organization under evaluation**.**

The last step in this stage is dedicated to creating a comprehensive report that includes all the assessment results of the company. This report will also incorporate action plans related to specific targets aimed at enhancing the capacity of the pharmaceutical company to comply with the requirements of the RDC 658/2022.

5. Discussion and final remarks

This paper presented a self-assessment model for pharmaceutical companies to measure their capacity to meet the requirements and items of the RDC 658/2022. Identifying and interpreting the requirements and their corresponding items in this Resolution allows us to develop a conceptual model based on the analytical hierarchical structure represented in Fig. 1.

To obtain the weights of the 41 items that make up the Resolution, the use of the AHP method [17] is recommended due to the advantages presented previously and proven during the development of previous research within the PósMQI Program at PUC-Rio, focusing on the development of self-assessment models based on standards and regulations applicable to organizations in different socio-productive contexts [e.g., 34, 35].

One of the model's main contributions is the monitoring of pharmaceutical companies' capacity to meet the nine requirements of the Resolution through regular management meetings. With the support of the IPA matrices, it is possible to objectively identify and prioritize improvement points associated with the nine RDC 658/2022 requirements.

The application of the self-assessment model will allow pharmaceutical companies to identify any gaps in their pharmaceutical quality management systems, which can be the subject of initiatives aimed at strengthening the company's capacity to comply with the requirements of the RDC 658/2022 and achieve higher levels of performance in the markets they operate.

References

[1] Bunn G P 2019 *Good Manufacturing Practices for Pharmaceuticals* 7th ed. Boca Raton: Florida CRC Press

[2] Carmo A C M et al. 2017 *Accreditation Qual. Assur.* **22** (4) 199

[3] Haleem R M et al.2015 *Saudi Pharm J* **23**(5) 463

[4] Woodcock J 2004 *Am. Pharm. Rev.* **7**(6) 10

[5] World Health Organization WHO 2014 *Good Manufacturing Practices for Pharmaceutical Products*: main principles: Annex 2. Geneve: World Health Organization

[6] Pharmaceutical Inspection Cooperative Scheme PIC/S 2018 *Guide to Good Manufacturing Practices for Medicinal Products.* PIC/S, PE 009-14 (Intro)

[7] Brasil Agência Nacional de Vigilância Sanitária Anvisa 2022 *Resolução nº 658 de 30 de março de 2022*

[8] Interfarma *Guia Interfarma 2022*. Available at https://www.interfarma.org.br/guia/guia-2022

[9] European Medicines Agency EMA 2007 *Good Manufacturing Practice* Doc. Ref. EMEA/INS/GMP/23022/2007 London: EMA

[10] Pharmaceutical Inspection Cooperative Scheme PIC/S 2012 *A Recommended Model for Risk-based Inspection Planning in the GMP Environment* Available at http://www.picscheme.org

[11] Pharmaceutical Inspection Cooperative Scheme PIC/S *Guide to Good Manufacturing Practice for Medicinal Products.* PE 009-14 (Part I) 2018 Geneve: PIC/S
[12] Pan American Health Organization PAHO 2010 *Resolution CD50. R9.* Available at http://new.paho.org/hq/dmdocuments/2010/CD50.R9-e.pdf
[13] International Conference on Harmonisation ICH 2019 *Quality Guidelines* Available at https://www.ich.org/products/guidelines/quality/article/quality-guidelines.html
[14] Jochem R, Geers D and Heinze P 2011 *TQM Journal* **23** (4) 377
[15] Dufry J 2011 *Strategy Leadersh.* **29** (6) 19
[16] De Bruin T, Rosemann M, Freeze R and Kulkarni U 2005 In *ACIS 2005 Proceedings - 16th Australasian Conference on Information Systems*
[17] Saaty T L 2008 *Int. J. Services Sciences* **1**(1) 83
[18] Martilla J A, James J C 1977 *J. Mark.* **41**(1) 77
[19] Slack N 1994 *Int. J. Oper. Prod. Manag.* **14**(5) 59
[20] Geyer A R C 2019 *Boas Práticas de Fabricação de Medicamentos no Brasil* Tese (doutorado) Universidade de Brasília
[21] Nwokike J, Clark A and Nguyen, P P 2018 *Bull. World Health Organ.* **96** (2)135
[22] Vogler M 2018 *Boas Práticas de Fabricação de Medicamentos* Tese (doutorado) Universidade de Brasília
[23] Vogler M *et al.* 2017 *Vigilância Sanitária em Debate: Sociedade, Ciência & Tecnologia* **5**(2) 34
[24] Ravinetto R *et al*. 2016 *J. Pharm. Policy Pract.* **9**(1) 16
[25] Hubert C *et al.* 2014 *J. Pharm. Biomed.* **88** 401
[26] Yu L *et al.* 2014 *The AAPS Journal* **16**(4) 771
[27] Ravinetto R M *et al.* 2012 *Trop. Med. Int. Health* **17**(11) 1412
[28] Linna A *et al.* 2008 *Eur. J. Pharm. Biopharm.* **69** 786.
[29] Rocha W L L, Almeida M F L and Calili R F 2023 *Sustainability* **15**(1) article ID 682
[30] Verma D 2014 IOSR *J. Bus. Manag* **16**(2) 171
[31] Costa H G 2006 *IPÊ. Version 1.0.* Available at http://www.producao.uff.br/index.php/aplicativos/130-ipe
[32] Zadeh L A 1965 *Inf. Control.* **8** 338
[33] Mosley H, Mayer A 1999 *Benchmarking National Labour Market Performance* Wissenschaftszentrum Berlin für Sozialforschung Discussion Paper March 1999 ISSN Nr. 1011-9523
[34] Santos M D C B, Almeida M F L 2022 In IEEE 28th International Conference on Engineering, Technology and Innovation, ICE/ITMC 2022 and 31st International Association for Management of Technology, IAMOT 2022 Joint Conference – Proceedings
[35] Belezia L C, Almeida M F L 2022 *Journal of Physics: Conference Series* **1826**(1) article ID 012026