A TALE OF THREE REGIONS: QUALITY CULTURE AND ITS IMPACT ON PHARMACEUTICAL PRODUCTION

B. Swartz[1*] & S. Singh[2]

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Contact details
* Corresponding author
SWARTZB@cput.ac.za

Author affiliations
1 Department of Industrial and Systems Engineering, Cape Peninsula University of Technology, South Africa

2 Department of Operations and Quality Management, Durban University of Technology, South Africa

ORCID® identifiers
B. Swartz
0000-0003-0752-7211

S. Singh
0000-0002-6178-6006

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ABSTRACT

This study presents a comparative literature examination of the pharmaceutical industry in Japan, Europe, and the United States, focusing on quality culture, which historically has impacted operations in these regions. It aims to highlight generic pitfalls that result from cultural influences so that these can be avoided when designing a conceptual model of quality management practices for South African organisations. Simultaneously, the literature illuminates areas where culture promotes operational excellence (OpEx) in production. Quadrants of the organisational cultural analysis instrument (OCAI) are used to collect and examine research data from 72 literature sources. An activity theory research approach is adopted to perform a comparative study to ensure a consistent formal examination of the three geographical regions. During this analysis, industry traits presumed to be supported by culture types are highlighted and examined. Findings from this examination will be used in a future study to develop an OpEx model for South Africa, based on quality culture.

OPSOMMING

Hierdie studie bied 'n vergelykende literatuurondersoek van die farmaseutiese industrie in Japan, Europa en die Verenigde State, met die fokus op die kwaliteitskultuur, wat histories bedrywighede in hierdie streke beïnvloed het. Dit het ten doel om generiese valstrikke wat ontstaan as gevolg van kulturele invloede uit te lig, sodat die valstrikke vermy kan word wanneer 'n konseptuele model van kwaliteitbestuurspraktyke vir Suid-Afrikaanse organisasies ontwerp word. Terselfdertyd het die literatuur gebiede belig waar kultuur operasionele uitnemendheid (OpEx) in produksie bevorder. Kwadrante van die organisatoriese kultuuranalise-instrument (OCAI) word gebruik om navorsingsdata uit 72 literatuurbronne in te samel en te ondersoek. 'n Aktiwiteitsteoretiese navorsingsbenadering is gebruik om die vergelykende studie uit te voer en dus 'n konsekwente formele ondersoek van die drie geografiese streke te verseker. Tydens hierdie ontleding, word veronderstel dat bedryfseienskappe ondersteun word deur kultuurtipes wat uitgelig en ondersoek is. Bevindinge van hierdie ondersoek sal in 'n toekomstige studie gebruik word om 'n operasionele uitnemendheidsmodel vir Suid Afrika te ontwikkel wat gebaseer is op kwaliteitskultuur.

1. INTRODUCTION

Quality culture is essential for organisational success in this highly competitive world [1]. A point of departure for understanding quality culture is to acknowledge that organisational culture is defined as a set of shared values and assumptions that a group maintains [2], [3], [4], [5], [6]. Roldán, Leal-Rodríguez and Leal [7] argued that quality culture is a subsidiary component of organisational culture, and that it refers to values about and interpretations of quality.

Citing Cameron and Sine [6], they noted that:

> *…the quality culture of an organisation is a subset of an organisation's overall culture. It reflects the general approach, the values, and the orientation towards quality that permeate organisational actions.*

Evans and Lindsay [2] highlighted a robust association between quality culture and an excellent standard of operations (OpEx) in pharmaceutical manufacturing. They argued that a successful OpEx strategy fits into an organisation's existing culture and is associated with quality management. Success is only achieved when every employee embraces the organisation's quality vision, values, and goals as a way of life. Such an organisation possesses a quality culture. Quality culture is a shared vision, and ultimately culture has a powerful influence on people's behaviour [2]. Essentially, the presence of a culture of quality leads to OpEx. Thus, this literature review is rooted in the belief that an OpEx model based on quality culture can be developed for South African pharmaceutical organisations.

2. BACKGROUND

The effective operation of the pharmaceutical industry is critical for global health. Therefore, pharmaceutical products worldwide must be produced according to the highest quality standards. The minimum acceptable standard for granting a pharmaceutical organisation authorisation to manufacture and market any pharmaceutical product in South Africa is the set of good manufacturing practice (GMP) guidelines. The International Council for Harmonisation (ICH) is one body that is a custodian of quality standards, such as GMP, in the global pharmaceutical industry. The ICH is the most widely recognised international association of pharmaceutical stakeholders [8] and is best known for its efforts to harmonise global pharmaceutical regulation. The ICH originally consisted of the three biggest market segments that historically have dominated the global pharmaceutical industry: the United States, Europe, and Japan [9].

Before the 1990s, pharmaceutical organisations worldwide were experiencing difficulties marketing their products in different countries owing to differing regulatory expectations. Thus, in the 1980s, discussions took place between Japan, Europe, and the United States on the possibilities for harmonisation [10]. These discussions led to a joint regulatory-industry initiative on international harmonisation, conceived in Paris in 1989. The initiative's primary purpose was to identify ways in which greater harmonisation could be achieved in the interpretation and application of technical guidelines and requirements for product registration and pharmaceutical production. This purpose was rooted in the desire for a more economical use of resources and the elimination of unnecessary delays in the development and availability of new medicines.

The primary objective of this comparative study is to uncover any common features, distinctions, and dichotomous aspects associated with the ICH regions. The purpose is to highlight generic pitfalls that arise because of cultural influences so that these can be avoided when a conceptual OpEx model is designed for South African organisations. Simultaneously, this study identifies areas where culture promotes OpEx in pharmaceutical production. During this analysis, industry traits that are presumed to be supported by one (or more) culture type are highlighted and examined. The findings of this examination will be used as a foundation to develop an OpEx model based on quality culture for South Africa.

3. METHODS

An activity theory research approach was adopted for this comparative study to ensure a consistent formal, structured approach to analysing the three geographical ICH regions. While this was used as a general research method, the organisational cultural analysis instrument (OCAI) was used as a research lens within the activity theory approach. Notably, all of the literature sources examined in this comparative analysis evaluated the pharmaceutical industry from a distinctly different perspective than that considered by this examination of the literature. The literature sources were written for a different purpose from that of this comparative study. Essentially, this literature exploration sets out to examine the underpinning cultural context in the three regions from a fresh perspective; this has not been attempted previously, and so it closes a research gap.

It should be noted that this study is contextual, and is not intended to identify transferable OpEx practices, even though ICH regions are compared. The intention, instead, is to examine the influence of culture on pharmaceutical production and to draw inferences on how culture can add value to a South African OpEx model (consisting of quality management practices) in the pharmaceutical industry. An extensive number of publications was examined (n=2078), and from them certain publications were selected (n=72) based on their value and explanatory power and, importantly, only if the same type of publication could be found in all three regions.

3.1. Activity theory

Activity theory is an ideal approach for studying a situation from a cultural perspective, since it offers a robust framework for a cultural examination [11], [12]. Activity theory offers a holistic and contextual method of discovery that is especially valuable in a qualitative enquiry into culture. There are seven elements in the activity theory approach, as shown in Figure 1. During an activity theory examination, three known elements pertaining to the problem at hand are specified to explore the remaining four elements. The known elements are the subject who performs the activity, the activity that takes place, and the goal of the activity. In this study, three geographical ICH regions are the subject, pharmaceutical production is the activity, and the goal of the activity is OpEx.

The unexplained elements are the tools used during the activity, the rules or norms regulating the activity, the stakeholders who play a role in the activity, and the division of labour that affects the activity. Activity theory adds practical value in understanding a situation by defining each element in a systematic review process and then exposing the interfaces between the elements, as seen in Figure 1. Contradictions, tensions, or problems within and between the various elements are identified. Contradictions and tensions are ‘agents of change’ and the ‘root causes for innovation’ [13]. They serve as triggers for development and are good for the continuous improvement of the system in which activity occurs. This paper highlights all of the contradictory OCAI cultural values that influence pharmaceutical production.

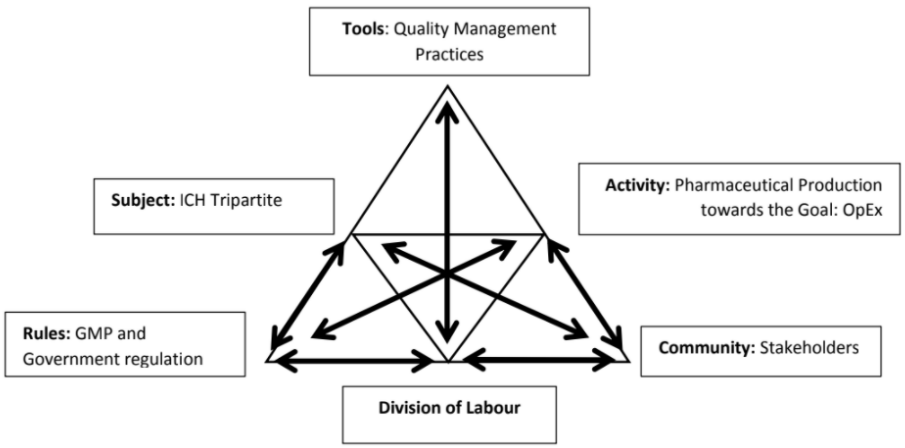

Figure 1: Activity theory framework/approach (adapted by the researcher)

3.2. The organisational cultural analysis instrument

Numerous studies [5], [7], [14], [15], [16], [17], [18] have demonstrated that, when measuring quality culture, it is advantageous to use a ‘competing values framework’ such as the OCAI to classify culture and to study its effect on quality management. This instrument, originally proposed by Cameron and Quinn [19], recommends the typification of culture based on its flexibility or rigidness and its outward or inward focus. This typification adds value to any study of culture, as it allows quality practitioners to view quality culture from a fresh perspective that enables vital decision-making on the adoption of business strategies, based on an organisation’s cultural characteristics.

The OCAI measures competing values in an organisation across two different dimensions. Each dimension represents a continuum, with contrasting values (which reflect organisational aptitude) at opposite ends. The first dimension differentiates an organisation's focus in terms of flexibility and dynamism at one end of the continuum from its focus on stability, order, and control at the other end. Some organisations are effective because they can change and be adaptable and agile, and thus be more flexible and dynamic. Conversely, other organisations are effective because they are stable, predictable, and mechanistic, and so more ordered and controlled [16], [18]. Certain organisations are effective because they are more flexible, while others are effective because they are more stable.

The second dimension differentiates organisations on their internal or external orientation. Internally orientated organisations have strong elements of internal harmonisation and integration, while externally orientated organisations are fiercely competitive and engage in rivalry with others outside their borders [16], [18]. When the two dimensions are united, they form four quadrants. Each quadrant represents a distinct organisational cultural type with different characteristics, as seen in Figure 2. Each culture type indicates how people in a particular organisation operate, and the behaviour that is considered appropriate and is valued in that organisation.

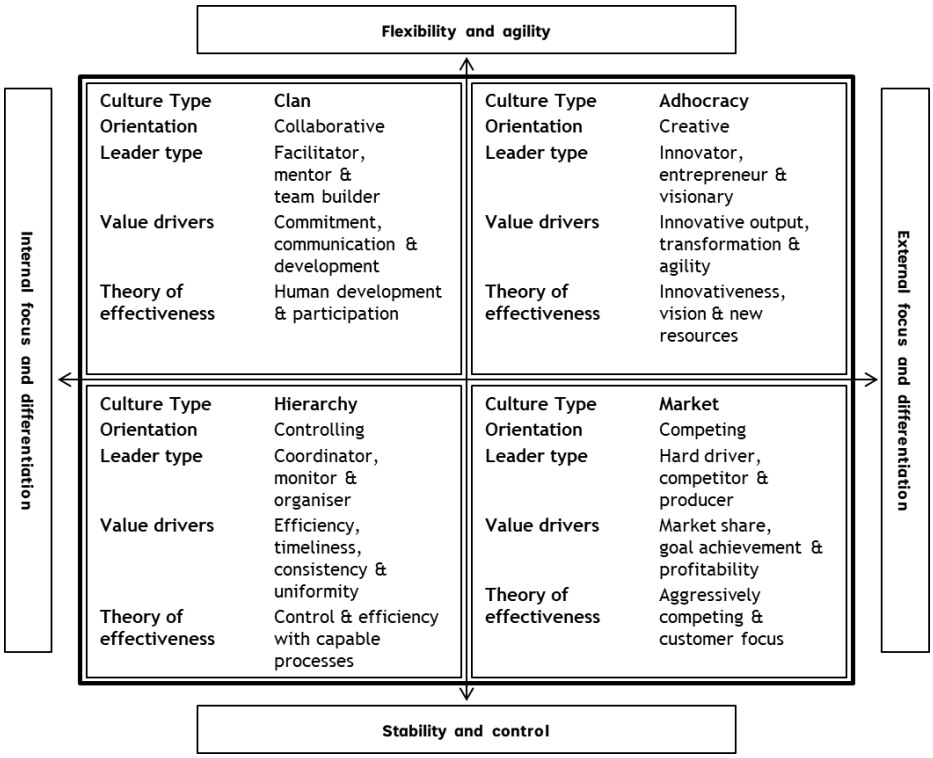

Figure 2: Competing values framework (adapted from Cameron and Quinn [19])

The group culture is positioned on the flexible end of the flexibility–rigidness axis [5], [18]. This culture emphasises the internal adaptability of the organisation. Teamwork, participation, empowerment, and concern for ideas are key characteristics of group culture, referred to as 'clan culture'. The developmental culture also resides at the flexible end of the flexibility–rigidness axis; however, the focus of this culture type is external to the organisation. Growth, innovation, creativity, and continual adaption to the external environment are valued in the developmental culture type, referred to as the 'adhocracy culture'.

The rational culture exists at the rigid end of the flexibility–rigidness axis and, like the adhocracy culture, is also focused on the external environment. The rational culture is control-orientated and emphasises competition, goal achievement, performance, and productivity. Task focus and clarity, efficiency, and high performance characterise this culture type, also referred to as the 'market culture'. The final culture type, hierarchical culture, is also control-orientated and, therefore, positioned at the rigid end of the flexibility–rigidness axis. This culture type has a more inward internal focus than the rational culture, and it values stability, centralisation, and predictable outcomes.

Although it would appear that the cultural types located in opposite quadrants are contradictory, they are not mutually exclusive [16], [20]. Since organisations exist in dynamic environments, one organisation can simultaneously exhibit competing values. In essence, different components of the various cultural types work in an interrelated way to establish balance and effectiveness. Most organisations tend to have one dominant cultural profile. However, the prevailing environmental factors that an organisation faces could result in its exhibiting traits from all four quadrants at any given time [16], [20]. The OCAI cultural analysis tool provides this study with a research lens to evaluate the ICH tripartite (Japan, Europe, and the United States) from an activity theory perspective, as outlined in Table 1. The limited amount of literature on Japan's pharmaceutical industry restricted the scope of this study. Consistent with the findings of other researchers [21], [22] a significantly small number of publications on the Japanese pharmaceutical industry were written in English. Only literature sources that enabled the comparison of all three geographical regions could be used to conduct this comparative study.

Table 1: Outline of the activity theory examination of the literature

Unknown elements in the activity theory framework presented in Figure 1	Number of literature sources examined
Tools for OpEx	28
Rule and regulations	26
Stakeholders and division of labour	31

4. ACTIVITY THEORY EXAMINATION

4.1. Activity theory examination of pharmaceutical production in ICH regions

The discussion and findings of the examination of the literature on the ICH regions are presented in four sequential sections, as directed by the activity theory approach. They are (1) Focus A: Tools for OpEx; (2) Focus B: Rules and regulations; (3) Focus C: Stakeholders and division of labour' and (4) Triangulation of focus areas to explore tensions.

4.1.1. Focus A: Tools for operational excellence (n=28)

The global pharmaceutical industry is inherently rigid and regulated [22], [23]. Thus, this study presumes that the basic quality management tools mandated by GMP are used in pharmaceutical organisations in Japan, Europe, and the United States, since GMP is legislated in all three geographical ICH regions. This study cannot confirm the names of the specific quality management practices employed in Japan owing to the unavailability of specific literature on those practices in the Japanese pharmaceutical industry. The reason for the limited amount of public information on these practices is the Japanese pharmaceutical industry's strong domestic orientation [21]. Japanese people are traditionally primarily concerned with their internal affairs and, therefore, do not see the need to publish literature on their work for the general public. This is compounded by the ranked nature of Japanese society in general. There are three distinct causes for Japan not publicly sharing information [21]. These are Japanese government policy, the industrial structure of the pharmaceutical industry, and Japanese medical culture. Based on this, it is presumed that the Japanese pharmaceutical industry has a very strong hierarchical orientation.

Notwithstanding the above comments, the Japan Pharmaceutical Manufacturers Association [24] reports that Japan's Ministry of Health, Labour and Welfare (MHLW) actively works with Japanese pharmaceutical organisations to guarantee a high level of implementation of internationally recognised GMP rules. Thus, an assumption is that selected quality management tools are integral to operations in Japanese pharmaceutical organisations to ensure and promote international standardisation and conformity to GMP. Moreover, Japan has garnered a reputation as a leader in quality management practices [25], [26]. Japanese manufacturing organisations have developed internationally recognised quality strategies with quality management tools such as Quality Circles, 5S, Poka Yoke, Kaizen Opportunities, Hoskin Kanri, and Lean. Based on this, it is assumed that a hierarchical culture underpins standard operating tools in Japanese quality management, given that all of these tools are highly structured. Control-orientated values are, however, particularly compounded in Japanese organisations, where the bureaucratic influence of government protectionist policies towards the pharmaceutical industry also plays a significant role [21].

As this study's focus shifts to tools used in European pharmaceutical organisations, a stark contrast is noted between the bureaucratic, inward-focused, and relatively closed Japanese pharmaceutical industry [27], [28] and the European pharmaceutical industry. The top ten pharmaceutical organisations in Europe in 2017 were multinational [29], reflecting the nature of the European pharmaceutical industry. This emphasises the harmonisation of quality management practices, aligned with the increasing trend of the internationalisation of pharmaceutical organisations. The literature [30], [31], [32], [33], [34], [35], [36], [37], [38] suggests that a melange of tools is used by European pharmaceutical organisations, in addition to those prescribed by GMP. The tools for OpEx include Lean, cLean (current Lean), RFT, Six Sigma, and a combination of JIT, TPM, and TQM.

Two prominent features that emerge from the evaluation of the European cases are the integration of a variety of quality management tools into the organisations' business strategies, and the substantial value placed on people management. This is consistent with the high-level structure of the most prestigious quality award in the European region, namely EFQM, and confirms that these are valued features in quality management. 'People' are considered a valuable resource in the quality strategies adopted by European organisations. The workforce creates value; therefore, the organisation is responsible for training and rewarding employees to increase their motivation, well-being, and satisfaction [39]. Thus, clan culture predominantly supports quality management practices in European organisations.

The literature on the pharmaceutical industry in the United States [9], [40], [41], [42], [43], [44], [45] is similar to that on the European region. Here, various quality management practices are used as tools in OpEx strategies. These tools are Change Control Management, Management Review, TQM, Lean, Six Sigma, and RFT. A significant feature noted in all of the cases examined in the United States pharmaceutical industry is a threefold emphasis on 'business strategy', 'people', and 'operations'. In the United States, OpEx strategies must be agile and relevant to be successful. They must meet customer demand and the needs of the business [40], [41], [42].

Furthermore, quality risk management and training are enablers that are ingrained in an organisation's mindset and are essential in daily decision-making. One study [44] describes the United States pharmaceutical industry as a successful global leader in OpEx. This study suggests that a requirement for success in the operations sector in pharmaceutical manufacturing in the United States is a degree of both hierarchy and clan culture, with a measure of innovation and market-driven culture as well. A deduction is made that a balanced underlying culture is the best approach to supporting the implementation and maintenance of quality management tools for OpEx. The United States region shows that balancing all of these cultural archetypes supports OpEx.

4.1.2. Focus B: Rules and regulations (n=26)

The pharmaceutical industry is an environment with onerous regulatory requirements [23] that impact quality management. The role of the ICH in this environment is merely to provide guidance and to promote harmonisation to foster international trade. The legal requirements are promulgated by national pharmaceutical regulating authorities (NPRAs) and governments in the respective regions.

Notification of GMP took place in Japan in 1974 [46], consistent with the global trend observed in pharmaceutical manufacturing in the 1970s. Significantly, another six years elapsed before GMP was officially legislated in Japan. This late adoption of GMP was a result of Japan's politicised, unscientific, and non-transparent governmental policies [23] in the pharmaceutical industry under the custodianship of MHW. Studies [21], [22] agree that a consequence of the devastation of Japan's entire industrial sector during World War II was that the Japanese government adopted a very controlling stance towards the pharmaceutical industry in particular. Even though this industry had caught up with the Western world by the 1970s, the MHW and the Japanese government maintained a very protective stance towards pharmaceutical organisations. Foreign competition was restricted by law from entering the Japanese market. Simultaneously, public health agendas were prioritised to ensure low-cost medication for the Japanese population. Researchers [27], [47], [48] state that stifled development in the Japanese pharmaceutical industry was the unintended result of Japan's protective governmental regulation of its pharmaceutical organisations, and that this compromised the ability of Japanese pharmaceutical manufacturers to compete with their western counterparts. International pressure through the ICH was a critical factor that eventually forced Japan to consider a more open approach to the pharmaceutical trade in the 1990s. This study regards this as evidence that a very hierarchical culture permeates Japanese society and impacts pharmaceutical manufacturing.

Regarding rules and regulations, this study notes parallels with the differences observed between Japan and Europe when examining quality management tools. The European Medicines Regulatory Network (EMRN) oversees the regulatory system in Europe, and is a partnership between four primary stakeholders: the European Commission (EC), the European Medicines Agency (EMA), the European Economic Area (EEA), and NPRAs in the European Union (EU) member states. This regulatory system has a consistent region-specific approach to regulating pharmaceutical products in greater Europe [49]. It leans towards a clan orientation. The system promotes quality management [50] and facilitates the exchange of information between stakeholders on GMP inspections, among other things, to help control pharmaceutical production in the region. The success of this system is contingent on supportive legislation within member countries. In addition to the 28 EU member states, three other countries in the European ICH region are part of the network of stakeholders. GMP is a platform for quality management from which all parties in the network connect to harmonise regulation and promote transparency [51]. The NPRAs work closely with EMA and EEC, meeting four times a year to discuss strategic issues in regulation, best practices, and information technology (IT) considerations. Ultimately, they aim to streamline processes and operations. This reveals a clan approach to regulation and quality management in the European region.

Directing the research lens towards the United States, its pharmaceutical industry is the largest in the world. It is also the only pharmaceutical industry that is not directly government-regulated [9]. Hu, Scherngell, Nga Man, and Wang [52] confirm that the United States is globally dominant and leads the way in terms of regulation of the global pharmaceutical industry. The NRA in the United States pharmaceutical industry is the internationally recognised Food and Drug Administration (FDA) [53], a consumer protection agency and the custodian of GMP in the United States. It develops regulations based on federal laws. Furthermore, although the FDA is internationally recognised as a stringent protector of the American public, it also has a progressive approach to regulation [52]. Since 1991, there has been strong political and public support for the relaxation of regulations by the FDA in the United States [54], [55].

Over-regulation stifles new pharmaceutical product innovation, and delays manufacturing and public access to much-needed medical products [9]. Researchers [9], [54], [55] call for a balance between the need for strong scientifically based regulatory policies and the need to understand the complex relationship between the social and economic requirements of a sustainable pharmaceutical industry. This accentuates the adhocracy and market cultural characteristics of the United States region, and so highlights a noteworthy difference between the cultural orientations in Japan, Europe, and the United States regarding regulatory concerns.

4.1.3. Focus C: Stakeholders and division of labour (n=31)

This section of the comparative study explores the pharmaceutical manufacturing stakeholders of the ICH tripartite and the division of labour among those stakeholders. The literature [9], [56], [57] suggests that stakeholders and the division of labour are closely interlinked, since different stakeholders perform different functions. The stakeholders examined in this section are NPRAs, governments, sellers, and buyers in the pharmaceutical industry.

Earlier in this literature review, it was emphasised that the ICH was a stakeholder in all three pharmaceutical industries because of its role to promote harmonisation between the industries. The function performed by the ICH means that an element of clan culture is necessary to promote and ensure effective quality management in the global pharmaceutical industry. The ICH supports NPRAs in all three geographical regions. The NPRAs, in turn, serve as the World Health Organization's (WHO) vehicle for regulating pharmaceutical production in organisations. The activities of the NPRAs vary between the three geographical regions in terms of the scope of their authority and the implementation of their requirements; however, the principal regulatory roles of the NPRAs in all three regions are the same [58], [59]. These include issuing market authorisations, the inspection and surveillance of pharmaceutical manufacturers, monitoring and controlling the quality of pharmaceuticals already on the market, and controlling the promotion and advertising of pharmaceuticals. Thus, it can be deduced that the duties of NPRAs in each region are similar and that a hierarchical culture is necessary to support pharmaceutical manufacturing in all three regions.

Significant distinctions between the influences of stakeholders on the ICH geographical regions only begin to emerge when the effect of government on pharmaceutical production in these regions is examined. Governments play an important role in policy development. They assist with regulating pharmaceutical industries to varying degrees in these three regions. In the Japanese pharmaceutical industry, the government is the most influential stakeholder [27], [60]. From after World War II until the 1990s, the

Japanese government fiercely protected the pharmaceutical industry; however, the unintentional consequence of this was that the industry stagnated [48]. When this was realised in the early 1990s, the Japanese government began to harmonise with other countries. In June 2013, the Japanese government initiated a Japan Revitalisation Strategy to achieve international competitiveness in the healthcare and medical sector, including the pharmaceutical industry. Through the MHLW, the Japanese government reviewed the regulatory processes to enhance efficiency and productivity [27], and in 2015 it established the Agency for Medical Research and Development (AMED) to promote OpEx in the pharmaceutical industry [27]. It is presumed that the move away from the previous hierarchical approach was because of a realisation that exclusive hierarchy does not promote OpEx.

From a European perspective, there is minimal empirical evidence to support an argument that there is any benefit in direct government involvement in pharmaceutical production [61], [62] beyond establishing a stable economic and political environment. Some European governments, such as France and Italy, have set objectives to establish state-managed production operations for pharmaceutical products. However, these objectives are not realisable, given the complexity of pharmaceutical production. Thus, a trend in Europe is that governments work in close collaboration with NPRAs, which this study regards as an inclination towards clan culture.

When comparing the United States government with others, it seems to exert the least influence on its pharmaceutical industry [9]. The rationale is that the FDA already performs these functions in the United States. The FDA is a science-based, comprehensively established and robust agency [9], [63] that is engaged in multiple efforts to ensure global health security and to protect public health in the United States and abroad. The United States government passes legislation that the FDA then regulates. However, in addition to the regulatory role, more than any of the other NPRAs, the FDA actively provides very detailed and comprehensive guidance actively to support manufacturing in the pharmaceutical industry [9], [52], [63], [64], [65], [66]. The conclusion derived from the literature evaluation is that the role of the FDA overshadows the government's role in the United States pharmaceutical industry. The government has, therefore, adopted an open, flexible stance on pharmaceutical manufacturing. The government supports the FDA with legislation; however, the FDA assumes the more proactive role and performs actions to ensure pharmaceutical consumers' safety and to promote OpEx. The underpinning culture is, therefore, adhocracy and market-driven.

Sellers and buyers do not have equal influence in the pharmaceutical industry. For the most part, pharmaceutical suppliers offer very widely available chemical commodities, and thus have little power, since commodities are available from numerous sources [9], [44], [48], [67]. This moderates the price of supplies. A distinction noted in Japanese supplier relationships was that, before the 1990s, a typical feature of the Japanese pharmaceutical industry was the presence of *keiretsu* relationships, which are characterised by commitment and a long-standing and loyal partnership [48]. This also restricted the development of the pharmaceutical manufacturing sector of the industry, since a feature of *keiretsu* is the restriction of modernisation and innovation. Following harmonisation in the 1990s, these relationships began to unravel, and the Japanese pharmaceutical industry began to resemble those in Europe and the United States. This study sees this as a move away from an unpinning hierarchical culture in Japan towards a more market-driven culture.

Buyers of pharmaceutical products in the ICH regions have a more significant impact on the activity of pharmaceutical production in general. In all three regions, patients are the final consumers of pharmaceutical products; however, the primary buyers of the products are the medical fraternity or the government in the ICH region [9], [21], [61], [63], since patients rely on the medical fraternity to decide on the most appropriate pharmaceutical product for them. Japan has a culturally distinct approach to medical therapy [60], [68] that has affected pharmaceutical manufacturing, and was especially pronounced from 1960 to 1970. Medical doctors were unwilling to inform cancer patients of their illnesses because of the belief that receiving a cancer diagnosis was a death sentence, and so was not welcome. Thus, doctors prescribed cancer medication with the fewest side effects to prevent patients from discovering that they had a near-fatal disease. This practice only changed at the beginning of the 21st century. Innovation and growth in the Japanese pharmaceutical industry also stagnated because of this practice [60], owing to the modest demand for pharmaceutical products. This study argues that this conservative medical culture was another form of the entrenched hierarchical culture that affected OpEx in the Japanese pharmaceutical industry.

In Europe, national healthcare systems are the primary buyers of pharmaceutical products [39], [69]. Furthermore, European nations prize solidarity and public health [70]. Thus, an inclination observed in this region is a unified approach to providing widespread access to pharmaceutical therapies. In European countries, a pharmaceutical product must be deemed cost-effective by a national committee before it can be made available for prescription [49], [71]. Therefore, healthy price competition is difficult to achieve because of the unified approach to satisfying buyers. This is in stark contrast to the United States, where sources in the literature [35], [72], [73] indicate that organisations use quality management (including traditionally recognised Japanese practices such as Hoskin Kanri) to gain a competitive edge over other organisations and to secure buyers. The primary buyers in the United States region are the United States government and medical insurance schemes. The priorities of United States pharmaceutical producers are set by market demand from the buyers [67], [70]; thus an underlying market-driven culture is foregrounded in this region. Market priorities then drive innovation [73] in United States organisations. This study deduces, therefore, that United States pharmaceutical manufacturers are more competitive and innovative than manufacturers in the other two regions.

4.2. Triangulation and tensions

The activity theory framework allows this study to illuminate the areas in the global pharmaceutical industry where transformation is required [11]. The resolution of the tensions showcased by this literature study identifies the broad areas where improvements towards OpEx occurred in the ICH regions. These findings provide guidance when developing an OpEx model for South Africa. The examination of tensions foregrounds an awareness of the underlying culture that directs behaviour. This provides an organisation with a vantage point from which to evaluate and tailor its OpEx strategy. In essence, this comparative study demonstrates that measuring culture should be an essential part of any quality strategy.

Research finds that, despite the absence of a literature on the specific quality tools used during pharmaceutical manufacturing in Japan, the Japanese are internationally recognised as experts in quality management [25]. Notwithstanding this status, the Japanese pharmaceutical industry has never achieved the same global status and level of OpEx as Europe or the United States. This is partly the result of contradictions between the reasons for GMP, restrictive government regulations, and the Japanese medical culture. A bureaucratic regulatory culture has overshadowed their quality management efforts, which would typically elevate performance levels in pharmaceutical manufacturing. Significantly, the secretive Japanese medical culture has also played a role in undermining the growth of the industry there.

The overruling culture in Japan is hierarchical. International pressure has led to the relaxation of regulation in the industry and to openness to harmonisation. While the initiatives have been successful, the contradictions associated with culture highlighted by this comparative study have harmed the success of OpEx in the Japanese pharmaceutical industry.

In Europe, a region-specific emphasis on strategy and people was observed. The GMP guidelines lend themselves to every pharmaceutical manufacturer's underlying hierarchical cultural approach. However, a movement towards a balance between hierarchy and clan culture was noted in addition to a primary hierarchical culture. The literature [61], [62] also indicates less direct government involvement in the pharmaceutical industry in the European region than in Japan. European pharmaceutical manufacturers collectively work towards a unified approach to regulation in collaboration with the EMRN and towards meeting customer needs in collaboration with European NPRAs. Clan culture firmly underpins efforts towards OpEx in pharmaceutical manufacturing in the European region. No tensions were noted in the European region regarding quality management tools, regulations, stakeholders, and the division of labour. However, dichotomies emerged when comparing Europe with Japan and Europe with the United States.

As stated, the United States is the most successful global pharmaceutical industry in relation to global sales and market share [74]. When comparing it with the Japanese and European regions in general, it was found that the United States adopted a more aggressively competitive approach to pharmaceutical manufacturing. Significantly, the quality management tools promoted by the FDA have a non-prescriptive threefold emphasis on 'strategy', 'people', and 'operations'. Tensions were observed in the United States pharmaceutical industry within the regulatory element of activity theory. Since the 1990s, there has been strong political and public support for the relaxation of regulation by the FDA. Although such relaxation has not occurred [75], this points to an underlying culture that is more flexible than a rigid hierarchical culture. The most significant tension in the United States is between regulation and the open market. Innovation and market-driven traits are valued in the United States.

This study highlights the most valued traits that direct the behaviour towards OpEx in each region. Collectively valued traits constitute culture; thus, culture influences the progression of OpEx in each region. In general, Japan values order, procedures, and instructions; Europe values being part of a team; and in the United States, innovation and continuous improvement are valued, as well as being recognised in the market. The finding of this comparative study is that all of these values are required for sustainable quality management that leads to OpEx. Thus, the OCAI is a tool to measure the proportion of each culture type in an organisation.

5. CONCLUSION

This literature study has drawn attention to the variety and balance of OCAI culture types that support continuous improvement and development in the pharmaceutical industry. The OCAI cultural research lens scrutinises the underpinning culture in each geographical region, and highlights tensions that emerge during each region's transition to improved OpEx levels. The ultimate objective of this literature study was to examine the role of the four culture types in pharmaceutical manufacturing in the ICH regions. A conclusion from this review of the literature is that adopting quality management practices would enable an organisation to improve itself continuously in all dimensions. An underlying quality culture that supports quality management practices is also a vital independent variable on which OpEx rests. The finding of this study is thus that culture directs the behaviour of people, that it is an unseen control mechanism for the daily routines and execution of operational tasks; and accordingly, culture must not be overlooked while managing quality. The findings of this study lay a foundation for future research, which will be to develop an OpEx model (based on culture) for South Africa.

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