Multi-Sourcing in the South African Pharmaceutical Industry

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DECLARATION

I, Dipesh Daya, declare that this research report is my own work except as indicated in the references and acknowledgements. It is submitted in partial fulfilment of the requirements for the degree of Master of Business Administration in the Graduate School of Business Administration, University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in this or any other university.

Dipesh Daya

Signed at ……

On the …….. day of …… 20…..

DEDICATION

This research report is dedicated to my family, friends, mentors and colleagues who have taken an active role in guiding and supporting me through my MBA journey.

It is especially dedicated to my mother, who has been my pillar of strength throughout my life.

I would also like to dedicate this research to my friends and family that have departed, who have played a major role in guiding and inspiring me to this day.

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SUPPLEMENTARY INFORMATION

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Supplementary files:	Research Survey Data (Including survey questions)
	Statistical analysis for Research Survey Results

EXECUTIVE SUMMARY (ABSTRACT)

Pharmaceutical supply chains play a major role in the management of the integrated process from the procurement of raw materials to the administration of the drug or drug product to the patient. This process spans across multiple business units, businesses and industries which can pose challenges to the performance of supply chains within the industry (Kokilam, 2016).

This research report was undertaken to look into the challenges of multi-sourcing in the South African pharmaceutical industry with particular reference to sourcing challenges, vendor challenges, compliance challenges and regulatory challenges.

Following a review of existing literature, an online survey was generated, specifically targeted at individuals involved in the related roles within the pharmaceutical industry. The survey was sent out to individuals at most of the currently operational pharmaceutical companies in South Africa and involved a combination of multinational organisations and local organisations. The survey data was intended to determine the industry view on the extent of challenges posed to multi-sourcing in the current pharmaceutical environment.

The key challenges identified in the literature review were the availability of alternate material, product and intermediate sources; the quality and regulatory requirements and the timelines thereof; the cost implications of the change process; and the disadvantaged state of fully local organisations in comparison to multinational organisations specifically operating in the South African pharmaceutical industry.

A total of 90 responses were logged with 74 fully completed surveys. The data used for purposes of this research report was extracted from the fully completed surveys only. The analysis of data was primarily through the use of descriptive statistics and variance testing.

The challenges encountered are significant to the local industry, as confirmed by participant responses to the research survey. These challenges may be overcome

through the use of networking, the use of agents and increased local pharmaceutical activity.

As much as profit is a key commercial driver to the industry, of greater concern for the local market is business continuity and the need for giving the end user a cost effective product that is safe and of good quality. The greatest impact of local pharmaceutical organisations is on the livelihoods of the patients using acute, chronic and life-saving medicines. In a highly competitive generic environment this can be guaranteed through multi-sourcing, making this process a key business practice that should align with the procurement goals of every pharmaceutical organisation operating in the country.

KEY DEFINITIONS

Supply Chain Management	The management of the flow of materials and products into, within and out of the business, including all intermediate processes required in making the product available to the market.
Regulatory Compliance	Compliance to the requirements of the local health authority board (SAHPRA – Formerly MCC in South Africa)
Quality Compliance	Compliance to the principles defined internally per company that ensures that patients receive effective and quality medicines and medical products.
MOQ	Minimum order quantity determined by material suppliers as the smallest possible order size for a business transaction to be secured.

SAHPRA / MCC	South African Health Products Regulatory Authority, previously known as the Medicines Control Council, which serves as the regulatory authority responsible for the control of medicines and related substances in South Africa and the neighbouring countries.
GxP	Standardised industry practices based on Good Practice guidelines. The “x” is a variable and may apply to Manufacturing (GMP), Laboratory (GLP), Clinical Studies (GCP), etc.
Chronic Patients	Patients taking medication on an ongoing basis for the treatment of chronic health conditions
Acute Patients	Patients taking medication on a once-off or short term basis for the resolution of an acute medical condition.
ERP	Enterprise resource planning. This is often facilitated by a business tool that has oversight over the status of products and materials as well as the movement of all materials and products within the system.
OpEx	Operational Excellence is a term used to describe the team and the efforts introduced in the industry that facilitates process and product optimisation. In larger organisations this forms a separate department, however, in smaller organisations it forms part of the production, projects or finance teams.

INTRODUCTION

In the supply chain management, of products and services, in all industries, the capability of building in a choice mechanism through multi-sourcing creates an ideal business scenario (Lambert, 1998; Ayhan, 2013). Similarly, this applies to the pharmaceutical industry, where multi-sourcing of materials, intermediates and products can have a positive impact on the sustainability of pharmaceutical organisations and a resultant impact on maintaining product availability for the end user. This process requires an integrated approach, however, is still riddled by industry and organisational challenges that result in deterring the multi-sourcing process.

This study serves to understand the challenges to multi-sourcing encountered by the South African pharmaceutical industry with the aim of either confirming or refuting the hypothesis that multi-sourcing in the pharmaceutical industry is hampered by the processes behind the technical, regulatory and quality compliance requirements. In the process, this study delves into the views of individuals employed in related roles within the South African pharmaceutical industry in relation to the specific challenges encountered.

Evolution of the Pharmaceutical Supply Chain

Globally, the pharmaceutical industry is a sophisticated and unique industry that is riddled by regulatory, compliance (quality and legal) and development challenges (Srai, 2015). These challenges arise with globalisation, process complexities (including the technical processes) and compliance (quality and regulatory) (Busfield, 2003; Rosenkranz, 2015). These challenges largely impact supply chain processes as the quality and regulatory requirements and timelines often result in major delays and stops in the supply of raw materials, intermediates, bulk product and packed product. If inadequately planned, the organisations and market has to endure significant delays and stock outs until an adequate resolution can be obtained (Shah, 2004; Srai, 2015). The South African pharmaceutical supply chain

endures the same challenges, often made worse by the lack of local material and product suppliers (Christopher, 2004).

Supply chain has evolved from being a purely back-office function to being an integrated business function that plays a role in the monitoring and control of processing steps within each division of the industry (Kokilam, 2016). This includes sourcing as the starting point through to warehousing and distribution as the final point before the product is retailed to the end user. The supply chain function was initially based around the logistics of products and materials. This was later integrated with the procurement function, followed by demand and material planning. This has incorporated full business functionality ranging from the initial functions of supply chain management to the integration, and monitoring of all processes and functions making it an essential core function within the business (Harland, 1996; Chae, 2013).

This type of approach gives companies the advantage of using track and trace applications and having definite timelines for deliverables at each stage or sub-stage of material transfer, processing and delivery. This process starts at the point of working with demand planning and forecasting as well as customer orders to adequately plan the timelines within which the product must be delivered. All of this can be facilitated through the use of ERP systems. The supply chain team can then plan for materials, which includes the sourcing, ordering and shipping of the materials, equipment and labour times for the product processing form the raw material form to the packed product form that can then be put into stock or shipped to the customer to be sold to and consumed by the patient (in conjunction with the relevant department managers). These processes must be adequately aligned to ensure a good and realistic flow of materials and product throughout the defined processes (Croxton, 2001; De Soete, 2016). The details in the process may differ between organisations, but the framework essentially remains the same.

These challenges become evident in supply chain or sourcing (procurement) however, have a much greater scope and can result in widespread and cross border stock-outs, patient supply disruptions, breakdown and loss in patient control

systems and opportunistic capitalisation of the market by available players (Enyinda, 2010). In this fragile business environment, timing is critical. When considering market share, there is a difference between the first to market and the first follower to market, with the first to market taking the greatest gains whether it is a new launch or bringing out improved or cheaper alternatives (Suh, 2000; Schoenherr, 2015). Timing therefore becomes a critical factor of the quality, regulatory and development work required in ensuring the availability of the pharmaceutical product.

The impact of globalisation

Globalisation has become a growing and significant factor in the pharmaceutical industry, with the need for companies to obtain materials and products from other business units or companies abroad introducing the requirement for control of logistic functions. The same applies of the sales function in controlling the warehousing and distribution flow of products (Busfield, 2003). Hence the need to manage and control the cross-company business functions in such a way that streamlines these functions. This drives pharmaceutical and other businesses to have fully integrated supply chains that either incorporates demand planning, forecasting, material planning, procurement, production planning, quality control, warehousing and logistics(in-bound and out-bound) functions (Semin, 2008).

Quality and Regulatory Compliance

The pharmaceutical industry is further challenged by the compliance requirements and regulatory commitments. This is not a direct supply chain management function, however it greatly impacts the supply chain management operations and requires the supply chain team to work closely with quality and regulatory departments (Marc, 2001).

Quality requirements are often organisation specific and are defined by internal manuals and directives that find origin in general industry guidelines and best practices. On the other hand, regulatory requirements are stringently defined by

the health regulatory authorities of the country or region. These requirements make it difficult for companies to change processes, procedures and techniques as it often requires long term variations to be filed with the regulatory authority (Locally, The South African Health Products Regulatory Authority – SAHPRA) for assessment prior to making any changes to currently registered processes, procedures and details. Depending on the change, there may also be the requirement to submit additional info in the form of test batches, test results, product stability data and supplier information (Rosenkranz, 2015).

A major risk that is inherent to many pharmaceutical companies, is that during development, only one registered and active material supplier was used for each material. For most, the non-active ingredients are available from alternate suppliers and can be supplemented through a minor variation (considered Type A or Type B variation as per the MCC amendment guidelines) to the health authority registration with some basic testing, a process validation if considered a Type B change and comparative studies. In these cases the risk to continuous supply is minimal and can be done without any market impact. With the active pharmaceutical ingredient (the actual drug substance) changes, the process is much more detailed, being considered a Type C change (Nash, 2000). Apart from the submission of the variation, this requires further comparative studies with the inclusion of full process validation and stability studies with an average timeline for a type C change being 18 to 36 months (Keyter, 2018).

Key limitations

Limitations to this study have been identified during the review of the literature, as well as the sample selection and data collection.

The study has been focussed around pharmaceutical organisations only operating within the South Africa and does not include organisations with no local production operations. All non-pharmaceutical and imported product suppliers are therefore excluded from the study.

Review of existing literature brought about limited recent literature on an international level relating specifically to the concept of multi-sourcing in the pharmaceutical industry, with older literature available and recent non-pharmaceutical supply chain related literature being available.

As this study was targeted at individuals in specific roles within the industry, the range of participants was narrowed by the scope and experience requirements. This had allowed for responses from individuals experienced in the related roles for the study.

The pharmaceutical market in South Africa is limited to only a few organisations, however, even within these organisations, data collection was limited due to non-disclosure agreements imposed on key personnel within the industry. This had a limiting effect on the collection of data from individuals in certain larger organisations.

Key Assumptions

The research conducted was formulated under the assumption that local pharmaceutical organisations are impacted by being single sourced for most products and materials, impacting the supply to market when supplier challenges are encountered.

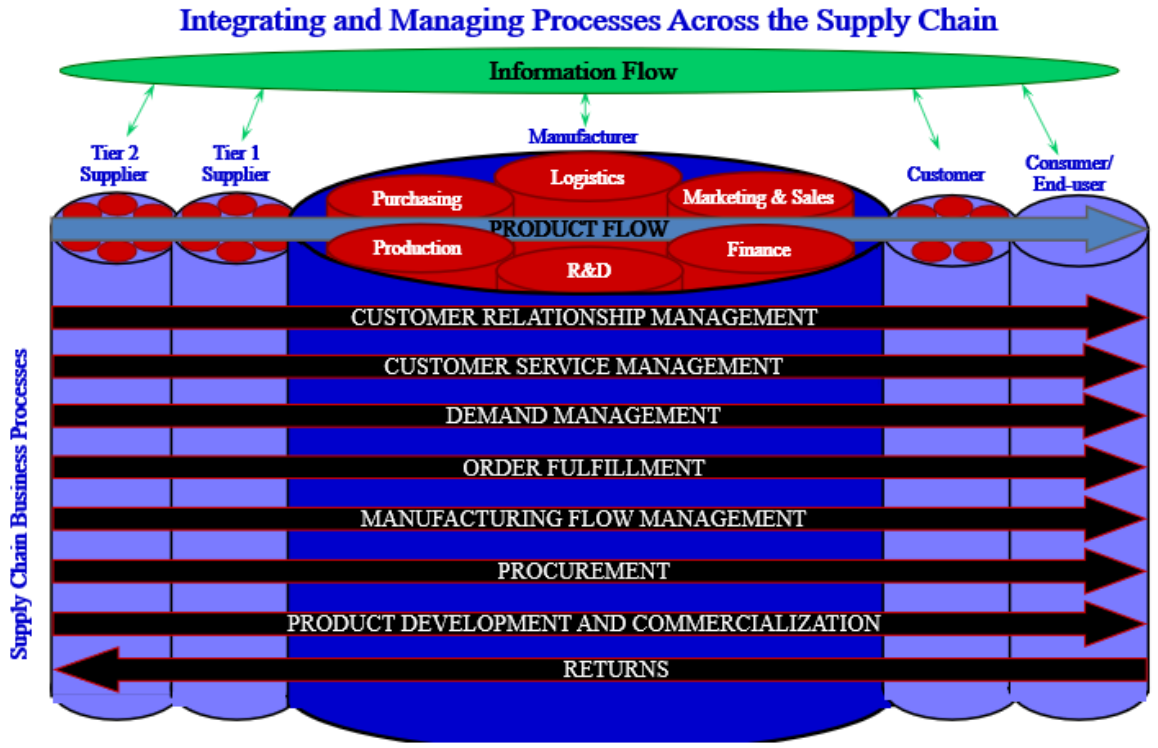
A further assumption in the form of the timelines required for fulfilling the quality and regulatory requirements can be considered standardised across all organisations being subjected to the local medicines authority, SAHPRA.

The availability of additional sources of products and materials are limited locally and challenged by the requirements for implementation of the alternate sources. The challenges affect the cost, timelines and compliance requirements in ensuring adequate availability of product to the market.

APPLICATION OF PRIOR RESEARCH

With the current supply chain management direction, Croxton, et al, describes the supply chain management function as streamlining cross company processes to the next great frontier for reducing costs, enhancing quality, and speeding operations (Croxton, 2001; Schoenherr, 2015).

The 8 management processes identified by the Global Supply Chain Forum as the framework of the function are: customer relations, customer service, demand, order fulfilment, production flows, procurement, product development and returns (Croxton, 2001; Bechtel, 1997). All of these functions apply to the sourcing, production and distribution of pharmaceutical products, materials and intermediates.



Source: Douglas M. Lambert, Martha C. Cooper, Janus D. Pagh, "Supply Chain Management: Implementation Issues and Research Opportunities", *The International Journal of Logistics Management*, Vol. 9, No. 2, 1998, p. 2.

Figure 1: Lambert's Integrating and Managing Processes across the Supply Chain (Lambert, 1998)

Chopra and Sodhi had later identified generic supply chain challenges and mitigation strategies in their 2005 article. In the pharmaceutical industry the same identified risks apply, however, with the addition of regulatory and compliance risks. The key risks from the Chopra and Sodhi model (on the right) that apply to the sourcing of materials include supply disruptions, supply delays, forecast risks, capacity risk, and inventory risk and depending on the function of the company, receivables risk (Chopra, 2004). Enyinda et al had developed a similar view after evaluating the risks and resilience of the pharmaceutical industry in developing countries (Enyinda, 2010). From Chopra and Sodhi as well as Enyinda, mitigation strategies included added capacity, inventory, additional or redundant suppliers, and demand pooling, can all be directly applied to make an impact on the overall supply chain, however, the regulatory and compliance challenges make it gruelling to increase responsiveness, flexibility or adding additional suppliers (Nash, 2000). These could be implemented as mid-term improvement strategies (3-5 years) and have no immediate impact in improving material or product supply. The challenge with this is that once customers or patients have changed to another product or generic, it is difficult to gain them back (Jones, 1995). With the nature of the industry, this could be detrimental to a product or group of products.

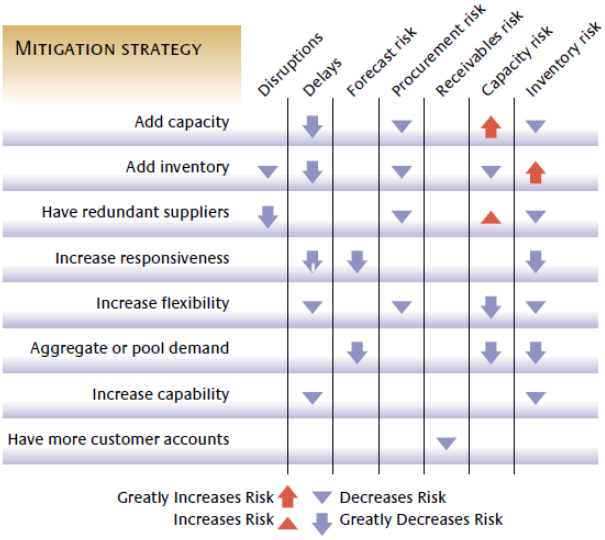


Figure 2: Chopra and Sodhi's Risk and Mitigation Matrix

The integration of supply chain management in the planning and production processes makes it a key structural component in the efficient running of pharmaceutical production plants with the consideration of campaign time and cycle time. Typical production, efficiency and operational excellence teams wanting to maximise campaign run time through consolidating orders and doing as much as

feasibly possible as per orders and forecasts, taking into account the availability of the material combinations (Susarla, 2012).

Multinational Pharmaceutical Businesses

Multinational pharmaceutical companies make use of highly complex supply chain units that are able to drive the business processes. This is due to the requirement for amalgamated multiple stakeholders and multi-site alignment in processes. These companies ideally have full alignment in processes and timing between the different sites to ensure an efficient continuous supply of materials and product taking into account specific differences in the handling, control, transport and manufacture of each supplier and product/material (Susarla, 2012).

The challenges introduced by the quality and regulatory requirements in the pharmaceutical industry

The high regulatory and quality compliance focus in the industry makes the pharmaceutical industry a high cost industry. In conjunction with the costs of patents, equipment, research and development (or science and technology), as well as high operational and maintenance costs for the operation of a pharmaceutical manufacturing facility, the excessive raw material and freight costs drive many pharmaceutical companies to operate from facilities close to that of their major cost driving API suppliers to avoid massive import duties and corporate taxes on unprocessed materials and product (Susarla, 2012). These challenges often lead pharmaceuticals into supplier deals with a single material supplier per required material. The products are then designed, developed and registered this way, creating a logistical, quality and regulatory challenge when change is to be considered. In extreme circumstances, such as suppliers closing down or stopping product lines, change is needed, however can be hampered as a result of the same processes. Susarla had discussed the need for supply chain integration between sites and businesses in order to simplify the supply chain process and in parallel reduce the risk of single sourcing through multi-sourcing where possible.

Susarla's idea of multi-sourcing is one that cannot be immediately implemented as a result of the regulatory and compliance requirements (Keyter, 2018). It also brings in the challenge of minimum order quantities from suppliers making the decision for many organisations close to impossible unless there is adequate demand for the products requiring the specific raw materials. However, in Susarla's model, there is the possibility of the use of intermediaries (Susarla, 2012). These intermediaries could serve as secondary distributors for materials and intermediates. This would mean that the intermediary buys material from the direct suppliers/manufacturers at quantities above the MOQ and sells part quantities of the materials to various other companies. This approach makes multi-sourcing more practical, however, with the added costs of the intermediary as well as added logistics costs to the product, the material costs to end user pharmaceutical companies goes higher, putting more cost pressures on most companies that are already financially stretched.

The need for Quality Risk Management in the sourcing of pharmaceutical materials is highlighted by Moreton in a guideline that prescribes a quality by design model (Moreton, 2010). Quality risk management is a function taken by an integrated procurement team in conjunction with internal quality teams that involves setting up quality agreements with suppliers, supplier facility and quality process audits and has major input in the service level agreements in the pharmaceutical industry. The quality aspect of the business takes precedence over all other functions in this industry. Suppliers are partly managed through strict quality agreements and service level agreements defining the minimum standards required for the materials being purchased (Stolle, 2008). Where quality risks are identified, stakeholders are given immediate notification to resolve and often results in disuse of the supplier until the identified findings are adequately resolved, or in the case of the inclusion of a regulatory authority, it may result in temporary or permanent closure of a supplier site. With the temporary closure, a defined period will be allowed to the management of the site in order to resolve the compliance risks before a re-inspection will be warranted. The site would then not be able to produce or supply until the authority is satisfied with the corrective action taken and the restriction is

lifted. This translates to supply shortages and stock out risks in the market where materials and products are single sourced (Shah, 2004; Videau, 2000).

Product recalls due to processing and supplier issues are common in the pharmaceutical environment. With the quality of the product and safety of the patient being of greatest importance, a recall can be warranted at any time (Steven, 2014). If no replacement stock is available market stock out is imminent. If the recall is warranted by a supplier or material quality issue and there is no alternate supplier available, qualified and registered for use, the company would be at risk of a long term stock out (Shah, 2004).

Forecasting

Managing material availability through the planning and procurement is always challenged by erratic orders and forecasts. If the market demand drops, the business will be holding on to stagnant stock that may end up being written off. If market demand spikes suddenly, the business will not have enough raw material, intermediates and product on hand to address the market demand. This combination can ultimately result in erratic supply to the market (Croxton, 2001; Lambert 1998; Hansen, 2015). These scenarios have a direct knock on effect on the suppliers of raw materials, intermediates and products as these suppliers also base their production plans and processes on their market demand. Although some level of safety stock may be kept on hand, erratic forecasts and irregular orders can quickly deplete the stored product and material. As with the end user organisations, material suppliers are also posed with write off risks when there are significant unexpected reductions in the demand of their products. Changes in demand are often not adequately planned and budgeted for, hence reduced demand as a result of customers purchasing from alternate sources leaves suppliers with excess product and increased demand from increased use by customers quickly depletes safety stock levels. The sudden changes in demand can, at times, put suppliers in a position where they may increase prices to manage the demand or they may start to ration the available material between customers to minimise impact on the market (Susarla, 2012).

There is a difference in the organisational processes between materials used in multiple products and those used in single products. It is easier for procurement teams to justify the need to secure and activate multiple sources of a material that is used in many products, however it becomes difficult to manage multi-sourcing of materials used in one product only. This is the case for most Active Pharmaceutical ingredients (APIs). With the sourcing of APIs, apart from the initial task of identifying alternate suppliers, minimum order quantities (MOQ) become a factor and more importantly, the costs of assessments and implementation are often astounding. .These costs include a range of compliance activities such as audits, registrations, trials, validations and stability studies become evident and will require more than a high level business continuity justification (Keyter, 2018; Susarla, 2012).

Expiry of materials poses a risk in production facilities where intermediary warehouses and suppliers do not adequately exercise the FEFO (first expiry, first out) policy. Without adequate control, good inventory levels are worthless as the expired materials are rendered useless. The incorporation of an ERP system that provides adequate material detail and control is an easy way around this and can prohibit movement of materials when not following the FEFO policy. It would also flag planners and procurement teams of materials that are close to expiry to promote the discussion of the need and timing of replacement stock. This can become a risk to suppliers as organisations aim to balance orders between multiple sources when attempting to implement multi-sourcing practices (Lambert, 1998; Shah, 2004).

Standardization of pricing

Reference pricing (or single exit pricing as known in South Africa) is a means of regulating the pharmaceutical industry pricing and the retail sector through standardising prices or price ranges per product. It requires adequate justification for a product price and limits the extent to which a price may be marked up by retailers (Pretorius, 2011). Reference pricing makes it difficult for organisations to absorb big fluctuations in product price that may be a result of changes in material costs due to a change in supplier or change in process (Galizzi, 2011). This is a

challenge to most as fluctuations in material prices are common and are based on demand, freight and urgency. If a reference price has been set using an API source that is no longer available, a new reference price would need to be defined and in most cases may only be done in the next review making the process largely disadvantageous when a new material suppler or alternate material supplier is much more expensive than the current supplier (Pretorius, 2011).

The Economic Nature of the industry

The pharmaceutical industry can typically be described as a combination of monopolistic and oligopolistic business markets (Caves, 1991). The originator, otherwise known as ethical companies drive a typically monopolistic industry, bringing novel drugs, treatments and devices onto the market at a high starting price with the aim of recovering investment costs as quickly as possible (Scherer, 2004). The oligopolistic nature of the industry is brought about by the generic companies that bring in the same drugs, devices and treatments as the originators, at the end of the patent period. The generic organisations drive multi-sourcing as cheaper alternatives increase the ability of these organisations to create products at lower costs making them more competitive on the market (Masoumi, 2012).

With the pure R&D, patent driven, drug originator companies fairing on the monopolistic end of the scale, the supply chain models of the originator companies are entirely different from that of the generic or hybrid companies. Originator companies often are linked to researchers that conduct the chemical synthesis of drug molecules or have these functions internally. The function is therefore not cost and mass production driven and the focus is on new target markets. With generic and hybrid companies, even though considered oligopolistic in nature, the focus is on cost as once a drug product patent has expired, multiple generics are made available and the competition grows for the first generic product to market and the cheapest generic product (Caves, 1991). Most generics are launched with the drug molecule sourced from the originator, however, over time other companies are able to clone the molecule created by the originator, making a cheaper active drug substance available. The drive for these companies is on cost (minimisation) and

making high volumes available to the market and at the same time challenging the supply chain management, production, compliance and regulatory teams to implement the most cost effective materials and methods while maintaining safe and effective products of high quality (Suh, 2000).

The view of Local vs Multinational companies

A related dynamic is brought about though the split between multinational and fully local organisations. The multinational companies have a significant advantage in the form of quality and compliance support as well as buying power from raw material suppliers. On the regulatory and compliance front, for a multinational organisation, the use of regional or group networks allows for compliance activities such as audits and review on material suppliers to be conducted by teams in close proximity to the supplier site, reducing the cost implications of the audit and also allowing for the audit outcome to be used by all of the linked business units that use or prospectively will use the materials from that particular supplier, on a positive audit or review outcome. This becomes highly challenging for smaller local companies. From a regulatory perspective, there is a need to have supplier quality audits (Keyter, 2018). The costs of putting together an audit team and funding an audit trip anywhere in the world for each major material supplier can cause budgetary strains for companies (Susarla, 2012; Shah, 2004).

Large multinational companies also have the advantage of long term planning and decision making as well as strong bargaining power through placing consolidated supplier orders for the multiple business units the company may have globally (Shah, 2004). There is also the possibility of managing logistics and supporting sites through a holding warehouse and site-to-site material transfers. This further mitigates the risk of material write offs as a result of a decline in demand in a particular country (Susarla, 2012). If lead times are adequately planned in, this could improve business efficiencies on the global level.

Some multinationals are able to strategically evade the risks of single sourcing through specialising production facilities for specific products and functions. This

strategy starts off by supplying the markets within the scope of the responsible regulatory authority. The business then drives for approval of other regulatory authorities globally in order then allow it to partially or fully manufacture and pack the product at the dedicated facility and export either bulk product or finished dose forms to other markets. This is a long term exercise but improves the business performance, scope and efficiency (Caves, 1991; Susarla, 2012). The use of common production and packaging systems and sites allows the business to maximise equipment outputs and at the same time obtain product availability in many countries through the use of packaging and labelling that is specific to the countries from which the orders have been received. This strategy allows for organisations to negotiate with multiple sources of materials, intermediates and products within the local scope as the organisation mass produces for local and export consumption, ensuring that quantities required are high and sustainable for the organisation and the multiple sources being used (Shah, 2004)

An overview of the literature

The supply chain plays a critical role in business continuity within the industry. The three major influential forces identified in the area of pharmaceutical supply chain are compensation, alternate channels and product forces. These forces drive the direction of the market and global pharmaceutical industry in ensuring market activity with the key stakeholders that results in business continuity (Rossetti, 2011).

The need for multiple sources is a key consideration when the discussion of business continuity arises. Sustainability of the industry in light of the planned NHI (National Health Insurance) implementation puts the need for cost effectives drug, drug products and medical services as a high priority on the industry visions (Pharasi, 2012). The risk of being non-competitive in tenders and other forms of government business will lead to major losses in the companies that are unable to keep up with the requirements, especially with the importation of low cost products and materials form highly efficient factories elsewhere (Barber, 2018; Rowe 2013). This highlights the need for effective and efficient management of supply chain and related functions by each competing business as well as the need to remain in the

front line of change to ensure constant competitive behaviour, control, planning and timing of changes (change management); and active business participation in the industry and business continuity (Shah, 2004).

Global integration is a route that can be used to support global and multinational organisations but raises a question as to what happens to the local manufacturers and whether these companies will be able to absorb the costs of multi-sourcing if indeed it is needed in the highly regulated industry.

On the basis of the views of professionals within the South African pharmaceutical industry the questions of the availability of alternate sources locally and internationally as well as the evaluation of the challenges around the implementation of the use of materials and products from alternate sources. This includes delving into the perception of extended timelines as a result of quality and regulatory requirements and the implementation costs of the potential multi-sourcing exercise.

DATA COLLECTION AND ANALYSIS

The data required for this research report was collected through a survey for the sole purpose of this research. The survey tool included 19 questions that were designed to obtain the views of industry experts, pertaining to multi-sourcing in the pharmaceutical industry. The questions were defined and structured to obtain maximum engagement and responses from the participants. The survey was adequate in obtaining the required data. It was designed to allow for best possible participation from the limited number of individuals in the functions in the local pharmaceutical industry (requiring a maximum of 10 minutes to complete the survey).

The data collection method selected was primarily quantitative, focussing on the standardised survey response views of all participants. Responses were coded into a numerical format. The research undertaken was not intended to analyse individual responses, and the focus was on gathering individual survey responses

to analyse the data statistically for the industry. The choice of using quantitative data also allows for the standardization of data for the evaluation, analysis and interpretation of data.

There are approximately 11 operational pharmaceutical manufacturing companies in South Africa. The sample size selection was based on the average of 25 employees in the functional roles selected for this study. This totals a population of 275 individuals, however, it was not possible to reach and obtain a response from the full population. A sample size of 50- 80 participants was therefore proposed for the completion of the survey to be analysed in this study. This would provide adequate information for the required statistical analysis

The questions posed in the survey were directed towards the obtaining information from the participant around the sector within the industry in which the participant operates (supply chain management, general management / commercial management, quality compliance and regulatory compliance); the participant's total duration of industry experience; the participant's views on the requirements single sourcing and multi-sourcing of materials and products; as well as the participant's views of average timelines for the implementation of supplier replacements or additions and the limitations introduced by the various quality and regulatory requirements and guidelines. The selection of these roles is based on the functional exposure to the scope of this research report and is elaborated further in Table 1 below.

The anonymity of the survey participants was maintained throughout the process and the data could not be linked to the organisation to whom the survey participant was affiliated. No individual information was collated and analysed for the purposes of this study. The survey was posed to participants working within the defined functions in the local manufacturing sector of the pharmaceutical industry only.

The survey was generated on the concept of the five response scale of the Likert response format, Participants were able to select the most appropriate response to a statement along the scale of Strongly Agree, Agree, Neutral, Disagree or Strongly Disagree.

This data collection and analysis conducted was in the form of a formal cross-sectional study using a statistical sample within the industry with the aim of obtaining the actual routine perceptions from the respondents.

The target population is defined in the table below. These are representatives of the sector of the industry that would have the best understanding of the challenges around single and multi-sourced materials and products. As this population is relatively small within companies based in South Africa, the sampling method to be applied will be true random sampling with surveys targeted to the selected groups below.

Analysis of the collected data included the use of descriptive statistics as well ANOVA (Baur, 2007) (regression) analysis in order to generate an overall view of the perceptions of the challenges within the total sample, thereafter breaking down the analysis in to sub samples depending on the area of expertise of the participants.

Potential research participants:

Participant group	**Reason for participation**
Supply Chain Management Professionals	This function is directly involved in the supply chain management within the respective company/industry. Members of this group have a full view of the current supply chain roles and challenges.
General Management	Business management to whom supply chain decision making is critical. This function requires a strong understanding of the impact of not having the product available to the market on time

Regulatory Professionals	Involvement in the regulatory aspects of product registrations as well as dealing with queries from the health authorities with regard to updates and submissions.
Quality Assurance/Control Professionals	Involvement in the control of the quality aspect of the business requirements and take on the major compliance role within the business.

Table 1: Participant groups selected for the research survey

The key limitation to this study is the limited number of participants in that may be approached as part of the data collection. Many of the participants operated from segmented regions and may not be reachable for data collection. Another limitation may be in the form of possible denial from privacy and compliance units within these businesses that would prevent participants from partaking in the survey.

The validity and reliability of the survey was assessed against the scope of the project prior to the circulation of the survey. This was conducted through an initial pilot study with five participants followed by a discussion on the concepts and survey questions raised. The pilot study had assisted in aligning the survey with the key concerns and concepts raised around multi-souring. The survey was also assessed for homogeneity, convergence and applicability to the theory. (Heale, 2015).

The external validity of this study was justified through the concept that this study delves into the details of challenges in a specific sector of the pharmaceutical industry. The challenges that are being assessed are evident globally and with the current trend of globalization among multinational companies, the highlighted challenges may have a significant impact on smaller business units and organisations (Onwuegbuzie, 2000). Although this study could be applicable globally, this report has been scoped to a local level in the South African pharmaceutical industry.

The reliability of the research is on the basis that the data was collected from participants employed in specific roles in the pharmaceutical industry making them subject matter experts in the field. The data source therefore can confirm the reliability of the data and research conducted.

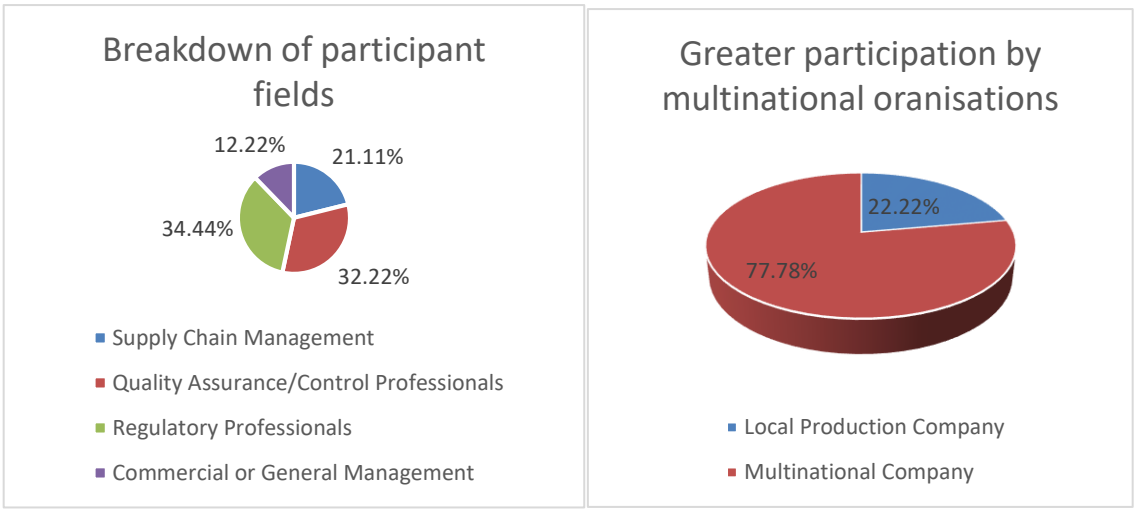
Ethical Considerations

No ethical issues have been identified in the preparation of the protocol and are anticipated during the data collection and processing. Ethical clearance to proceed with this research was granted through the University of the Witwatersrand research ethics committee.

RESULTS

All data generated for this study was confirmed to be through the voluntary completion of a research survey targeted at the narrow range of participants, being professionals in various pharmaceutical companies, that would have adequate knowledge and understanding of the processes and requirements of multi-sourcing in the South African pharmaceutical industry.

The survey was sent out to colleagues in various pharmaceutical companies, and had a total of 90 voluntary responses. Of the 90 participants and 77 complete survey responses, 21% were supply chain management professionals, 32% were quality assurance professionals, 35% were regulatory compliance professionals and 12% were individuals in commercial and general management roles within the industry. Therefore confirming a strong representation of participants, in the small industry population and a diverse range of professionals within the targeted fields.



Figures 3: Graphical representation of employment fields of participants and the breakdown of participants between local and multinational organisations

Further, 78% of the respondents were employed in multinational pharmaceutical companies at the time of the study and 52% of the respondents had working experience in more than one of the defined fields within the industry, with a further 37% of respondents having some exposure to multiple fields within the industry, giving them a working knowledge of the various functions required for the survey data.

The data obtained from the sample can also be considered to be a good representation of the industry as 52% of the participants have more than 8 years of experience in the industry and essentially, 81% of the participants being in the industry for more than 5 years. This indicates that most of the participants are well experienced and familiar with the industry being studied.

DATA AND ANALYSIS

The data was further evaluated, and analysed through the use of descriptive statistics and regression analysis to yield the analysis detailed below.

The use of the ANOVA analysis on the data yielded an overall variance in the raw data of a maximum of 2.32. This was further viewed per survey question. In order to determine this, the data was codes by the use of a numbering system based on the option chosen by the participant as a response, e.g. the first response option was allocated number 1, while the second response option was allocated number 2, to the highest number, 5, based on the maximum of five response options in the survey. This has been broken down into three key topics in addressing the questions around multi-sourcing in the pharmaceutical industry, viz. the need for multi-sourcing, the impact of the regulatory and compliance on multi-sourcing in the pharmaceutical industry and the cost implications of multi-sourcing on the decision making process.

Assessing the need for multi-sourcing through analysis of the responses of the survey participants yielded the following responses:

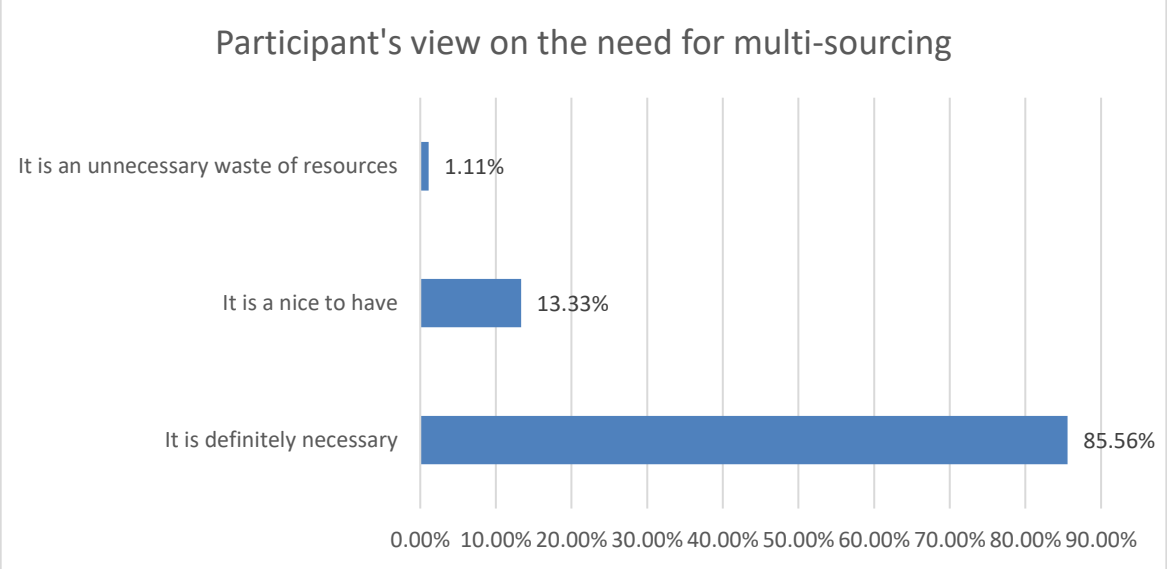


Figure 4: A graphical representation of participant's views on the need for multi-sourcing

The graphical representation above indicates that 85.56% had indicated the need for multi-sourcing, with a further 13.33% seeing some advantage in multi-sourcing. Only 1.11% of the respondents had a response indicated no value in multi-sourcing. This indicates a strong view within the industry supporting multi-sourcing for the South African pharmaceutical industry. The variance detected in response to this

topic was calculated as 0.15, confirming the majority view as multi-sourcing being definitely necessary in the industry.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.06; Quality professionals as 0.29; Regulatory professionals as 0.11; and commercial and general management professionals as 0.

Delving further into this topic, the possible advantage of multi-sourcing of raw materials, intermediates, and finished products was evaluated, yielding the following results:

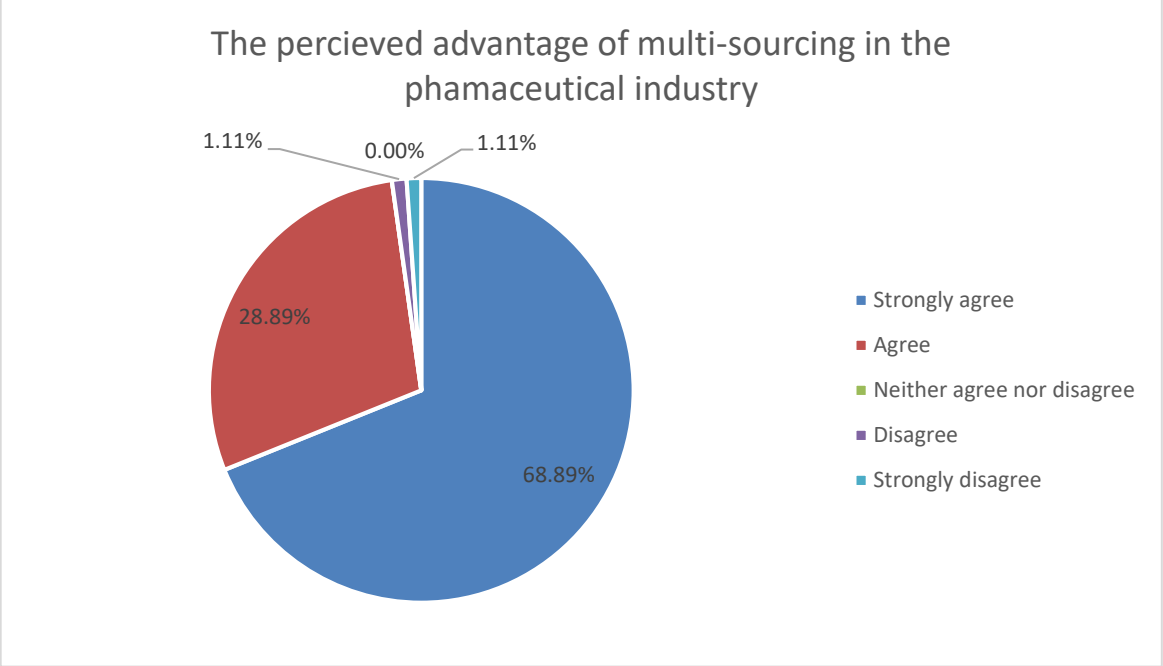


Figure 5: A graphical representation of the industry perception of multi-sourcing in the pharmaceutical industry

The graphical representation above further highlights the view in the industry supporting multi-sourcing. The total positive response obtained through the inclusion of strongly-agree and agree responses (the dark blue and red areas in the chart above) is equivalent to 97.78%, with only 2.22% of respondents not in support of the view of multi-sourcing being advantageous in the industry. The variance in response was identified as 0.43, with a high response in the strongly agree and agree options.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.15; Quality professionals as 0.49; Regulatory professionals as 0.73; and commercial and general management professionals as 0.14

Evaluating the need for multi-sourcing as a key business process that would form part of the procurement function indicated the following:

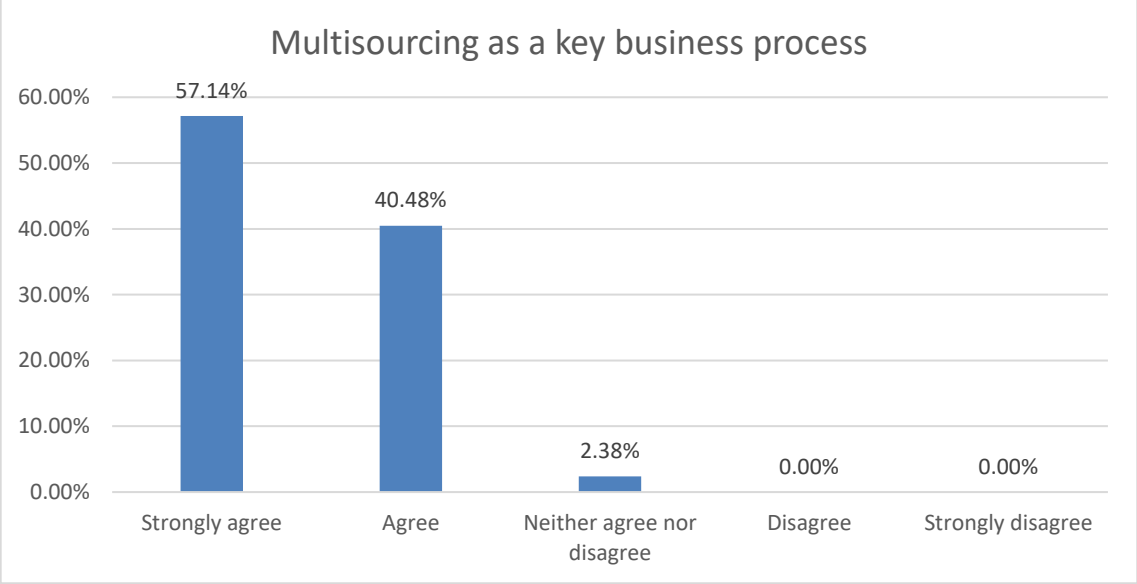


Figure 6: A graphical representation of the industry view of multi-sourcing as a key business process

This is a clear indication that the professionals from all the targeted job functions within the pharmaceutical industry, recognise the need for multi-sourcing as a key business process, with a total of 97.62% of participants agreeing that multi-sourcing should be a key business process within the industry. This would support the need for most organisations to have an individual or team constantly sourcing compatible alternate sources in the scope of raw materials, intermediates and finished products. The variance in response was detected as 0.30, with the greater split evidently between the strongly and agree responses.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.26; Quality professionals as 0.33; Regulatory professionals as 0.33; and commercial and general management professionals as 0.28.

When considering the cost impact of multi-sourcing of products and materials on the final product cost to the patient, the participant responses were strongly supportive of the perception that multi-sourcing would result in an overall cost benefit to the patient.

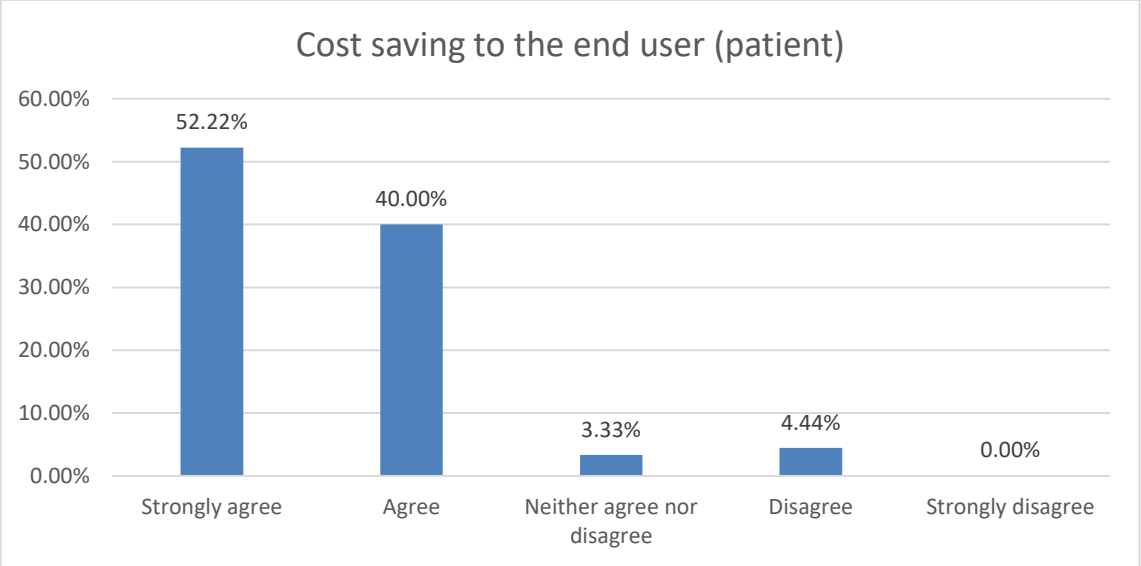


Figure 7: The possibility of cost saving to the end user through the implementation of multi-sourcing

The graph above indicates a strongly supportive view among the participants through a combined total of 92.2% of participants indicating awareness of the possible cost saving to the patient. Interestingly, 3.33% of the participants had a neutral response, with 4.44% of the participants not in agreement with the view of possible cost saving to the patient. This is possibly due to factoring in the costs of sourcing, trial work on products, testing and regulatory submissions that would absorb a significant portion of the cost saving before it can be transferred to the patient, or a complete alternate view in which cost saving would not be transferred to the patient at all. The responses to this statement had a variance of 0.67, with most responses in the “agree” and “strongly agree” options.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.61; Quality professionals as 0.79; Regulatory professionals as 0.32; and commercial and general management professionals as 0.90.

The focus of the data collection was then changed to the availability of alternate suppliers and the supporting processes required in multi-sourcing of materials and products. This section highlights the availability, regulatory and compliance aspects of the evaluation and approval process for alternate sources.

When evaluating the availability of alternate suppliers for South African Pharmaceutical companies, it was found that there appears to be a dissonance in the responses of participants, with 22.62% of responses indicating that adequate alternate suppliers of materials and products are available.

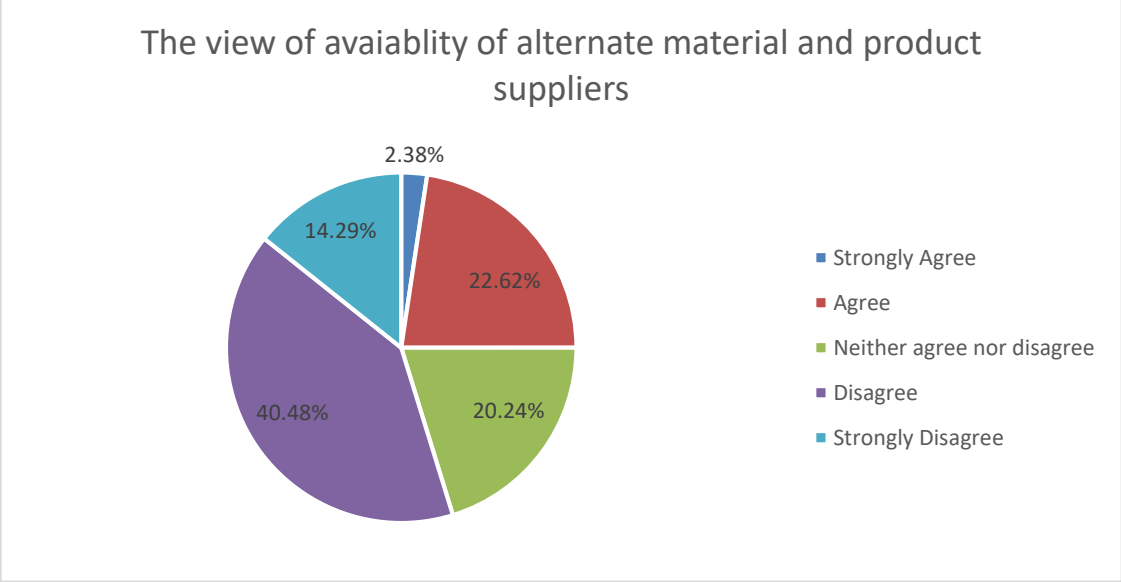


Figure 8: A graphical representation of the view of the availability of alternate suppliers

However, on the other end of the scale, 40.48% of participants disagree and a further 14.29% of research participants strongly disagree, resulting in more than half (54.77%) of the participants identifying that even though alternate suppliers may be available, these are not adequate. The variance in response to this statement was calculated to be 1.12 indicating a wider spread of responses.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 1.65; Quality professionals as 0.95; Regulatory professionals as 1.21; and commercial and general management professionals as 0.90.

When evaluating the practicality of a change, often one of the key decision drivers is related to the efficiency of the change. In the highly regulated environment, this can be complex with multiple factors to consider. Participant responses had highlighted this.

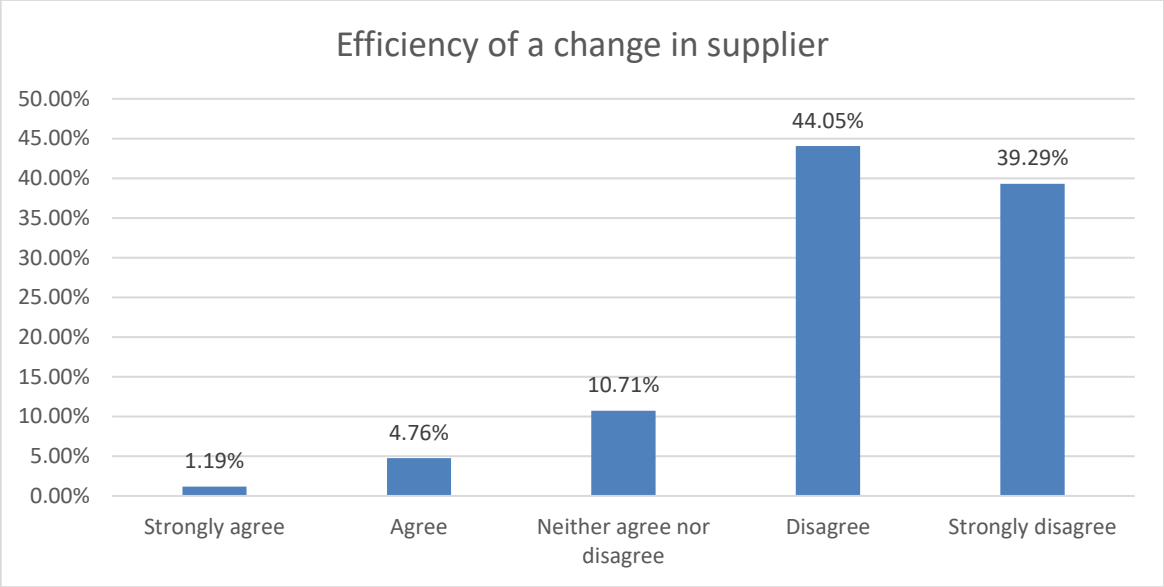


Figure 9: An industry view of the efficiency of the change process

Supplier changes are seen by majority of the participants as a long-winded, slow and inefficient process. The response of 83.33% of participants confirms that supplier and material changes can be very time and resource constraining, definitely not aligning with the fast paced nature of the industry. The statement has a resultant variance of 0.77 with most participant disagreeing to the perception that the change process may be considered efficient.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.37; Quality professionals as 0.82; Regulatory professionals as 0.72; and commercial and general management professionals as 1.14.

This is further confirmed by majority of the participants indicating that the (30.95%) indicating that the material change process is on average greater than two years.

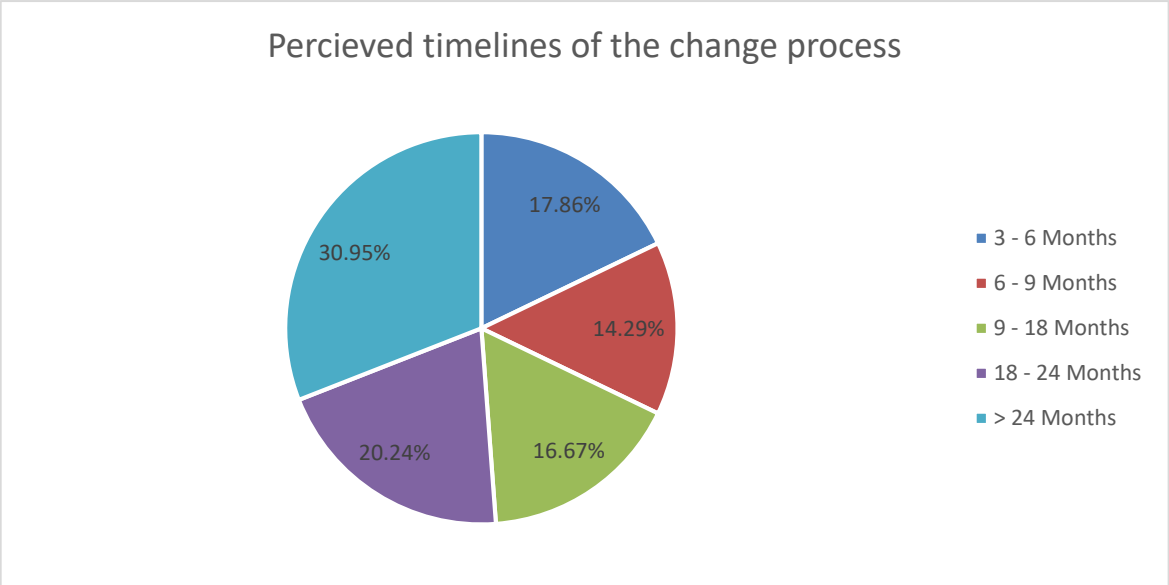


Figure 10: A graphical representation of the industry view of the change process timelines

The perceived timelines for the change in supplier has varied responses, with 17.86 respondents indicating an average of 3 - 6 months, 14.29% indication 6 - 9 months, 16.67% of respondents indicating 9 - 18 months, 20.24% indicating 18 – 24 months, and the majority, 30.95% of respondents indicating greater than 24 months. The variability in responses to this is likely a result of the influence of exposure and experience of the respondents to different aspects of the business, hence not fully evaluating the entire process and timelines thereof. The response to the perceived timelines resulted in the greatest variance, with a fair spread of varied responses.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 2.59; Quality professionals as 2.10; Regulatory professionals as 2.40; and commercial and general management professionals as 2.24.

This timeline can become a deterrent to organisations that have resource constraints and are unable to set aside adequate finding for trial batches that will have to be rejected and not made available to the market.

In determining the root cause of this, the survey was then directed toward gaining further views in the industry around the regulatory and compliance requirements

and the impact thereof on the ability for organisations to implement multiple sources of pharmaceutical raw materials, intermediates and finished product.

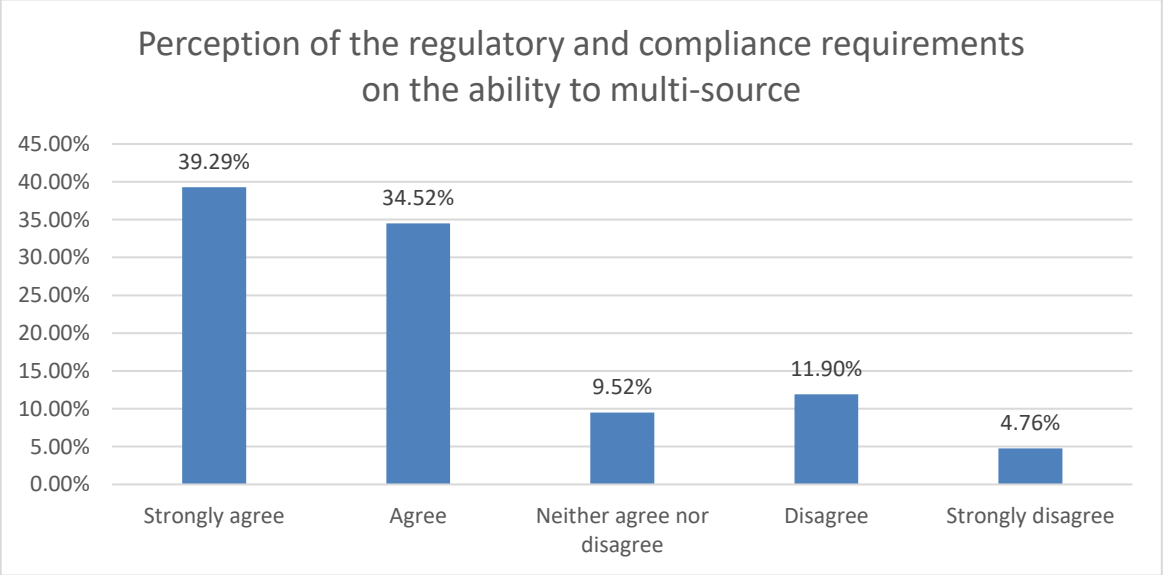


Figure 11: A graphical representation of the perception of the impact of regulatory and compliance requirements on the ability for organisations to multi-source

The survey responses clearly indicate the extent to which regulatory and compliance requirements form barriers to the ideal concept of multi-sourcing in the South African pharmaceutical environment. 73.91% of respondents had agreed and strongly agreed to the statement that regulatory and compliance requirements serve as a barrier to multi-sourcing, with only 15.66% of respondents on the other end of the spectrum. Responses to this statement resulted in a variance of 1.39.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 1.06; Quality professionals as 1.60; Regulatory professionals as 1.03; and commercial and general management professionals as 1.33.

In an attempt to link possible cost saving initiatives that could be introduced through multi-sourcing, the impact of regulatory timelines on material changes and multi-sourcing was evaluated. The graphical representation below indicates an almost even distribution of responses from those whom agree and those whom disagree to the regulatory timelines being supportive to the business need to implement cost

effective changes. There is, however, a slightly greater population of the respondents that strongly believed that the regulatory timelines do not support the business need for the timely implementation of cost effective changes. This highlights the highly regulated nature of the industry, with individuals at every level of these organisations ensuring the regulatory compliance requirements are maintained with a high priority.

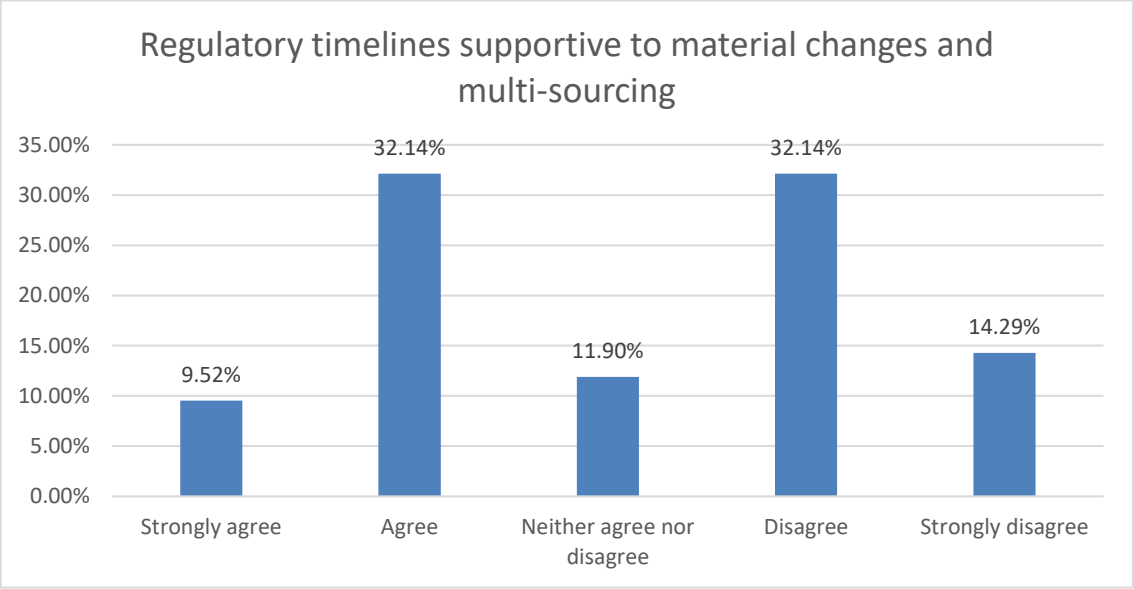


Figure 12: An industry view of the impact of regulatory timelines on the multi-sourcing process

The above representation, highlights the nature of the industry in that as much as cost remains a key business performance indicator, quality still remains high on the priority of those in the industry, with the need of ensuring that the end user (the patient) gets a safe and effective product of good quality.

An important part of the regulatory commitment of the pharmaceutical organisations in the need of quality and regulatory authority audits. This is often a combination of internal organisational baseline requirements as well as the regulatory authority audit requirements that are imposed on all organisations that intend to market their product or products within the jurisdiction of the regulatory authority. The graphical representation below indicates strongly that the regulatory authority audits, by SAHPRA, FDA, WHO, EU, etc. are adequate for a source to be considered as an alternate source of material, intermediates or product by local pharmaceutical

companies. This is emphasised through the 17.86% of participants that strongly agree and the 53.57% of participants that agree to regulatory authority audits being adequate to allow for the approval and use of an alternate source. The variance detected for the response to regulatory timelines being aligned with the need for efficient multi-sourcing was calculated to be 1.59.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 1.76; Quality professionals as 1.33; Regulatory professionals as 1.74; and commercial and general management professionals as 1.80.

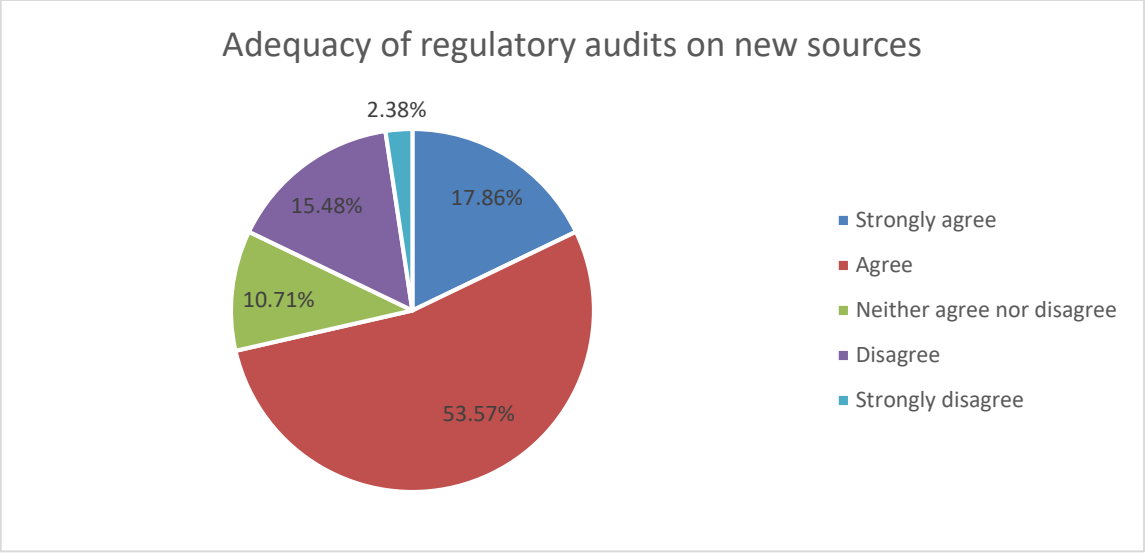


Figure 13: A graphical representation of the view of adequacy of regulatory audits for implementation of alternate sources

The 15.48% of participants that disagree and 2.38% that strongly disagree are likely members of more stringent organisations that enforce internally driven quality and compliance audits in addition to regulatory authority audits, on these suppliers.

One must also take into consideration that regulatory authority audits are imposed primarily to the finished product, intermediate drug product and active drug product sources and not to the other inactive drug products that are required as part of drug and medicine formulae. In these cases the decision to audit the inactive material or inactive intermediate supplier is left to the organisation. This statement resulted in a variance in response of 1.02.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 1.27; Quality professionals as 1.10; Regulatory professionals as 0.87; and commercial and general management professionals as 1.29.

The willingness of suppliers to support the various levels of organisation specific compliance requirements and regulatory authority audit, and related requirements is understood to be dependent on the desired order quantities of an organisation. This is a common perception held by various members of the industry and is evident, even with currently active suppliers where further regulatory or compliance support is required. It is often easier to gain the necessary support when order quantities are high. Where order quantities are low or not guaranteed, it becomes a challenge to obtain adequate support from the supplier. This is confirmed in the participant responses represented below.

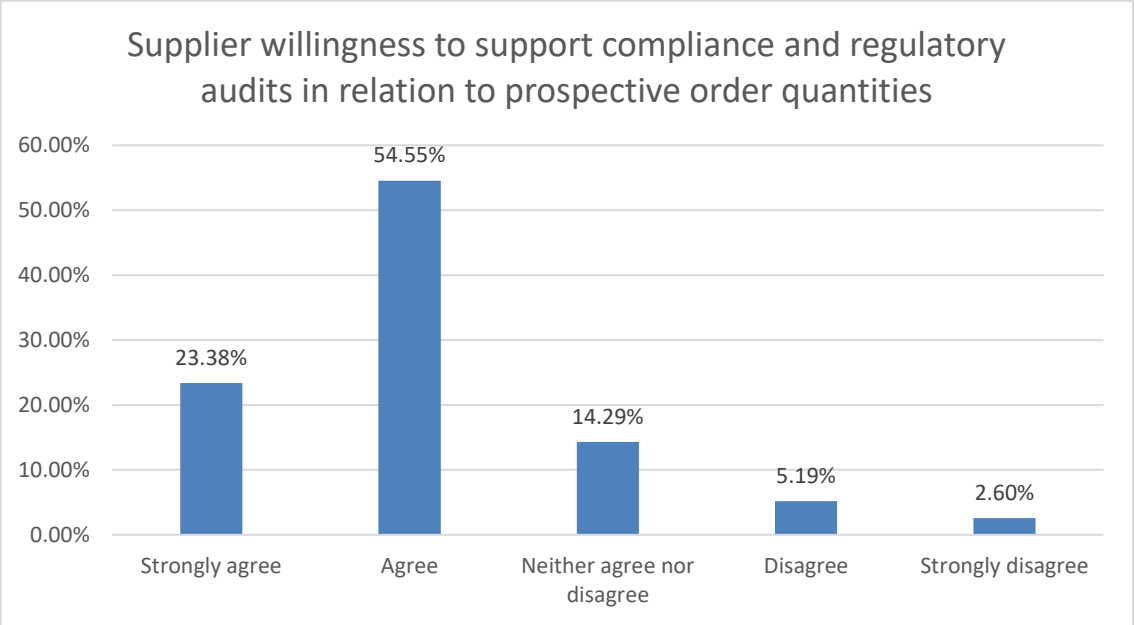


Figure 14: A graphical representation of the view of supplier willingness to support regulatory and compliance audits

The figure above indicates a strong stance (23.38% strongly agreeing and 54.55% agreeing) in the industry in which it is noticed that material, intermediate and finished product suppliers are often reluctant to support quality and regulatory requirements including regulatory authority audits without adequate confirmation of

expected order quantities. The variance in response to this statement was calculated to be 0.90.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.29; Quality professionals as 0.98; Regulatory professionals as 0.84; and commercial and general management professionals as 1.62.

This is possibly due to the quality and regulatory requirements often being highly detailed requiring specific and well-reviewed data as well as expert teams and can have major interruptions in the daily operations of the supplier, with key personnel required in the audits and further audit related downtime. It then becomes a business decision of the supplier, in order to determine whether investment in fulfilling the quality and regulatory audit requirements is in fact aligned with the business plan of the supplier.

From the perspective of pharmaceutical companies, the multi-sourcing decision and background work needed to fulfil the related requirements are often left to an individual within the routine procurement team. This approach often forces the process to fail as it can be circumvented by other stakeholders within the individual organisations, frequently as a result of lack of support or inadequate background detail by the procurement team.

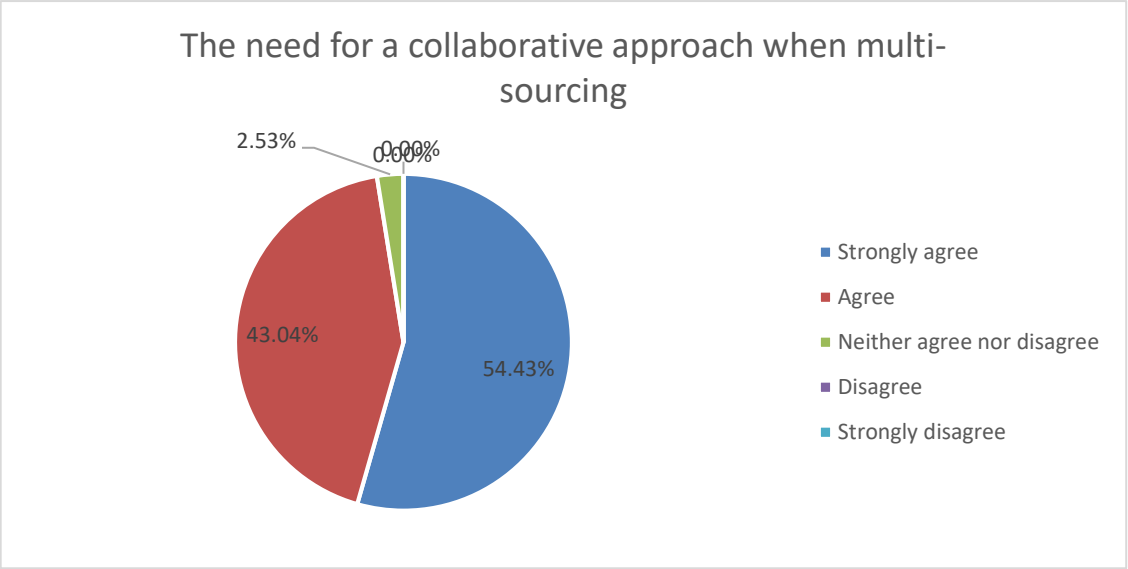


Figure 15: The industry view of the need for a collaborative approach to multi-sourcing efforts within organisations

This approach is well supported by the participants in the industry, with no responses disagreeing to this statement. The use of a collaborative approach and possibly a project management type approach would be best suited for the identification, preparation, documentation, auditing, trial work, validation work, stability data generation, review and submission of the required compliance and regulatory requirements for the addition of the new source. The list of activities required certainly does require input from various departments and teams and will therefore require a strong lead in a project management type approach. The process can still be led by a procurement or supply chain management professional, with a fully briefed support and implementation team. This is further reiterated by the all survey participants being in support for the need for management, technical and financial support in the multi-sourcing process. The response to this statement resulted in a low variance of 0.30, with most participants either agreeing or strongly agreeing to the statement.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.38; Quality professionals as 0.33; Regulatory professionals as 0.26; and commercial and general management professionals as 0.24.

The financial support further links to the significant internal initiation costs. From the data obtained through participant responses to the survey; and the graphical representation below, it is evident that majority of the participants (93.67%) are of the opinion that the internal initiation costs related to the addition of sources for raw materials, intermediates and finished products are significant enough to play a major role in the final multi-sourcing decision.

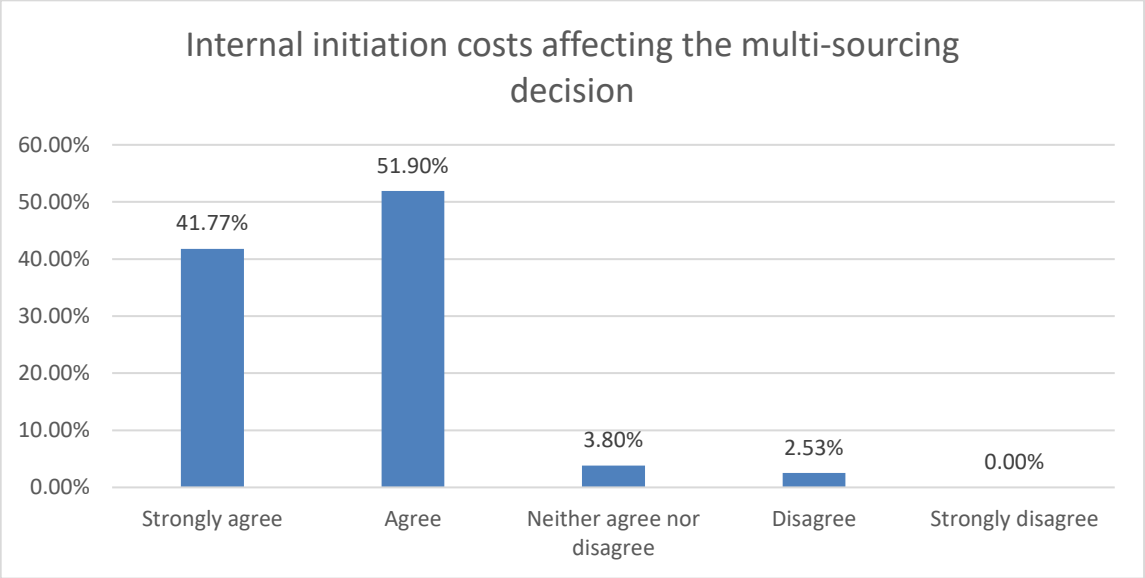


Figure 16: A graphical representation of the industry view of the cost impact on the multi-sourcing process

Apart from material costs, which may vary from supplier to supplier, the internal initiation costs of sourcing an alternate material, intermediate or finished product which includes procurement costs, transport costs, site visits, audits, documentation, trial work, validation work, analytical testing, stability studies, regulatory assessments and regulatory amendment costs are often incremental and can discourage the multi-sourcing process. The variance in response detected was 0.45, hence most responses aligned to the concern of initiation costs related to sourcing of new materials in the industry

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.65; Quality professionals as 0.30; Regulatory professionals as 0.33; and commercial and general management professionals as 1.24.

This directly links to the power larger multinational and networked organisations have over the smaller local pharmaceutical manufacturing companies. From the participant responses to the survey most participants are in agreement that the larger market players have an advantage in successfully implementing alternate sources in comparison to the smaller individual manufacturers in the market.

The representation below highlights the understanding in the industry with 43.04% of participants strongly agreeing, 36.71% of participants agreeing and only 12.66% of participants neutral with a minor 7.50% of participants disagreeing with the view of larger organisations holding a significant advantage in the ability to multi-source at all levels (raw materials, intermediates and finished products) than the smaller counterparts in the South African pharmaceutical industry. An overall variance of 0.84 indicates that although multiple views were selected, most responses are aligned in the belief that larger organisations have an advantage over the smaller organisations when multi-sourcing is considered.

When breaking down responses per participant group the variance detected was noted as follows: supply chain management professionals as 0.88; Quality professionals as 0.82; Regulatory professionals as 0.90; and commercial and general management professionals as 1.14.

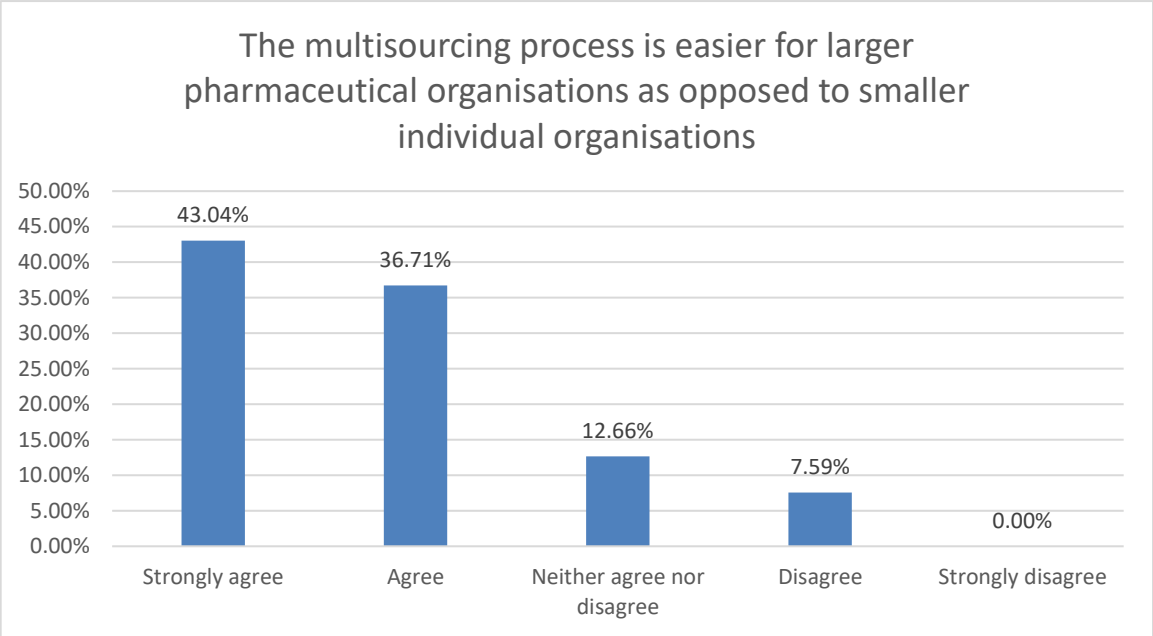


Figure 17: An industry view of multi-sourcing for multinational organisations vs. local organisations

The implications of these links to the ability of multinational pharmaceutical companies to make use of global networks to successfully implement multi-sourcing which is more demanding on smaller local organisations.

Discussion

The data and analysis emphasised key findings in relation to the research questions posed. Of the 90 participants that had initiated the research survey, 77 participants had completed the entire survey. The data, analysis and discussion has therefore been generated on the basis of the fully completed survey responses in order to generate adequately informed conclusions.

The influence of work experience on the survey responses

As it would be expected, the work experience of survey participants has a level of influence on the responses of survey participants. This includes the influence of the number of years of experience within the industry as well as the number of related roles in which the individual has experience 52% of the survey participants

had experience in more than one of the related roles and a further 38% had at least a working knowledge of more than one of the related roles.

This translated to a lower variability in responses, with the survey population responses mostly strongly aligning with or strongly opposing to the statements made around the need for multi-sourcing, the quality and regulatory implications, the support of new suppliers and the intrinsic factors of organisations that may impact the multi-sourcing process, in the survey.

Further, 80% of the participants have greater than 5 years of working experience in the industry. This could imply a more accurate understanding of the industry and industry processes in relation to the topic of research.

The determination of the variance in responses had clearly indicated a low variance within the responses of the individual roles surveyed, although the overall variance for the full data sets may have been higher. This aligns with the assumption that most individuals in the same or similar types of roles carry the same views on multi-sourcing within the South African pharmaceutical industry.

The response data also indicated that participants in commercial and general management roles as well as in the supply chain management professionals, that a more holistic view of the business and processes is taken, with greater alignment to longer timelines implying that they have given greater consideration to the multiple factors that have a role in these changes. This differs from those in specialist roles such as regulatory and quality professionals, who may have a somewhat limited view on the overall process.

Views on multi-sourcing

The views expressed by the participants amongst both the multinational organisations as well as the local pharmaceutical organisations are strongly in support of multi-sourcing. This aligns with the literature of Harland, Masoumi and Shah whom had all supported the need of multi-sourcing in supply chain in general. The benefit of having alternate sources is therefore clearly understood in the industry as multi-sourcing supports not only the end user or patient's need for

having the right medication available when needed, but also strongly supports cost reduction initiatives and most importantly business continuity (Shah, 2004; Harland, 1996; Masoumi, 2012).

From the business perspective, in a highly competitive market where for most locally produced pharmaceutical products there are various generics and alternatives, giving the customer the right price is not always adequate as in this type of business, the customer is a patient, who is accustomed to taking the same medication when needed, therefore highlighting the important of maintaining market presence through ensuring that there are no, or minimal, delays in getting the product to the customer and that stock-outs are averted (Schoenherr, 2015).

The greatest risk for local companies, mostly being generic manufacturers is that once a customer has changed over to an alternative it is near impossible to get that customer back on your product. Hence the need of prioritisation and a good business continuity plan that highlights and strategizes to address the risks to product supply and the action plans for the greatest risks with urgency, while maintaining visibility on the smaller risks to the point where all possible risks can be reduced or averted completely (Shah, 2004). This further supports the industry view of multi-sourcing being a key business process.

The cost impact of multi-sourcing to the patient

Being a highly specialised industry, pharmaceutical industry processes often come at a high cost with multiple stops, checks and the need for highly skilled and specialised personnel at multiple levels in order to ensure the best quality product is made available to the end user (Kokilam, 2016; Papavasileiou, 2007).

This often leaves cost reduction strategies primarily in the procurement of materials. The possibility of the implementation of alternate sources often comes with significant trial, validation, analysis, quality and regulatory work and may require changes to the production processes, however, also have the potential for significant gains through cost reduction (Rosenkranz, 2015). In the competitive environment, the investment required can be recovered and if there is adequate

cost gain, it will not only ensure that the products are constantly available, but also that the reduction in costs can be transferred to the end use as a price reduction on the product.

In terms of marketing and sales, an effective, good quality product that works well at a reduced price ensures a returning customer. It also makes the customer conscious of the brand the product carries and can drive a conscious decision to buy the brand for other related products if needed (Rosenberg, 1984; Royo-Vela, 2016).

This ideal can be used to further incentivise the need for local pharmaceutical companies to pursue cost reductions and ensure business continuity through multi-sourcing.

Alternate source availability

The survey responses indicate a lack of availability of alternate sources of required raw material, intermediates and products. Locally, the pharmaceutical market is very relatively small, with no local chemical manufacturing facilities that manufacture active pharmaceutical ingredients (APIs), and very few pharmaceutical grade raw material suppliers. Most materials are used in the industry are imported, adding the costs of freight, material taxes and customs related costs that further push up material costs. These additional costs pose a challenge to sourcing, and can serve as a deterrent to multi-sourcing if there is a risk of the alternate source causing any further processing related uncertainties.

This can, in part, be linked to the choice of globalisation among organisations within the industry as it limits the production and sourcing of certain products and materials to specific regions only. With South Africa being situated at the bottom extreme of the African continent and very few other pharmaceutically active countries in the sub-Saharan region, materials are imported from Asian, European, and American states (Kookana, 2014).

The change process

The vast majority of survey participants indicated that changes or additions of suppliers in the pharmaceutical sector is not a quick and efficient process. Apart from the scarcity of alternative suppliers, other related process and industry specific factors play a role. These factors are often linked to the quality and regulatory requirements for the addition of the source. However, these factors are coupled with the risk of processing challenges. An alternate source may be available with the same quality grade and specification of a material, however, this does not necessarily mean that the material will behave the same in the manufacturing process and in the product as a minor material difference can have major changes to the product properties and parameters. These challenges can at times be detected through the detailed review and material comparison, in vivo, however, a true reflection can only be obtained during full scale trial batch production.

Trial batch production is a costly process as, in most cases, these are exploratory batches only and will not be marketable unless it can be proven that the alternate material has not change to the product or process. The trail batch gives a full view of how the alternate material behaves during the production process and it can be informative if any process changes are required to implement the use of the alternate material. It also allows for adequate control testing and stability studies that will give production and quality personnel a full indication of changes the new material may make to the product (Kookana, 2014). This process can take a significant amount of time, however, the regulatory and quality change requirements would still be required before the material may be used on commercial batches.

From a quality perspective, the material would need to be approved. This means it would need to be tested on receipt and it would need to comply with a stringent set of globally defined control requirements. If any of these requirements are not met, the material batch will be failed and rejected. The supplying source of the material would need to be audited for compliance to the organisations defined quality and documentation standards (Steven, 2014).

Once production and quality have confirmed that the material is compatible with the product and have made the relevant process changes, the change must be submitted through regulatory professionals to the regulatory authority in the country, SAHPRA. The regulatory authority will then evaluate the change prior to approving the alternate source. This can take a further three to four years if it is considered a "Type C" variation to the product or process, requiring further batches, analysis, studies and documentation to be produced. Depending on the material being changed, it may also require a regulatory authority audit. Hence, the lengthy and costly process which many organisations cannot afford. The multi-sourcing process therefore needs to be managed through a strategic development or project management channel (Keyter, 2018).

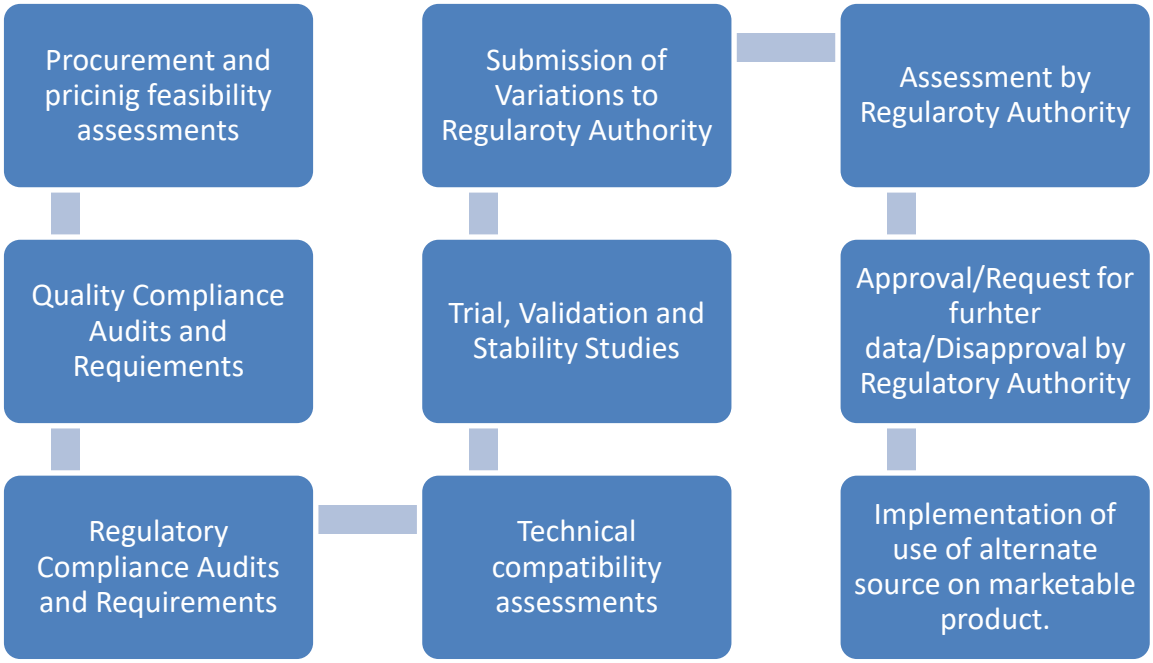


Figure 18: A high level flow chart indicating the generic business process involved in the process of changing or adding sources for materials, intermediates and products

Auditing of new or alternate sources

A major component of the quality and regulatory compliance activity is a baseline GxP audit. For all active pharmaceutical ingredients, intermediates and products, the regulatory authority, SAHPRA, has a requirement that the manufacturing site of the new source be audited, either by SAHPRA or an affiliate global regulatory body

such as the FDA or WHO. As most suppliers have no local presence in South Africa, this poses the challenge to the organisation planning to make the change to undertake the costs to arrange and conduct the audit with the regulatory body if a recent has not been conducted (Marc, 2001).

Further to the regulatory authority requirements, many local pharmaceutical companies follow the direction of the larger multinational organisations with the aim of keeping up with the quality standard of conducting a baseline quality and GxP audit at the inactive pharmaceutical suppliers in addition to the regulatory requirements for the active pharmaceutical suppliers. This brings not only cost implications, but personnel and time constraints as well.

In order to successfully complete the regulatory and quality audits, the new source or supplier that is being audited must provide a team to support the auditors. In most instances this requires a great deal of preparation and involvement of operational and middle and senior management personnel and can be quite strenuous on smaller organisations as the audit will entail plant and site walkthroughs, review of working procedures and operations, review of documentation as well as an overview of business controls, utilities and environmental implications (Chae, 2013).

In some instances, the new source or supplier may reject the request on the bases of lack of resources or preparation for the audit or incorporate the use of consultants for the audit purposes at the cost of the organisation planning to use the new supplier. Suppliers may also not support auditing requirements as a result of not having a guarantee of future orders, with the knowledge that they are being sourced as an alternate source or the proposed order quantities do not support the investment needed to fulfil the audit requirements.

Impact on local organisations

The local organisations that find it most challenging to gain adequate support to multi-source are the smaller fully local organisations that are not linked to multinational organisations. In most instances the time and cost requirements

imposed on the organisation reduce the feasibility of the task and these organisations often continue to operate single sourced until a change is forced due to supply failure, which can be detrimental to these organisations.

Multinational organisations and networked organisations have the ability to share prior audits that may have been done for any of the other sites, hence reducing and possibly excluding audit requirements for the use of the new supplier. This challenge affects the individual local organisations to a much greater extent than the multinational and networked organisations (Masoumi, 2012).

Further, local organisations have limited order capacities as the orders are of one manufacturing facility only whereas multinationals and networked organisations could group orders and negotiate for better pricing and better service from the supplier.

Minimum order quantities may further exclude smaller organisations from gaining the opportunity to have the supplier as an alternate source.

Timelines to implement multi-sourcing

Although multi-sourcing is a highly needed concept in the local pharmaceutical industry as the benefits far outweighs the risks, the timelines to implementation are not aligned with the need to implement. This incorporates the regulatory, quality and technical timelines that depending on the material and processes affected can take a few years to implement and carries a definite write off risk to the organisation.

Aligning with the views of Nash and Keyter, more than half of the participants had indicated that the time required to implement multi-sourcing of a single product or material takes above 18 months, with 30% of the participants indicating greater than 24 months. This is applicable to the process, documentation and approval for the quality and regulatory compliance requirements. Where technical product development work is required this process can be extended further. A process change for a single material can therefore take longer than 3 years (Keyter, 2018; Nash, 2000).

Taking heed of the fact that these products compose of multiple raw materials and intermediates, the multi-sourcing process of single product could take over a decade. It is therefore important for organisations to plan and prioritise the materials, intermediates and products that have the greatest business impact to the organisation and market impact to the end user.

The incorporation of internal and technical costs

The material, quality and regulatory costs are often considered as these processes are better known and are easily considered for costing purposes, however, the internal costs that need to be considered forms a significant factor to the production divisions of these organisations as the internal costs of trial and validation batches; analytical development, quality control testing, comparison studies and stability studies can be exorbitant. An additional major cost factor is the technical specialists required in the change process (Barber, 2018). This becomes a major decision driving factor for the smaller local organisations in which costs are under tight control and has the potential to drive the decision toward remaining single sourced for as long as possible.

Essentially all challenges studied and discussed above form part of an overall process flow that in the visual form, may assist in driving a solution based approach in the local pharmaceutical industry.

Addressing these challenges

Networking

Through networking, smaller local organisations have the potential to form larger networks that could, for the purposes of multi-sourcing, mimic the approach of multinational organisations. In this way the organisations would be teaming up to meet the required technical quality and regulatory requirements in order to successfully implement the use of alternate sources of materials, intermediates and products as the general workload would be decreased, with the exception of the internal product and organisation specific activities that would be required, and the network would have better negotiating power with the suppliers that could allow for

the use of products with high minimum order quantities and reduce the price that would be afforded to smaller orders of individual organisations.

The use of agents

Individuals familiar with the requirements and processes could for businesses that facilitate the process of sourcing materials for the local and locally operating multinational organisations. These businesses can take on the task of addressing the general quality and regulatory requirements and based on the demand for products and materials, order and hold large quantities of materials from suppliers abroad. These products and materials can then be sold to the local organisations that would, in other instances, not have access to these materials.

The agents would be charging a higher price for these materials and products than the manufacturers, however, the agents will effectively reduce the development, quality and regulatory costs that would otherwise have been incurred directly by the local organisation. The agent would also be holding defined quantities of materials locally, ensuring that the required materials and products are available at the time required with minimal delay to the purchasing organisation.

Pharmaceutical activity

Increased pharmaceutical activity locally, would increase the need to locally manufactured materials, intermediates and products. The major advantage with locally sourced materials and products is in the form of a short lead time between order and delivery dates. Local organisations would likely be able to turnaround orders at a greater rate as the import process would no longer be required. This could also reduce the freight costs incurred while importing products.

Further Academic Research

This study could be further supported by evaluation of standardized suppliers within the food and pharmaceutical industries. This will increase the available supplier base for organizations to drive multi-sourcing as even though the same materials may be used in both industries, the grades, documentation, quality and regulatory

requirements of the pharmaceutical industry is much greater. This could introduce the added advantage of a better regulated local food industry.

Further research could also be conducted on the introduction of material and product supply agents on the local pharmaceutical industry for local pharmaceutical companies. The resource constrained nature of local organizations limits the availability of personnel and processes to adequately conduct the multi-sourcing exercise. The introduction of local agents for souring of materials may facilitate this and as a result may impact the operations of both local and multinational organisations within the South African pharmaceutical industry.

Academic evaluation of the current regulatory processes and the practicality of quality and regulatory requirements on the change management process for the introduction of alternate or multiple sources of products of materials can be advantageous to the industry as this may result in the suggestion of possible improvements and actions that could reduce or streamline the process. This can grow the industry as the compliance requirements often become a deterrent to new entrants.

Conclusion

Through conducting an evaluation of multi-sourcing in the South African pharmaceutical industry some key competencies and challenges around multi-sourcing were uncovered. The evaluation is in the form of a research report based on survey responses by industry experts in the South African pharmaceutical industry and spans across local and multinational organisations. The competencies are evident in the form of the ability of the industry to act on forced changes when required through a combination of technical and compliance related activities with the aim of maintaining continuity of the industry. The challenges have been highlighted as the quality and regulatory compliance processes, the change processes (technical and compliance), the availability of alternate sources and most importantly, the resultant timelines of these combined factors on the organisation.

On the basis of industry expert views, the research conducted confirmed the following:

- Multi-sourcing of materials, intermediates and products is definitely needed in the industry.
- The quality and regulatory requirements are often seen as a challenge to the multi-sourcing or alternate sourcing process.
- There are limited sources available locally, posing a challenge to the need to multisource and requiring further work to be done for importing the required products.
- The costs of setting up alternate sources are often not fully understood and evaluated in the industry as these costs are product and process dependant.
- Multinational and networked organisations have the advantage of group activities for quality and regulatory functions as well as bulk buying power that allows for management of supplier MOQs and costs.

With the view that most specialists in the industry (quality, regulatory and supply chain individuals), focus on their specific roles and functions, the concept of silo operations is evident as the full realistic view of costs and timelines are better understood by individuals with broader industry experience and the senior general management teams. There is definite consensus, among the range of selected experts in the industry, around the complexities of multi-sourcing and the lengthy timeframes for the implementation of alternate sources as most participants, even though responses were focussed on individual views, have highlighted long time-frame requirements for the implementation process.

Costs incurred are considered excessive as the cumulative costs are often too high for smaller individual organisations to budget and implement the possible changes. This is due to the extent of risk required for each material change requires. If the change fails or is not implemented the write-off costs associated to the process can significantly impact the financials of the organisation.

Multinational organisations have a significant advantage in the process of multi-sourcing through the global regulatory authority approvals as well as minimised

internal processes required for the change to a new material if the material has already been implemented elsewhere. Multinationals also have the advantage to bulk ordering which often translates to cost reductions as larger quantities can be ordered and distributed to multiple facilities. Larger order quantities also assists in negotiating better prices with suppliers. Price gains can be transferred to the patient which gives multinational organisations an advantage over the smaller local organisations through overall customer perspectives.

This report has detailed the challenges detected and possible solutions such as:

- The creation and use of local agents. Local agents would have the ability to procure and hold stock to supply to the range of local organisations. This may increase material costs to a small extent, but will aid the smaller organisations in circumventing the challenges around minimum order quantities and compliance support requirements from alternate sources. These agents would be able to ensure compliance to all the required quality and regulatory compliance requirements, leaving the local organisation to focus on the internal requirements and processes only. ,
- The use of networking between organisations. This allows for sharing of knowledge and processes between linked local organisations. This may compromise internal systems, however, in the greater scheme collaboration within the industry can be beneficial to all organisations within the industry and will have an impact on the satisfaction of the end user.
- Increased pharmaceutical activity locally and in surrounding countries. This can drive up the need for more local sources creating a niche for current or new organisations to enter either through the generation of new sources or supplier facilitating agents. .

The proposed solutions can impact the industry as a whole and possibly reduce the extent of the disparity between multinational organisations and fully local organisations. These solutions may also impact the food and other FMCG

industries that rely on related materials and products used within the pharmaceutical industry.

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