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KEY CHALLENGES IN THE OUTBOUND PHARMACEUTICAL COLD CHAIN

by

Sarantis Kosmas

200606630

DISSERTATION

Submitted in fulfilment of the requirements for the degree

MAGISTER COMMERCII

in

LOGISTICS MANAGEMENT

in the

FACULTY OF MANAGEMENT

at the

UNIVERSITY OF JOHANNESBURG

Supervisor: Prof Johan du Plessis

October 2016
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<td>AEFI</td>
<td>Adverse Effects After Immunisation</td>
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<tr>
<td>AFRO</td>
<td>World Health Organisation Regional Office for Africa</td>
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<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
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<td>BOM</td>
<td>Bureau of Meteorology</td>
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<td>CAPA</td>
<td>Corrective Action Preventive Action</td>
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<td>First Expiry First Out</td>
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<td>KPI</td>
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<td>Mean Kinetic Temperature</td>
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ANNEXURE 3 – Benchmark Model B cost schedule

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ANNEXURE 5 – Scenario A2 cost schedule

ANNEXURE 6 – Scenario B1 cost schedule

ANNEXURE 7 – Scenario B2 cost schedule
DECLARATION

I certify that the dissertation submitted by me for the degree Master’s of Commerce (Logistics Management) at the University of Johannesburg is my independent work and has not been submitted by me for a degree at another university.

Sarantis Kosmas
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‘Things don’t end wrong, they start wrong’ - Prof Johan du Plessis
ABSTRACT

The South African pharmaceutical cold chain industry has a fundamental challenge in balancing the quality requirements, driven by the Medicines Control Council (MCC), within a constrained revenue model that caps the possible income from distribution activities through single exit pricing (SEP) regulations. This research seeks to understand the key challenges in the pharmaceutical cold chain industry.

Through the use of a survey and cost analysis, both a qualitative and quantitative view of the research on the outbound distribution operations for fine distribution, distribution to pharmacies and hospitals, of cold chain pharmaceuticals were obtained. The research takes a structured approach to identifying relationships between various elements of the pharmaceutical cold chain, as well as ascertaining the key factors and risk ratings of these elements. This information was analysed to identify the key challenges in the pharmaceutical cold chain industry. Using the Lambert and Stock total cost model, a framework was developed to guide both the survey and cost analysis research. As both components were structured in this manner, these components could be cross-referenced for consistency.

The findings of the research identified that there was a significant relationship between the outbound distribution and the quality elements of the supply chain. The most important key factors were determined to be transportation volume, product write-offs, cold room validation, duration of the cold chain packaging system, type of temperature monitoring equipment, and cold room and freezer storage. The key risks were identified as being in the transport, validation/qualification and cold chain packaging elements.

The research concluded that quality elements related to the warehousing function are well controlled, while the highest risk is within the transportation element. The research successfully identified six key challenges all related to the transportation element of the pharmaceutical cold chain industry. These challenges related to cold chain packaging, temperature monitoring as well as validation/qualification of cold chain packaging systems.
CHAPTER 1 – PHARMACEUTICAL COLD CHAIN MANAGEMENT

1.1. Introduction
Logistics and supply chain management are very broad fields of study in that they are applicable to many different industries. In each of these industries, there are many fundamental principles that may be applied. However, there are often unique considerations in these industries that must be factored in over and above these fundamental principles. The intention of this research is to elaborate on some of the unique challenges in the pharmaceutical cold chain, in the context of supply chain management. Chapter 1 will provide a broad overview of cold chain management, why this research is important and what objectives the research was seeking to achieve. The research methodology will also be discussed, leading to a dissection of the research chapters.

1.1.1. The importance of cold chain management
According to the Therapeutic Research Centre, failure to store pharmaceuticals at their required storage temperature can result in sub-potent products and in turn, therapeutic failure (Therapeutic Research Centre, 2008:1). In the case of life-saving drugs, which are ‘drugs which require immediate administration within minutes post or during a medical emergency’, a therapeutic failure can be fatal (Chaudhury, 2003:1). This makes cold chain management a critically important component of the pharmaceutical supply chain.

1.1.2. History and evolution of supply chain and pharmaceutical cold chain management

1.1.2.1. Origins and evolution of cold chain management
While ‘cold chain’ as a term suggests a cold supply chain, as a concept it is more broadly used to define a temperature-controlled supply chain. The term has its origins in the food industry where the requirement to control the storage and transportation temperature of the product is key to halting the growth of microorganisms. The term ‘cold’ typically refers to temperatures ranging between 2 °C and 8 °C as stated on the labels of pharmaceuticals that need to be stored in cold temperatures (Walker, 2011).
The focus on the pharmaceutical cold chain has been driven by three key factors:

1. In the late 1990s the Food and Drug Administration (FDA) and the United States Department of Agriculture implemented a system of hazard analysis and critical control points (HACCP).
2. In 1992, one-time disposable data loggers made it economical to collect and create databases of temperature data.
3. Increased mail-order prescriptions, which are less controlled, led to higher quality complaints in detectable physical drug characteristics (Walker, 2011).

1.1.2.2. Origins and evolution of supply chain management
Supply chain management (SCM) has its roots in the 1960s, in the development of physical distribution, with the key focus being on outbound logistics. This focus was due to the higher value of finished goods when compared to, for example, raw materials. During this time there was a significant level of fragmentation of concepts ranging from demand forecasting through to customer service. These concepts began to merge around the 1980s into two main categories, namely inbound and outbound logistics, which ultimately merged again to form the logistics supply chain in a process that began in the 1990s and reached total integration in the year 2000 (Coyle, Langley, Gibson, Novack & Bardi, 2009:16-17) (see Figure 1).
Fragmentation refers to the silo orientated nature of the various supply chain concepts. This leads to the consolidation which may be considered the process of the concepts merging into broader concepts of materials management and physical distribution. These broader concepts evolve becoming functionally integrated, meaning all the functions are viewed as one aggregated concept referred to as logistics. Lastly supply chain management delivers value capture, through the reduction of costs and improved efficiencies and information flows.

1.1.2.2.1. 1960s: Fragmented concepts

The evolution of SCM is characterised by the degree of integration across the various concepts. In the 1960s integration was limited and each concept was managed in its own silo (Coyle et al., 2009:16).
1.1.2.2. 1980s: Consolidation

By 1980, demand forecasting through to manufacturing inventory had been consolidated into the concept of materials management. Warehousing, materials handling and packaging remained fragmented concepts, while finished goods through to customer services merged into the concept known as physical distribution (Rodrigue, 2012). Greater levels of integration were achieved through the consolidation of these concepts.

1.1.2.2.3. 1990s–2000: Functional integration and SCM

In 1990 all the elements were further integrated into the singular management concept of logistics.

Figure 2 Integrated supply chain (Coyle et al., 2009: 16 & 17)

With significant advances in information technology, it became possible to achieve full integration (see Figure 2) of all the concepts which started as single silos in the 1960s (Rodrigue, 2012). This resulted in improved flow of products/services, information and finances across suppliers, distributors, manufacturers, wholesalers as well as retailers and customers.
1.1.2.3. Brief overview of the evolution and development of supply chain and cold chain management

Figure 3 Supply chain and cold chain evolution

The author compiled Figure 3 above based on the following sources:
1.1. to 1.4. Rodrigue, 2012
2.1. Rice, 2007:1
2.2. World Health Organisation, n.d.:1
2.3. Walker, 2011
2.4. Bloomberg, n.d.

Figure 3 gives a brief overview of the evolution of the key supply chain and cold chain concepts and events as they progressed to the current day. In Chapter 2 this will be expanded and the detail of the events and developments that have been fundamental to the cold chain as we know it investigated.

1.1.3. Research scope

As previously stated cold chain management is a term loosely used to refer to the concept of a temperature-sensitive supply chain. However, for the purposes of this research it is required that the term is strictly defined in terms of a temperature range, in order to focus the scope of the research.
1.1.3.1. Temperature range

1.1.3.1.1. Possible temperature ranges
In order to review the various possible storage temperatures, this research will categorise pharmaceutical drugs as follows:

- Over the counter (OTC)
- Prescription (Rx)
- Vaccines

In the FDA Code of Federal Regulations (CFR) Title 21 part 201, which deals with the labelling requirements for drugs, both OTC and Rx have a requirement to state any special storage conditions (FDA, 2010a:1). It is within this section of the label that the storage requirement of the pharmaceutical is stated, if applicable.

In researching label databases and other sources for the above categories, the following temperature ranges applicable to the storage of pharmaceutical products have been identified:

- Below zero – Some vaccines, such as the measles vaccine, can be stored at −20 °C (WHO, 2006f:2)
- 2 °C to 8 °C – Most vaccines must be stored in this range (WHO, 2006f:2)
- 20 °C to 25 °C – Identified based on a review of the FDA OTC label database (Dailymed, 2011)
- 15 °C to 30 °C – Identified based on a review of the FDA Rx label database (Dailymed, 2011)

1.1.3.1.2. Global temperature
The global population was divided into five climate zones by the Australian Bureau of Meteorology (BOM) (see Table 1).
Analysing these climate zones in relation to the temperature ranges required for pharmaceutical products, it becomes evident where the primary concern around temperature is likely to be. According to Table 1, 82% of the world’s population resides in climatic zones with a mean temperature of above 9.6 °C. This therefore implies that for 82% of the world’s population, pharmaceutical drugs that are required to be stored between 2 °C to 8 °C must be actively controlled to that temperature, as the ambient environment in these climate zones is outside of the required range.

It is for the above reason that cold chain management, specifically in the 2 °C to 8 °C range, is such a challenge for global pharmaceutical storage and distribution. It is on this justification that this research will focus on cold chain management at the 2 °C to 8 °C temperature range.
1.1.3.2. Selecting the supply chain segment

Within the scope of cold chain, it is necessary to define specifically what segment of the cold chain the research will focus on.

A typical supply chain consists of the following stages (Chopra & Peter, 2004:2):

- Component/raw material supplier
- Manufacturer
- Wholesaler/distributor
- Retailer
- Customer

The manufacturer operates according to good manufacturing practice (GMP)-based processes; consequently, their processes are ‘highly controlled’. Figure 4 illustrates the more variable, and hence, less controlled processes in the distribution segment (Bishara, 2004:4).

![Figure 4 GCCMP - Qualification vs Validation (Bishara, 2004:4).](image)

The ‘last mile’ (the last leg of the distribution to the end consumer) is the most variable and less controlled component of the supply chain. It is in this segment of the supply chain where the greatest risk of a cold chain breach exists, as identified by the gap analysis conducted by Thermal Packaging Solutions (2010:44), which identified a key gap in the cold chain with regard to the distribution from the wholesaler to the hospital (see Figure
5). The two key issues identified were frozen packs in direct contact with the pharmaceutical product as well as inconsistent pack outs.

Due to the 'highly controlled' GMP-based processes that manufacturers use, the focus of the research will be within the fine distribution component of the last mile from the wholesaler/distributor to the pharmacy/hospital. This is where the greatest risks lie, and will be referred to as the outbound distribution.

1.1.4. What is cold chain management?

From a pharmaceutical perspective, cold chain management may be defined as:

- ‘a system used for keeping and distributing vaccines at the correct temperature so they remain sterile and potent until they reach the end user. It consists of a series of cold storage and transport links, such as refrigerators, cold boxes and vaccine carriers with cool packs. Most vaccines should be kept at between 2 °C and 8 °C. While some are damaged by freezing, others are damaged by excessive heat’ (Gavi Alliance, n.d.:1).
- ‘all of the materials, equipment, processes and procedures used to maintain all products (which require cold chain conditions) within the required temperature
range of 2 °C to 8 °C from the time of manufacture until the products are administered to individuals’ (MCC, 2012: 5).

Although the definitions have significant overlap the definition as defined by the MCC will be used.

Cold chain management is the practice of structuring the supply chain with the required equipment and methodologies to maintain the required temperature range over the entire supply chain. This would include active monitoring of the cold chain to ensure the integrity of the product once it reaches its final destination (Tamimi, Sandarakani & Vel, 2010:2).

1.1.5. Industries within which cold chain management is relevant

Although many industries may require the transport and storage of temperature-sensitive products, each industry has its individual challenges. In some industries, either these challenges are easy to overcome or the need to meet the temperature requirement is not stringent. In these industries, the need for cold chain management may not be as critical as in others. This is largely linked to the risk factor involved in the event of a failure in the cold chain.

In Table 2 the risks of each of the industries initially considered for this research (pharmaceutical, biotechnology and food) are evaluated from a qualitative point of view, based on two factors: detectability, which is the ability to identify that the product is not fit for consumption; and lethality, which is the likelihood of harm or death due to the consumption of such products.
Table 2 Industry cold chain risk level

<table>
<thead>
<tr>
<th>Industry</th>
<th>Detectability of cold chain failure</th>
<th>Lethality</th>
<th>Overall risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutical</td>
<td>Low – While a shake test can be used to check if a vaccine has dropped below freezing, there are questions around the validity of such tests. In a study conducted, only 37% of participants were able to identify frozen vaccines using this method (Grover &amp; Singh, 2005: 724).</td>
<td>High – As in the case of life-saving drugs. Furthermore, therapeutic failure in vaccines can be fatal as the patient is technically not vaccinated (Ram, 2011a:1).</td>
<td>High</td>
</tr>
<tr>
<td>Food</td>
<td>High – Sensory indications, sight and smell, that product is not fit for consumption (Thrall, 2011:1).</td>
<td>Medium – Can lead to dehydration; death is a risk only if not treated correctly (WHO, 2007:1).</td>
<td>Medium</td>
</tr>
<tr>
<td>Biotechnology</td>
<td>Medium – Being a raw material for other products, biotech products will be tested before being used in the manufacturing process (Canadian Health Products and Food Inspectorate, 2009:20).</td>
<td>Low – Typically not used by the end consumer.</td>
<td>Low</td>
</tr>
</tbody>
</table>

Where biotechnology products are used, testing is conducted on the product itself prior to use in further manufacture (Canadian Health Products and Food Inspectorate, 2009:20). This implies that at worst the product is written off and replaced, resulting in only financial implications. This is not the case with pharmaceuticals, as the product is already packaged and ready for the consumer or patient, therefore no testing can be done (Grover & Singh, 2005:724). The only way to ensure that the product does not impact the consumer is by ensuring that the product does not breach its temperature limits. It is for this reason that the cold chain is so critical in the pharmaceutical supply chain. With this comes the importance of temperature data and data integrity. First, the data may be used
to pick up a failure prior to reaching the end consumer. Secondly, in the event a consumer is negatively affected, it is critical to be able to trace the temperature history of the product (Bishara, 2006a:3).

The common thread between these three industries is that they all have some impact on consumer health. The fundamental differentiator in the industries identified is the degree to which a failure in the cold chain may harm a consumer.

The outcome of a breach in the cold chain in the case of pharmaceuticals may result in the drug losing its efficacy. In the case of life-saving drugs this may result in death if the breach in the cold chain is not identified. If the breach is identified, the efficacy period may be reduced resulting in a decreased shelf life of the product (FDA, 2010b:1).

The importance of cold chain management can be illustrated when one considers:

- **Adverse effects after immunisation (AEFI):** ‘Adverse effects after immunisation (AEFI) is a general term that covers various reasons, including bad vaccine quality due to breaks in the cold chain, contamination and complications due to pre-existing conditions of the child.’ According to Union Health Ministry Statistics in India, the number of children who died in India due to AEFI rose during the period 2008 to 2010 from 111 to 128 respectively (Ram, 2011b). Although not all AEFI may be attributed to breaches in the cold chain, it is a contributing factor.

- **Lack of cold chain distribution infrastructure:** ‘At least 2 million people die each year from vaccine preventable diseases.’ Ironically the deaths are not all linked to the lack of vaccines, but rather to the challenge of distributing and maintaining the cold chain during the distribution process (Ruben, 2011:74).

- **Life-saving drugs:** As mentioned previously, these ‘drugs which require immediate administration within minutes post or during a medical emergency’, a therapeutic failure can be fatal (Chaudhury, 2003:1).

Due to the significant impact that cold chain management can have on people’s lives around the world, and the challenges in ‘last mile’ distribution, the scope of this research will be the outbound distribution of pharmaceutical cold chain products, from the wholesaler/distributor to the pharmacy/hospital in South Africa.
1.2. Problem statement
A fundamental challenge in pharmaceutical cold chain management is the contradictory requirements of quality management and outbound distribution. Quality management seeks to maintain and improve the quality of products through various activities. These activities increase outbound distribution costs making cost control a challenge. This requires a significant effort to balance the fundamental trade-off between quality and outbound operations; this trade-off is viewed as the baseline challenge pivotal to this research. The impact of such contradictory requirements, if not properly balanced, could result in poor quality levels for pharmaceutical chain products, in the case where logistics service providers are unable to profitably distribute these crucial products. Alternatively, logistics service providers may choose not to distribute these items, which would be of significant concern in terms of access to these medicines.

1.2.1. Research Gap
Pharmaceutical cold chain management is a relatively new concept in South Africa as a result there is little research available. Specifically, there is no research which addresses the challenges related to the increasing quality requirements in relation to regulations which govern how pharmaceutical logistics costs are priced and recovered by logistics service providers. This research intends to bridge this gap, by identifying what challenges emerge from these contradictory regulatory requirements, which increase the cost of logistics while limiting the possible recovery of these costs.

1.2.2. Core requirement for cold chain management
Before one attempts to understand the intricacies of cold chain management it is important to understand what drives cold chain management. The fundamental driving force comes down to the critical concept of quality management.

‘Quality management includes all the activities that organisations use to direct, control and coordinate quality. These activities include formulating a quality policy and setting quality objectives. They also include quality planning, quality control, quality assurance, and quality improvement’ (Praxiom Research Group Limited, 2011:14-17).
As the definition indicates, quality management is the overriding concept and includes quality planning, control, assurance and improvement (Harvey & Dalrymple, n.d.:10).

Quality management is specifically important in the pharmaceutical industry due to the major health implications to the end consumer in the event that quality is not properly maintained. Failure to meet these requirements may result in injury or death (Ram, 2011:1). A fundamental aspect of these requirements is temperature related and as such falls under the scope of this research.

1.2.3. The fundamental challenge, counter requirements of quality management and outbound distribution
Cold chain pharmaceutical product sales have increased by 27% versus the 13% increase of global bio pharma product sales from 2008 to 2011 (Figure 6). It is estimated that cold chain costs represent 12% ($5.2billion) of the total supply chain costs related to bio pharma products sales (Figure 7). With these figures in mind organisations cannot ignore the significant cost impact cold chain has on the overall cost structure (Basta, 2010:1-2).
Cold chain management adds the critical component to SCM of ensuring the supply chain can be maintained between the specific temperature parameters as defined by the perishable characteristics of the product. The temperature requirement of the product creates an increased requirement for quality management. Where a product not requiring a specific temperature condition may have quality issues linked to raw material, manufacture, damages and so forth, cold chain products have the added complexity of being impacted by variations in the ambient temperature (Bishara, 2011). In order to counteract this, the temperature of the cold chain needs to be actively controlled and monitored using various mechanisms to maintain and report on the environment within which these products are stored and transported.

Costs associated with quality management include (Larson, 2009):

- Prevention costs – associated with designing, implementing and maintaining a quality management system
- Appraisal costs – relating to evaluation of materials used
- Internal failure costs – which occur when the process fails to operate as required, for example, scrap, rework etc.
- External failure costs – due to quality issues only being picked up once the product reaches the intended consumer, for example, repairs and returns.
These costs typically impact outbound distribution costs as the equipment required to maintain these temperatures is used in the outbound distribution, for instance: refrigerators, refrigerated trucks, and cold chain packaging systems related to the storage and distribution of the pharmaceutical products (Wei & Quanyue, n.d.:660). This may not sit well with operations executives as a key performance indicator (KPI) for operations often includes overall cost effectiveness (KPI Drafting Group, 2001:11). This potentially results in resistance, perhaps even conflict, when trying to maintain quality through proper cold chain management. Outbound distribution managers may resist the implementation of proper cold chain practices or alternatively may provide token compliance, which in turn may result in shortcuts being taken. On the other hand, the quality department may create undue pressure by taking an ‘overkill’ approach to quality.

Balancing these requirements is crucial in meeting the business objective and ensuring the pharmaceutical products reach the patient in the appropriate state.

‘Without significant improvements in the supply chain that delivers the correct amount of these valuable products safely and efficiently – ensuring little is wasted, lost, broken, or exposed to excessive heat or cold – they may never reach the people who need them most’ (PATH, 2008:3). These unique challenges in the pharmaceutical cold chain form the foundation of the motivation for this research.
1.3. Research motivation

Cold chain distribution in the pharmaceutical industry is extremely specialised due to the very tight quality requirements of the product. This results in processes in pharmaceutical cold chain management such as validation and qualification that require an extremely scientific approach, running temperature mapping studies under controlled, simulated and extreme conditions in order to provide a level of confidence that the product will remain within its quality levels during its distribution life cycle (Pharmaceutical and Medical Packaging News, 2007:2). The challenge in cold chain distribution is evident when one tries to maintain the required temperature range throughout the logistical, operation and business processes (International Society for Biological and Environmental Repositories, 2009:1).

In the pharmaceutical distribution industry people are typically either focused on the quality aspects (pharmacists, doctors, quality department) or the operational aspects (operations management, shareholders). This highlights the need for the supply chain philosophy of providing the best overall service, at the required quality levels, at the lowest possible cost (Geiger & Dooley, 1998:50). This can only be achieved through a better understanding of both quality and outbound distribution in the pharmaceutical cold chain.

![Figure 8 Quality vs cost](PriceWaterHouseCooper, n.d., 4)
The objective should be to identify the optimum levels to which the operation should strive for cost reduction and the quality department’s drive for quality improvements. The motivation behind this research is born out of the need for integration between the contrary requirements of quality (risk reduction and compliance) and operations (cost reduction and shareholder returns) (PriceWaterhouseCooper, n.d.:4). The balancing act of quality and operational cost and efficiency is the fundamental challenge in the pharmaceutical cold chain which this research seeks to understand (see Figure 8).

1.4. Study objectives

1.4.1. Primary objective

- To identify key challenges between pharmaceutical quality requirements and outbound distribution functions in the pharmaceutical cold chain of the private sector
  - In order to gain a better understanding of how an organisation can improve the balance between the quality requirements intrinsic to the pharmaceutical cold chain, and the fundamental commercial requirements of an efficient and effective outbound operation.

1.4.2. Secondary objectives

- To identify the relationships between cost elements within the quality and outbound distribution functions
  - Based on the fundamental challenge of the contradictory requirements between the quality and outbound distribution functions, specific relationships between elements within these functions will be identified.

- To identify the key factors to be considered within each of the relationship elements identified, from highest to lowest priority
  - In order to provide context to the nature of the relationships, the key factors will provide the detail necessary to identify the key challenges.
1.5. Methodology

1.5.1. Paradigm
Due to the complex nature and difficulty in acquiring detailed data in the pharmaceutical cold chain, a mixed method approach will be employed to meet the objectives of the research. This method originates from a multi-paradigmatic approach which seeks to obtain the best of both the traditional positivist paradigm as well as the interpretive paradigm (Taylor, 2013:2-8).

1.5.2. Research design and execution
Based on the mixed method approach, both descriptive and exploratory techniques will be used.

- Descriptive:
  - The first secondary objective of this research will be met in part by determining if there is a relationship between elements within the pharmaceutical cold chain. The identification of these relationships will set the context for further analysis of key factors within each cost element. Relationships between the elements will be verified through industry-based surveys, and confirmed through a cost analysis.

- Exploratory:
  - The second secondary objective seeks to identify what factors are important to consider within each of these elements. The exploratory component of the research design will deal with this question.

The descriptive data will be collected through a survey as well as a cost analysis; the exploratory data will be collected purely through the survey.

The primary objective of the research will be met by combining the outputs from both the descriptive and exploratory components of the research. The descriptive component will identify relationships between elements. The exploratory component will identify the key factors within each cost element. The key factors between the relationships of the elements will be analysed in order to determine key challenges, which make up the
fundamental challenge of contradictory requirements between quality and outbound operations.

1.6. Dissection of the study
The study consists of seven chapters, beginning with an introduction to the study in Chapter 1.

1.6.1. Chapter 2 – Overview of the development of pharmaceutical regulation and current standards and guidelines
Chapter 2 provides the necessary insight into the historical development of pharmaceutical regulation, guidelines and standards. The understanding of various industry bodies clarifies and provides the necessary context for the balance of the research as these bodies and the requirements of these bodies define the fundamental quality requirements within the pharmaceutical cold chain. In addition, the key regulations, guidelines and standards available are reviewed and summarised in order to provide the detail of the underlying requirements for the pharmaceutical cold chain.

1.6.2. Chapter 3 – Pharmaceutical cold chain context
Over and above the regulatory component there are other considerations in terms of the history and development of the pharmaceutical supply chain that must be understood; these considerations are discussed in detail in Chapter 3. The components which make up the pharmaceutical cold chain are broken down and discussed individually in order to fully explore the many aspects which must be considered in the pharmaceutical cold chain.

1.6.3. Chapter 4 – Development of the relationship model
There are many different cost elements that must be considered in any supply chain. The research is not able to investigate every one of the many different elements that exist. Therefore, to focus the research, a framework was used. This framework model assists in structuring the research, allowing the development of a survey and cost analysis that can be compared to one another. The development of the new model was based on
research of available models to determine the most suitable model. This new model was then be augmented and adjusted to serve the purposes of the research.

1.6.4. Chapter 5 – Research methodology
The research methodology was guided by a multi-paradigmatic paradigm. This paradigm and its associated methods allowed for the necessary flexibility in the approach to meet the outcomes of the research. Both descriptive and exploratory research was used, structured in the form of a survey and cost analysis.

1.6.5. Chapter 6 – Research results and findings
Chapter 6 encapsulates the outcomes of the research summarising and analysing the results of the survey and cost analysis. The relationships and key factors identified in the research were integrated to identify the key challenges as illustrated by the research. The results of the cost analysis were used to support the outcomes of the survey.

1.6.6. Chapter 7 – Conclusion and recommendations
Finally, in Chapter 7 the entire study was summarised highlighting the key findings. Focus was placed on results of the research to ensure that the objectives of the research were met. The potential application of the research was explored, and recommendations and opportunities for further research identified.

1.7. Conclusion
The fundamental starting point for this research originates from the identification of regulatory requirements which drive both reduction in the price of pharmaceuticals and increased quality. These two requirements create a conundrum for the pharmaceutical cold chain industry due to the need to improve quality without the ability to increase pricing.

In order to operate successfully in such a situation, it is necessary to think creatively and identify opportunities for improved quality without increasing cost or reduce costs to fund improved quality. This requires an understanding of the interaction between operational and quality focused cost elements, and the impact in changes of these cost elements on one another, and ultimately on patient safety.
This research will attempt to understand these relationships and provide a framework to allow further analysis and research to take place. This will be achieved through the use of mixed method research in line with a multi-paradigmatic paradigm.

Due to their highly complex nature, understanding the two fundamental components of the pharmaceutical cold chain will be the starting point. Both the regulatory aspects which define the quality requirements and the supply chain context will need to be reviewed in depth. The regulatory structure will be discussed first as this is the unique and most complex component of the pharmaceutical cold chain.
CHAPTER 2 – OVERVIEW OF THE DEVELOPMENT OF PHARMACEUTICAL REGULATION AND CURRENT STANDARDS AND GUIDELINES

2.1. Introduction
In order to gain an understanding of the pharmaceutical cold chain, it is necessary to understand the development of pharmaceutical regulation, as well as some of the current available standards and guidelines, as these drive the quality requirements for cold chain management. In Chapter 2 the countries of significance will be established. This is important as it will guide the literature overview in terms of what regulations, standards and guidelines are relevant for this research. The balance of the chapter will provide an overview of the development and summary of these regulations, standards and guidelines.

2.1.1. Legislation and regulation
With the cold chain having such a significant impact on the safety and efficacy of certain drugs and vaccines, legislation and regulation form a fundamental base underpinning the legal requirements for proper cold chain management.

The main focus of the research is pharmaceutical cold chain management and its interaction with outbound distribution operations. Pharmaceutical cold chain management forms part of the temperature storage and transport conditions, which have a significant impact on drug safety and efficacy. Drug quality did not start with cold chain management. Many other aspects may affect drug safety and efficacy, such as chemical mixes which resulted in the sulphanilamide tragedy (Ballentine, 1981) and other factors such as humidity, light and oxygen (United States Pharmacopeia, 2010). In this chapter, the development of legislation and regulation will be highlighted in order to provide a background as to the origins of today’s current regulations, standards and guidelines.

The development of legislation and regulation will be discussed on a global level with reference to some of the key bodies and events that have shaped today’s regulatory landscape, including that of South Africa.
2.2. Countries of significance

Pharmaceuticals are distributed worldwide; by default, therefore, cold chain is a worldwide requirement. As a result, when looking at the development of cold chain and related concepts (regulation, distribution, etc.) one would need to analyse its development on a global scale.

Many of the industry methodologies and developments are influenced to a large extent by global learnings, methodologies and regulations, and therefore, reference will be made to the information and experience gained from other countries and organisations. In particular, the United States of America (USA) and the World Health Organisation (WHO) will form a core foundation for much of this chapter for the following two reasons: First, there is a very high concentration of global manufacturers based in the United States. There are 12 pharmaceutical manufacturers in the top 500 companies in the world (see Table 3). These companies represent $434 billion of global pharmaceutical revenue, of which seven are based in the USA and make up $230 billion of the total revenue. To put this into perspective, these USA-based companies represent just under 53% of the total revenue, with the closest country thereafter being Switzerland at 19.75% (see Figure 9) (CNNMoney, 2009).

Table 3 Global 500 pharmaceutical revenues (CNNMoney, 2009)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Country</th>
<th>Global 500 rank</th>
<th>Revenue ($ m)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Johnson &amp; Johnson</td>
<td>United States</td>
<td>103</td>
<td>63 747</td>
<td>14.68%</td>
</tr>
<tr>
<td>2</td>
<td>Pfizer</td>
<td>United States</td>
<td>152</td>
<td>48 296</td>
<td>11.12%</td>
</tr>
<tr>
<td>3</td>
<td>GlaxoSmithKline</td>
<td>United Kingdom</td>
<td>168</td>
<td>44 654</td>
<td>10.29%</td>
</tr>
<tr>
<td>4</td>
<td>Roche Group</td>
<td>Switzerland</td>
<td>171</td>
<td>44 268</td>
<td>10.20%</td>
</tr>
<tr>
<td>5</td>
<td>Sanofi-Aventis</td>
<td>France</td>
<td>181</td>
<td>42 179</td>
<td>9.72%</td>
</tr>
<tr>
<td>6</td>
<td>Novartis</td>
<td>Switzerland</td>
<td>183</td>
<td>41 459</td>
<td>9.55%</td>
</tr>
<tr>
<td>7</td>
<td>AstraZeneca</td>
<td>United Kingdom</td>
<td>268</td>
<td>31 601</td>
<td>7.28%</td>
</tr>
<tr>
<td>8</td>
<td>Abbott Laboratories</td>
<td>United States</td>
<td>294</td>
<td>29 528</td>
<td>6.80%</td>
</tr>
<tr>
<td>9</td>
<td>Merck</td>
<td>United States</td>
<td>378</td>
<td>23 850</td>
<td>5.49%</td>
</tr>
<tr>
<td>10</td>
<td>Wyeth</td>
<td>United States</td>
<td>401</td>
<td>22 834</td>
<td>5.26%</td>
</tr>
<tr>
<td>11</td>
<td>Bristol-Myers Squibb</td>
<td>United States</td>
<td>435</td>
<td>21 366</td>
<td>4.92%</td>
</tr>
<tr>
<td>12</td>
<td>Eli Lilly</td>
<td>United States</td>
<td>455</td>
<td>20 378</td>
<td>4.69%</td>
</tr>
</tbody>
</table>
Figure 9 Top 12 Pharmaceutical manufacturers’ revenue by country (source data: CNNMoney, 2009)

Due to the fact that the large majority, by revenue, of pharmaceutical manufacturers are based in the USA, the development and evolution of regulation in the USA becomes significant to global quality requirements. Switzerland follows second (in terms of revenue) to the USA. With the headquarters based in Switzerland, the WHO is of interest with regard to the development of cold chain.

Secondly, the FDA and WHO were significant regulatory pioneers. If one considers the establishment of a regulatory body to be the initiation of regulation in the pharmaceutical industry, South Africa followed the USA in the establishment of such a body. With the WHO being established in 1948 and the United States FDA in 1927 (Siedman and Warren, 2001), South Africa established the MCC as part of the Medicines and Related Substance Control Act of 1965 (SA Government, 1965:4), a full 38 years after the FDA.

A bilateral agreement between the FDA and MCC indicates that channels for information sharing between the two government agencies are in place (FDA, 2004).
2.3. Development of legislation and regulation in the pharmaceutical industry

2.3.1. Legislation and regulation
Legislation refers specifically to the creation of new laws, while regulations on the other hand are the specific rules created by the agency that interpret and enforce the laws (Worthan, 2006:20). A South African example would be the South African Pharmacy Council (SAPC), which is the regulator of the Pharmacy Act of 1974 (South African Pharmacy Council, 2011), which forms the legislator framework. The SAPC is a body that was created as a result of the Pharmacy Act of 1974, which was passed by the South African Government (SA Government, 1974:3). Legislation and regulation therefore represent the underlying requirements which must be met by all participants in the industry without exception.

2.3.2. Origins of legislation
In today’s society we have the confidence to assume that the medicines we consume have been produced, labelled and tested rigorously in accordance with government legislation. While this may be true, it was not always the case. In the USA the quality of drugs was in effect unregulated until the 1900s (Siedman & Warren, 2001). Prior to 1900, drug regulation was limited to the Drug Importation Act, which focused solely on imported drugs (FDA, 2006a:1).

The first legislation published with regard to the pharmaceutical industry was the Drug Importation Act of 1884 and Biologics Control Act of 1902. While these Acts preceded the Pure Food and Drug Act of 1906, it was the 1906 Act that first gained the awareness of the consumer. This increased level of awareness was partially as a result of The Jungle, a novel published by Upton Sinclair (Worthan, 2006:20).

The novel’s original intent was to explore and expose the conditions within which immigrants worked in the meat-packing industry in the USA in the early 1900s. The novel instead caught the attention of the American public in a mere 12 pages which discussed food safety. Upton said it best himself: ‘I aimed for the hearts of the public and by accident hit their stomach.’ The fictional novel led to a public outcry in the meat-packing industry,
which resulted in a significant drop in meat sales. Ironically, the meat-packing industry then lobbied the government for increased regulation to restore public confidence (Wilson, 2010:1).

The Pure Food and Drug Act dealt with ‘preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes’. On review of the Act, it is clear that at that stage there was still no specific legislation related to the temperature storage conditions of pharmaceuticals and drugs (US Government, 1906).

It was this sequence of events that ultimately led to a heightened sense of awareness and the passing of the Pure Food and Drug Act in 1906, to better protect the public (FDA, 2009a:1).

2.3.3. The sulphanilamide tragedy: The spark to regulation reform

In 1927 the FDA was created to enforce food and drug laws. Unfortunately, the Pure Food and Drug Act did not cover drug safety and efficacy; as a result, the FDA recommended a review of the Act, to include drug safety, which fell on deaf ears (Siedman & Warren, 2001).

It was only until the 1937 sulphanilamide disaster that the calls for legislation reform were heard. Sulphanilamide, a drug used to treat streptococcal infections, had worked well for some time in tablet form. However, when demand for the same treatment in liquid form arose, a company, S.E. Massengill CO., identified that the tablet could be successfully diluted in diethylene glycol. At the time legislation did not require new drugs to be tested for toxicity, and so what turned out to be a toxic concoction was shipped to 633 locations throughout the USA. The toxic Elixir Sulphanilamide resulted in the death of over 100 people and the first major drug recall. It was this incident that hastened the enactment of the 1938 Food Drug and Cosmetic Act (FDCA), which is still the basis on which drugs in the USA are regulated today (Ballentine, 1981:1).
2.3.4. First legislation relevant to cold chain management

The FDCA has two fundamental goals. The first is to protect public safety; the FDCA mandates the safety, purity and effectiveness of drugs. Secondly, the FDCA provides a legal ground to regulate the truthfulness and completeness of product labelling and marketing (Ruger, 2004).

One can see the clear link between the goals of the FDCA and the cold chain when considering the impact that a breach in the cold chain would have on both the safe and effective use of cold chain pharmaceutical products.

It was in the FDCA that guidelines for the storage of pharmaceuticals first became a requirement for any entity distributing pharmaceuticals. ‘The Secretary shall by regulation issue guidelines establishing minimum standards, terms, and conditions for the licensing of persons to make wholesale distributions in interstate commerce of drugs subject to subsection (b). Such guidelines shall prescribe requirements for the storage and handling of such drugs and for the establishment and maintenance of records of the distributions of such drugs.’ (FDA, 2009b). The minimum standards for distribution, and in turn storage and handling, begin to indicate the considerations of the impact of environmental factors on the quality of drugs.

Little happened with regard to legislation in the USA between the years 1938 and 1960, other than the 1952 Durham–Humphrey Amendment. This amendment codified the two classes: prescription and non-prescription (Worthan, 2006:20).

2.3.5. Enter the World Health Organisation

2.3.5.1. Establishment of WHO

According to McCarthy (2002), pre-1945 there were several international health agencies which lacked integration and had little success in dealing with disease outbreaks such as the cholera outbreaks in 1830 to 1847. These organisations included:

- International Sanitary Bureau (Americas)
- Pan American Health Organisation (Americas)
- L’Office International d’Hygiene Publique (Europe)
• Health Organisation (League of Nations)

In 1945, at the end of World War 2, the United Nations voted to establish a single integrated international health organisation. In 1948 the WHO Constitution obtained enough signatures for it to be established. The WHO comprised six regional organisations with its headquarters in Geneva (see Figure 10). The six regional offices are:

- Regional Office for Europe (EURO)
- Regional Office for Western Pacific (WPRO)
- Regional Office for Africa (AFRO)
- Regional Office for Eastern Mediterranean (EMRO)
- Regional Office for South East Asia (SEARO)
- Pan American Health Organisations (PAHO)

![WHO Regional Offices](image)

Figure 10 WHO regional offices (McCarthy, 2002)

2.3.5.2. WHO Constitution

An organisation’s constitution can be defined as, ‘a body of fundamental principles according to which a state or other organisation is governed’ (Concise Oxford Dictionary, 1982:202).

As the central agency that assists in coordinating health efforts across the globe, between various countries and their relevant health agencies, the WHO Constitution provides some insights into the development of regulation.
2.3.5.2.1. Objectives and functions

The WHO’s objective is ‘the attainment by all peoples of the highest possible level of health’ (WHO, 2006a:2). The WHO works to achieve this ultimate goal through the following functions (WHO, 2006c:iii):

- Leadership in developing partnerships and matters critical to health
- Shaping the research agenda and stimulating research activities and sharing of knowledge
- Developing standards and monitoring their implementation
- Articulating policy options
- Providing technical support, catalysing change, and building sustainable institutional capacity
- Monitoring the health situation and assessing health trends

Based on its objectives and functions, the WHO can be considered to be a body which acts as an international regulatory body.

2.3.5.3. WHO as a regulatory body

Using the WHO Constitution and the International Health Regulations (IHR), which is a legal instrument binding 194 countries around the world, the WHO plays a regulatory role in global health. The IHR obligates its members to report certain disease outbreaks and health events, in order to uphold global public health security (WHO, 2008).

2.3.5.3.1. WHO Constitution

The three articles of the WHO Constitution that are of particular interest with regard to the WHO and regulation are (WHO, 2006b:7-8):

- Article 19 – ‘The Health Assembly shall have authority to adopt conventions or agreements with respect to any matter within the competence of the Organisation’
- Article 21 – ‘The Health Assembly shall have authority to adopt regulations concerning:
  - Sanitary and quarantine requirements
- Terminology with regard to diseases
- Diagnostic standards
- Standards with respect to safety, purity and potency of pharmaceuticals and related products
- Labelling and advertising of pharmaceuticals and related products’

- Article 23 – ‘The Health Assembly shall have authority to make recommendations to Members with respect to any matter within the competence of the Organisation.’

It is important to note that the above articles and the WHO’s ability to regulate is specific to that of the international functioning of the pharmaceutical industry and the member states of the WHO Constitution.

Article 19 makes provision for the adaptation of conventions and agreements between member states. Furthermore, Article 21 allows the WHO to promulgate regulations with regard to the stated items above, while Article 23 gives the WHO the authority to make recommendations with regard to topics within its scope (Georgetown University, 2010).

These three articles provide a solid foundation for the WHO to regulate its member states within the given scope of the articles. Perhaps the most relevant aspects of this research are Article 21 items D and E.

- Item D refers to ‘safety, purity and potency’. Cold chain management has a significant impact on meeting the related ‘standards’ in this regard.
- Item E refers to the ‘labelling’ of pharmaceuticals, and what one needs to take note of in this particular item is that while there are many aspects that need to be considered with regard to labelling requirements, storage temperature is a key aspect that needs to be stated on the product (US Pharmacopeia, 2010:234). This illustrates the foundation for the mechanisms that ultimately provide for the regulation of cold chain requirements, within the WHO member states.

Article 23 takes the WHO’s responsibility further than simply standards and regulations, and makes provision for the WHO to provide guidelines for subject matter within its expertise. We will explore this in further detail later on, where guidelines such as the ‘Guidelines for the International Shipping of Vaccines’ will be reviewed as the WHO
provides some fundamental principles and guidance with regard to good cold chain management (WHO, 2005c:1)

2.3.5.3.2. WHO Regulations – International Health Regulations

In the research conducted, the key WHO regulatory document is the International Health Regulations (IHR). It was originally published in 1969 with the second addition being published in 2005 (WHO, 2008:1).

The origins of the IHR are rooted in the first International Sanitary Conference in Paris, France in 1951, with the primary focus being on the cholera outbreaks across Europe from 1830 to 1847. From this point, ten international sanitary conferences were held with no agreements coming into place, until the first convention was adopted in Venice, Italy in 1892. In the early 20th century the international organisations discussed earlier in the establishment of the WHO came into being to enforce the agreed-to conventions. In 1951 the International Sanitary Regulations were signed which were renamed as the International Health Regulations in 1969 (Lawrence & Gostin, 2004).

According to the Pan American Health Organisation (2005), and corroborated by Mankan and Pinto (2009:222), the original IHR of 1969 was developed to monitor, report and control the following six communicable diseases:

- Cholera
- Plague
- Yellow fever
- Smallpox
- Relapsing fever
- Typhus

An important point to note in terms of the development of cold chain management is that of the above six communicable diseases, four have a cold chain requirement:

- Cholera: 2 °C to 8 °C (WHO, 2006f:40)
- Plague: 2 °C to 8 °C (WHO, 1995:1)
- Smallpox: 2 °C to 8 °C (Centre for Disease Control and Prevention, 2006:2).
- Typhus: below 4 °C (WHO, 1982:74)

According to the Icelandic Directorate of Health (2008), in 1974 the IHR was amended to include provisions with regard to cholera. A further amendment of the IHR was made in 1981 to remove smallpox from the regulation due to the eradication of the disease. In 1995 the need for a comprehensive review of the IHR was identified at the 48th World Health Assembly. This was identified on the basis of some inherent limitations of the IHR, including:

- Narrow scope of diseases
- Dependence on official country notification
- Lack of formal international coordinated mechanism

In 2003 the World Health Assembly established an Intergovernmental Working Group to review and provide recommendations for a draft revision of the IHR. This revision of the IHR was adopted in 2005 and was enforced by 2007, with its purpose being ‘to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade’ (WHO, 2005c:1).

In order to assist in achieving the above purpose, significant changes were made to the IHR, with some key changes being highlighted in Table 4. The scope of the regulations was significantly expanded, communication channels were updated in line with modern technologies, and the WHO was given increased authority, among others (Kats & Fischer, 2010:3).
### Table 4 Comparison of IHR (Katz & Fischer, 2010:3)

<table>
<thead>
<tr>
<th>IHR component</th>
<th>1951–2007</th>
<th>2007–Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scope</td>
<td>Cholera, plague, yellow fever and smallpox (removed after eradication); control at borders</td>
<td>Public health emergency of international concern; detection and containment at source</td>
</tr>
<tr>
<td>Communication</td>
<td>Countries fax reports to WHO</td>
<td>IHR national focal points (NFP) and WHO’s secure website</td>
</tr>
<tr>
<td>Notification</td>
<td>Report to WHO within 24 hours</td>
<td>Report to WHO within 24 hours; 72 hours to respond to follow up request</td>
</tr>
<tr>
<td>Coordinated response</td>
<td>No mechanism for coordinated international response to contain disease</td>
<td>Assistance in response/recommended measures</td>
</tr>
<tr>
<td>Authority</td>
<td>WHO not able to initiate an inquiry: Dependence on official country notification</td>
<td>WHO can initiate request for information based on unofficial sources; can ask for additional information</td>
</tr>
<tr>
<td>National capacity</td>
<td>Provide disease inspection and control at port of entry</td>
<td>Provide disease inspection and controls at port of entry. Meet minimum core capacity for detection, reporting and assessment</td>
</tr>
<tr>
<td>Response capabilities</td>
<td>Predetermined public health controls at point of entry</td>
<td>Flexible, evidence-based responses adapted to nature of threat</td>
</tr>
</tbody>
</table>

### 2.3.6. The thalidomide tragedy: History repeats
Thalidomide was first developed by a German pharmaceutical company in 1954, and was originally marketed as an anticonvulsant to be used for epilepsy patients. The drug however was not effective for this purpose, but worked well as a hypnotic, sedative and tranquilliser, and was prescribed to pregnant woman to treat morning sickness (Randall, 1990).

The drug was made available for sale from 1957 onward, in a time when legal requirements for testing of medicines was far from the legislation in place today. In
October 1959, reports started emerging of two side effects; the first was nerve damage in the hands and feet of the user, at which point the company applied for prescription status for the drug. Suspicion of the second horrifying side effect first arose with an increase in deformities in unborn children. In 1961, shortly after the suspicions began to rise, the product was withdrawn from the market. However, the market recall was too late as a year later in 1962, it was identified through animal testing that the drug thalidomide had a propensity to cause defects (Granenthal, 2012) (see Figure 11).

One of the FDA’s greatest success stories is that the thalidomide drug was never approved for sale in the United States. Dr Francis Kelsey, who was overseeing the New Drug Approval (NDA) at the time, had concerns that the drug could cause neuropathy, a nerve disease. On this basis she declined the application, which kept the company busy with the completion of the application until the side effects were discovered in 1961. As a
result, preventing another thalidomide-type tragedy became a key focus for the FDA, and
has been a driving force in regulation reform (Glauberman, 1997:2-5).

If the legislation of the day had been sufficient to prevent the thalidomide tragedy from
spreading to the USA, why was there still a need for reform? The answer was provided
in an article published by the *Washington Post* titled ‘Heroine of FDA Keeps Bad Drug off
Market’. In the article it became apparent that the reason the tragedy was averted was
not due to robust legislation but rather to the right person; Dr Francis Oldham Kelsey was
in the right place at the right time. It was her suspicion of its different effects on humans
versus animals, and the fact that it was not a life-saving drug, that prompted her to use
loopholes in the approval process to drive the manufacturer to provide additional evidence
of its safety and efficacy. As a result of this tragedy, the Kefauver–Harris Amendments
were unanimously passed in 1962 signed by President Kennedy in the presence of Dr
Francis Kelsey (Rice, 2007:5-6).

According to Worthan (2006), the 1962 Kefauver–Harris Amendments had the following
key changes added to the 1938 Food Drug and Cosmetic Act:

- Efficacy as premarketing condition
- Establishment of good manufacturing practice (GMP)
- Nomenclature being addressed

2.3.7. FDA: Pharmaceutical good manufacturing practice regulations

2.3.7.1. Introduction to good manufacturing practice

Good manufacturing practice (GMP) is a standard that allows for control, management
and quality testing during the manufacturing process of pharmaceuticals, and is
recognised worldwide. GMP forms the foundation for 21 Code of Federal Regulations
(CFR) Parts 210 and 211, which govern legislation for pharmaceutical manufacture.
Being the basis for regulation, GMP is a requirement for pharmaceutical manufacturers
(Metric Stream, 2008).

The scope of GMP is applicable to the manufacturing, processing, packing and holding
of a drug (FDA, 2011). This scope is of particular importance as it refers to the holding,
or storage, of the drugs at manufacture, which is relevant to this research in terms of the storage temperature of these drugs. These temperature storage requirements would likely influence other guidelines to be discussed later such as good distribution practice (GDP).

2.3.7.2. 21 CFR Parts 210 and 211

On review of 21 CFR Parts 210 and 211, the following key points relevant to cold chain were identified (FDA, 2011):

- Product should be stored at appropriate temperature conditions – These would be defined by the conditions stated on the label, for example 2 °C to 8 °C in the case of cold chain products.
- Potency or therapeutic activity of the drug – Not storing the product at the required temperature could impact the potency of the drug.
- Reference to labelling requirements – Labelling would require a statement of the required storage conditions.
- A system for monitoring environmental conditions – This would include the cold room in the case of cold chain products.

While no reference is made to the cold chain specifically, all the above requirements would be defined by the storage requirement of the drug itself. Where the drug has a cold chain storage requirement, for example 2 °C to 8 °C, the above aspects would become relevant to the cold chain, for example, monitoring of the cold room.

2.3.7.3. Foundations of GMP

According to Lombardi, in 1962, after the thalidomide tragedy the first GMPs were established in the CFR for drug manufacturers. He summarises the then GMP as follows (2005: 14-15):

- Write procedures and work instructions.
- Follow procedures and instructions.
- Document your work.
- Validate/qualify processes and equipment.
• Design proper facilities and equipment.
• Maintain and cleanse facilities, equipment and self.
• Define, develop and demonstrate job competence.
• Protect against contamination.
• Control components and product-related processes.
• Conduct planned and periodic audits.

The GMP requirements as stated by the FDA require the manufacturer to ‘consider storage and shipment requirements to meet special handling needs’; in the case of cold chain pharmaceuticals, refrigeration would be required (FDA, 2006b:23).

It is at this stage that we begin to see specific reference to the storage requirements of pharmaceuticals, and more specifically to the requirement of their being stored in a ‘cold’ environment.

2.3.8. Current FDA regulations
The latest significant amendments to the FDA regulations are found in the Food and Drug Modernization Act (FDAMA) of 1997. Most of these amendments focused on reducing bureaucracy (FDA, 1997). No amendments significant to the cold chain were made.

2.3.9. Development of regulation in South Africa

2.3.9.1. Medical, Dental and Pharmacy Act 13 of 1928
At the heart of today’s South African pharmaceutical regulation lies the Medicines and Related Substances Control Act 101, which was implemented in 1965.

Prof Johann Schlebusch, who was a Registrar of Medicines at the MCC, provides insight into the historical development of regulation in South Africa (personal communication, 1 January 2012). Prof Johann Schlebusch joined the MCC in 1972 as a medicine controller and was later appointed as the Registrar of Medicines in 1985 (What’s New Doc, 2010:3). The Medical, Dental and Pharmacy Act 13 of 1928 was a broad, principle-based piece of legislation. The Act provided for regulation related to rules, ethics and training within the medical, dental and pharmacy professions. For example, the Act required pharmacists to
ensure proper control of medicines. The requirement was stated in a general manner and relied on the competence of the pharmacist to ensure that medicines were properly handled and controlled. The Act at this point had a different scheduling system compared to today’s.

2.3.9.2. The Hendrik Snyman Commission

On 15 January 1960 the then Minister of Health, Dr Albert Hertzog, commissioned Hendrik Snyman, who was a Professor of Pharmacology, to conduct an inquiry into the high cost of medicinal services and medicines. The task of this commission of enquiry was to investigate all factors influencing the high cost of medicinal services and medicines and how the costs could be reduced. In April 1962 the report conducted and compiled by Hendrik Snyman and his team was published. One of the conclusions of the report was that ineffective, dangerous and inappropriate use of medicines had a significant indirect impact on the cost, due to the need for further medicines or medicinal services as a result of the above stated reasons. A total of 49 recommendations were provided in the report, including the following (Schlebusch, personal communication, 1 January 2012):

- The safety and efficacy of drugs should be investigated.
- Information of drugs should be provided to the end user.
- A need for a medicines control system was identified.
- A central control body was suggested.

It is important to note that during this period South Africa was not part of the WHO due to apartheid. The Minister instructed Hendrik Snyman to investigate medicines control systems around the world, including (Schlebusch, personal communication, 1 January 2012):

- Dunlop Commission (United Kingdom) – which dealt with safety but not efficacy
- Hinchcliffe Committee 1959 (United Kingdom) – which focused on the cost of medicines
- Douglas Committee 1959 (Scotland)
- Kefauver Senate Committee 1961 (USA)
Some of the key outcomes of the Hendrik Snyman Commission were (Schlebusch, personal communication, 1 January 2012):

- Registration of drugs must be done through a modern medicine/drug control council.
- It promoted information to end users through package inserts.
- The Department of Health could issue inserts to practitioners.
- Drugs had to be pre-screened for efficacy.
- New drug scheduling systems (Schedules 1–7) were developed.
- The Medicines and Related Substances Act 101 of 1965 came into effect.
- The MCC was established, of which Hendrik Snyman became the chairman.
- The broad-based Medical, Dental and Pharmacy Act was removed and replaced with a specific Act to handle each segment, as follows:
  - Medical: Medicines and Related Substances Act 101 of 1965
  - Dental: Health Professions Act 56 of 1974
    - Established Health Professions Council of South Africa (HPCSA) which handles the registration, education and training of health professionals in South Africa (Health Professions Council South Africa, n.d.)
  - Pharmacy: Pharmacy Act 53 of 1974
    - Established Pharmacy Council to regulate pharmacists, pharmacy support personnel and premises (South African Pharmacy Council, 2011).

The thalidomide tragedy did not have a direct impact on the South African regulatory framework as the drug did not make it to South Africa. At the time, while the term ‘good manufacturing practice’ had not yet been coined, the principles of GMP were being used. In 1965 the Medicines and Related Substances Act 101 enforced GMP by law (Schlebusch, personal communication, 1 January 2012).
2.3.9.3. **Medicines and Related Substances Control Act 101 of 1965 and the Medicines Control Council**

The MCC is a statutory, regulatory body that was established in accordance with the Medicines and Related Substances Control Act 101 of 1965 (Health Systems Trust, 2011).

The mandate of the MCC is as follows (SA Department of Health, n.d.):

- Advise the minister on any matter referred to by the minister or arising from the application of the Act.
- Keep the medicines register.
- Register new medicines.
- Amend entries in the register.
- Prohibit the sale of unregistered medicines.
- Transfer certificates of registration.
- Cancel the registration of medicines.
- Approve medicine labels and advertisements.
- Authorise the sale of unregistered medicines for certain purposes.

The Act does not make reference to a specific temperature requirement, but rather refers to the packaging insert for guidance as to the required storage conditions, including the temperature requirement which is of particular importance. The MCC is also a signatory of the WHO certification scheme. In 2007 the MCC joined the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) and has adopted their standards and guidelines, according to Hevan van der Westhuizen who was previously an MCC inspector (personal communication, 15 November 2011). This is corroborated by the PIC/S website which states the MCC is a member (Pharmaceutical Inspection Co-operation Scheme, n.d.).
2.4. Current global and local standards and guidelines

A myriad standards and guidelines may be related to the cold chain in some way. In order to provide a reasonable scope of standards and guidelines to refer to, this research will be guided by the scope selected for a review of the Cold Chain Forum of South Africa.

The Cold Chain Forum of South Africa is a recently established industry forum with the purpose of (SA Pharmaceutical Journal, 2011:42):

- Creating a platform to share professional and technical information as it pertains to cold chain and temperature control of pharmaceuticals
- Prioritising challenges encountered through the pharmaceutical industry supply chain
- Facilitating cost-effective, compliant, total supply chain solutions, including the control of last-mile distribution of all pharmaceutical and related products
- Educating all role players, in order to continue to provide safe, effective and quality pharmaceutical products

At a meeting of the Cold Chain Forum South Africa a list of relevant standards and guidelines was compiled, on the basis of which the following list was compiled for review (2011):

- Good Distribution Practice (WHO)
- Good Wholesale Practice (MCC)
- Good Pharmacy Practice (Pharmacy Council)
- PDA Technical Report 52 – Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain
- WHO – Guidelines on the International Packaging and Shipping of Vaccines
- United States Pharmacopeia (USP) 1079 – Good Storage and Shipping Practice
- PIC/S GMP Guide
As regulations have already been discussed, some of the key standards and guidelines will be covered at a high level to provide an overview of the available standards and guidelines. The latest revisions of the guidelines have been used where possible.

2.4.1. Good distribution practice (WHO)

While a GMP guideline based on regulation and other guidance documents is available for the manufacture of pharmaceutical products, there are only a few meaningful documents for the GMP-compliant shipping of pharmaceuticals. It is for this reason that a good distribution practice (GDP) guidance document for GMP-compliant shipping is so significant (Becker, 2004). Below is a summary of the concept of GDP and the WHO GDP guideline for pharmaceutical products.

2.4.1.1. Introduction to GDP

Good distribution practice (GDP) ‘is that part of quality assurance which ensures that products are consistently stored, transported and handled under suitable conditions as required by the Marketing Authorisation (MA) or product specification’ (Medicines and Healthcare Products Regulatory Agency, 2012) (see Figure 12) which illustrates the scope of GDP across the supply chain starting at the primary manufacturing of the active ingredient and ending at the hospital, pharmacy and final customer.
According to the Irish Exporters Association (2010), GDP has the following outcomes:

- A compliant and consistent supply chain of pharmaceutical products
- Reduced counterfeit risk
- Reduced transport and storage risk
- More safety to the final consumer

Of these outcomes cold chain management has a direct impact on all except counterfeit risk. While GDP may be relevant to all aspects of the supply chain, primary sourcing included, only the aspects relevant to distribution of finished pharmaceutical products will be discussed.

2.4.1.2. Review of good distribution practice guidelines
A summary of the key aspects of the WHO GDP guidelines (2005a:4-16) relevant to cold chain management follows.
The document defines GDP as ‘that part of quality assurance that ensures that the quality of a pharmaceutical product is maintained through adequate control throughout the numerous activities which occur during the distribution process’.

Due to the fact that there are many risks in the distribution of pharmaceuticals that are similar to those present during and after the manufacture of drugs, GDP states that GMP principles should be considered during the distribution process.

‘The quality of pharmaceutical products can be affected by a lack of adequate control over numerous activities.’ This statement is particularly relevant to cold chain management, as a lack of temperature control can have a significant impact on the quality and efficacy of a drug.

‘Where special storage conditions are required on the label (for example, temperature, relative humidity), these should be provided, checked, monitored and recorded.’ Similar to the statement identified in the GMP guidelines, this statement further reinforces the need to not only control but also monitor and record the temperature in these ‘special’ storage conditions.

Monitoring of storage conditions:

- Recorded temperature should be available, and kept for at least the life of the product, plus one year or as defined by legislation.
- Temperature mapping should show uniformity of temperatures across the facility.
- Temperature monitors should be placed in areas most likely to show fluctuations.
- Equipment used for monitoring should be calibrated.
  - Calibration is defined as: ‘The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established.’
This is of particular importance to the measurement of temperatures as inaccuracies in the data recorded could have implications with respect to the decisions being made. This concept of inaccurate data will be discussed later with particular reference to 'Uncertainty of measurement'.

‘Vehicles and equipment used to distribute, store, or handle pharmaceutical products should be suitable for their use and appropriately protect the products to prevent exposure to conditions that could affect their stability.’ This aspect of GDP would be relevant in two specific aspects of cold chain transportation. First, as specified, is the vehicle itself, be it a normal, insulated, refrigerated or temperature-controlled vehicle. Secondly, where the cold chain product is distributed in a cold chain packaging system, this container should meet the above requirement. Both the vehicles and cold chain packaging systems will be discussed in further detail later on in the research.

‘Where special storage conditions (for example, temperature and/or relative humidity), different from or limiting the expected environmental conditions, are required during transit these should be provided, checked, monitored and recorded. Recorded monitoring data should be reviewed on receipt of pharmaceutical products to assess whether required storage conditions have been met.’

GDP as a concept provides a solid base for guidance on cold chain management. Other standards and guidelines provide additional details to supplement GDP.

2.4.2. Good wholesale practice (MCC)

In 2012 the MCC published a revision of the 2004 Good Wholesale Practice Guidelines (effectively a good distribution guideline), titled Good Wholesaling Practice for Wholesalers, Distributor and Bonded Warehouses. This document provides significant guidance to the pharmaceutical distribution industry and represents the primary compliance requirements in South Africa. This document will be used as the primary point of reference for South African cold chain requirements. In review of the document, the following key requirement categories relating to cold chain management were identified (MCC, 2012:1-47):
• Cold storage, which is required to store cold chain pharmaceuticals
• Lagged containers, which makes reference to the cold chain packaging requirement
• Temperature monitoring of cold storage
• Validation of cold storage including temperature mapping, lagged containers and cold chain processes

2.4.3. Pharmacy Council – Good pharmacy practice
In 2015 the Pharmacy Council released an amendment to the Good Pharmacy Practice guideline document. As all wholesalers and distributors are also registered with the Pharmacy Council this guideline falls within the scope of the requirements with which they need to comply.

The amendment made changes to multiple aspects of the guideline, most notably the changes to Section 2.7.3.: ‘Minimum standards relating to the collection and the delivery of medicines to patients from a community or institutional pharmacy’. The following key additions are important to note for this research (SA Pharmacy Council, 2015:15-17):

• Storage: Cold chain pharmaceuticals should be stored in a cold room, which has been temperature mapped and is temperature monitored. The cold room or refrigerator should be connected to a backup power source.
• Distribution and transportation: Cold chain pharmaceuticals should be transported in packaging systems which have been thermally designed and validated. The validated container should also have a temperature-monitoring device within it during transportation.

2.4.4. PDA Technical Report 39 – Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment
The Parenteral Drug Association (PDA) was founded in 1946 as a non-profit organisation that provides science, technology and regulatory information as well as education to the pharmaceutical and biotechnology industry (Parenteral Drug Association, 2012).
According to Mishra from Wyeth (2007:13-15) the key concepts covered in the PDA Technical Report 39 are:

- Cold chain – looking at the cold supply chain, key points of risk, transit and storage
- Medicinal products – pharmaceuticals, vaccines, diagnostics and animal products
- Products types – finished products, active ingredients and samples
- Maintaining quality during shipping – according to the Certificate of Analysis, testing, shipping, stability or temperature/time limit requirements
- Temperature-sensitive products – specialised packaging, controlled environment and time out of refrigerator
- Transportation environment – agents, forwarders and customers’ inspections

2.4.5. PDA Technical Report 46 – Last Mile: Guidance for Good Distribution Practice for Pharmaceutical Products to the End Users

This technical report focuses on the key risk, the ‘last mile’. The document covers proper handling of the product through the final leg of the journey all the way to patient administration (Masy Systems, 2010).

Technical Report 46, drafted by the PDA (2010), states that healthcare professionals, patients and most retailers are not fully aware of the challenges experienced in the 'last mile' and that the practical knowledge and experience required to handle any deviations during this process are unknown or unavailable to the end users. Technical Report 46 is intended to be a complementary document to Technical Report 39, with specific focus on bridging the gap of knowledge to the ‘last mile’. The document covers two broad categories as follows:

- Distribution of temperature-sensitive pharmaceutical products
  - Transport conditions for last mile logistics
  - Wholesaler distribution for refrigerated pharmaceuticals
  - Stability data
  - Mail service pharmacy
  - Disaster plan
- Education to provide to end user/recipients
2.4.6. PDA Technical Report 52 – Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain

Technical Report 52 is the PDA’s contribution to the GDP library, joining recent publications by the WHO and United States Pharmacopeia (USP) (International Pharmaceutical Quality, 2011).

The guideline breaks down GDP for pharmaceuticals into seven key pillars of which Technical Report 52 (Parenteral Drug Association, 2011) handles the first four of these pillars, namely:

- Stability
- Distribution control management
- Performance management
- Supplier chain partner management

The last three pillars are:

- Quality/validation
- Continuous improvement
- Import/export compliance

2.4.7. WHO – Guidelines on the International Packaging and Shipping of Vaccines

This guideline, last revised in 2005, is one of the most widely used in the field of immunisation. It is recommended by the WHO that all governments that are part of the United Nations (UN), use the manual as part of the technical specification in their procurement agencies (WHO, 2005b).

The document covers the following topics:

- Insulated packaging
- Temperature monitoring devices
• Storage volume standards
• Labelling and packaging
• Standard shipping and arrival practices

2.4.8. United States Pharmacopeia 1079 – Good Storage and Shipping Practice
The United States Pharmacopeia Convention (USP) is a scientific non-profit organisation that sets quality standards for pharmaceuticals, food ingredients and dietary supplements manufactured, distributed and consumed worldwide. The FDA is the regulatory authority that then enforces these standards within the United States (United States Pharmacopeia, 2012).

USP 1079 provides guidance to distributors, wholesalers, repackagers and transport logistics providers as to the proper handling of pharmaceutical products. The guide covers warehouses, pharmacies, trucks, shipping docks and other locations (Sensitech, 2006:1). The document discusses key issues related to the cold chain such as: refrigerated equipment, qualification, temperature challenges (US Pharmacopeia, 2010:238-39) and other aspects related to cold chain management.

2.4.9. EU Good Distribution Practice of Medicinal Products for Human Use
In 2013 the European Commission updated the Good Distribution Guidelines to factor in advances in practices for the storage and distribution of medicines. From a temperature management perspective, the guideline addresses the following key points (Official Journal of the European Union, 2013:4-11):

• Temperature mapping – An initial temperature mapping should be conducted on the storage area. In the case of temperature-controlled vehicles these should be temperature mapped as well.
• Temperature monitoring – Monitoring positions should be defined by a temperature mapping exercise.
• Transportation temperature – Temperature should be maintained within acceptable limits during transportation. In the case of temperature-sensitive products qualified, i.e. thermal, packaging should be used.
• Validation and qualification – Key equipment should be identified and validated or qualified as appropriate.

2.4.10. International Air Transport Association Perishable Cargo Regulation

'IATA is an international trade body, created over 60 years ago by a group of airlines. Today, IATA represents some 230 airlines comprising 93% of scheduled international air traffic. The organisation also represents, leads and serves the airline industry in general’ (International Air Transport Association, 2012).

According to the Time and Temperature Task Force (2009:5) set up by the USP, ‘as much as 54% of temperature excursions of healthcare freight occurs while in possession of the airlines’. This illustrates the need for some kind of guidance in terms of air transportation of temperature-sensitive goods. The Perishables Cargo Regulations (PCR) provide a comprehensive review of the requirements for temperature control and cold chain management of pharmaceutical and food-related temperature-sensitive goods, specifically focused on air transport. The document also provides airlines with specific rules in terms of the handling of such products (International Air Transport Association, 2011).

2.5. Conclusion

The outcome of regulation is to ensure that a safe and effective product is delivered to the end consumer. On the basis of the critical impact of the cold chain, on the above outcome, cold chain management must be aligned to appropriate regulations, standards and guidelines.

While regulations state the requirement, it is in the standards and guidelines that the industry finds the majority of the guidance needed to meet the requirements set out by the regulations. Having said this there are a multitude of guidelines, which may take different standpoints on specific methodologies or aspects of cold chain and related activities.

The regulatory and guidance framework discussed above is what drives quality and will form the context of the quality component of this research. Fundamentally this research
leverages off two bodies of knowledge, one being pharmaceutical cold chain management and the other being SCM. The next chapter will set the context within which the pharmaceutical cold chain operates from a supply chain perspective.
CHAPTER 3 – PHARMACEUTICAL COLD CHAIN CONTEXT

3.1. Introduction
Chapter 3 will provide a broader cold chain context, relating to the different considerations that must be factored into account in a pharmaceutical cold chain compared to a supply chain management as a concept. This will be achieved by assessing the two components which make the pharmaceutical cold chain unique. In terms of the cold chain component the impact of maintain temperature across the supply chain will be discussed, while from a pharmaceutical perspective there are specific considerations which impact the pharmaceutical supply chain more broadly. It is imperative to understand these two unique aspects of the pharmaceutical cold chain as these considerations must be factored into the execution of the research.

3.2. Key components of pharmaceutical cold chain management
As previously discussed, a pharmaceutical cold chain is a specialised supply chain. It is specialised on two levels. First, the requirement to maintain the product between a specific set of temperature criteria implies that specialised processes, equipment and training are required in order to ensure the product reaches its end destination within the specified quality requirements. Secondly, the highly regulated, controlled and specialised pharmaceutical industry places further unique conditions and requirements on the supply chain process. These unique considerations will be reviewed by understanding the components that make up pharmaceutical cold chain management. The author considers the components of pharmaceutical cold chain management to be:

- Supply chain management – As within any other product-related industry the pharmaceutical cold chain must consider traditional supply chain challenges and approaches to ensure an efficient and effective supply chain.
- Cold chain management – The temperature component of the pharmaceutical cold chain introduces unique challenges related to the maintenance of the temperature during distribution.
• Pharmaceutical supply chain management – Being of a highly regulated nature, pharmaceutical supply chains have further regulatory challenges and requirements that must be met.

These three components combine (see Figure 13), creating challenges unique to pharmaceutical cold chain management. The pharmaceutical cold chain must meet the requirements as defined by each of the above components. This chapter seeks to identify some of the unique aspects of the pharmaceutical cold chain that may be relevant to this research. Understanding the three core components that make up the pharmaceutical cold chain will provide the necessary background for this research.

![Figure 13 Components of pharmaceutical cold chain management](image)

### 3.1.1. Supply chain management

For the purposes of this research, supply chain management (SCM) is defined as ‘the integration of key business processes from end user through original suppliers that provides the products, services, and information that add value for customers and other shareholders’ (Stock & Lambert, 2001:54).

In order to achieve the right quality at the right price, the total cost concept will be used as a guiding principle. This principle along with the associated cost trade-off principle will be applied to the pharmaceutical cold chain, in order to provide a framework to assist in meeting the objectives of the research.
The trade-off model will serve as a framework for the research on the basis that a trade-off may be considered a type of relationship. In the context of a purely logistics research paper, a trade-off model could be appropriately quantified. However, due to the fact that quality and non-conformance in the pharmaceutical industry is a much more difficult element to quantify, the structure of the trade-off model will be used to identify relationships as opposed to trade-offs. It should be noted that the relationships identified could potentially be trade-offs; however, the objective only seeks to identify if a relationship exists, as this will be used to determine key challenges.

3.1.1.1. Supply chain business processes
The supply chain model illustrated in Figure 14 below will be used to discuss some of the unique aspects in the pharmaceutical cold chain. First these processes will be discussed from a typical supply chain perspective, then from a general cold chain management perspective and lastly from a pharmaceutical supply chain point of view. This will provide all the necessary angles to fully understand the context of pharmaceutical cold chain management perspective.
Supply chain management has the following key business processes (Stock & Lambert, 2001:54).

3.1.1.1.1. Customer relationship management

In order to achieve an integrated supply chain one needs to identify customer groups that are key to the business’s success. Once identified service levels need to be geared towards meeting the customer’s needs. These service levels should be agreed formally and partnerships developed to ensure the achievement of the defined service levels. Furthermore, information from the customer is fed back into the operation to eliminate root cause issues that may result in problems during demand fulfilment.

3.1.1.1.2. Customer service management

Critically customer service management must ensure a single source of customer information. Customer information in this context is broader than information about the customer, and includes order information such as lead times, expected delivery dates, agreed service levels, etc. Additionally, technical support related to the products must readily available to the customers. All of this information should be available in real time.
3.1.1.3. Demand management
Demand management requires an organisation to balance customer requirements against its supply capabilities. Sales data reaching as far as point of sale flowing up the supply chain reduces uncertainty and improves efficiencies, in a good demand management system.

3.1.1.4. Order fulfilment
The objective is to execute a seamless integrated process, to achieve high order fill rates at both a line item and order level. Furthermore, partnerships with supply chain members should be established in order to reduce the ‘total delivered cost’ to the customer.

3.1.1.5. Returns management
Returns management provides a further opportunity to achieve a sustainable competitive advantage. Managing the returns process allows for the identification of productivity improvement opportunities.

For the purposes of this research, manufacturing flow management, procurement/supplier relationship management, and product development and commercialisation will not be discussed as these processes are not directly relevant to the scope of this research, with its focus on outbound distribution.

3.1.2. Cold chain management
In Chapter 1, cold chain management was defined from a pharmaceutical standpoint. While this definition is used for the research, this section will focus on cold chain management from a generic perspective, i.e. as it applies to any industry.

An interdisciplinary Cold Chain Working Group at the Rheinische Friedrich-Wilhelms-University of Bonn, view cold chain management as dealing with ‘efficient control and organisation of production and logistics regarding temperature’. Additionally ‘The principal aims of Cold Chain Management are optimisation of product quality and product safety and minimisation of wastage’ (2008).
3.1.2.1. Supply chain business processes (cold chain perspective)

3.1.2.1.1. Customer relationship management (CRM)
A study conducted by Deloitte in conjunction with the University of Arkansas found that produce in transit from farms in Latin America to the United States, had temperature variations from pallet to pallet of up to 35%. The conclusion of this study was that real-time bi-lateral data communication may result in improved customer service, brand value, market share and financial results (2006:7).

With the temperature component introduced into the supply chain it becomes necessary to provide the customer with confidence that the product is being stored and transported within the required temperature ranges, to ensure the quality of the product. Figure 15 below illustrates the ‘customer portal’ which would provide the customer with information to provide such confidence. Temperature data from the vehicle is routed to a central database allowing the customer to access the data regarding the transport temperature of their products.

![Figure 15 Intelligent cold chain architecture (Deloitte, 2006:8)]
3.1.2.1.2. Customer service management

The distribution centres have focused all their resources to meet McDonald’s expectation of “Cold, Clean, and On Time Delivery” and plays a very vital role in maintaining the integrity of products throughout the entire “Cold Chain” (Khan, 2011:32). This example illustrates the importance of on-time delivery in the cold chain. Due to the temperature-sensitive nature of cold chain products, there is an elevated importance in ensuring that systems are in place to achieve the appropriate storage and transportation temperatures.

A survey conducted in China in 2006 found that the top three areas which require improvement in the cold chain are service levels, cost efficiency and lead times (China Supply Chain Council, 2006:2). Of these, both service levels and lead times are related to customer service management. This illustrates the additional challenges that the cold chain introduces to customer service management.

3.1.2.1.3. Demand management

Approximately 30% to 50% of the value of fruit and vegetables is reportedly lost, due to quality degradation or direct losses of spoiled product. Such losses are the direct result of poor or lack of cold chain management (Bledsoe, 2009:20). The perishable nature of cold chain products means proper cold chain management is crucial in order to ensure the available product capacity is not diminished by product write-offs due to poor product quality. This should be considered within demand management to ensure cold chain issues do not negatively impact the outcome of meeting customer demand.

Understanding demand requirements is not only crucial in terms of understanding the product required to meet the demand, but cold chain infrastructure capacity must be sufficient to meet product demand requirements. Demand management is crucial for the planning of purchasing of cold chain facilities and equipment to ensure the ‘cold supply chain’ has sufficient capacity to meet the product demand requirements (Zhang, Xu & Zheng, 2012:2).

3.1.2.1.4. Order fulfilment

Being more susceptible to quality degradation, an additional dimension is added to order fulfilment in cold chain management. ‘Fill rate is the percentage of orders shipped in the
right quantity at the right time with the right quality’ (Martichenko & Grabe, 2010:51). High order fill rates for example are not only affected by stock levels and effective process management, but order fulfilment in the cold chain may be impacted by poor cold chain management. A poor quality product delivered is as bad as not being delivered at all, if not worse.

3.1.2.1.5. Returns management

Returns management within the cold chain, must be considered from two perspectives, the first of which is managing the cold chain within the return leg of the supply chain. This is important in order:

- To ensure stock that is to be resold is suitable and of sufficient quality. Resale of returned cold chain goods may not always be possible, and must be undertaken with caution. For example, the Medicines and Healthcare Products Regulatory Agency (MHRA) has issued guidance that if cold chain product is to be returned it should take place 24 hours after the original dispatch; thereafter the returns should not be accepted (Todd, 2008:3).
- To confirm that stock damaged due to a breach in the forward distribution cycle was indeed damaged in the forward cycle rather than the return cycle of the supply chain.

Secondly, returns information regarding damages as a result of poor cold chain management, is important to:

- Measure the effectiveness of the cold chain
- Improve cold chain processes to reduce damaged stock as a result of poor cold chain practices

3.1.3. Pharmaceutical supply chain management

The pharmaceutical supply chain must deal with unique supply chain challenges as well as regulatory issues, in order to ensure consumer safety (Kinaxis, 2010: 2). The regulatory issues in particular introduce a significant challenge as regulatory requirements are not optional and must be adhered to.
3.1.3.1. Supply chain business processes (Pharmaceutical supply chain management perspective)

3.1.3.1.1. Customer relationship management
The end consumer and principle product customer are not always the same in the pharmaceutical industry. The customer may be the administrating doctor or pharmacist, while the consumer is the patient. Therefore, CRM activities are not necessarily focused on the patient (Michels, 2014). While this may be the case, CRM could be extended to include the patient; this specialised form of CRM is known as patient relationship management (PRM). PRM allows for increased patient satisfaction, coordinated care delivery, proactive management of chronic illnesses and improved community relationships (Microsoft, 2008:9-10).

3.1.3.1.2. Customer service management
While manufacturers may have spent many years developing drugs to save lives, these drugs are of no use if they are not available at the required time, in the required condition, when a medical emergency arises. Furthermore, delivery of life-saving drugs needs to be possible 24 hours a day, 7 days a week, 365 days a year (Sweeney, 2012). Due to the high cost and perishable nature of drugs, storing medicines in the required quantities is not always possible. Customer service management is crucial in terms of meeting delivery lead times and ensuring the required medicines arrive on time at the required quality standards.

Customers, especially the hospitals, often charge hefty fines in the event that the service levels are not met (Boulaksil, 2010: 13). This further reinforces the critical nature of proper customer service management.

3.1.3.1.3. Demand management
Pharmaceutical manufacturers need to deal with each country’s drug regulator in order to get approval to sell the drug in a specific country (Tan, 2006:40). This may result in spikes in demand as and when the drug is approved for sale.
In the event of an epidemic or outbreak, modelling the geographical spread (factoring in
time and population density) of the outbreak becomes crucial to treating ill patients and
controlling the outbreak (Graves, Lei, Melamed, Pinedo, Qi, Shen & Xu, 2009:3-4). Such
considerations need to be built into the demand planning process.

3.1.3.1.4. Order fulfilment
Outsourcing order fulfilment continues to be an industry trend, which allows companies
to focus on their core business. Pharmaceutical order fulfilment is a niche example of
such outsourcing (Tagg Logistics, 2011:1). Outsourcing order fulfilment can result in
significant reduction in costs. However, due to the highly regulated nature of the
pharmaceutical industry, pharmaceutical manufacturers typically want direct control over
the supply chain activities (Beerens, 2005:6). This makes taking advantage of outsourced
order fulfilment more challenging than in other industries. More effort, in the form of quality
agreements and audits, is required to ensure quality standards are maintained.

3.1.3.1.5. Returns management
Reverse logistics, which deals with product returns as well as product recalls, is a key
element of the pharmaceutical supply chain (Sartori, 2009:18).

A product recall is the process of removing products from the market that have been found
to have some sort of defect. Product recalls may result from a customer complaint, a
company discovery during testing or regulatory authority observation (Cafmeyer & Lewis,
2011). Of critical importance in managing recalls is batch traceability in order to identify
which batch was delivered to which customers (WHO, 2010a:67). Managing product
recalls provides further unique challenges in the returns management of pharmaceuticals
and needs to be planned for so that batches that need to be recalled can be traced and
returned, as quickly as possible to prevent harm to customers.

3.1.4. Pharmaceutical cold chain management
The pharmaceutical cold chain is a specialised supply chain that is made up of the three
components discussed above, namely supply chain, cold chain and pharmaceutical
supply chain. Each of these components introduces a unique challenge or requirement
to the business processes of the pharmaceutical cold chain.
These unique challenges and requirements combine within each business process of the pharmaceutical cold chain, making the pharmaceutical cold chain an extremely specialised and niche supply chain industry – having to meet requirements of efficiency and effectiveness (supply chain perspective), temperature acceptance criteria (cold chain perspective) and quality and regulatory requirements (pharmaceutical supply chain perspective).

Against this backdrop, this chapter will proceed into further detail of the unique requirements and how these requirements may affect the pharmaceutical cold chain.

3.2. Pharmaceutical industry supply chain considerations
Every industry has its own unique supply chain challenges. The pharmaceutical industry may be one of the most challenging due to:

- Supply chain regulation
- Price control
- Barriers to entry
- Pharmaceutical industry consolidation

These factors will be discussed in order to further understand how some of the industry’s unique dynamics influence the distribution of pharmaceuticals.

3.3. Supply chain regulation
While regulation was discussed in depth in Chapter 2 as it pertains to the quality aspect of this research, in Chapter 3 the implications of regulation on the operational aspects of the supply chain will be investigated.

Being such a highly regulated industry, the pharmaceutical distribution and the relevant distribution models used are to a large degree influenced by the complexity of the relevant regulations related to the distribution of pharmaceuticals and quality. The regulatory impact is summarised by the European Commission in the following statement: ‘It is a complex industry due to its complicated supply chain and the extent of government regulations in all aspects of the trade’ (ECORYS Research and Consulting, 2009:12).
3.3.1. Regulatory factors affecting pharmaceutical distribution

3.3.1.1. Cold chain requirements
Due to the perishable nature of cold chain pharmaceuticals, the MCC Guidelines for Licence to Act as a Wholesaler or Distributor requires that storage areas be maintained and monitored at appropriate temperatures. Refrigerators or cold rooms are required for cold chain product, the appropriate temperature for which is normally between 2 °C and 8 °C (2012). At the very least, in order to meet this requirement an organisation needs to consider the following:

- Cold storage
- Freezer storage
- Temperature mapping
- Temperature monitoring
- Cold chain distribution (refrigerated vehicles or cold chain packaging system)
- Validation and qualification of the above (which will be discussed in Chapter 4)

All the above requirements will have some implication on cost and/or complexity on the operation, and need to be considered when balancing operational and quality requirements.

3.3.1.2. Packaging and label requirements
The Medicines and Related Substances Act 101 (SA Department of Health, 1965:8), requires that 'Medicines that are parallel imported shall be labelled, packaged and have package inserts and patient information leaflets as prescribed in terms of regulations 9 and 10'.

According to Whewell (2010:83), packaging requirements are defined by each country, which creates the following supply chain challenges:

- Complex inventory control, due to product packaging differentiation
- Small packaging batch sizes, which impacts costs as it reduces the benefit of economies of scale
- Centralised distribution and customisation become more difficult
• Quality standards may differ, increasing the cost of analysis

3.3.1.3. Staff
A responsible pharmacist (RP), who must be a qualified pharmacist, is required to safeguard product users against potential hazards. Additionally, it is the responsibility of the RP to ensure that good wholesale practice (GWP) and good distribution practice (GDP) are met (MCC, 2004:5). Certain products may be handled only by a pharmacist, which creates an additional constraint that some products need to be physically 'picked and packed' by a pharmacist (SA Department of Health, 1965).

3.3.1.4. Complex stock control
Under the Medicines and Related Substances Act, manufacturers are required to adhere to storage, batch control and product compliant handling requirements (SBP, 2005:25). The following regulatory requirements increase the complexity of managing stock:

• Storage – specific storage requirements of stock such as first expiry first out (FEFO), separation of damaged stock from usable stock and storage conditions that should be in line with recommendations from manufacturer, need to be adhered to (WHO, 2010b:248-50).
• Batch control – traceability of batches through the supply chain (WHO, 2010a:67).

3.4. Price control
Although this may be considered a regulatory factor, the extent to which it influences the supply chain warrants the discussion of price control in more depth. While the implications of price controls can be debated to some extent in terms of the influence on the ‘free market system’, the reality is that at present price controls are in place and enforced through regulation. This research will not discuss the appropriateness of such controls but rather the implications that these controls have on a pharmaceutical supply chain.

The price of medicines is regulated as part of the Medicines and Related Substances Act (SA Department of Health, 2004:3-8). The legislation provides for the regulation of the price of medicines on three distinct levels:
• Single exit price (SEP) – As part of the introduction of a ‘transparent pricing system’, the SEP requires that a manufacturer or importer must set a price at which the product will be sold to any person (other than the state), regardless of the volumes purchased.
• Appropriate dispensing fee – This relates to the fee a pharmacy can charge to dispense the product. This fee is a percentage of the SEP price, with a defined cap, and represents the maximum that a pharmacy can charge to dispense medicines.
• Appropriate wholesale/distribution fee – This relates to the fee a wholesaler or distributor can charge to distribute the product. This fee is a percentage of the SEP price, with a defined cap, and represent the maximum that a wholesaler or distributor can charge to distribute medicines.

One can understand the significant impact that SEP might have on the distribution of medicines. Considering that purchasing power does not impact the purchase price of the product, large wholesalers cannot leverage bulk buying to reduce product cost. Furthermore, the defined fees, relating to dispensing and more specifically distribution costs related to the product, are of particular importance to this research as this sets a maximum cost within which pharmaceutical products (including cold chain pharmaceutical products) must not only be delivered to the end consumer, but must be delivered within the required temperature limits. The achievement of this in cold chain products ultimately incurs a cost that must be managed within the legislated capped fee structure.

It should also be noted that the legislative move to SEP had a major impact on the wholesale market and how they make a profit. This will be discussed in further detail later in this chapter.

On 4 April 2011, the Department of Health released a new draft amendment for the Medicines and Related Substances Act 101 1965, which referred to the ‘logistics fee component of a transparent pricing system’. The amendments have the following key updates (SA Department of Health, 2011b:3-6):
• Definition of logistics fee – the fee paid to logistics providers by manufacturers for logistics services
• Definition of logistics services – services provided for distribution of medicines to the end dispenser
• If the ex-manufacture price (the price the manufacturer charges to produce the medicine) is: (all figures exclude VAT)
  o Less than R100.00, the logistics fee may be no more than 6%
  o Between R100.00 and R500.00 (inclusive), the logistics fee may be no more than 4% plus R2.00
  o Between R500.00 and R1 000.00 (inclusive), the logistics fee may be no more than 3% plus R5.00
  o Greater than R1 000.00 the logistics fee may be no more than 2% plus R10.00
• Where multiple logistics providers are used, the logistics fee is estimated by the negotiated fee multiplied by the estimated number of units to be distributed by provider in 12-month period, divided by the total units to be sold in the 12-month period.
• At the end of the year, the logistics fee must be reconciled with actual values, against the initial estimates.
• Over and under recovery must then be factored into the calculation for the next 12 months.

Such a move towards further regulation of logistics fees could have significant implications for cold chain management. Reinforcing the capped structure of logistics pricing as well as the introduction of additional administration, further increases the difficulty of distributing a cold chain product which requires additional packaging, service level and care in distribution.

This legislated price control is a key consideration when assessing the challenges between pharmaceutical quality requirements and outbound distribution in a context of a capped pricing structure; this makes cost a much more significant consideration as costs cannot be recouped through increased pricing.
3.5. Fewer distribution market players due to barriers to entry

Barriers to entry restrict the companies that are able to participate in pharmaceutical distribution. This in turn influences the supply chain landscape as fewer companies are able to compete on a large scale.

Based on the MCC Guidelines to Act as a Wholesaler or Distributor (2004), ‘it is unlawful for medicines or medical devices to be marketed, manufactured, distributed and sold or supplied in the Republic except in accordance with the appropriate authorisation, registration certificates, licences, clinical trial approvals or exemptions obtained from the Medicines Control Council’. Acquiring the licence becomes a barrier to entry as it is a prerequisite before a company can distribute pharmaceutical products. This may discourage new entrants into the pharmaceutical distribution market, resulting in fewer companies competing in the pharmaceutical distribution landscape.

3.6. Pharmaceutical industry consolidation

‘Consolidation in the bio pharm sector and the industry trend towards preferred provider partnerships has reduced the number of solution providers that will be required to support clinical needs of the industry,’ according to Pervaaz (2010). This indicates the significant impact that consolidation of pharmaceutical manufacturers may have on their suppliers, including the logistics support providers.

The implications of industry consolidation are further reinforced from a risk perspective. Deloitte (2011:no. 21) have identified consolidation as a trend that introduces risk in the pharmaceutical industry. Three factors are mentioned:

- Supply chain complexity, due in part to industry consolidation
- Mergers and acquisition-related process disruption, for example, two merging companies may have processes that work well individually but neither may work for both companies combined
- Post-merger integration risk, which relates to a variety of risks that may result after a merger
The high degree of pharmaceutical industry consolidation must be considered when reviewing the pharmaceutical industry supply chain, due to the impact it has on the pharmaceutical supply chain landscape.

### 3.6.1. Pharmaceutical patents

A patent is an exclusive right granted by a government to an inventor (the pharmaceutical company for the purposes of this research) for a period of time, normally 20 years. The patent excludes all others from making, using or selling the invention/product, in this case the medicine, made by the invented process (Pipers Patent Attorneys, 2011).

Trade-related aspects of intellectual property rights (TRIPS) is to date the most comprehensive multilateral agreement and has been in force since 1995. The TRIPS agreement introduced global minimum standards for protecting most forms of intellectual property rights (IPR). Prior to the TRIPS agreement 40 countries did not provide patent protection for pharmaceutical companies (WHO, 2005d:238-39).

According to Innovation.org (n.d.:5-6) the significance of patents is that they provide an incentive to innovate. Patents provide the patent holder with the necessary protection to justify investment into research and development for potential future profits. 'It is widely acknowledged that patents are a fundamental incentive to innovative activities in pharmaceuticals and biotechnology.' The process of bringing a drug to market is an extremely expensive and lengthy one, considering that (see Figure 16):

- Only one in every 5 000–10 000 compounds tested ever reach the consumer.
- Only two out of ten compounds pass clinical testing.
- Drugs that reach the market have on average 11–12 years of effective patent life left.
- Only three out of ten drugs match or exceed the average research and development cost.
On the other hand, some argue that the current patent system neglects the needs of the public health system. The argument is that patents prevent access to or increase prices of the particular medicine as the patent holder has the sole right and effectively a monopoly to produce that particular product (World Intellectual Property Organisation, n.d.).

A good example of the negative effect that patents may have on the public health system occurred in South Africa. In 2001, 40 multinational pharmaceutical companies brought litigation against South Africa. At the time the cost of antiretroviral drugs (ARVs) was around $15 000 per patient per year. The South African government was in the process of passing legislation, through the Medicines Act, that would allow the generic production and importation of ARV pharmaceuticals. Strong international support for the South African government, from the WHO, European Union, Dutch government, Germany and France, emerged which ultimately led to the litigation being dropped. This in turn dropped the cost of the drugs from $15 000 to between $148 and $159 per annum. This event of global interest ultimately led to the Doha Declaration by the World Trade Organisation (WTO), later on in 2001, which articulated, in respect of TRIPS, that members of the WTO had ‘the right to protect public health, in particular, to promote access for all’ (Helfer & Austin, 2011:145-48).

3.6.2. The rise of generics
A generic drug may be considered to be ‘a drug that is comparable to a brand/reference listed drug product in dosage form, strength, route of administration, quality and
performance characteristics and intended use’ (Center for Drug Evaluation and Research, n.d.).

According to the Generic Pharmaceutical Association (2012), in the 1960s a USA government drive to prove the safety and effectiveness of drugs manufactured prior to 1962, served as a launch pad for the generic pharmaceutical industry. The National Research Council of the National Academy of Research Sciences was instructed to conduct a drug efficacy study. In the Drug Efficacy Study Implementation (DESI) programme, over 300 products were reviewed and categorised as one of three classes:

- Effective for all claimed indications
- Probably/possibly effective for claimed indications
- Ineffective for claimed indications

It was on this basis that generic manufacturers were able to produce drugs that were ruled effective without the need to conduct bio-studies (see Figure 17), provided the drug was manufactured to the prescribed chemical formula. While the above study made it safe to produce generics, the legal framework that truly allowed the generic industry to flourish, by allowing the approval of generic drugs, was the Drug Price and Patent Term Restoration Act of 1984 (Generic Pharmaceutical Association, 2012).
3.6.3. Pharmaceutical industry consolidation and its impact on the pharmaceutical supply chain

The pharmaceutical industry has undergone significant consolidation through the process of mergers and acquisitions, as indicated in Figure 18 below.

![Drug Industry Consolidation](image)

**Figure 18 Drug industry consolidation (New York Times, 2009)**

Competition from generic drug companies was minimal until the 1980s. This is an important factor driving industry consolidation when one considers that the entry of a generic can take up to 90% of the brand name’s sales (Bloom, 2012). This can be seen in Figure 19 below which illustrates how, as more manufacturers enter the market, the cost of the drug is pushed lower and lower.
According to Tomkins International (n.d.), mergers and acquisitions are a viable way for the pharmaceutical companies to improve new product pipelines, expand market growth prospects and face the challenge of pending patent expirations. Of the many driving forces of mergers and acquisitions, the three relevant to this section are:

- Reinvigorating a dwindling drug pipeline, to compensate for patent expirations
- Participating in generics to maintain market share
- Leveraging operations to achieve greater economies of scale

By default, mergers and acquisitions result in supply chain consolidation (Hook, 2010). While the objective of supply chain consolidation may be to achieve greater economies of scale, the reality of the end result of consolidation may not necessarily achieve this.

The Accenture Supply Chain Post Merger Study, which surveyed 154 managers involved in mergers and acquisitions in the pharmaceutical and other industries, found that problems arising from mergers included (Partridge, 2007):

- Diminished product/service quality (53%)
- Orders fill rate problems (52%)
- Stock outs (46%)
- Inventory build-up (44%)
- Increased supply disruptions (36%)
These post-consolidation issues should be considered as part of the pharmaceutical industry context which this chapter sets out to explore.

3.7. Pharmaceutical distribution models

A fundamental aspect of understanding the supply chain context within which the pharmaceutical cold chain operates, is understanding the types of distribution models used for pharmaceutical products.

A distribution model may be considered as the manner in which a product moves from the manufacturer to the consumer. In some cases, this channel may be complex including distributors, wholesalers, agents, etc. (Entrepreneur, 2014).

Traditionally there have been three main models for distribution of pharmaceutical products (Deloitte, 2008), namely:

- **Wholesaler model** – This allows logistics efficiencies across multiple manufacturers, while the wholesaler focuses on demand fulfilment.
- **Limited distribution model** – By limiting the wholesaler relationship, manufacturers attempt to improve inventory management, reduce costs and mitigate concerns about product and supply integrity.
- **Direct distribution model** – Particularly used for high-priced biological products with limited supplier base, bulk shipments to customers with their own distribution centres may be a viable option.

According to Iain Barton (personal communication, 22 February 2012), pharmaceutical distribution models can be broken down as follows:

- Wholesaler model
- Vertically integrated model
  - Owned
  - Agency
- Distributor model
3.7.1. Wholesaler model

Wholesalers purchase stock from the manufacturers, and thus take ownership of the stock and sell to retailers. The wholesaler model relies on the difference between the purchase price of the stock and the selling price of the stock in order to make a profit. This difference is based on a discount off the list price provided to the wholesaler by the manufacturer (Hartzenburg, 2001:9).

A significant issue with the wholesaler model is that the focus for the wholesaler is often more on turning a profit rather than the quality of the product provided, which may result in substandard processes (business.com, n.d.). An assessment of pharmaceutical wholesalers in Ghana found that wholesalers have weak incentives to conduct quality testing of medicines and would rather rely on others in the supply chain to assure the quality of the medicines they sell (Anum, Mankartah & Anaman, 2010). This may be due to the fact that the wholesaler takes ownership of the product, and as a result the manufacturer no longer has authority over the storage and distribution of the product, and therefore cannot enforce its quality standards effectively.

3.7.2. Vertically integrated (distributor)

Vertical integration may be described as the merger of companies at different stages of production or distribution. Merger with an input supplier is known as backward integration while merger with the distribution chain is known as forward integration (BusinessDictionary.com, n.d.).

This model for the distribution of pharmaceuticals originated when manufacturers opted to establish their own distribution firms. These distribution firms were then used as the exclusive distributors for the manufacturers (Labuschagne, 2006).

The fundamental shift from the wholesaler model to the distributor model was due to the removal of the discount structure (Hartzenburg, 2001) as a result of SEP; the distribution firm made its profit from a fee-for-service structure rather.

‘Fee for service (FFS) contracts limit the amount of inventory distributors can carry at any time (by imposing an inventory cap) and requiring inventory information sharing from the...
distributors to the manufacturers while compensating the distributors with a per-unit fee for distribution’ (Zhoa, Xiong, n.d.:1)

3.7.3. Vertically integrated (owned)
In 1993 International Healthcare Distributors (IHD, now UTi Pharma), was founded as a joint exclusivity distribution venture among four multinational pharmaceutical companies in order to distribute the products of these pharmaceutical companies in South Africa. This was a strong vertical relationship in that the manufacturers jointly owned the distributor, and forms a prime example of owned vertical integration (Hartzenburg, 2001:9).

3.7.4. Vertically integrated (agency)
Another example of vertical integration is Kinesis. Kinesis, similarly to IHD, was a joint exclusive distribution agency owned by Synergistic Alliance Investments (SAI) which was formed by five pharmaceutical manufacturers in 1998. The Kinesis example is slightly different from the IHD example in that while IHD only distributed for companies that had ownership in IHD, Kinesis distributed for other companies which had no ownership or vertical relationship with it. Kinesis distributed for other pharmaceutical companies on an agency basis (Hartzenburg, 2001:6).

3.7.5. Distributor model
The distributor model provides for a fee-for-service relationship to any company that may want to use the company for distribution of pharmaceutical goods. The distributor is not owned by the manufacturer so no vertical integration is present and the ownership of product remains with the manufacturer.

A prime example of this model is PHD. In 2000 PHD, a distribution firm, entered into a sole distribution agreement with a multinational pharmaceutical company to warehouse and distribute (which included order generation, credit control and debt management) their products, on a fee-for-service basis (Hartzenburg, 2001:6). PHD was bought by RTT, to become RTT Medical, changing its name to RTT Health Sciences in 2013. Not too long after this, Imperial acquired the organisation to become Imperial Health Sciences (Imperial Health Sciences, n.d.).
It should be noted that IHD was acquired by UTi in 2004 (UTi, 2011) and by default, is no longer owned by pharmaceutical manufacturers, following a similar model to Imperial Health Sciences in that it provides distribution services to companies that have no shareholding in it. The traditional wholesaler has also had to make a shift in the way it operates; as a result of SEP, wholesalers now have to operate on a fee-for-service basis (Gerber, 2006:9).

3.8. Conclusion
Pharmaceutical distribution has some unique challenges, as this chapter has indicated. Most of these challenges stem from the high degree of regulation in the industry, while others are linked to economic aspects such as patents, generics as well as mergers and acquisitions. These factors have in some way or other influenced the distribution models that are used and how the supply chain operates. Chapter 3 has provided the supply chain frame and context within which the primary objective of this research lies.

In order to construct a research methodology that will meet the objectives as defined in Chapter 1, a framework or model will be necessary to structure the various elements in a logical form. This will take the form of a relationship model, and will be used for the purposes of the identification and verification of relationships. This model will be discussed in detail in Chapter 4.
1.1. Introduction

Chapters 2 and 3 provided a detailed review of the macro level context of the pharmaceutical cold chain industry, both from a regulatory perspective as well as a supply chain perspective. In the context of the pharmaceutical cold chain industry, a framework or model to structure the research will be developed. The specific model used to investigate the primary objective will be identified and discussed. This will be achieved by reviewing available total cost models as the foundation for the relationship model, and integrating key elements highlighted in South African regulations. This will then provide the structure to guide the research to be conducted.

1.2. Key supply chain concept

Two concepts, the total cost concept and cost/benefit trade-off, are directly related to one another. The total cost concept has the ultimate objective of achieving the lowest total cost across an operation while the cost/benefit trade-off provides the framework for the application required to achieve the lowest total cost.

It is these concepts that will be applied to the cold chain in order to provide a framework for the identification and verification of relationships between quality and outbound distribution elements. These concepts will form the supply chain foundation for this research.

1.2.1. Total cost concept and cost trade-off

‘Total cost analysis is the key to managing the logistics function. One of the major goals of the organisation should be to reduce the total cost of logistics activities rather than focusing on each activity in isolation’ (Stock & Lambert, 2001:28). If a ‘silo’ or focused approach is taken on one specific cost element, any cost reductions may be offset by increases in cost due to the changes made in the initial action to reduce cost (Somuyiwa, 2010:387). Therefore, it is critical to understand the trade-offs or relationship between various costs elements, in order to reduce the total cost. The intention of this research is to apply this principle to the pharmaceutical cold chain, in order to discover if there are
such relationships which could be used to identify the key challenges within the pharmaceutical cold chain.

The total cost model was first used by Culliton, Lewis and Steele in 1950 to calculate the value of air freight; however, today there are multiple cost models. It is important to identify an appropriate model that includes the appropriate costs as suggested by Zackrisson (2007:29): ‘In order to perform the total cost analysis it needs to be based on a suitable total cost model which includes the costs necessary to perform the logistic activities.’

The concept is best described by example. In Figure 20 below the relationship between three key cost components – transport cost, warehousing/storage cost and inventory carrying cost – is demonstrated. Moving from left to right on the horizontal axis, transport costs drastically decrease as the number of warehouses increases, due to the closer proximity to customers. However, as the transport cost decreases so the inventory carrying costs (increased safety stock required) and warehousing costs (additional warehouses) increase. The graph illustrates the need to balance costs at an optimal point where the total cost (red line) is at its lowest.

![Figure 20 Total distribution cost graph (McKinnon, 2003:19)](image-url)
In the case of quality and outbound distribution cost, which this research deals with, the structure of the total cost concept will serve as the foundation, while the cost elements will be replaced with costs relevant to the pharmaceutical cold chain. These cost elements will be discussed and analysed as they relate to the pharmaceutical cold chain specifically.

Before this can be done, a total cost model must be selected to serve as the structure of the new model that will be developed as part of this research. Three models will be briefly reviewed in order to select the appropriate model. They are:

- Aronsson, Ekdahl and Oskarsson
- Coyle, Bardi and Langley
- Lambert and Stock

1.2.1.1. Aronsson, Ekdahl and Oskarsson

This total cost model divides costs according to five broad categories. Borowiec and Liedberg (2009:38) provide some insight into these categories (see Figure 21):

- Inventory holding costs: These include the cost of binding capital, risk, incurrence and insurance, which arise as a result of holding stock.
- Handling costs: These include buildings, equipment, personnel and internal transport, which all relate to the handling of stock.
- Transport costs: These include all costs related to the administration and carrying out of transportation from suppliers, between facilities and to customers.
- Administrative costs: These include goods receiving, invoicing, payment of wages, and economic follow-up.
- Other costs: This category provides for all other costs, such as information systems, packaging costs, indirect logistics costs and material costs.
1.2.1.2. Coyle, Bardi and Langley

Described as the ‘total system cost model’, this model is fundamentally the same as the other total cost models. The model focuses on analysing trade-off scenarios in order to arrive at the lowest physical distribution cost (Coyle, Bardi & Langley, 2003:13) (see Figure 22).
The total cost analysis should not only include current costs but should consider future cost elements that may come into effect as volumes increase. The author of the model suggests that the model is futile without considering customer service, as measured through the cost of lost sales (Zackrisson, 2007:27-28).

1.2.1.3. Lambert and Stock
Lambert and Stock view the total cost model from a base that logistics costs are generated in the process of serving the customer (Finskas, 2011:18). Lambert and Stock break the logistics costs into the following elements (Stock & Lambert, 2001:28-31) (see Figure 23):

- **Customer service levels**: The cost related to customer service levels is that of lost sales, both present and future. It is suggested that the best approach to this model is to define the desired customer service level and on this basis define the implications for all the other logistics costs.
- **Transportation cost**: The costs associated with supporting transportation can be analysed in many different ways based on the unit of categorisation (customer, product, channel type, etc.). Volume, weight, distance, points of origin and destination, and mode of transportation are significant factors to be considered.
- **Warehousing costs**: The driving factors for warehousing costs are the physical warehouse, storage costs as well as plant and warehouse selection. Costs related to the number of warehouse locations are also included in this category.
- **Order processing/information systems costs**: Activities related to order processes, distribution communication and demand forecasting drive this cost element. In particular, costs related to information systems to improve customer service are of significant focus.
- **Lot quantity costs**: Largely as a result of production and procurement activities, which influence costs depending on production lot quantity or order quantity size, these costs include:
  - Production set-up costs including time lost, scrap and operating inefficiencies
  - Capacity lost to downtime due to line or supplier changeover
1.2.1.4. Comparison and model selection

Figure 24 below is a graphical representation of the difference between the various total cost models. The most obvious common elements are those of inventory carrying, warehousing and transport costs, which feature in all the above models. Cost of lost sales feature as a significant element in the Lambert and Stock as well as the Coyle, Bardi and Langley models. Although other differences exist between the models, fundamentally these differences are related to naming the costs more broadly as in the Aronsson model’s ‘administrative costs’, or more specifically as in the Lambert and Stock model’s ‘lot quantity costs’ (Zackrisson, 2007:28).
The Lambert and Stock model has been selected on the basis that the graphical representation of the model best reflects the interrelatedness of the various elements in that each element has a bilateral link to all the other elements. This is therefore a more accurate representation of any relationships between the cost elements identified. A new model will be developed for the purposes of this research using the structure of the Lambert and Stock model.

1.3. Identification and discussion of pharmaceutical cold chain elements to be used in the pharmaceutical cold chain model
Due to the highly unique and technical nature of pharmaceutical cold chain management, each element must be understood in the context of the pharmaceutical cold chain. In this
section of Chapter 4 the intention is to provide the specific background to these elements, which will assist in understanding the impacts on supply chain cost later on in the research.

Based on a review of the MCC’s wholesale and distribution guidance document (MCC, 2012), the following elements have been selected for integration into the model:

- **Non-conformance cost**: Representing the cost of poor quality management, all costs resulting from product excursions are incorporated into this element. This is a primary outcome for good customer service in the context of pharmaceutical products.
- **Validation/qualification cost**: A key requirement by regulators, validation increases costs due to the significant testing and documentation required to ensure processes and equipment meet stated requirements.
- **Cold chain packaging cost**: Regulators require that cold chain products be distributed in ‘lagged’ containers which provide insulation and thermal protection; these containers increase the packaging costs related to the distribution of such products.
- **Temperature monitoring cost**: Also a regulatory requirement, temperature must be monitored during storage and transportation in order to ensure that distribution has happened within the stated product temperature requirements.
- **Warehouse cost**: This element represents all costs that result from unique storage requirements related to temperature-sensitive pharmaceuticals, for example, heating and cooling of the warehouse to maintain the temperature within the acceptable limits.
- **Transport cost**: This element represents all costs that result from unique transport requirements related to temperature-sensitive pharmaceuticals, such as the need to maintain temperatures within acceptable limits during transportation.

Non-conformance, validation/qualification, packaging and temperature monitoring costs will represent the quality elements in the new model, while warehousing and transport will
represent the distribution cost elements of the model. These concepts will now be discussed in detail as they relate to the pharmaceutical cold chain.

1.3.1. Non-conformance cost
The concepts below relate to the non-conformance cost element, as these concepts need to be understood as they relate to the cold chain.

1.3.1.1. Non-conformance
A non-conformance is a failure to fulfil a specified requirement. (MCC, 2012:7). A primary example of a non-conformance in the pharmaceutical cold chain is a temperature excursion (temperature exceeding the acceptable limits of the product) during storage and transport. For the purposes of this research, non-conformance cost will refer specifically to the risk of cold chain pharmaceutical product being exposed to inappropriate temperatures, and the associated cost.

1.3.1.2. Quality management system
The United Kingdom Department of Trade and Industry defines quality management system (QMS) as ‘a set of coordinated activities to direct and control an organisation in order to continually improve the effectiveness and efficiency of its performance’ (n.d.:1). A QMS system relates to but is not limited to, organisation, roles and responsibilities, process, training, implementation planning, compliance, change control, on-time delivery, quality metrics, continuous improvement and customer satisfaction (Bishara, 2006b:3). A QMS is critical to the management of the cold chain as it is within the structure of the QMS that the cold chain management activities will be defined and documented, in order to limit non-conformances.

1.3.1.3. Corrective and preventive action
A corrective action is an action taken to rectify a non-conformance after it has occurred, while preventive action is an action taken to avoid repetition of the same non-conformance (Cardiff University, 2009:3). A corrective action preventive action (CAPA) system allows for the proper management of such actions and should include, but not be limited to: investigation, root cause and appropriate short term and permanent solutions, due date and responsibilities (Parenteral Drug Association, 2011:10).
1.3.1.4. Acceptance criteria and product excursions
Due to the fact that pharmaceuticals must be stored and transported at the temperature range indicated when submitting for approval to the regulatory authorities, this temperature range typically becomes the acceptance criteria for temperature requirements during the storage and transport of the product. The MCC defines the cold chain range as 2 °C to 8 °C, this is considered the acceptance criteria for storage and transportation of pharmaceutical cold chain products (MCC, 2012:5).

When conducting validation or qualification testing of equipment and systems in the pharmaceutical cold chain, the acceptance criteria are the key parameters on which basis the equipment or system will be passed.

1.3.1.5. Product stability and product excursions
A pharmaceutical product may be considered stable when its essential properties do not change or the change is negligible over a period of time (Association Française du Froid & SFSTP, 2009:22).

The MCC (2011:16-18) stability guidelines define stability as ‘the capacity of an API (active pharmaceutical ingredient) or dosage form to remain within specifications established to assure its identity, purity, strength and critical physico-chemical characteristics’.

In order to demonstrate stability, manufacturers must execute stability testing, which provides evidence of how the quality of the drug varies over time when exposed to a variety of environmental conditions (for example, temperature, humidity and light). Furthermore, stability testing is used to establish the product shelf life and recommended storage conditions (European Medicines Agency, 2003:4).

Acceptable timelines for product excursions, or time out of refrigerator (TOR), should be defined, controlled and justified, based on the appropriate stability data for the product. Data should available to support such timeframes outside of labelled temperatures (Parenteral Drug Association, 2011:5).
1.3.1.6. Mean kinetic temperature

The mean kinetic temperature (MKT) is a representation of the effects of temperature on temperature-sensitive goods such as foods and pharmaceuticals. This is calculated by applying a greater weight to higher temperatures, as opposed to a simple mean. In many instances there is a relation between the MKT and the shelf life of a product (Scigiene Corporation, n.d.:1). The International Convention for Harmonisation defines MKT as ‘a single derived temperature that, if maintained over a defined period of time, affords the same thermal challenge to a drug substance or drug product as would be experienced over a range of both higher and lower temperatures for an equivalent defined period’ (European Medicines Agency, 2003:18). The MKT is used to determine if the storage conditions to which a product has been exposed have affected the stability of the product. It should be used with caution as it may provide a false sense of security when applied to the distribution of a product. The MKT was developed for the application to long-term storage and may not accurately reflect the temperature impact during transportation (O’Donnell, 2008).

1.3.1.7. Product recalls

The MCC defines a product recall as ‘removal of specific batch/batches of a pharmaceutical product from the market for reasons relating to deficiencies in quality, safety or efficacy’ (2012:8).

1.3.2. Validation and qualification

The MCC (2012:23) requires that distributors validate, at minimum, the following:

- Warehouse premises and cold room, including temperature mapping
- Lagged containers (cold chain packaging system used to transport cold chain products)
- Cold chain processes
- Computerised systems

It is therefore vital to understand the validation process and ensure that the validation requirements are met during the distribution process, and that the costs to meet these requirements are managed to ensure a cost-effective supply chain.
The WHO defines validation and qualification, where the concept of validation typically incorporates the concept of qualification, as follows (WHO, 2006d:3):

- **Validation** – ‘Action of proving, in accordance with the principles of GMP, that any procedure, process, equipment, material, activity or system actually leads to the expected results’
- **Qualification** – ‘Action of proving that any premises, systems and items of equipment work correctly and actually lead to the expected results’

The MCC of South Africa adopts the same definitions as the WHO which can be found in the MCC Good Wholesaling Practice for Wholesalers, Distributors and Bonded Warehouses guideline (2012).

The Parenteral Drug Association defines validation and qualification slightly differently (2007):

- **Validation** – ‘Documented testing performed under highly controlled conditions, demonstrating that processes, methods, and systems consistently produce results meeting pre-determined acceptance criteria’
- **Qualification** – ‘Documented testing that demonstrates with a high degree of assurance that a specific process will meet its pre-determined acceptance criteria’

The above definitions will serve as the foundation for validation and qualification in this research. The difference between validation and qualification is best illustrated by Bishara (2005:4), in Figure 25 below.
Validation is applied to highly controlled processes, and as per the PDA definitions seeks to provide ‘consistent’ results. Such highly controlled processes are typically only achieved in the manufacturing and storage stage of the supply chain.

Qualification on the other hand is applied to uncontrolled/variable process, and seeks to provide a ‘high degree’ of assurance in the results. Hence qualification is applied to processes in the distribution stage of the supply chain.

Conceptually, however, both validation and qualification follow a similar process, and are often used interchangeably.
1.3.3. Cold chain packaging systems

The MCC guidelines require that lagged containers be used to transport cold chain products at a constant temperature of between 2 °C and 8 °C. A lagged container is an ‘insulated container that has been tested and internally validated to meet the requirements of storing and transporting pharmaceutical products at the required temperatures for the necessary duration of time’ (2012:7, 37).

This section will discuss the various types of components and packaging that are used in such lagged/cold chain packaging systems, as well as provide some background to these systems.

Cold chain packaging systems typically have two configurations: summer and winter. The configuration refers to how the insulated container is packed or the temperature to which the cooling packs are conditioned. Such configurations are required to compensate for the shifts in temperature from one season to another (Kosmas, 2011:37). Managing the changeover from one configuration to another is important in terms of maintaining product quality.

It should be noted that ‘pre-qualified’ insulated systems, which have been designed, tested and qualified/validated by the manufacturer of the system, can be purchased. Alternatively, the system can be designed, tested and qualified/validated internally by the organisation or an external testing company. Pre-qualified systems are significantly more expensive than in-house validated systems.
1.3.3.1. Components

Cold chain packaging systems are made of multiple components to achieve the desired outcome of maintaining the temperature between 2 °C and 8 °C. Figure 26 illustrates the various components required, including:

- Outer cardboard shipper
- Insulated container
- Cooling packs
- Inner cardboard shipper
- Insulated sheets

1.3.3.1.1. Outer container

The outer container serves two main purposes. First, the outer cardboard shipper can be used to display printed company logos and specific handling information. Based on experience in the development of such packaging, the handling instructions provided are critically important as the handling of cold chain packaging systems can affect the cold chain performance. For example, placing the container on its side may change the thermal flow within the container. Another example would be placing the container in a refrigerator, which may result in temperatures going too low due to the cold ambient environment. Secondly, the outer container protects the insulated shipper from damage.
during transportation and handling. There are two types of outer containers: cardboard outer containers are cheap and are typically used for disposable systems, whereas hard plastic outer containers are more expensive but provide a greater degree of protection. They are therefore ideal for reusable systems.

1.3.3.1.2. Insulated container
The insulated container is the primary source of insulation, which resists heat transfer based on the properties of the type of insulating material used. The most common types of insulating material are expanded polystyrene (EPS) and polyurethane (PUR) (Coolpack, n.d.). Table 5 below illustrates the key differences between EPS and PUR.

**Table 5 EPS vs PUR (Cool Pack, n.d.)**

<table>
<thead>
<tr>
<th>Expanded polystyrene (EPS)</th>
<th>Polyurethane (PUR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low weight</td>
<td>Higher weight</td>
</tr>
<tr>
<td>Low cost</td>
<td>Higher cost</td>
</tr>
<tr>
<td>Flexibility (moulded and fabricated)</td>
<td>NA</td>
</tr>
<tr>
<td>Broad availability</td>
<td>Broad availability</td>
</tr>
<tr>
<td>Low insulation capabilities</td>
<td>Higher insulation and durability</td>
</tr>
<tr>
<td>Low recyclability</td>
<td>Low recyclability</td>
</tr>
</tbody>
</table>

Other methods of insulation include:

- Vacuum insulated panels – A vacuum insulated panel (VIP) is an insulated material like EPS or PUR core surrounded by a thin foil, metallic or plastic material (Figure 27). The opened cell core allows a vacuum to be pulled through an assembly. This
results in a very high R value (thermal resistance, a measure of insulation performance) (Shampain, Letizia & De Weese 2009:53).

- **Airliners** – This is an inflatable insulated liner, which provide greater levels of protection and is more eco-friendly than traditional alternatives (Figure 28). Perhaps its greatest benefit is due to the fact that it is an inflatable solution, which reduces supply chain costs by taking up less transport and storage space prior to use (Welch, 2009).

- **Wool packaging** – By using 100% wool as the insulator, wool packaging is biodegradable and recyclable (Figure 29). Wool packaging has the further advantage of assisting in reducing humidity exposure as it can absorb 35% of its weight in moisture (Wool Cool, 2010).
1.3.3.1.3. Cooling packs

Eutectic and cooling packs refer to the components that provide the ‘cooling’ to keep the cold chain packaging system within the required temperature range for the required duration. These packs are typically either chilled between 2 °C and 8 °C or frozen. They are then placed within the cold chain packaging system according to a predetermined configuration. Cooling packs have two key components, the cooling material and the container:

- **Cooling material**
  - Water/ice – Water is a phase change material as it changes from a solid to liquid and vice versa at 0 °C. Water is often used due to the fact that it is ‘free’ and has good latent heat properties; however, due to the 0 °C phase change there is a risk of freezing product unless there is a buffer between the frozen pack and the product (Cryopack, 2012).
  - Gels – By adding a thickener to a water pack, a gel substance is formed, which thickens the material and increases the viscosity of the gel pack. This, in turn, results in an increased release duration that improves the performance of the cooling pack (Association Française du Froid & SFSTP, 2009:42). The increased performance is due to the increased viscosity of the material, which reduces convection within the cooling pack.
  - Phase change materials (PCM) – ‘PCMs are materials that change their physical state due to temperature.’ While water and gels are technically PCMs, because they change phase at 0 °C, they have been excluded from this category for the purposes of this study. Therefore, all references made to PCMs in this document are specifically to specialty PCMs which provide greater control of the temperature requirement. For example, a specialty PCM formula (using other materials such as paraffin wax and hydroscopic polymers) may remain at a constant 4 °C during its phase change (Cook, 2006:5). The benefits of such PCMs are obvious when considering the challenge of keeping an insulated container at 2 °C to 8 °C. As mentioned, when water-based packs have a phase change of 0 °C, buffers and insulators need to be used to protect the product from the freezing point.
temperatures during phase change. However, with PCMs as described above, the phase change is within the required temperature range.

- **Container**
  - Rigid packs are made of a hard plastic material. The advantage of this is that the cooling pack maintains its shape during freezing and thawing, resulting in a lower likelihood of leakage. The cooling pack also has a greater life expectancy making it ideal for reusable systems (Association Française du Froid & SFSTP, 2009:41). These packs are typically more expensive than flexible packs.
  - Flexible packs are made of flexible plastic. The drawbacks of such cooling packs are that their shape varies depending on how the pack was frozen; and they are less robust, and so have a lower life expectancy (Association Française du Froid & SFSTP, 2009:41) These packs are less expensive, making them ideal for disposable systems.

1.3.3.1.4. Miscellaneous

Further to the items discussed above, the following items are typically used in insulated packaging:

- **Inner shipper** – used to contain the individual pharmaceutical units. The inner shipper provides a container to pack the product items into, as well as insuring that the payload space remains consistent even if only half the payload space is used.
- **Insulated sheet** – used to provide insulation from the cooling source. Insulated sheets may also be repositioned to adjust for different seasons, namely winter and summer. These sheets are typically made from EPS or PUR.

1.3.4. Temperature monitoring

1.3.4.1. Key considerations

- What needs to be monitored:
  - Temperature and humidity – The MCC Good Wholesale Practice guidance document (2012:35-38) explicitly requires that temperature be continuously (i.e. ongoing monitoring using digital technology) monitored in product
storage locations. For cold chain products, ‘checks should be done to ensure that the cold chain has been maintained during transportation’, which suggests monitoring may be required during transportation. Humidity monitoring may be required where the product label specifies that humidity should be controlled.

- Probe placement and alarms:
  - Probes should be placed in positions representing temperature extremes (based on temperature mapping). Furthermore, alarms should activate in the event the temperature exceeds the defined product limits (MCC, 2012:35-36).
- Calibration:
  - Calibration is the process of comparing the value indicated by a measurement device against a known value in order to determine the accuracy of the device, so as to ensure it operates within the required limits. The accuracy of the device is confirmed and corrected (if possible) by calibrating the device on an annual basis. (MCC, 2012:4-35). The WHO (2005b:4) recommends a device with an accuracy of ±0.5 °C or better.

1.3.5. Warehousing

1.3.5.1. Managing varying temperature requirements
Based on the research in Chapter 1, the three broad temperature range requirements can be identified as:

- Freezing temperatures
- Cold temperatures
- Ambient/room temperature

Therefore, when storing pharmaceuticals, a warehouse needs to be equipped to store products at the appropriate temperature range. The specific temperature range would be stated on the product itself, and the relevant equipment would need to be set to achieve the range specified.
While the stated scope of this research is cold temperatures at 2 °C to 8 °C, all three ranges will be touched on as they may all have an impact on cold chain in that:

- The cold room is likely to be within a warehouse environment, the temperature of which could impact the cold room temperatures or functioning.
- Cold chain shipments typically require the gel packs or other eutectics to be conditioned in freezing temperatures prior to use.

1.3.5.1.1. Freezing and cold temperatures
The temperature range for frozen products is typically −15 °C to −25 °C (WHO, 2002:12). A small but increasing number of pharmaceutical products require storage at freezing temperatures (ABB, 2009:5). To meet this requirement, freezing temperatures are achieved through the use of either a freezer room or free-standing freezer.

- Freezer rooms are designed to replace multiple smaller free-standing units. Freezer rooms provide a larger volume of storage space controlled by a central refrigeration unit (Cincinnati Sub-Zero, 2011).
- Household-style freezer units could be used provided that independent testing illustrates that the equipment performs as required (WHO, 2011:340).

As mentioned above, freezer storage may also be required to store components used in cold chain insulated packaging, for example, gel packs, eutectic plates, etc.

1.3.5.1.2. Cold temperatures
The temperature range for cold products is typically 2 °C to 8 °C (WHO, 2002:4). Temperature-sensitive products should be stored in a refrigerator or cold room according to the MCC (2012).

- Domestic refrigerators may be suitable for cold chain products that are not particularly sensitive to brief excursions outside of the specified temperature range. However, domestic refrigerators are not suitable for sensitive pharmaceutical products. Refrigerators specifically designed for pharmaceutical products are available and preferred to domestic refrigerators (Taylor, 2001:128).
1.3.5.1.3. Ambient/room temperatures

Heating, ventilation and air-conditioning systems (HVAC) are able to assist in the control of particles, pressure, humidity and temperature (Bhatia, n.d.:2-3). The primary focus for this research will be on its ability to control temperature. Used appropriately, they can control the temperatures for products at ambient or room temperatures.

1.3.5.2. Power requirements

According the WHO (2011:338-39), the following should be considered regarding the power requirements for storage of pharmaceutical products:

- Uninterruptable power supply (UPS): Where possible or required, equipment such as HVAC, refrigerators, freezers, etc. should be connected to a UPS system.
- Generator: Where a generator is used it should:
  - Have sufficient capacity for all the connected temperature controlling and monitoring equipment
  - Not exceed the mains supply limits
  - Have automatic start/shutdown functionality
  - Sufficient fuel capacity for a prolonged power outage
- Power contingency plan: A contingency plan to protect temperature-sensitive products should be in place. Emergency alternatives such as liquid nitrogen or dry ice could be considered, depending on the nature of the product.

1.3.6. Transport

Transportation of cold chain pharmaceuticals may make use of air, ocean and ground transportation methods.

It is necessary to understand that all forms of cold chain transportation are either active or passive systems of temperature control:

- Active systems: ‘Systems with active temperature control (for example, air/sea freight containers, refrigerated vehicles)’ (Parenteral Drug Association, 2007:4). Such systems typically have thermostats and are capable of creating warmer or cooler temperatures as required.
• Passive systems: ‘Systems without active temperature control (for example, insulated containers with or without refrigerants)’ (Parenteral Drug Association, 2007:4). These systems are packed with an inherent thermal capacity which depletes during the course of distribution.

A significant consideration between active and passive systems relates to risk. As active systems require some type of power source, in the event of a power source not being available the unit will no longer provide the required cooling/heating. On the other hand, passive systems are designed to maintain their temperature for a specified period of time regardless of power.

1.3.6.1. Refrigerated vehicles

A refrigerated vehicle has two key components: an insulated body and a refrigeration unit. The insulated body reduces the amount of heat that is able to penetrate through to the cargo area. The refrigeration unit is used to reduce or maintain the temperature at the desired range (Hubbard, n.d.).

![Figure 30 Refrigerated vehicle (Hubbard, n.d.)](image)

The refrigeration unit cools down the air and provides air circulation within the cargo area of the vehicle. The warm air is then dispersed outside the vehicle (see Figure 30).

1.3.6.2. Air/sea freight refrigerated containers

1.3.6.2.1. Sea freight refrigerated containers

These containers have refrigerator units built in which allow the unit to be maintained between the required temperatures. As a result, reefer containers require electricity and
therefore have to be placed in specific slots at shipyards and once on the ship. Reefer containers are typically painted white to reduce heat absorption (Rodrigue, 2012). Figure 31 below provides an illustration of the airflow within such a unit. The floor of the unit has gratings and the sidewalls are ‘corrugated’; these attributes allow for the required airflow within the unit (Transport Information Services, 2011).

1.3.6.2.2. Air freight refrigerated containers
The concept of the refrigerated container above has been extended for use in air freight. One such example is the Envirotainer® which is specifically designed for the transport of temperature-sensitive medicines (see Figure 32). Temperature sensors within the unit monitor the temperature and ensure the required temperature is maintained. Furthermore, these monitoring sensors provide information as to the status of the container (Envirotainer, n.d.).
Some of the key features of such a device are as follows (Envirotainer, n.d.):

- Insulated shell
- Temperature data logging
- Rechargeable batteries
- Fully redundant heat/cooling systems

1.4. **The pharmaceutical cold chain model**

Using the Lambert and Stock model as a foundation, a new model will be developed to fit the unique elements as they apply to the pharmaceutical cold chain. It is important to note that the original model still applies to a pharmaceutical cold chain management as it would to any supply chain; therefore, only unique factors as they relate to the pharmaceutical cold chain will be discussed. The new pharmaceutical cold chain model provides a structure within which to assess pharmaceutical cold chain elements and their relationships. These elements increase the complexity of the cost decisions as they may influence the fundamental element of quality and hence patient safety.

For the purposes of this research, the term ‘cost’ will refer to three primary cost categories, namely quality, money and time, and may make reference to direct or indirect cost implications.

1.4.1. **Development of the pharmaceutical cold chain model**

Each element of the pharmaceutical cold chain model will be discussed. Through this process the structure will be developed for the pharmaceutical cold chain model, which will serve as the framework for the research to be executed.

1.4.1.1. **Non-conformance cost**

Identifying the required product quality level is a key element of defining the customer service standard or level (Government of South Australia, 2007:7). Having a significant impact on quality and patient safety, non-conformance will represent the fundamental cost element at the apex of the pharmaceutical cold chain model.
At the 2011 International Conference on Harmonisation, Macher presented the findings of a survey into the cost of poor quality systems in the pharmaceutical industry. She identified the following key costs associated with poor quality (Macher, 2011:4-5):

- **Internal costs**
  - Direct costs – arise as a direct result of the product failure, for example, product write-off
  - Remediation costs – related to the identification, correction and reporting

- **External costs**
  - Regulatory action costs – due to legal action, product recalls and suspended operations
  - Market share costs – decreased supply may result in lost sales
  - Reputational costs – associated with negative impact on brand value

**1.4.1.2. Validation/qualification costs**

Validation costs relate to all activities associated with the validation and qualification of equipment, processes and systems – a requirement for the storage and distribution of pharmaceuticals (MCC, 2012:23). Significant time and money is required to validate the outbound distribution of a pharmaceutical supply chain, which includes the validation of:

- Enterprise resource planning (ERP) systems and temperature monitoring systems
- Warehouse
- Cold room
- Freezer room
- Cold chain shippers

**1.4.1.3. Cold chain packaging costs**

Cold chain packaging costs refer to all costs related to the packaging of pharmaceutical cold chain products for transportation.

According to the MCC, pharmaceutical cold chain product is usually transported in cold chain packaging systems with sufficient ice packs to maintain the required temperature for the duration of the journey (2012:37). The cost associated with this additional...
packaging requirement should be factored into the total cost of distribution. The impact of such cold chain containers may include:

- Duration capability of the cold chain packaging – Typically, longer duration containers require increased thermal capacity which may impact cost.
- Payload size/volume – The amount of product shipped within a cold chain container will influence its efficiency in terms of cost per volume of product.
- Complexity of packaging configuration – The more complex a packing configuration, the longer it may take to pack, which affects the efficiency of the packing process. Furthermore, increased complexity may increase the risk of incorrectly packed cold chain shippers, which could result in non-conforming product.
- Cost of packaging – The most significant cost element is the packaging itself, which increases costs due the nature and multiple components required to maintain the temperature.
- Reusability of packaging components: Due to the high cost of cold chain shippers, the ability to reuse the shippers could significantly reduce cost over a period of time.

### 1.4.1.4. Temperature monitoring costs

Temperature monitoring introduces a requirement for data and information related to the temperature across the supply chain.

Monitoring of refrigerators, cold rooms and freezers is a requirement for the storage of cold chain pharmaceuticals. Furthermore, 'checks should be done to ensure that the cold chain has been maintained during transportation’ (MCC, 2012:36). Temperature monitoring of the parcel may be required, or alternative methods of temperature verification may be used. The WHO provides some suggestions on some of these alternatives, which will be discussed further in this chapter (1999:1).

Temperature monitoring introduces three key cost factors:

- Cost of the actual temperature monitoring (Mousavi, 2010:10)
• Cost of data harvesting and management (Mousavi, 2010:10)
• Cost of annual calibration (MCC, 2012:35)

With regard to the actual temperature monitoring the following key aspects should be considered:

• The actual device and types of probes, as these affect the accuracy of readings
• The number and position of monitoring probes
• Alarms and alerts functionality

1.4.1.5. Warehousing costs
For the purposes of the pharmaceutical cold chain model only aspects unique to cold chain product storage and warehousing will be considered. These factors include:

• Cold room/refrigerator and freezer – Pharmaceutical cold chain products are required to be stored in a cold environment, i.e. cold room or refrigerator. Products which are required to be frozen must be stored in a freezer (MCC, 2012:35). The need for such infrastructure introduces many new cost factors to consider.
• Packaging storage – The packaging results in additional space being required to store the packaging, as well as increased complexity and training.
• Electrical consumption – In order to run the various temperature control systems additional power is required to keep these systems running.
• Generator/backup power requirements – As temperature control is so key for pharmaceutical products, it is imperative to have backup available in the event of a power failure to ensure pharmaceutical products are maintained within the required temperature range.

1.4.1.6. Transport costs
As with the warehousing element, only unique elements of pharmaceutical cold chain transportation will be considered under the transportation element.

Although volume, weight and mode of transport are the critical factors that are important in any supply chain, the pharmaceutical cold chain model will see these components only in terms of unique considerations of the pharmaceutical cold chain management.
• Volume – Due to the fact that a pharmaceutical cold chain product needs to be transported in an insulated system, the volumetric space is significantly increased relative to the amount of product transported. In Table 6 below, a listing of technical specifications of a common cold chain packaging system, the volumetric impact becomes clear when comparing the internal volume to the external volume:
  o EN2-48: Internal – 2000 cm³ | External – 28830 cm³, 14.4 time the internal volume
  o EN4-48: Internal – 3564 cm³ | External – 69148.8 cm³, 19.4 times the internal volume
  o EN6-72: Internal – 5760 cm³ | External - 115612.42 cm³, 20 times the internal volume

It is therefore crucial to understand the implications of distribution volume and cost per cubic centimetre of product delivered.

Table 6 Technical specification for Sherpa Cold Box (Sherpa Systems, n.d.)

<table>
<thead>
<tr>
<th>Code</th>
<th>Dimensions (mm)</th>
<th>Internal Product Volume (lt)</th>
<th>Duration (hrs)</th>
<th>Volumetric Weight (kgs)</th>
<th>Total System Weight (kgs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN2-48</td>
<td>Int 200 x 200 x 50 Ext 310 x 310 x 306</td>
<td>2</td>
<td>48</td>
<td>4.9</td>
<td>4.9</td>
</tr>
<tr>
<td>EN4-48</td>
<td>Int 180 x 180 x 110 Ext 392 x 392 x 450</td>
<td>4</td>
<td>48</td>
<td>11.5</td>
<td>9.8</td>
</tr>
<tr>
<td>EN6-72</td>
<td>Int 240 x 240 x 100 Ext 456 x 456 x 436</td>
<td>6</td>
<td>72</td>
<td>15.1</td>
<td>14.6</td>
</tr>
</tbody>
</table>

• Weight – Weight has a similar characteristic to volume in that the cold chain packaging system requires coolant components such as gel packs and PCMs to maintain the required temperature. These components as well as the cold chain packaging system itself significantly increase the weight of the shipment. Using the same table above, an additional 4.9, 9.8 and 14.6 kg will be added to every delivery using the respective systems. This would in turn have an impact on transportation cost.

• Mode of transport – As this research is based on pharmaceutical cold chain distribution within South Africa, sea and rail freight are not used for distribution. Road and air transport are the only options. Due to the time and temperature-
sensitive nature of pharmaceutical cold chain, air transport may be the only option for long-distance routes. This may significantly impact cost (McPherson, 2011:1).

- Vehicle type – This refers to whether the vehicle is a standard body, insulated body, refrigerated or temperature-controlled vehicle; the more specialised vehicles will increase cost.
- Duration to destination – This aspect refers to the transportation service level defining how long it will take for the parcel to reach its end delivery point.

1.4.2. Relationships
As the primary focus of this research is to determine the key challenges within the pharmaceutical cold chain, the following relationships will be investigated in order to meet the objectives of the research:

- Transport and non-conformance
- Transport and validation
- Transport and packaging
- Transport and temperature monitoring
- Transport and warehouse
- Warehouse and quality
- Warehouse and validation
- Warehouse and packaging
- Warehouse and temperature monitoring
While other relationships not defined above (see Figure 33) may also be of value, they will not be considered as part of the scope of this research.

1.5. Conclusion

With the objective of this research in mind it is crucial to constantly balance the drive for supply chain cost and efficiency against the absolute requirement of quality in the pharmaceutical cold chain. The detail within each of these cost elements has been provided in order to lay the foundation for the detailed analysis of the pharmaceutical cold chain model. Chapter 4 brings together in one concise model all the key aspects and considerations from the previous chapters. The framework that has been developed will now form the skeletal structure for the execution of the research. In order to execute the research, the methodology and details of how the research will be executed must be defined and discussed. Together the framework and research methodology will form the foundation for the execution of the research.
CHAPTER 5 – RESEARCH METHODOLOGY

5.1. Introduction

The framework defined in Chapter 4 requires a defined research methodology to provide the detail on how the research will be executed. This is a crucial aspect in terms of the reliability of the findings of the research. Chapter 5 will address the logic and approach of the research, including the research paradigm, research design, data collection, population and sampling as well as the specific methods for the execution of the research.

The research methodology for this study had two significant challenges that hinder the ability to collect suitable data. First, pharmaceutical cold chain management is a relatively new and highly specialised industry. The complexities described in Chapter 3 demonstrate the many considerations that must be balanced in order to ensure patient safety and supply chain efficiency. Due to its specialised nature, finding sources of data was more challenging and less likely as it is not yet a mainstream subject of study. Secondly, cold chain management as a concept is still in its infancy in South Africa, lagging behind international counterparts. This statement is supported by:

- The recent (2011) establishment of the Cold Chain Forum of South Africa
- The recent update of the Good Wholesale Practice guideline to bring it in line with international requirements (MCC, 2012)
- Analysis by industry that illustrates the MCC is about 2 years behind their international counterparts in terms of audit topics (Imperial Health Sciences, 2014:6,7)

It was extremely difficult to find data to use as an input to this study. It is therefore necessary to create the data. However, this was not without its challenges. Being a young concept, caution must be exercised as to the sources of data and information.

It was therefore necessary to take a structured approach to identifying the research methodology in order to ensure the results of the study were robust. To achieve this, this chapter will analyse and discuss the key aspects of the research methodology, taking a top-down approach in order to align the structure of the study.
5.2. Research paradigm

5.2.1. Paradigm selection

5.2.1.1. Supply chain management research paradigm

In her research to identify dominant research paradigms in SCM, Wolf asked the following question: ‘What are the dominant research paradigms in Supply Chain Management and how did these evolve over time?’ (2008:154,155). The conclusion may be summarised as follows:

- Four major periods in SCM research were identified:
  - Emergence period, 1990–1994: A limited number of articles dedicated to SCM, marking SCM as a specific area of scientific interest
  - Acceptance period, 1995–1999: Increased institutionalisation of SCM-related research
  - Growth period, 2000–2002: A large increase in SCM-related articles
  - Normal science period, 2003–2006: No further growth in the number of articles; stagnates at a high level

- The outcome of the research was that ‘Supply Chain Management has strongly been influenced by, and rooted in, the positivist tradition’.

Therefore, in the progression to identify the paradigm for this study the point of origin was positivism. However due to the complex nature of the objective of this study and the lack of usable data, it was necessary to augment this paradigm further.

5.2.1.2. Types of paradigms

Taylor (2013:2-8) categorises paradigms into two broad categories. The traditional category covers positivism and post-positivism paradigms. The relatively new paradigms cover interpretive, critical, and post-modern paradigms.

Based on these various paradigm options, the appropriate paradigm was selected for the research as this set the foundation for the structure and execution of the research.
5.2.1.3. Paradigm selection and discussion

In analysing possible paradigms for the research, the limitations in positivism, post-positivism and interpretivism become clear (Wahyuni, 2012:70). Within each of these paradigms, restrictive choices must be made in order to meet the criteria of the paradigm. The post-positivist paradigm begins to bridge the gap between positivist and interpretive paradigms, by allowing certain elements of the interpretivist approach to be used. However, the pragmatist approach provides the greatest flexibility in the application of methods and techniques. This allowed for the appropriate tools to be used based on the problem at hand.

According to Robson (2002): ‘There are situations and topics where a scientific quantitative approach is called for and others where a qualitative naturalistic study is appropriate. But there are still others [which] will be better served by a marriage of the two traditions.’ The nature of this research was best served by the multi-paradigmatic or pragmatism approach which will provide the necessary flexibility of both quantitative and qualitative methods.

The intention of this research was to identify key challenges in the pharmaceutical cold chain and provide a practical framework to assist in decision-making. While the research must have an objective departure point, a key source of data was the views of respondents within the industry. It was therefore important not to be bound by paradigm restraints.

Valuable data can be gathered from both scientific quantifiable sources as well as qualitative sources. Being able to tap into the many years of experience of the respondents within the industry provides a sound source of data to be interpreted.

Perhaps the strongest benefit of the pragmatic approach was the ability to use qualitative and quantitative approaches in meeting the research objectives. This was fundamental to meeting the outcomes of this study as the data required to execute this research in a purely quantitative manner is typically company confidential and not readily available, while a qualitative approach alone could be criticised in its validity to meet the outcomes.
5.3. Research design

According to Babbie (2012:89) the research design defines the strategy and plan for finding something out. Key elements that must be defined are, what the research was trying to find out, how the research will find this out and why.

The ‘what’ has been defined in Chapter 1. This chapter will discuss and define the ‘how’, with pragmatism as the guiding principle.

It was at this point that the reason for selecting the pragmatic paradigm, and its associated methodology of mixed method research, becomes evident.

- Descriptive research can use either quantitative or qualitative methodologies (Gerseten, 2014). This study made use of both methodologies within the ambit of mixed method research. The two methods that were used were survey and cost analysis:
  - Survey – Formed the qualitative component and provided an industry perspective to determine if there were relationships between the elements identified in Chapter 4, as well as the nature of these relationships. While the results of the survey were statistically analysed in a quantitative manner, the survey was considered qualitative as the data will be based on the views and opinions of the respondents.
  - Cost analysis – The quantitative component was a cost analysis based on primary cost data collected from various sources. The objectives of this analysis was:
    - To corroborate the findings related to relationships between elements of the survey. Through the cost analysis, the impact of a change in one element was assessed on the other elements. The greater the impact on a specific element, the greater the relationship between these elements was considered to be.
    - To provide input into identifying key challenges by analysing and interpreting the results of the scenario-based cost analysis.
- Exploratory research – In this component of the study, a qualitative survey provided the input required to define the factors that should be considered within
each of the primary elements. In a similar way to the descriptive part of the research, the survey was considered qualitative as the data gathered was based on the respondents’ views and opinions.

5.4. Data collection

Data collection can be discussed in two segments (see Figure 34):

- New data, will need to be generated to fulfil the exploratory research and part of the descriptive research. This primary data will be collected through a survey which will be sent to appropriate respondents in the industry.
- Existing data, will be collected in order to conduct the secondary data analysis which is required to fulfil the balance of the descriptive research through the cost analysis. This data will be collected from the following sources:
  - Official sources such as the Road Freight Association (RFA)
  - Quotes from suppliers to the industry
The survey data was collected through an online survey platform. Respondents were first contacted via personal communication to confirm if they would be willing to complete the survey. An email link was then sent to them which allowed the respondents to complete the survey online.

5.5. Research population and sampling
Both the exploratory and descriptive questions will be handled in one survey. The population and sample size must be determined for the survey. The population is a group selected for study and from whom conclusions will be drawn. In the case of this study, this group refers to pharmaceutical distribution companies. As it is not always possible to study the full population a sample is selected for the study (Babbie, 2012:115).

5.5.1. Population size
As it is a legal requirement to be licensed to store or distribute pharmaceutical products, the population will be defined as all companies licensed by the MCC. Based on the licences issued (MCC, 2013), there are 471 registered entities, owned by 388 legal entities. Based on this data the registered entities are summarised and categorised in Table 7 below as wholesalers, manufacturers, import and export and other licences. It should be noted that the table below has been simplified for analytical purposes, as some entities may have multiple licence types. Furthermore, the MCC does not distinguish between wholesalers and distributors as their principle function is the same; therefore, distributors are licensed as wholesalers.
Due to the focus of the study being fine distribution of cold chain pharmaceuticals, only
the wholesaler category will be considered as part of the population size. It is important
to note that while only entities in the wholesale licence list will be used, some of these
entities may be manufacturers as some companies can have more than one licence type.

Of the 194 wholesaler licences (i.e. 194 premises, as each physical premise requires a
licence) there are 151 unique entities/companies that could form the population size.

There is however a further dimension that must be considered. Based on a desk review
of these 151 companies, they can be further categorised as per Table 8 below.

**Table 8 Wholesalers licence breakdown**

<table>
<thead>
<tr>
<th>Categories</th>
<th>Sum of No of sites</th>
<th>Count of Company Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trials distributor</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Consumer</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Dental</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Distributor</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Retail</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Vet</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>Wholesale</td>
<td>94</td>
<td>82</td>
</tr>
<tr>
<td>Government</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>194</strong></td>
<td><strong>151</strong></td>
</tr>
</tbody>
</table>

Only the wholesale, distributor, retail pharmacy, manufacturer and government
categories will be used, as the other categories are too specialised to provide a fair
representation of the target population of this study. This therefore leaves 110 entities
that will be considered as the population size.
5.6. Sample size

Babbie (2012:129) suggest that the purposive/judgmental sampling technique, while useful in initial stages of survey design, does not represent the population in a meaningful way. However, this method is appropriate for application in this study.

A fundamental consideration in the selection of the sampling technique is the research question, as the research question will drive the research objectives on which the sampling technique will be selected. Purposive sampling is a non-probability sampling technique, which may be used with both qualitative and quantitative research. It is most effective where one needs to study a specific domain with knowledgeable experts within an industry (Dolores & Tongco, 2007:1).

The nature of this study fits with the above rationale, as the understating of the distribution of temperature-sensitive pharmaceuticals in South Africa is still in the early stages of its development. The appropriate respondents to provide the necessary input into the research will need to have had exposure to international trends, regulations, audits, or be large enough to attract appropriate attention and rigorous audits from the MCC. This will therefore form a fundamental base in the selection of respondents to ensure that the appropriate 'knowledgeable experts' are identified.

Therefore, the following considerations will guide the selection of companies/entities to be selected from the sample:

- Johannesburg Stock Exchange (JSE) listed manufacturers
- Distributors who distribute on behalf of international pharmaceutical companies
- Wholesalers who have more than one physical distribution site
- Retail pharmacy chains
- Local entities of the top five multinational pharmaceutical companies will be included, namely Johnson & Johnson, Pfizer, GlaxoSmithKline, Roche, Sanofi

Within each selected company, at least one operationally focused individual and one quality focused individual will be approached to complete the survey.

Based on the above rationale 27 companies were selected as the sample size.
5.7. Questionnaire Design

Due to the significant and recent changes to the regulations the pharmaceutical distribution industry in South Africa, the questionnaire design was guided by discussions, conferences and interviews with industry experts. The questionnaire consisted of 5 key sections: General, Risk Analysis, Estimated Costs, Key Factors, Relationships Between Elements. Each section contributed to a specific input required for the research as follows:

- General: These questions were demographic in nature and would be used to confirm that the sample was indeed appropriate to meet the objectives of the research.
- Risk analysis: The cost impact of non-conforming product was assessed through a risk analysis and what risk the various elements pose to pharmaceutical cold chain products.
- Estimated costs: Cost estimates were used to cross reference against the cost information collected in the survey.
- Key factors: This section provided contextual information for interpretation related to what the respondents considered to be the key factors within each defined element. This information was used in the analysis of the survey in conjunction with the relationship between elements to determine the key challenges.
- Relationships between elements: While the key factors provided context of each element, this section provided additional information with regard to the degree to which elements were related from a cost, time and quality perspective.

The risk analysis, key factors and relationship between elements were analysed to determine key challenges within the pharmaceutical industry.

The two primary measurement scales were used in the survey. Firstly a 5-point scale was used as this would allow respondents to provide a midpoint response rather than forcing respondents to be bias to the lower or upper end of the scale. This was important as it ensures a better representation of how the respondent felt about the question. Secondly a ranking scale was used to provide a comparative result of the importance of the factors.
5.8. Cost Analysis Method
To conduct the cost analysis a pharmaceutical distribution organisation was simulated. In each scenario, various cost aspects were then adjusted as appropriate to that scenario. The costs were then grouped per element. As cost factors were adjusted it was possible to assess the cost impact (increases and decreases) between the various cost elements. Each scenario resulted in different cost impacts on the various elements. These cost impacts could then be used to determine from a quantitative perspective the cost relationship between the various elements, and was cross referenced to the results from the relationship between elements from the survey.

5.9. Data Analysis
The approach to data analysis must be discussed in two parts, survey data analysis and cost analysis.

The survey data analysis required the consolidation of the data into a single data set. General questions were analysed on the basis of the percentage of respondents which selected the specific options. All other questions were analysed by determining the average response rating, including the standard deviation and margin of error. Where appropriate tabular and graphical representation of the questions also provided insight into the distribution of responses across the multiple options.

In the case of the costing analysis each element had specific cost components with variables which influenced these costs, for example the cost per trip for transportation, was influenced by the service level. For each scenario the appropriate variables were adjusted to determine the cost for each element. These costs were then represented in graphical format also providing a comparative difference to a benchmark. The degree to which the cost changed was an indication of the degree to which the specific elements have an impact on one another.

5.10. Ethical considerations
As no company confidential information formed part of the mandatory questions, there was no significant ethical considerations to factor into the approach of the study.
Nonetheless all information gathered will be kept confidential in that only aggregated data will be published. No reference will be made to any specific company or respondent. A statement reflecting the above will be included on distribution of the online survey.

5.11. Conclusion
The mixed method approach was most suited to the research due to the challenges in collecting appropriate data. Furthermore, this approach allowed cross-referencing between the qualitative and quantitative aspects of the research which further supported the veracity of the outcomes of the research.

The complexity of the research objectives made it appropriate to use the mixed method approach. While this introduces complexity into the research process, it was offset by the relatively small population size. By filtering the sample down to ensure a higher probability of knowledge experts, the sample was reduced to a manageable size, making the execution of the mixed method approach viable.

Ultimately the effectiveness of the approach as defined in this chapter was demonstrated in the outcomes of the research as well as the cross-referencing and statistical analysis. The next chapter provides details on this analysis, which will form the base for interpretation of the data in the final chapter.
CHAPTER 6 – RESEARCH RESULTS AND FINDINGS

6.1. Introduction
Having conducted the research, detailed analysis on the data was executed in order to meet the objectives of the study. This chapter will summarise, with the necessary level of detail, the outcomes of the analysis. Due to the mixed method approach of this research, there is a significant amount of information that must be logically structured, analysed and interpreted. It is important therefore to assess each aspect of the research individually and to integrate the outcomes of the research for interpretation.

6.2. Overview of research
The fundamental approach to the research was to juxtapose two methods in order to meet the research objectives. First, the survey provided an industry perspective and relied on the experience of industry experts to identify if there are indeed relationships between the elements identified and what the key factors of these elements are. The cost analysis served as a cross-check of the survey as it relates to the relationships between cost elements. The purpose of this chapter is to summarise, analyse and interpret the findings of the above two-pronged approach. The structure of this chapter will analyse each approach (survey and cost analysis) separately and then integrate the outputs to identify the key challenges.

In terms of the objectives of this research, it was important to understand the distinction between what elements are well documented and researched versus the elements which were not. From a cost and supply chain relationship perspective, the transport and warehousing elements have been well documented as discussed in Chapter 4. The other four elements (non-conformance, validation and qualification, cold chain packaging and temperature monitoring), while well documented from a technical perspective, have not been very well documented in terms of the impact on the supply chain. It is for this reason that the dual approach has been selected as defined in Chapter 5. The survey, see annexure 1, provides the insight and experience of knowledgeable experts in the industry, while the cost analysis illustrates the same principles from a quantitative perspective.
The diagram in Figure 35 above illustrates how the survey and cost analysis are related to one another in order to meet the outcomes of the research.

In order verify the baseline cost (2.1.) which the scenarios were based on, cost estimate (1.3.) questions from the survey were used as a reference point for comparison. It is crucial to note that it was not possible to develop a cost analysis that was representative of all organisations in the industry due to the varied nature of different operations. This was not necessary as the objective of the research was to identify if there are relationships between cost elements, rather than to determine the actual cost. Therefore, the verification of the baseline costs (2.1.) was performed in a manner that would provide confidence that the costs were realistic estimates and could be related to the South African pharmaceutical distribution industry.
The outcome of the cost analysis (2.3.) was to determine the impact of changes to specific cost elements on the other elements. This was used to support the outcomes of the survey which identified from a qualitative perspective if there was indeed a relationship (1.5.) between the various elements and if so, the nature of the relationship.

It was not possible to quantify the non-conformance cost due to the irregular nature of such costs. This was therefore quantified in the form of risk using a risk analysis (1.2.) conducted in the survey. The risks for each cost element were then used to quantify the overall non-conformance risk and the risk of each relationship identified (5.).

Based on the survey results, the key factors (1.4.) were prioritised and incorporated into the relationship model. The result of the cost analysis (2.3.) was reviewed and interpreted to support the relationship determination of the survey.

The relationships (3.), key factors (4.) and risk review (5.) were then reviewed and interpreted in order to identify the key challenges (6.).

### 6.3. Survey results

In constructing the survey, it was important to ensure that the questions, once answered, would provide the necessary information to meet the objectives of the research. It was therefore imperative to understand the intention of the various questions and why they were included in the survey. This would also assist in interpreting the results of the survey.

#### 6.3.1. Rationale, results, analysis and interpretation of survey

In this section each question will be discussed in terms of the rationale and intent of the question; a summary of the results; and analysis and interpretation of the question.

#### 6.3.1.1. General questions

##### 6.3.1.1.1. Question 1 – Do you work in the pharmaceutical industry?

**Rationale**

This was a fundamental filter question in that it confirmed that the respondents were indeed operating in the pharmaceutical industry. Furthermore, it served to clarify that the respondents believed themselves to operate in the pharmaceutical industry.
Results, analysis and interpretation

Table 9 Question 1 – Do you work in the pharmaceutical industry?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>100.0%</td>
</tr>
<tr>
<td>No</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

All respondents answered yes. The result clearly indicates that all respondents were and perceived themselves to be in the pharmaceutical industry.

6.3.1.1.2. Question 2 – Which of the following storage temperature ranges do your products require?

Rationale
The stated scope of the research is specific to cold chain products, specifically at the 2 °C to 8 °C range. It was therefore important to ensure that respondents do have operations with the requirements of distributing within this range.

Results, analysis and interpretation

Table 10 Question 2 – Which of the following storage temperature ranges do your products require?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra-low (below −40 °C)</td>
<td>10.0%</td>
</tr>
<tr>
<td>Frozen (−15 °C to −25 °C)</td>
<td>30.0%</td>
</tr>
<tr>
<td>Cold (2 °C to 8 °C)</td>
<td>95.0%</td>
</tr>
<tr>
<td>Controlled room temperature (15 °C to 25 °C)</td>
<td>80.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Most (95%) respondents had operations in the 2 °C to 8 °C range. This indicates that the sample does have cold chain requirements and therefore would be appropriate to provide the required information for the survey. All responses were used as the intention of this question was to determine the appropriateness of the sample, rather than to exclude respondents.
6.3.1.1.3. Question 3 – What is the nature of the organisation?

Rationale
The objective of the research was not intended to identify differences between the several organisation types (for example, wholesalers and manufacturers); however, this question was intended to provide insights into the types of organisations that respondents originate and could assist in the interpretation of the data if required.

Results, analysis and interpretation
Table 11 Question 3 – What is the nature of the organisation?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>35.0%</td>
</tr>
<tr>
<td>Distributor</td>
<td>40.0%</td>
</tr>
<tr>
<td>Wholesaler</td>
<td>20.0%</td>
</tr>
<tr>
<td>Retail pharmacy</td>
<td>0.0%</td>
</tr>
<tr>
<td>Government agency/department</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

No responses were received from retail pharmacy and government agencies. In the case of retail pharmacy, this may have been that while a company may be part of a retail pharmacy group, the distribution arm of the company is technically a wholesaler and therefore when responding to this question the responses may be captured as wholesaler. The lack of responses for these two categories (government and retail pharmacy) is not of concern as this question was primarily for information purposes. In terms of the implications for the representativeness of the sample, while there may be a difference between the different organisations, the fundamental requirements for all these organisation types are the same. Having said this there may be a variation in terms of government agencies, and therefore this research should be interpreted with care if it is to be used in the context of a government-based agency.

The ‘other’ category (5%) was recorded as a ‘third party logistics provider’, and for the context of this research, this will be interpreted as a wholesaler as this is the nature of the licence that all organisations in the sample hold.
Notwithstanding the comments above, there was a reasonable distribution across the remaining categories with most of the respondents being distributors.

6.3.1.1.4. Question 4 – Does your organisation outsource the warehousing function?

Rationale
Responses were interpreted in the context within which the organisations operate. For example, while an organisation may operate in the distribution of pharmaceuticals, the actual operation itself may not be within their direct control, which could be the case if operational aspects were outsourced. This is not to say that a respondent whose organisation outsources aspects of the operation would not understand the requirements; however, outsourced operations may influence the hands-on experience related to the challenges of the cold chain. This question indicated the degree to which respondent organisations outsource warehouse activities.

Results, analysis and interpretation

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>10.0%</td>
</tr>
<tr>
<td>Some warehousing is outsourced</td>
<td>35.0%</td>
</tr>
<tr>
<td>No</td>
<td>55.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Most respondents had at least some level of warehousing under direct control, with only 10% of respondents outsourcing operations. The low level of outright outsourcing is positive as it indicates a higher level of hands-on experience of respondents. As the sample population is based on organisations with a wholesale licence it is expected that 90% of the respondents have some level of their own warehousing. In some instances, these entities are third party providers who distribute on behalf of the manufacturers.
6.3.1.1.5. Question 5 – Does your organisation outsource the majority of the transportation functions?

Rationale
As discussed above this question aims for the same objective but from a transportation point of view.

Results, analysis and interpretation
Table 13 Question 5 – Does your organisation outsource the majority of the transportation functions?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>55.0%</td>
</tr>
<tr>
<td>Some transportation is outsourced</td>
<td>35.0%</td>
</tr>
<tr>
<td>No</td>
<td>10.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

The converse was true for transportation outsourcing where only 10% did not outsource transportation. Although there is a high level of transportation outsourcing when compared to the warehousing function, this is of less importance as the transportation vehicle is not the primary control point for quality but rather the cold chain packaging which is designed to maintain the required temperatures during transportation.

6.3.1.1.6. Question 6 – What is your job title?

Rationale
Job titles provided insight into the nature of the respondent’s job to ensure that the respondent was appropriate to provide insight for the research. In order to provide an indication of the appropriateness of respondents, job titles were analysed in terms of the nature of position. This would indicate that the respondents were of an appropriate level within the organisation to have the required expertise to provide the necessary insight for the survey.
Results, analysis and interpretation

Table 14 Question 6 – What is your job title?

<table>
<thead>
<tr>
<th>Category</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Director/executive</td>
<td>25%</td>
</tr>
<tr>
<td>Manager</td>
<td>55%</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>15%</td>
</tr>
<tr>
<td>Supervisor</td>
<td>5%</td>
</tr>
</tbody>
</table>

The results indicate that a high proportion (80%) of respondents were manager level and up which suggests that respondents were appropriate for the research. These findings would need to be corroborated by further questions related to experience.

6.3.1.1.7. Question 7 – What is the highest level of education you have completed?

Rationale

Level of education served as a further indicator of the degree to which respondents were suitable to provide the required insights for the survey. This is not to say that education is the only indicator; experience was also a crucial if not more relevant indicator. This will be discussed in Question 9.

Results, analysis and interpretation

Table 15 Question 7 – What is the highest level of education you have completed?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matric</td>
<td>15.0%</td>
</tr>
<tr>
<td>1 year post matric course (e.g. diploma/certificate)</td>
<td>0.0%</td>
</tr>
<tr>
<td>3 year post matric course (e.g. diploma/degree)</td>
<td>10.0%</td>
</tr>
<tr>
<td>4 year post matric course (e.g. Honours degree/B Tech)</td>
<td>30.0%</td>
</tr>
<tr>
<td>Master's degree or equivalent</td>
<td>40.0%</td>
</tr>
<tr>
<td>Doctorate degree or equivalent</td>
<td>0.0%</td>
</tr>
<tr>
<td>Post-doctorate degree</td>
<td>5.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
All respondents had at least a matric or higher qualification. A total of 85% of respondents had a 3-year degree/diploma or higher, with a relatively large proportion of them having a Master’s degree or equivalent, or higher.

6.3.1.1.8. Question 8 – Is your job primarily focused on quality or operations?

Rationale
As the research deals with both operational and quality aspects of cold chain management, it was crucial to ensure that the mix of respondents was not skewed to either side as this may have affected the conclusions of the research. The primary focus of the respondent’s job was used to categorise the respondent to ensure balanced results.

Results, analysis and interpretation
Table 16 Question 8 – Is your job primarily focused on quality or operations?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality</td>
<td>55.0%</td>
</tr>
<tr>
<td>Operations</td>
<td>45.0%</td>
</tr>
</tbody>
</table>

Although there was a slight bias towards the quality function, respondents were well balanced between the operational and quality functions of their organisations. This suggests that the results were not skewed in terms of a quality versus operations bias.

6.3.1.1.9. Question 9 – How long have you worked in the pharmaceutical industry (years)?

Rationale
Perhaps one of the most important indicators related to the appropriateness of respondents, the experience of respondents in the pharmaceutical industry was a key question to verify the sample.

Results, analysis and interpretation
On average respondents had 13.7 years’ pharmaceutical industry experience, with a minimum of 3 years and the maximum 40 years. The significant level of experience indicates a strong foundation to support the reliability of the results from respondents.
6.3.1.1.10. Question 10 – Rate your knowledge of distribution of temperature-sensitive pharmaceutical products

Rationale
As Question 9 related to the appropriateness of respondents, a self-rating of knowledge from a quality and operational point of view would indicate how the respondents view themselves. While this particular question could be highly subjective, the results were viewed in the context of previous questions related to job title, education and experience.

Results, analysis and interpretation

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Poor (1)</th>
<th>Low (2)</th>
<th>Medium (3)</th>
<th>High (4)</th>
<th>Very good (5)</th>
<th>Rating average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality knowledge</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>6</td>
<td>8</td>
<td>4.10</td>
</tr>
<tr>
<td>Operations knowledge</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>4</td>
<td>9</td>
<td>4.10</td>
</tr>
</tbody>
</table>

No respondents rated themselves below medium, while on average the scores were high levels of knowledge for both quality and operational aspects. Perhaps more importantly, ratings are the same for quality and operations, suggesting that results should not be skewed due to a bias related to a respondent’s inclination for either quality or operations.

6.3.1.1.11. Question 11 – What type of vehicles does your company use to distribute?

Rationale
Many factors may influence outbound operational costs. A key variable which may have an impact on the transportation cost component of outbound operational costs is the type of vehicle used, as there are a few options for an organisation. The results of this question were intended to assist in interpretation of other questions related to cost factors. Additionally, the results assisted in the identification of potential variability or consistency of transportation costs.
Results, analysis and interpretation

Table 18 Question 11 – What type of vehicles does your company use to distribute?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard bodied</td>
<td>25.0%</td>
</tr>
<tr>
<td>Insulated bodies</td>
<td>60.0%</td>
</tr>
<tr>
<td>Refrigerated (cooling only)</td>
<td>15.0%</td>
</tr>
<tr>
<td>Temperature-controlled (heating and cooling)</td>
<td>25.0%</td>
</tr>
<tr>
<td>Don’t know</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>10.0%</td>
</tr>
</tbody>
</table>

Most (60%) respondents’ organisations used insulated body vehicles for transportation of their products. However, the broad distribution may indicate potential variability in transportation costs across respondents, which is supported by the high level of outsourcing of transportation.

6.3.1.1.12. Question 12 – Which of the following delivery types do you do?

Rationale

Similar to the above question, the nature of the delivery types may influence the costs associated with transportation. For example, if a particular organisation has a significantly larger number of deliveries in outlying areas, they may experience higher transportation costs. This question therefore sought to identify if there were any significant variances across the categories specified.

Results, analysis and interpretation

Table 19 Question 12 – Which of the following delivery types do you do?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter DC (distribution centre)/between provinces</td>
<td>70.0%</td>
</tr>
<tr>
<td>Fine distribution</td>
<td>65.0%</td>
</tr>
<tr>
<td>Outlying areas</td>
<td>65.0%</td>
</tr>
<tr>
<td>Temperature-controlled (heating and cooling)</td>
<td>45.0%</td>
</tr>
<tr>
<td>Don’t know</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>10.0%</td>
</tr>
</tbody>
</table>
Results indicated relatively consistent delivery types across respondents. There was a slightly higher response rate for inter DC, which may be due to manufacturers who may do more inter DC and less fine distribution.

6.3.1.1.13. Question 13 – What size vehicles do you make use of?

Rationale

In line with Question 12, this question provided further context on cost variability related to transportation. Larger vehicles are likely to provide better economies of scale and in turn may affect the interpretation of transportation costs.

Results, analysis and interpretation

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small vehicle (±0.5 ton)</td>
<td>10.0%</td>
</tr>
<tr>
<td>Light vehicle (±1 ton to 4 tons)</td>
<td>80.0%</td>
</tr>
<tr>
<td>Medium vehicle (±8 tons)</td>
<td>45.0%</td>
</tr>
<tr>
<td>Large vehicle (±20-foot container or smaller)</td>
<td>45.0%</td>
</tr>
<tr>
<td>Very large (inter link/larger than 20-foot container)</td>
<td>35.0%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

The most commonly used vehicle was the light delivery vehicle (80%). This result would align with the logic that a larger number of smaller vehicles are required to distribute the same volume that can be transported in larger vehicles. Furthermore, the nature of fine distribution and outlying deliveries is conducive to smaller vehicle sizes. The ‘other’ category related to sea freight which was not considered as part of research. There was a fair response rate for large and very large vehicles, which would support the higher percentage of inter DC deliveries in Question 12 and which would likely be bulkier deliveries.
6.3.1.14. **Question 14 – Have you had to write off product due to failures in the cold chain?**

**Rationale**
Ultimately the need for cold chain management relates to the risk of temperature excursions. The most significant quantitative measure of the impact of such excursions would be product write-off related failures in the cold chain. However, respondents may not have figures at hand and may be apprehensive to indicate any quantitative data. Therefore, this question was only intended to identify if there had been any product write-offs at the respondents’ organisations, and was used as an indicator as to the scale of potential cold chain failure risks.

**Results, analysis and interpretation**

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Response per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>65.0%</td>
</tr>
<tr>
<td>No</td>
<td>35.0%</td>
</tr>
</tbody>
</table>

The respondents who indicated ‘no’ may not have been aware of excursions which had happened or may have had excursions but not necessarily written off product as the excursions may have not been extreme enough. Furthermore, considering that respondents may have been apprehensive to answer this question, 65% is a considerably high percentage. This supports the need for proper cold chain management and the potential for poor cold chain management to have a cost impact on the business.

**6.3.1.2. Risk rating**
The objective of the risk-related questions was to determine a risk rating for each element of the model. These ratings were a key component of the final analysis, in that they provided the required data to indicate the impact of the scenarios in the cost analysis on the non-conformance element. The overall risk rating was calculated by multiplying the results of Question 15 (probability/chance) by the results of Question 16 (degree/impact); these will be discussed later in this chapter.
6.3.1.2.1. Question 15 – Risk: Probability/chance

Rationale
The probability/chance rating of each element was used as one criterion to calculate the overall risk. The probability/chance represented the likelihood of a risk occurrence in the particular element.

Results, analysis and interpretation

Table 22 Question 15 - Risk: Probability/chance

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Highly improbable (1)</th>
<th>Unlikely (2)</th>
<th>Possible (3)</th>
<th>Likely (4)</th>
<th>Highly probable (5)</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>3.20</td>
<td>1.28</td>
<td>0.62</td>
</tr>
<tr>
<td>Warehouse/storage</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>2.15</td>
<td>0.88</td>
<td>0.42</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>3</td>
<td>6</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>2.45</td>
<td>0.83</td>
<td>0.40</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>2.35</td>
<td>0.93</td>
<td>0.45</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>2.35</td>
<td>1.09</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Transportation had the highest probability, while warehousing had the lowest probability. This is congruent with the rationale that warehousing provides a greater degree of control, while transportation has a lower level of control.

6.3.1.2.2. Question 16 – Risk degree/impact

Rationale
Question 16 provided the alternative criterion to question 15, namely the degree or impact, which represents the significance to which a risk, if it occurred, would affect the operation.
Results, analysis and interpretation

Table 23 Question 16 – Risk degree/impact

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Negligible impact</th>
<th>Slight impact</th>
<th>Tangible impact</th>
<th>Significant impact</th>
<th>Disastrous impact</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>4</td>
<td>3.45</td>
<td>1.05</td>
<td>0.50</td>
</tr>
<tr>
<td>Warehouse/ storage</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>3.50</td>
<td>1.32</td>
<td>0.63</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>2</td>
<td>9</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>2.90</td>
<td>1.37</td>
<td>0.66</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>4</td>
<td>3.35</td>
<td>1.27</td>
<td>0.61</td>
</tr>
<tr>
<td>Validation/ qualification</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>3.65</td>
<td>1.18</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Warehousing and validation had the highest risk in terms of impact, which makes sense in that, if something does go wrong the volume of stock exposed to the risk would be significant. Question 16 had higher overall risk composition, i.e. the chance of something going wrong is a lower contributor to the overall risk than the impact of when something does go wrong.

6.3.1.3. Estimated cost

Rationale

Question 17 very broadly determined the costs from highest to lowest, while Question 18 determined a broad percentage of total outbound costs for each element. These questions were cross-referenced against one another for consistency and used to cross-check the percentages determined in the cost analysis.

It was not likely that respondents would know or provide specific cost information and therefore it was necessary to determine this indicator in a broader manner.
6.3.1.3.1. Question 17 – Cost ranking

Results, analysis and interpretation

Table 24 Question 17 – Cost ranking

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>4</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>2.75</td>
<td>2.75</td>
<td>1.45</td>
<td>0.69</td>
</tr>
<tr>
<td>Warehousing</td>
<td>9</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>1.90</td>
<td>1.90</td>
<td>0.97</td>
<td>0.46</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3.25</td>
<td>3.25</td>
<td>1.33</td>
<td>0.64</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>10</td>
<td>1</td>
<td>3.25</td>
<td>3.25</td>
<td>1.12</td>
<td>0.54</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>11</td>
<td>3.85</td>
<td>3.85</td>
<td>1.50</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Average Rank

Noting that a lower rating means a higher cost, based on how this question was asked, the weighting was inverted in order to make comparison to Question 18 easier, i.e. a higher average rank indicates a higher cost. Based on this question the order of cost from highest to lowest was

- Warehousing
- Transportation
- Cold chain packaging and temperature monitoring (equal scores)
- Validation/qualification
6.3.1.3.2. Question 18 – Percentage estimate

Results, analysis and interpretation

Table 25 Question 18 – Percentage estimate

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Less than 5%</th>
<th>10% ±5%</th>
<th>20% ±5%</th>
<th>30% ±5%</th>
<th>40% ±5%</th>
<th>50% ±5%</th>
<th>60% ±5%</th>
<th>70% ±5%</th>
<th>80% ±5%</th>
<th>90% ±5%</th>
<th>Rating average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3.31</td>
</tr>
<tr>
<td>Warehousing</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2.81</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.53</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2.31</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.06</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation</td>
<td>30.63</td>
<td>25.16</td>
<td>13.41</td>
</tr>
<tr>
<td>Warehousing</td>
<td>25.00</td>
<td>20.00</td>
<td>10.66</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>7.33</td>
<td>7.99</td>
<td>4.28</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>18.13</td>
<td>19.05</td>
<td>10.15</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>13.75</td>
<td>15.00</td>
<td>7.99</td>
</tr>
</tbody>
</table>

Figure 37 Question 18 – Percentage estimate
This particular question required a deeper level of detail in that respondents were required to specify cost percentage ranges per cost element. Based on this question the order of total cost from highest to lowest was:

- Transportation
- Warehousing
- Cold chain packaging
- Validation/qualification
- Temperature monitoring

Although questions 17 and 18 are not fully aligned there are some consistencies which can be noted:

- Transportation and warehousing are the top two costs in both instances
- Cold chain packing is the middle cost in both instances
- Validation/qualification is in the bottom two costs in both instances
- The correlation between the two data sets is 0.65 which suggests a reasonably high correlation.

Furthermore, it must be considered that Question 18 is an aggregate of multiple responses with standard deviations ranging from 7.99 to 25.16 suggesting a high degree of variability, which would be expected considering the various types of respondent organisations. Nonetheless considering that it was not possible to collect specific cost figures, the above figures will be accepted as indicative for the purposes of the research. Furthermore, the actual figures are not the objective of the research but rather the determination of the relationship between the cost elements.

**6.3.1.4. Key factors**

**Rationale**

Questions related to key factors were used to determine what the respondents felt were the most important factors to consider within each element. This information was combined in the final interpretation in order to identify what the priority factors to consider would be based on the affected elements of a particular scenario.
Respondents were to rate the factors from highest importance to lowest importance, in the distribution of cold chain pharmaceutical products. It should be noted that a lower average rating is indicative of a higher rank/importance.

### 6.3.1.4.1. Question 19 – Non-conformance factors

Results, analysis and interpretation

Table 26 Question 19 – Non-conformance factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct - e.g. product write-offs</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>2.82</td>
<td>2.82</td>
<td>1.51</td>
<td>0.78</td>
</tr>
<tr>
<td>Remediation - e.g. identification, correction and reporting</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td>3.18</td>
<td>3.18</td>
<td>1.19</td>
<td>0.61</td>
</tr>
<tr>
<td>Regulatory - e.g. fines, legal action, recalls and suspended operations</td>
<td>8</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2.41</td>
<td>2.41</td>
<td>1.54</td>
<td>0.79</td>
</tr>
<tr>
<td>Market share - e.g. lost sales</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>3.29</td>
<td>3.29</td>
<td>1.45</td>
<td>0.74</td>
</tr>
<tr>
<td>Reputational - e.g. negative brand impact</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>3.29</td>
<td>3.29</td>
<td>1.36</td>
<td>0.70</td>
</tr>
</tbody>
</table>

- **Regulatory** – The regulatory factors introduce significant risk to the business if not appropriately adhered to; it therefore follows that these are rated as the most important factor for this question.
- **Direct** – Likely the most measurable of all the non-conformance factors, direct costs such as write-offs are rated as the second most important. These costs are the most tangible cost in this question resulting in a high rating.
- **Remediation** – Depending on the nature of issues to be corrected, these costs could be significant, for example, if air handling equipment must be installed to correct temperature excursions.
- **Market share** and **reputational** were rated as the least important factors. This may be due to these factors being less tangible and less likely in terms of risk.
6.3.1.4.2. Question 20 – Transport factors

Results, analysis and interpretation

Table 27 Question 20 – Transport factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume</strong> - physical size of the parcel to be transported</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>2.65</td>
<td>2.65</td>
<td>1.41</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>Weight</strong> - weight of the parcel to be transported</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>3.71</td>
<td>3.71</td>
<td>1.36</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>Mode of transport</strong> (i.e. road, air, sea, rail) - relates to the primary type of transportation e.g. road vehicle, airplane, ship or train</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>2.94</td>
<td>2.94</td>
<td>1.30</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>Type of transport equipment</strong> - based on the mode of transportation, the type of transport equipment relates to insulation, refrigeration and temperature control equipment</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>2.71</td>
<td>2.71</td>
<td>1.26</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Duration to destination</strong> - the total transportation time from dispatch to receipt at the specified end point</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>3.00</td>
<td>3.00</td>
<td>1.66</td>
<td>0.85</td>
</tr>
</tbody>
</table>

- Type of transport – The type of transport is a key factor in terms of the cost of transportation, and as such the type of transportation has been rated the most important factor.

- Volume and weight – Volume was rated as a significantly more important factor than weight. This may suggest that the typical cold chain shipment is bulkier than its weight and in turn transport is charged on volume rather than weight. This is likely to be due to the insulating materials used (such as polystyrene or polyurethane) which typically have a high volume-to-weight ratio as discussed in earlier chapters.

- Mode of transport and duration were rated very similarly; the mode of transport has a direct impact on the duration to destination. For example, an airfreight shipment to Cape Town is likely to reach the destination before a road shipment. Having said this, the impact on the cost still needs to be considered. This scenario will be discussed further in the cost analysis.
6.3.1.4.3. Question 21 – Warehouse factors

Results, analysis and interpretation

Table 28 Question 21 – Warehouse factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product storage</strong> (cold room and freezer) - cold room and freezer space required to hold cold chain packaging materials</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1.76</td>
<td>1.76</td>
<td>1.09</td>
<td>0.56</td>
</tr>
<tr>
<td><strong>Packaging storage</strong> (warehouse) - warehouse space required to hold cold chain packaging materials</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>3.29</td>
<td>3.29</td>
<td>1.16</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Electricity consumption</strong> - specifically related to the electricity required to power HVAC, air-conditioning, cold rooms and freezers</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>3.76</td>
<td>3.76</td>
<td>1.15</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>Packing of cold chain parcels</strong> - the activity of packaging a cold chain parcel for delivery to the end destination</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>3.53</td>
<td>3.53</td>
<td>1.46</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>Back-up power requirements</strong> - generators, UPS required to ensure consistent power to warehouse equipment</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2.65</td>
<td>2.65</td>
<td>1.37</td>
<td>0.70</td>
</tr>
</tbody>
</table>

- Product storage – It is a logical conclusion that this is the most important factor as this is the primary objective of the warehousing element.
- Backup power requirements – These follow second, probably due to the significant impact a risk occurrence would have on the bulk of the product being stored.
- Packaging storage – Being ranked third may come down to the bulky nature of the packaging material. As a result, the packaging material takes up more storage space and thus has a potentially significant impact on storage cost.
- Packing of cold chain parcels – This relates to the complexity and time required to pack cold chain parcels, which affect operational efficiencies as well as non-conformances in that a more complicated packing configuration may result in incorrectly packed parcels which may further result in product exposure and in turn impact the non-conformance element.
- Electricity consumption – These costs were ranked lowest in terms of importance.
6.3.1.4.4. Question 22 – Temperature monitoring factors

Results, analysis and interpretation

Table 29 Question 22 – Temperature monitoring factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of equipment (probes and recording device) used to monitor - the model and specifications of the equipment used to monitor temperature</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>2.65</td>
<td>2.65</td>
<td>1.22</td>
<td>0.63</td>
</tr>
<tr>
<td>Number of positions monitored - the number of probes used to monitor temperature</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2.88</td>
<td>2.88</td>
<td>1.22</td>
<td>0.63</td>
</tr>
<tr>
<td>Alarms and alerts - alarms that trigger when temperature exceeds predefined temperature limits</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>3.06</td>
<td>3.06</td>
<td>1.48</td>
<td>0.76</td>
</tr>
<tr>
<td>Harvesting, management and analysis of data - the process of collecting and interpreting temperature data</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>3.59</td>
<td>3.59</td>
<td>1.58</td>
<td>0.81</td>
</tr>
<tr>
<td>Calibration of probes - annual testing of probes to ensure they operate within the required accuracy limits</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2.82</td>
<td>2.82</td>
<td>1.55</td>
<td>0.80</td>
</tr>
</tbody>
</table>

- The type of equipment used – This is important because it will affect the cost of the system, functionality and accuracy of the data collected.
- Number of positions monitored and calibration – These were rated at a similar level of importance.
- Alarms and alerts – These are crucially important as they are a requirement of GDP.
- Harvesting – In last position this activity was not rated as a very high consideration, indicating that temperature monitoring may be more of a reactionary activity (in the event of an issue) rather than a proactive activity (monitoring for trends).
6.3.1.4.5. Question 23 – Cold chain packaging factors

Results, analysis and interpretation

Table 30 Question 23 – Cold chain packaging factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong> capability of cold chain shipper - the time that the cold chain shipper can maintain the temperature within the required temperature range</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>2.06</td>
<td>2.06</td>
<td>1.03</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Payload size</strong>/volume - the amount of product the cold chain shipper can hold</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>2.94</td>
<td>2.94</td>
<td>1.25</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Complexity</strong> of packaging configuration - the intricacy of the specific instructions used to pack the cold chain shipper</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>3.24</td>
<td>3.24</td>
<td>1.56</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Cost of packaging</strong> - the material cost of the packaging material, i.e. gel packs, insulated box and cardboard shippers, etc.</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>2.94</td>
<td>2.94</td>
<td>1.30</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>Reusability</strong> of packaging components - the capability and practicality of reusing cold chain shipping material</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td>3.82</td>
<td>3.82</td>
<td>1.47</td>
<td>0.75</td>
</tr>
</tbody>
</table>

- **Duration** – As the fundamental requirement of cold chain packaging is to sustain the temperature during transportation for a specific duration, it follows that this was rated as the highest importance.
- **Cost of packaging and payload size** – Cost of packaging was ranked slightly higher than the payload size. Both these factors have an impact on cost in that the payload affects the overall efficiency of the packaging when viewed from a cost per volume of product shipped.
- **Complexity** – This was rated relatively low. The complexity of the packing would be likely to have an impact on the factor related to the activity of packing the parcels in question 21. Both these factors were ranked at position number 4.
- **Reusability** was rated the lowest in terms of importance. This may be as a result of the challenges (cost, management and quality control) associated with the reverse logistics in trying to reuse cold chain packaging systems.
6.3.1.4.6. Question 24 – Validation/qualification factors

Results, analysis and interpretation

Table 31 Question 24 – Validation/qualification factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Rating average</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Margin of error (95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation of systems (ERP/accounting system and temperature monitoring)</td>
<td>7</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>2.59</td>
<td>2.59</td>
<td>1.54</td>
<td>0.79</td>
</tr>
<tr>
<td>Validation and temperature Mapping of warehouse</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2.65</td>
<td>2.65</td>
<td>1.54</td>
<td>0.79</td>
</tr>
<tr>
<td>Validation and temperature Mapping of cold room</td>
<td>4</td>
<td>6</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>2.18</td>
<td>2.18</td>
<td>0.81</td>
<td>0.42</td>
</tr>
<tr>
<td>Validation and temperature Mapping of freezer room</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>3.94</td>
<td>3.94</td>
<td>1.09</td>
<td>0.56</td>
</tr>
<tr>
<td>Validation and temperature Mapping of cold chain shippers</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>3.65</td>
<td>3.65</td>
<td>1.27</td>
<td>0.65</td>
</tr>
</tbody>
</table>

- Cold room and warehouse – The cold room runs at a tighter range than the warehouse (typically 2 °C to 8 °C vs 15 °C to 25°C respectively) so it follows that the validation of the cold room would be more important than the warehouse validation. Furthermore, it is the cold room where cold chain products are stored, making the validation of the cold room crucial to proper control of storage conditions.
- ERP/temperature monitoring system – Systems track and record all the data from the day-to-day operation, and thus validating these systems is crucial in order to ensure this information is reliable.
- Cold chain shipper – This is a surprising result as it would have been expected to be of higher importance considering the higher risk rating for transportation as a whole. Validation of the cold chain shipper could be viewed as a way of mitigating such risk.
- Freezer – As the freezer is typically used only to store gel packs and only seldom (only 29% of respondents) used for product storage, this result was expected.
6.3.1.5. Relationship between elements

The relationship-based questions were based on the structure shown in Table 32 below, where the underlined elements were swapped until each combination had been asked as follows:

- Transport and non-conformance
- Transport and validation/qualification
- Transport and cold chain packaging
- Transport and temperature monitoring
- Transport and warehouse
- Warehouse and quality
- Warehouse and validation/qualification
- Warehouse and cold chain packaging
- Warehouse and temperature monitoring

Table 32 Question example

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Time</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Quality</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Rationale

The questions related to the relationship between the six elements form the foundation to achieve the objective of the research. Each question allowed the respondent to provide a response in terms of three aspects of each relationship, namely cost, time and quality. This was done to ensure that the respondents could express partial agreement/disagreement from multiple aspects. Furthermore, the intention was to trigger deeper consideration from respondents and these three aspects allowed for more detailed analysis of the nature of the relationships between the cost elements.

Responses were assigned a weight based on the answer as given in Table 33 below.
Table 33 Response options

<table>
<thead>
<tr>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree nor agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2</td>
<td>-1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Using this weight scale, responses were categorised for analysis. Furthermore, responses were aggregated by element and the three aspects of cost, time and quality.

6.3.1.5.1. Questions 25 to 29 (Transportation)

Results, analysis and interpretation

Question 25 – Transportation and non-conformance

Table 34 Question 29 – Transportation and non-conformance

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation - Non-conformance</td>
<td>1.27</td>
<td>1.25</td>
<td>1.00</td>
<td>1.56</td>
</tr>
</tbody>
</table>

Figure 38 Question 29 – Transportation and non-conformance

Only one respondent strongly disagreed with the relationship between transportation and non-conformance, from a time perspective. The quality aspect had the highest rating, which supports the earlier risk rating assigned to transportation as one of the higher risk
elements. Cost and time have the same rating. Overall, respondents agree that there is a cost, time and quality relationship between transportation and non-conformance.

**Question 26 – Transportation and validation/qualification**

<table>
<thead>
<tr>
<th>Table 35 Question 26 – Transportation and validation/qualification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transportation - Validation/Qualification</strong></td>
</tr>
<tr>
<td>Transportation - Validation/Qualification</td>
</tr>
</tbody>
</table>

Only two respondents disagreed with the cost and one with the time aspect of the relationship between transportation and validation/qualification. Validation/qualification is a critical aspect of GDP and is primarily focused on the verification of equipment and processes to ensure product quality. It therefore makes sense that quality emerged as the most significant aspect followed by time and cost respectively.
Question 27 – Transportation and cold chain packaging

Table 36 Question 27 – Transportation and cold chain packaging

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation - Cold chain</td>
<td>1.33</td>
<td>1.44</td>
<td>1.13</td>
<td>1.44</td>
</tr>
<tr>
<td>packaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 40 Question 27 – Transportation and cold chain packaging

No respondents disagreed with any aspect within the relationship between transportation and cold chain packaging. Quality and time were the highest rated for this relationship. From a quality perspective, the cold chain packaging is the last line of protection for the product once it is out in the uncontrolled environment during transportation. The additional time required to pack cold chain parcels may also have an impact on the flexibility of managing dispatch and transportation. Cold chain parcels may need to be packed and dispatched at specific times of day due to: weather conditions; cut-off times of outsourced transportation service providers; or air freight flight times. Organisations must also consider that, once packed, the cold chain parcel may have a specific lifespan and the required temperature must be maintained for the duration of this transport.
Table 37 Question 28 – Transportation and temperature monitoring

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation – Temperature monitoring</td>
<td>1.02</td>
<td>0.81</td>
<td>0.88</td>
<td>1.38</td>
</tr>
</tbody>
</table>

Quality had the highest agreement level, which relates to the significant impact temperature monitoring has on quality in terms of detection of risk occurrences such as temperature excursions. Furthermore, temperature monitoring provides key information in terms of the determination of the corrective action in the event of an excursion; the duration and temperature reached is crucial in deciding if the product is still safe for the patient.
Question 29 – Transportation and warehousing

Table 38 Question 29 – Transportation and warehousing

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transportation - warehouse</td>
<td>0.92</td>
<td>0.81</td>
<td>0.75</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Figure 42 Question 29 – Transportation and warehousing

The quality component of this relationship had the highest rating at 1.19 compared to time and cost at 0.81 and 0.75 respectively. This may indicate that the significance of the relationship between transportation and warehousing lies in the potential impact on product quality rather than to time or cost.
6.3.1.5.2. Questions 30 to 33 (Warehousing)

Results, analysis and interpretation

**Question 30 – Warehousing and non-conformance**

**Table 39 Question 30 – Warehousing and non-conformance**

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warehouse - Non-conformance</td>
<td>1.00</td>
<td>0.94</td>
<td>0.75</td>
<td>1.31</td>
</tr>
</tbody>
</table>

*Figure 43 Question 30 – Warehousing and non-conformance*

The cost aspect in this relationship was rated as the lowest. This may once again relate back to the risk rating for warehousing in that the risk within the warehouse is lower in terms of the probability rating, which directly relates to a cost impact on non-conformance. This, therefore, may lower the perceived relationship between the warehousing element and non-conformance, in turn resulting in the slightly lower rating for the cost aspect.
In the warehousing category, the relationship between warehousing and validation/qualification is the highest. This may be due to the fact that the warehouse contains the majority of the equipment that must be validated/qualified, including the air handling system, cold room, temperature monitoring system, ERP system and generator.
**Question 32 – Warehousing and cold chain packaging**

**Table 41 Question 32 – Warehousing and cold chain packaging**

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warehouse - Cold chain packaging</td>
<td>1.06</td>
<td>1.06</td>
<td>1.00</td>
<td>1.13</td>
</tr>
</tbody>
</table>

**Figure 45 Question 32 – Warehousing and cold chain packaging**

No particular aspect stands out for the relationship between warehousing and cold chain packing. Nonetheless most respondents agreed that there is a relationship between the two elements.
Question 33 – Warehousing and temperature monitoring

Table 42 Question 33 – Warehousing and temperature monitoring

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>Time</th>
<th>Cost</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warehouse - Temperature monitoring</td>
<td>1.17</td>
<td>1.13</td>
<td>1.00</td>
<td>1.38</td>
</tr>
</tbody>
</table>

Figure 46 Question 33 – Warehousing and temperature monitoring

Similar to the transportation relationship with temperature monitoring, warehousing also had a high quality rating related to temperature monitoring. This is supported by the fact that temperature monitoring is a key component of GDP as discussed in earlier chapters.

6.3.1.5.3. Combined results and analysis

A 5-point scale was selected in order to ensure that respondents were not forced to choose an opinion either for or against if they did not feel strongly about that opinion. It is therefore important to note that overall there were very few respondents, namely 11%, who selected the option ‘neither disagree nor agree’. This therefore suggests that where alternative options were selected, respondents truly agreed/disagreed with the particular question, which supports the integrity of the research.
6.3.2. Summary of survey findings

6.3.2.1. Relationship determination

In order to provide an overview of the findings of the relationship determination questions, results were assessed on the average rating for each aspect (cost, time and quality) by relationship. Furthermore, each relationship was assigned an overall score based on the feedback from respondents (see Table 43).

Table 43 Summary of results by relationship

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Average Score</th>
<th>Score by Aspect</th>
<th>Average by Transportation and Warehousing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Time</td>
<td>Cost</td>
</tr>
<tr>
<td>Transport Cost - Non Conformance Cost</td>
<td>1.27</td>
<td>1.25</td>
<td>1.00</td>
</tr>
<tr>
<td>Transport Cost - Validation/ Qualification Cost</td>
<td>1.32</td>
<td>1.13</td>
<td>1.31</td>
</tr>
<tr>
<td>Transport Cost - Cold Chain Packaging Cost</td>
<td>1.33</td>
<td>1.44</td>
<td>1.13</td>
</tr>
<tr>
<td>Transport Cost - Temperature Monitoring Cost</td>
<td>1.02</td>
<td>0.81</td>
<td>0.88</td>
</tr>
<tr>
<td>Transport Cost - Warehouse Cost</td>
<td>0.92</td>
<td>0.81</td>
<td>0.75</td>
</tr>
<tr>
<td>Warehouse Cost - Non Conformance Cost</td>
<td>1.00</td>
<td>0.94</td>
<td>0.75</td>
</tr>
<tr>
<td>Warehouse Cost - Validation/ Qualification Cost</td>
<td>1.23</td>
<td>1.31</td>
<td>1.00</td>
</tr>
<tr>
<td>Warehouse Cost - Cold Chain Packaging Cost</td>
<td>1.06</td>
<td>1.06</td>
<td>1.00</td>
</tr>
<tr>
<td>Warehouse Cost - Temperature Monitoring Cost</td>
<td>1.17</td>
<td>1.13</td>
<td>1.00</td>
</tr>
<tr>
<td>Overall Average</td>
<td>1.15</td>
<td>1.10</td>
<td>0.98</td>
</tr>
</tbody>
</table>

On analysis of this data, the majority (eight) of the nine relationships had a rating of at least 1, which would translate to an ‘agree’ rating. The relationship with the lowest average rating (transportation and warehouse) was marginally below a rating of 1 at 0.92. Overall, it can therefore be accepted that the findings of the survey were that respondents in the sample agreed that there is a relationship between the six elements as defined by the nine relationships.

The strongest relationship was between transportation and validation, primarily driven by the high quality and cost aspects of this relationship. This could be related to the higher risk associated with transportation making validation/qualification a crucial requirement. Additionally, validation/qualification in the transportation element may be more difficult and costly due to the lower levels of control.
When comparing which aspect was the most significant within the relationships, quality (1.36) emerged as the most crucial of the three aspects. Time (1.10) and cost (0.98) were rated at very similar importance levels, marginally above and below the ‘agree’ rating of 1. There was no significant bias in terms of the nature of the position of respondents as there was a good balance between operational (45%) and quality (55%) focus, as per question 8. The high ‘quality’ relationship between cost elements is likely due to the fact that quality as a whole is a crucial aspect across the pharmaceutical supply chain.

When comparing the relationship between transport and warehouse cost against the other cost elements, it is clear that transport cost had a slightly stronger relationship with the other cost elements, at 1.17 compared to warehousing at 1.08. Considering that transport cost had a higher level of outsourcing, this could be a contributing factor to the stronger relationship in that the respondents have less control over the physical transportation and must therefore engage more in the other cost elements in order to influence the cost, time and quality aspects of transport cost.

The risk factor would directly correlate to non-conformance in that a non-conformance may be described as the occurrence and impact of a risk. The relationship of transport and warehouse cost with non-conformance cost is supported by the responses to the risk analysis in that that transportation (3.33) had a higher risk overall when compared to warehouse cost (2.83), risk figures will be discussed further in the risk analysis section below. A similar pattern is evident in the strength of the relationship between transport cost (1.27) and non-conformance cost being higher than warehouse cost (1.00). Furthermore, the relationship between transport cost and non-conformance cost had the highest rating (1.56) across all cost elements in terms of the quality aspect.

Overall, it is clear that respondents agree with the relationships indicated, and based on the survey results there is indeed a relationship between the elements identified. The results thus support the first of the secondary objectives of the research in confirming these relationships.
6.3.2.2. Key factors

Figure 47 below illustrates the various key factors based on the average ratings from respondents. Using this diagram, it is possible to identify which factors within each element respondents considered to be least and most important. The results of the key factors will be analysed further in Chapter 7.
6.3.2.3. Risk analysis

The weighted average for each risk aspect (probability and impact) was calculated in order to determine the total risk for each element. The risk rating was based on a 5-point scale as per Figure 48 below.

![Risk matrix](image)

The results of the risk analysis are indicated in Table 44 below.
Using the data collection in questions 15 (probability) and 16 (impact), the risk of each element was determined. The relationship risk rating was then determined using an average of the respective elements. The impact rating was higher for all elements when compared to probability. The probability may be rated lower due to the significant controls that GMP and GDP introduce into the supply chain. If a risk does occur, the impact would still be high due to the nature of the products being distributed and the potential impact on patient safety.

While probability was rated lower than impact overall, in the instance of the transport cost element it was rated significantly higher than other elements. This is likely to be because transportation, by its nature, is a higher risk element as a result of the high environmental variability and reduced control of the product. The transport cost element contrasts significantly with warehouse cost which has a much lower probability risk rating likely due to the higher degree of control over the product. Of interest is the impact rating for the warehouse cost element which is marginally higher than that of transport cost; it is probable that this is due to the quantity and value of product stored in the warehouse. In the event of a risk occurrence the exposure of product is significantly higher, i.e. a whole warehouse of product is at risk.
The highest impact rating was related to validation/qualification cost. If one considers that validation/qualification is the process of confirming that the required equipment or process performs as defined, it is not difficult to understand why a risk occurrence in this element would have a significant impact. If the equipment or process is being used under the impression that the equipment or process is suitable while it is in fact not, product could be exposed to undesirable conditions which in turn could have a significant impact on product quality.

The second part of Table 44 above has identified the risk between relationships by multiplying each elements’ risk with the transport and warehouse element risks respectively. This table demonstrates that the relationship between the transport and validation/qualification elements is the highest at 3.16, with the relationship between the warehouse and temperature monitoring elements being the lowest at 2.75.

6.4. Cost analysis results

The purpose of the cost analysis is to further confirm the relationships between the cost elements identified from a quantitative perspective, as well as to assess the practical impact of these relationships. The cost analysis together with the survey will both be key inputs into the final verification of the relationships between the various elements identified in Chapter 4.

6.4.1. Review and interpretation of cost analysis

Based on the researcher’s consulting experience, a baseline cost structure was developed for a pharmaceutical distribution organisation. This baseline cost was constructed in the context of two different supply chain models. The first model was a centralised distribution model, while the second was a decentralised distribution model. The baseline cost for each of the models served as a benchmark against which to compare a series of scenarios. Scenarios were developed based on possible changes to an outbound distribution operation. The benchmark was then replicated changing only the parameters as defined by the particular scenario being tested. The impact on total cost was then analysed to determine the impact of the scenario on the other cost elements.
Non-conformance cost was treated differently to other costs in that the monetary cost of non-conformance was not calculated directly. The reason for this was due to the many variables and the difficulty in measuring the non-conformance cost. For example, it is very difficult to measure the cost of potential penalties or litigations as these are not a standard cost of distribution. Therefore, non-conformance was reviewed qualitatively in terms of what the risk impact of the scenario change would potentially be.

It is important to note that while every effort was taken to ensure an accurate cost analysis, the costs could vary depending on the specific situation of an organisation. The costs used are based on quotes received and applied to the cost structure as mentioned above. The important consideration, however, is not the actual costs; rather, the key concern of this analysis is to determine the impact on the other cost elements.

6.4.1.1. Model A and B baseline cost determination and assumptions

The fundamental consideration in terms of the baseline cost determination is to ensure that the appropriate costs and proportion of cost were built into the total cost. This stems from the focus of the research in terms of outbound distribution of cold chain products.

- Costs that were included:
  - Any cost directly associated with the outbound distribution activity. For example, the picker’s salary was included while the warehouse manager’s salary was not, as it is not a direct cost associated with cold chain activity.

- Cost proportion:
  - Based on the nature of the cost, either the full cost or a proportion based on an appropriate unit of measure was used to allocate a portion of the cost. For example, the packaging cost associated with cold chain parcels was 100% allocated, while the warehouse rental cost was allocated based on the ratio of space utilisation for cold chain activities.

A key assumption was that only customers in the Johannesburg, Cape Town and Durban regions would be serviced in these scenarios. Certain outlying routes from these regions were considered as part of the scenarios. The outlying routes were determined in terms of distance (178 km) from these regions.
6.4.1.1.1. Model A – Centralised distribution (24-hour transport service level)

6.4.1.1.1. Transportation

Costs related directly to the transportation activities included:

- Vehicle capital cost – Based on the assumed delivery volumes and routes, three panel vans with a payload of 3 200 litres (3.2 cubic metres) were selected. The capital cost was calculated over 72 months at a 9% interest rate.
- Drivers’ salaries – Provision for three drivers was made at a market-related salary.
- Fuel, maintenance and insurance costs – Based on the average daily routes, mileage for each vehicle was determined over a monthly period. Based on this mileage and RFA cost schedules, the fuel, maintenance and insurance costs were calculated.
- Outsourced delivery costs – For each model it was assumed that regional deliveries were executed by an outsource partner, from the appropriate point of departure. Costs for Cape Town and Durban, local (city centre and surrounding) and outlying (outside of the city centre and surrounding), for each container size from a reputable courier company were used.

6.4.1.1.2. Warehousing

In the context of this study, warehousing refers to all space requirements related to the storage and distribution of cold chain products. This therefore primarily refers to the space required for the cold room and associated equipment and processes. Warehousing cost relates to the costs associated with the outbound distribution process from storage, picking, packing and dispatching of cold chain goods. Warehousing costs that were considered included:

- Warehouse rental – Based on the proportion of the area of the warehouse required for the cold room and cold chain packaging storage the appropriate amount of monthly rental was allocated.
- Handling equipment – Handling equipment was based on a monthly rental and maintenance agreement.
• Staff salaries – These were based on market-related salaries for two pickers/packers and one administrator.

• Generator – A 100 kVA generator which would support critical equipment only (i.e. cold room, monitoring equipment, etc.) was included.

• Cold room capital cost – The cold room was based on a 6 m × 7 m × 2.8 m area, including the cooling systems (coil, control board, blowers, etc.).

• Electrical consumption – This cost was calculated using a tool available from Eskom, assuming the two 13 kW condensers for the cold room run for a total of 20 hours per day, as these units run on an intermittent basis.

• Freezer unit – A commercially available 481 litre chest freezer was priced for the conditioning of gel packs for the cold chain packaging.

6.4.1.1.1.3. Temperature monitoring
Temperature monitoring costs are considered in terms of storage and transportation temperature monitoring as different types of technology are required to meet the requirements.

• Storage monitoring – A continuous monitoring system with the appropriate level of prequalification was selected. The prequalification of the system means less effort is required in order to qualify the system for use in a pharmaceutical environment. Eleven temperature monitoring probes were provisioned:
  o Five probes within the cold room as follows: two to monitor the warmest positions, two for the coldest positions and one at the door. The warmest and coldest positions were defined by the cold room temperature mapping and validation which is discussed under the validation/qualification cost element.
  o Two probes to monitor the warmest and coldest positions in the freezer, with one in each position.
  o Two probes to monitor the temperature within the warehouse around the cold room area.
- Two probes to monitor the temperatures outside the warehouse as external environment conditions could affect the warehouse and in turn the cold room.

- Transportation monitoring – In order to monitor temperatures during transportation a different technology is required due to the mobile nature of transportation. For this application a small temperature-monitoring device with a built-in battery, which is downloaded on retrieval of the device, was considered for the cost analysis. Due to the volume of shipments not every parcel can be monitored, therefore a sample-based approach to monitoring was used. The sample is based on three different routes being monitored on a daily basis five days a week. Up to three working days may be required to retrieve the loggers and therefore sufficient loggers for eight days were provisioned. On each route two loggers were provisioned, one to be placed within the parcel and one to be placed outside the parcel to gather environmental temperature data.

- Calibration – Pharmaceutical requirements state that all monitoring equipment should be calibrated on an annual basis. Therefore, all probes related to both storage and transportation monitoring would require calibration (MCC, 2012). These costs were included.

- Analysis – The above costs relate specifically to the collection of accurate data. The objective of temperature monitoring is not to collect data for the sake of collecting data. This data must be collated, analysed and interpreted to identify issues, non-conformances and trends that must be used to correct or improve the storage and transport temperature-related conditions. The associated costs were calculated on the average salary of a distribution pharmacist converted into an hourly rate and multiplied by the estimated time to review the number of data sets generated on a monthly basis.

6.4.1.1.1.4. Cold chain packaging

Cold chain packaging costs relate to the materials used to pack the cold chain packaging system. As there were two sizes of containers, a total cost for each container size was determined and multiplied by the number of shipments that would be required for each
container payload size. The costs of these containers were based on a 24-hour duration within the 2 °C to 8 °C requirement.

6.4.1.1.1.5. Validation/qualification
Validation/qualification was treated in a similar way to temperature monitoring in that there are two distinct categories, namely storage and transportation. Furthermore, both initial as well as ongoing validation and qualification costs have been considered.

- Storage validation/qualification – Costs were provisioned for the validation and qualification of: warehouse, cold room, freezer, temperature monitoring system, ERP system and the generator.
- Transportation validation and qualification – This cost specifically applies to validation of the insulated cold chain containers.

6.4.1.1.2. Model B – Decentralised distribution (24-hour transport service level)
In order to determine the baseline costs for Model B, the costs were primarily based on the same principles and costs as defined in Model A. The costs were adjusted as appropriate to account for the decentralised component of Model B.

6.4.1.1.2.1. Transportation
The following adjustments were made to the transportation costs:

- Drivers’ salaries – The number of drivers required for Model B was adjusted appropriately for the regional distribution centres.
- Owned vehicles – An additional vehicle was added dedicated to the replenishment of the regional distribution centres.
- Outsourced delivery costs – The regional distribution centres were costed on the basis of outsourced transportation in order to ensure consistency between the two models. The point of origin was adjusted to the appropriate region.

6.4.1.1.2.2. Warehousing
In order to calculate the costs related to the regional distribution centres, the costs were calculated based on the proportion of volume at the regional distribution centres, in
relation to the main distribution centre. Certain fixed cost components remained the same due to the nature of these costs.

6.4.1.1.2.3. Temperature monitoring
The additional distribution centres would require further monitoring for the storage at the regional distribution centres. From a transportation monitoring perspective, an additional route was added at the main distribution centre for the replenishment routes to the regional distribution centres.

6.4.1.1.2.4. Cold chain packaging
As the service level for Model A remains at 24 hours, the duration within the 2 °C to 8 °C requirements of the cold chain packaging remained at 24 hours for Model B as well.

6.4.1.1.2.5. Validation/qualification
From a validation perspective, the costs related to the validation of the cold chain packaging remain the same; however, the costs related to the validation of regional distribution centres were added to the validation and qualification costs.

6.4.1.2. Scenarios
The scenarios that were ultimately selected were based on the consideration of the impact on non-conformance. As the highest level of risk was determined to be during transportation, the transport service level was considered to be the primary driver of risk that could have an impact on the non-conformance element.

On this basis two scenarios were tested for each distribution model, resulting in four scenarios, related to transportation. First was a reduction in the transportation service level from 24 hours to 48 hours, and secondly an increase of the service level from 24 hours to 18 hours (see Figure 49).
These scenarios were then tested for each model resulting in four scenarios, namely A1, A2, B1 and B2. Each scenario was tested against the respective distribution model, adjusting each cost element within the cost analysis as appropriate based on the impact of the change in the transportation service level. In order to provide further depth to the analysis, a third scenario, a comparison between the two benchmark models, was also conducted resulting in a fifth scenario. Cost schedules for each scenario are available in Annexures 2, 3, 4, 5, 6 and 7. These schedules form a high level overview of the costs used for the analysis. Figure 50 below provides a summary of the benchmark and related scenarios.
6.4.2. Summary and analysis of cost analysis

6.4.2.1. Benchmark cost determination

6.4.2.1.1. Model A – Centralised distribution (24-hour service level)

Refer to Figures 51 and 52 above for the total cost of Benchmark A and cost breakdown of Model A respectively.

- Transport cost: The delivery split between local (i.e. within the province of the warehouse) and regional (outside of the province of the warehouse) was 66% and 34%, based on the data used for the cost analysis, respectively. As one might
expect, however, distribution to the regional areas was more expensive, driven by two key factors. First is the geographic increase in distance, and secondly, regional distribution was executed using third party couriers. When analysing the costs associated with transportation, local transportation costs attributed only 8% of total transportation costs while the regional cost attributed the balance at 92%.

- Cold chain packaging cost: Being the second most significant cost element, packaging costs are driven solely by the actual cost of the various packaging components, insulated containers, gel packs and shippers. While it may be possible to reuse some of these containers, the baseline cost model has assumed that there will be no reuse of these containers as the reverse logistics management can become challenging and the quality of returned containers cannot be guaranteed.

- Warehouse cost: Due to the centralised nature of the warehousing in the baseline cost, the warehousing costs were relatively low. Having said this, it is important to note that these costs were proportionate based on the volume of cold chain product (20%) relative to the total product distribution.

- Validation/qualification cost: 87% of the validation costs were related to the validation of the cold chain packaging system, while the balance was associated with infrastructure such as warehouse, cold room, temperature monitoring system, etc. The significant difference between these figures is largely due to the fact that some of the infrastructure costs were assigned with only the appropriate cost based on the volume of cold chain product, whereas the costs related to the cold chain packaging validation was 100% allocated as these validation activities are specific to cold chain product requirements.

- Temperature monitoring cost: Temperature monitoring came in as the lowest cost, with about 50% of this cost being driven by the human resource requirements to review the temperature monitoring data. This is a cost many organisations do not always consider as it is typically a sunk cost, i.e. the individual is already on the pay roll. The cost must be considered as this individual could be doing other productive activities. It should be noted that temperature monitoring was calculated
on the basis that parcels would be monitored on a sample basis. If every parcel were to be monitored this cost would be likely to increase significantly.

6.4.2.1.2. Model B – Decentralised distribution (24-hour service level)

Refer to Figures 53 and 54 above for the total cost of Benchmark B and cost breakdown of Model B respectively.
• Transport cost: As Model B is based on a decentralised model, it provides the potential opportunity for the use of owned vehicles at regional level. However, for the purposes of the research in order to maintain consistency, the regional distribution centres would continue to make use of the same third party courier for the distribution in the regions, the main difference being that the stock would already be in the region. Regional replenishment would take place with an additional vehicle dedicated to this function.

• Cold chain packaging cost: While it is likely that some routes and customers may experience an improved service level, the minimum transport service level remains 24 hours and therefore the cold chain packaging must still be able to sustain this timeframe as per Model A.

• Warehouse cost: In Model B the main distribution centre remained, although the cost was reduced proportionately to the reduction in space requirements for product that would now be distributed at a regional level. An additional two regional distribution centres were added to the cost analysis.

• Validation/qualification cost: Due to the additional regional distribution centres, additional validation activities would be required in order to ensure compliance of the facilities.

• Temperature monitoring cost: Similar to the validation/qualification cost element, additional temperature monitoring systems would be required for the additional two facilities. Additional monitoring probes for monitoring of packages on a sample basis were also provided for each facility. The additional monitoring data generated would also create additional time spent to analyse and report on the data which was also built into the cost analysis for Model B.

6.4.2.1.3. Cost cross-referencing (Survey and cost analysis)

In order to verify the costs used for the cost analysis, the benchmark costs determined above have been cross-referenced to Questions 17 and 18 of the survey for congruence. As it is not possible to verify actual cost figures, the verification will be done in terms of
ranking the costs from highest to lowest. Table 45 below has ranked each cost element in this manner for Questions 17 and 18, Benchmark A and Benchmark B.

Table 45 Cost cross-referencing – Survey and cost analysis

<table>
<thead>
<tr>
<th>Cost Score</th>
<th>Question 17</th>
<th>Question 18</th>
<th>Benchmark A</th>
<th>Benchmark B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest</td>
<td>Warehouse Cost</td>
<td>Transportation</td>
<td>Transportation</td>
<td>Transportation</td>
</tr>
<tr>
<td></td>
<td>Transportation</td>
<td>Warehouse Cost</td>
<td>Cold Chain Packaging Cost</td>
<td>Cold Chain Packaging Cost</td>
</tr>
<tr>
<td></td>
<td>Cold Chain Packaging Cost</td>
<td>Cold Chain Packaging Cost</td>
<td>Warehouse Cost</td>
<td>Warehouse Cost</td>
</tr>
<tr>
<td></td>
<td>Temperature Monitoring Cost</td>
<td>Validation/Qualification Cost</td>
<td>Validation/Qualification Cost</td>
<td>Validation/Qualification Cost</td>
</tr>
<tr>
<td>Lowest Cost</td>
<td>Validation/Qualification Cost</td>
<td>Temperature Monitoring Cost</td>
<td>Temperature Monitoring Cost</td>
<td>Temperature Monitoring Cost</td>
</tr>
</tbody>
</table>

Although each cost element is not in the exact same ranking across each of the above cost sources, there are some important consistencies that can be identified. First, the transport, warehouse and cold chain packaging costs are always in the top three highest costs, with transport being the highest cost in three instances. Validation/qualification and temperature monitoring costs are in the bottom two costs in all instances, with temperature monitoring being the lowest and validation/qualification being the second lowest in three instances. On this basis, the costs identified for the cost analysis are considered to be appropriate, understanding that exact costs are not imperative for this study.
6.4.2.2. Model A scenario analysis

6.4.2.2.1. Scenario A1: 24-hour service level to 48-hour service level

Figures 55 and 56 above provide a cost breakdown of Scenario A1 and the percentage change per element respectively.
The service level in this particular scenario makes specific reference to the duration within which it is expected that the third party transportation provider must deliver the goods. This is of particular importance in the case of cold chain pharmaceuticals, in that this service level could have a significant impact on non-conformance if the service level is not met. This is due to the fact that the cold chain packaging containers have a predetermined effective lifespan once they are packed, and therefore the parcel must be delivered within the lifespan of the cold chain packaging. As can be seen in the graph in Figure 56 above, Scenario A1 had cost implications for all elements except the warehousing element. On analysis, the initial cost reduction in the change to the transportation element showed a 39% reduction in transportation costs. However, on further analysis of the same scenario, in terms of the total cost, there was only a 10% decrease in total cost. This was due to the impact that the change had on the other elements.

- **Transport cost:** Adjusting the service level from 24 hours to 48 hours has a major impact on transportation costs. Specifically, the impact is on the regional distribution, which constitutes the majority of the transportation cost. By reducing the service level to 48 hours the regional distribution costs were reduced by an average of 51%, with a total decrease of 39% for the all the transportation costs.
- **Warehouse cost:** There was no specific impact on the warehousing element.
- **Temperature monitoring cost:** Due to the longer delivery time, more temperature monitoring devices were required as the return of the devices would take longer. Furthermore, these additional devices would need to be calibrated, and the data from the devices reviewed and analysed. This resulted in a 4% increase in temperature monitoring costs.
- **Cold chain packaging cost:** In order to maintain the required temperature for the increased duration of the service level, the configuration required additional thermal capacity, which increased the cost per cold chain package. This increase was due to two factors:
  - The increased thermal capacity was achieved through the addition of gel packs to the configuration. These additional gel packs resulted in a 10%
and 21% increase in the cost of the actual packaging for the small and large box respectively.

- In order to add this additional thermal capacity, the payload (available space for product) size was reduced to accommodate the additional gel packs. This in turn resulted in a 43% and 16% reduction in payload volume respectively, which ultimately meant a corresponding increase in the number of cold chain packages required to meet the same distribution volume requirements. The net effect of these factors resulted in a 48% increase in cold chain packing costs.

- Validation/qualification cost: The change in the cold chain configuration would require the new configuration be re-qualified. This cost was added to the validation/qualification costs and amortised over a five-year period. The result of this was a 10% increase in validation/qualification costs.

- Non-conformance cost: As previously discussed, non-conformance would be considered in terms of risk rather than actual cost. The risk factor to consider in terms of the change in Scenario A1 would be the increased time the packaging would spend in less controlled conditions during transportation. This would likely increase the probability of a risk occurrence, while the impact would remain the same. Therefore, there would be a likely increase in overall risk.
6.4.2.2.2. Scenario A2: 24-hour service level to 18-hour service level

Figures 57 and 58 above provide a cost breakdown of Scenario A2 and the percentage change per element respectively.

As per Scenario A1 the service level in this particular scenario makes specific reference to the duration within which it is expected that the third party transportation provider must
deliver the goods. This scenario is contrary to Scenario A1 as the service level is being improved from a 24-hour service level to an 18-hour service level.

Scenario A2 had an overall cost increase of 11% primarily driven by the increase in transport costs due to the shorter service level, which increased transportation costs by 28%. There was a reduction in packaging costs and an increase in validation costs.

- Transport cost: Changing the service level from 24 hours to 18 hours had a significant impact on the transportation cost resulting in an increase of 28%. It should be noted that this service level change was not made to outlying areas, as such a service level is not possible to these areas. The 28% increase is driven only by the increase in service level to city centre deliveries.
- Warehouse cost: There was no specific impact on the warehousing element.
- Temperature monitoring cost: There was no specific impact on the temperature monitoring cost element. Despite the shorter delivery time, the same number of loggers would still be required due to the turnaround time of recovering loggers.
- Cold chain packaging cost: With the faster lead time, there is an opportunity to reduce the amount of thermal energy required within the cold chain packaging system. The reduction was achieved through reducing the number of gel packs required. This reduction was applied and reduced the packaging cost. The reduction was significantly less proportionate to the increase in cost in Scenario A1. One of the key drivers of cost in Scenario A1 was not only the increased number of gel packs but the reduction in space availability. This required more containers to be used to deliver the goods. In Scenario A2 while there may be an improved capacity in the containers, the whole container still needs to be shipped, and therefore there was no reduction in the number of containers required.
- Validation/qualification cost: The change in the cold chain configuration would require the new configuration be re-qualified. This cost was added to the validation/qualification costs and amortised over a five-year period. The result of this was a 10% increase in validation/qualification costs. This aspect of the cost analysis has the same implications as Scenario A1.
• Non-conformance cost: Following the rationale of reviewing non-conformance cost in terms of risk, this scenario would represent a reduction in risk in that the deliveries sent with the faster service level would be exposed to environmental conditions and external factors for a shorter period, in turn reducing the chance of a risk occurrence.

6.4.2.3. Model B scenario analysis

6.4.2.3.1. Scenario B1: 24-hour service level to 48-hour service level

![Scenario B1 Cost Breakdown](image-url)

*Figure 59 Scenario B1 cost breakdown*
Figures 59 and 60 above provide a cost breakdown of Scenario B1 and the percentage change per element respectively.

- **Transport cost:** Transportation costs reduce by 22% largely due to the lower courier charges related to the increased delivery time (from 24 hours to 48 hours). Delivery charges make up 19.5% of this reduction while the fewer vehicles, driver and related costs make up the balance of the reduction.

- **Warehouse cost:** There was no specific impact on the warehousing element.

- **Temperature monitoring cost:** The increased delivery time resulted in increased temperature monitoring costs of 3% due to the longer turnaround time to retrieve the temperature logging devices. This resulted in the need for additional temperature logging devices, and associated costs.

- **Cold chain packaging cost:** In a similar way to Scenario A1, cold chain packaging costs increased by 48% in order to meet the requirement of a 48-hour delivery time as additional ‘thermal capacity’ had to be added to the cold chain container. This has the double impact of increasing cost as well as reducing payload size. The smaller payload size means more cold chain packaging systems are required to ship the same quality.

- **Validation/qualification cost:** Validation costs increase in the same manner as they did in Scenario A1.
• Non-conformance cost: As with Scenario A1, the increased time spent in uncontrolled conditions during delivery at a 48-hour service level represents an increase in risk.

6.4.2.3.2. Scenario B2: 24-hour service level to 18-hour service level

![Figure 61 Scenario B2 cost breakdown](image1)

![Figure 62 Scenario B2 – Percentage change per element](image2)
Figures 61 and 62 above provide a cost breakdown of Scenario B2 and the percentage change per element respectively.

- **Transport cost:** Similar to Scenario A2, there was a significant increase in cost due to the improved transport service level of 18 hours. The increase in Scenario B2 is however larger than that of Scenario A2 at 69%. This is as a result of the cost structure from the outsourced transport provider. For example, the cost to ship a consignment from Johannesburg to a Durban outlying area compared to the cost to ship from Durban central to the same area is the same. Therefore, the cost increase incurred in Scenario B2 is similar in absolute terms, but because Scenario B2 has a lower cost base to start, the cost increase is larger in percentage terms.

- **Warehouse cost:** There was no specific impact on the warehousing element.

- **Temperature monitoring cost:** There was no specific impact on the temperature monitoring cost element. Despite the shorter delivery time, the same number of loggers would still be required due to the turnaround time of recovering loggers.

- **Cold chain packaging cost:** The cost reduction in cold chain packaging is due to the reduction of the number of gel packs, as in Scenario A2, as well as the increased payload volume resulting in fewer cold chain boxes being required.

- **Validation/qualification cost:** The cost increase of validation and qualification requirements is driven by the cold chain packaging change as described in Scenario A2. The percentage is slightly different as the cost increase is on a slightly higher base compared to Scenario A2.

- **Non-conformance cost:** As per Scenario A2 this scenario would represent a reduction in risk due to the shorter delivery lead times. Furthermore, in comparison to Scenario A2, having regional distribution centres would further reduce risk in that it would allow for parcels to be returned to the controlled conditions in a shorter period of time than in the decentralised scenario.
6.4.2.4. **Scenario C: Comparison of Model A and Model B**

The comparison of Model A and B (see Figures 63 and 64) is based on changing from a centralised (Model A) to a decentralised (Model B) supply chain. There was a significant increase in warehouse costs of 124%, an 18% reduction in transport cost with an overall increase of 9% in total cost, when moving from a centralised to a decentralised distribution model.
• Transport cost: The reduction in transportation cost was driven by the weekly replenishment of the regional distribution centres which allowed increased economies of scale when compared to the fully centralised model.

• Warehouse cost: Regional warehousing space was provided for, based on the distribution volume for both the Durban and Cape Town distribution centres. The costs for the regional distribution centres were calculated using the same equipment as defined in the main centre in Gauteng except for handling equipment, and a reduction in the size of the cold room and generator. The net impact of this change resulted in a 124% increase in warehousing costs. Coming off a lower base than the transportation cost, the warehouse cost increase was less, in real terms, than the reduction in transportation cost. The relationship between the two elements (transport cost and warehouse cost) is primarily driven by the standard total cost model relationship. The interesting aspect of this relationship, as it applies to this research, is the impact that this change has on the other elements, as well as the overall risk impact.

• Temperature monitoring cost: Additional storage temperature monitoring devices were provided for the regional distribution centres. Additional calibration and analytical costs were calculated on the addition of the temperature monitoring devices required. The net impact of the additional temperature monitoring requirements was a 48% increase in temperature monitoring costs. It is important to note, however, that temperature monitoring costs were coming off a relatively low base in that these costs only accounted for 3% of the total benchmark cost.

• Cold chain packaging: No change was made to the cold chain packaging element.

• Validation and qualification: The increase in validation/qualification cost is due to the need to validate/qualify the additional two facilities. This results in a 22% increase in validation/qualification cost. There is a direct association with warehouse and transportation changes and validation/qualification cost, as in most cases any addition, expansion or change will require validation/qualification.

• Non-conformance: In terms of the risk impact to the product in this scenario, the implications are a reduction in the likelihood of a risk event due to the fact that product will endure less consecutive time in transportation, i.e. it would first be
transported to the regional distribution facility, where it would be unpacked from
the cold chain packaging and packed into the cold room. On receipt of orders,
product would then be repacked and sent on to the final destination. If there was
a risk occurrence during either the replenishment trips down to the regional
distribution centre or the transportation to the final destination, there would be more
time available to mitigate the risk and get the product into controlled conditions.
There would also be an increase in the impact of a risk event relating to the
replenishment shipments to the regional distribution facilities as there would be a
larger quantity of product at risk at a particular time.

6.4.3. **Summary of cost analysis findings**

6.4.3.1. **Impact on total cost**

![Figure 65 Total cost by scenario](image)

Overall Model A had a lower total cost than Model B as shown in Figure 65. This is
primarily driven by the increased warehousing cost required by the decentralisation in
Model B. Although there was a reduction in transport cost in Model B, this was less than the cost increase in warehousing cost.

In the case of Scenario A1 there was a cost decrease primarily driven by the reduction in the service level to a 48-hour service level. In the case of Scenario B2 the total cost increased due to the decrease in transport cost being less than the decrease experienced in Scenario A2 (as transport cost was already on a lower base in Scenario B2). As a result, the increased cost in cold chain packing requirements pushed the total cost higher.

Scenario A2 and B2 resulted in an increase cost primarily driven by the increased transport service level.

When comparing Models A and B in Scenario C there is an increase in cost, primarily driven by the increase in warehouse costs. The move from a centralised to decentralised model also results in potential non-conformance cost implications in that there is both an increase in risk, related to the size of the replenishment shipments, as well as a decrease in risk, related to the closer proximity to the end delivery point.

6.4.3.2. Cost analysis relationship determination

In order to determine if there is a cost relationship between the elements identified in Chapter 4, the cost impact of the various scenarios was analysed, the rationale being the greater the cost impact on a particular element the greater the cost relationship.

<table>
<thead>
<tr>
<th>Table 46 Absolute impact by scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Element</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Transport Cost</td>
</tr>
<tr>
<td>Warehouse Cost</td>
</tr>
<tr>
<td>Temperature Monitoring Cost</td>
</tr>
<tr>
<td>Cold Chain Packaging Cost</td>
</tr>
<tr>
<td>Validation/ Qualification Cost</td>
</tr>
<tr>
<td>Non-Conformance Cost</td>
</tr>
<tr>
<td>Total by scenario</td>
</tr>
</tbody>
</table>

Table 46 above demonstrates in absolute terms if there was a cost impact or not. Looking at the table from the perspective of transport, the validation and qualification and non-conformance cost elements were impacted in all scenarios (i.e. five of five scenarios).
Viewing the table from a scenario perspective, Scenarios A1, B1 and C impact five of the six elements while Scenario A2 and B2 impacted only four of six elements.

Table 47 Total cost increase/decrease by scenario

<table>
<thead>
<tr>
<th></th>
<th>Model A Benchmark</th>
<th>Model A</th>
<th>Scenario A1</th>
<th>Model A</th>
<th>Scenario A2</th>
<th>Model B</th>
<th>Scenario B1</th>
<th>Model B</th>
<th>Scenario B2</th>
<th>Model A Benchmark</th>
<th>Model A</th>
<th>Scenario A2</th>
<th>Scenario C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport Cost</td>
<td>R 206 255.05</td>
<td>R 125 122.28</td>
<td>R 263 947.43</td>
<td>R 169 115.39</td>
<td>R 151 444.87</td>
<td>R 285 600.86</td>
<td>R 206 255.05</td>
<td>R 169 115.39</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature Monitoring Cost</td>
<td>R 13 827.33</td>
<td>R 14 394.83</td>
<td>R 13 827.33</td>
<td>R 20 467.58</td>
<td>R 21 035.08</td>
<td>R 20 467.58</td>
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<td>R 20 467.58</td>
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<tr>
<td>Cold Chain Packaging Cost</td>
<td>R 130 546.85</td>
<td>R 192 586.03</td>
<td>R 116 572.05</td>
<td>R 130 546.85</td>
<td>R 192 586.03</td>
<td>R 116 572.05</td>
<td>R 130 546.85</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Validation/ Qualification Cost</td>
<td>R 31 576.67</td>
<td>R 34 756.67</td>
<td>R 34 756.67</td>
<td>R 38 643.33</td>
<td>R 41 823.33</td>
<td>R 41 823.33</td>
<td>R 31 576.67</td>
<td>R 38 643.33</td>
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</tr>
<tr>
<td>Non-Conformance Cost (Risk)</td>
<td>NA</td>
<td>Reduced</td>
<td>Increased</td>
<td>NA</td>
<td>Reduced</td>
<td>Increased</td>
<td>NA</td>
<td>Reduced</td>
<td>Increased</td>
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<tr>
<td>Total</td>
<td>R 433 184.26</td>
<td>R 417 838.18</td>
<td>R 480 081.84</td>
<td>R 473 142.70</td>
<td>R 501 258.86</td>
<td>R 578 833.37</td>
<td>R 433 184.26</td>
<td>R 473 142.70</td>
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</tbody>
</table>

When looking at the cost impact as per Table 47 above it is clear that transportation and cold chain packaging have the most significant impact on cost ranging from R13 974.8 (in the case of Model A Benchmark compared to Scenario A2/B2 Cold Chain Packaging) to R116 485.47 (in the case of Model B Benchmark compared to Scenario B2 Transport). Warehouse cost was a significant impact in Scenario C with a R63 391.18 increase in cost. Validation/qualification cost had a minor impact, while temperature monitoring had a slight impact.

![ABSOLUTE AVERAGE IMPACT](image)

Figure 66 Absolute average impact
The graph in Figure 66 above illustrates the total percentage impact of each element in absolute terms averaged across all scenarios (Scenario A1, A2, B1, B2 and C). It is clear that transport cost has the most significant impact on cost, followed by warehouse, cold chain packaging, validation/qualification and finally temperature monitoring cost. Furthermore, the above graph illustrates that a change in one element (transport cost) can influence other cost elements. The cost analysis has thus illustrated that there is indeed a relationship between these cost elements.

6.4.4. Interpretation and findings of cost analysis

Based on the analysis of the scenarios, there is a clear indication that there is a cost relationship between the various elements. The scenarios have not challenged every single relationship between all elements. The intention of the cost analysis was to illustrate, rather than prove, the principle of the cost relationship between elements and to determine where the most significant relationships exist. The findings of the cost analysis support the findings of the survey, which provided input from industry experts as to their opinions and experience as they relate to the defined elements.

After analysis, it was clear that a change to the transport service level or warehousing model affected most other elements, most significantly transportation, warehousing and cold chain packaging. We can therefore determine that while there may be a relationship between all these elements, a particular change in one element will not necessarily result in a change to all other elements. This should be considered in terms of how this research is interpreted: when making a change to one element, one should consider if there are implications to the other elements, and understand that the other elements may or may not be impacted depending on the nature of the change. The model defined in Chapter 4 is therefore not necessarily a rule but a guideline to assist in interrogating decisions and their implications.
6.5. Relationship confirmation

To verify the relationships identified in Chapter 4 for the pharmaceutical cold chain model, inputs from both the survey and cost analysis will be used.

6.5.1. Scoring method

Based on the research, the relationship between transport and warehouse cost, and the other cost elements was determined. Each relationship was rated on four parameters and assigned a score from 1 to 4. The parameters are:

a) Survey: Survey average rating – refers to the average rating defined by the survey for each relationship
b) Survey: Consistency – refers to consistency of the survey ratings of the relationships between the various elements across the aspects of time, cost and quality
c) Cost analysis: Impacted by scenarios – defines if an element has been impacted by a particular scenario, i.e. Impact or No impact
d) Cost analysis: Degree of impact – where an element was impacted by the scenario, the average impact was calculated in absolute percentage terms

The scoring criteria for each parameter is defined in Table 48 below.

Table 48 Relationship rating matrix

<table>
<thead>
<tr>
<th>Relationship rating</th>
<th>Survey parameters</th>
<th>Cost analysis parameters</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a. Survey average rating</td>
<td>c. Impacted by scenarios</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Consistency across aspects (i.e. time, cost, quality)</td>
<td>d. Degree of impact</td>
<td></td>
</tr>
<tr>
<td>Strong</td>
<td>1.5. to 2</td>
<td>Impacted by all five scenarios</td>
<td>4</td>
</tr>
<tr>
<td>Significant</td>
<td>1 to 1.49</td>
<td>Impact by four of five scenarios</td>
<td>3</td>
</tr>
<tr>
<td>Tangible</td>
<td>0 to 0.99</td>
<td>Impact by one to three of five scenarios</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>Below 0</td>
<td>Impact by zero of five scenarios</td>
<td>1</td>
</tr>
</tbody>
</table>
Based on the score for each of the four parameters, an average score was determined which was then rounded up or down as appropriate to determine the relationship rating as follows:

- Strong: 4 ± 0.5
- Significant: 3 ± 0.5
- Tangible: 2 ± 0.5
- None: 1 ± 0.5

6.5.2. Survey scoring

Table 49 below summarises the findings from the survey questions related to the relationships between the respective elements, based on the above relationship rating parameters. This table was used to define each relationship in terms of the survey average rating component of the above parameters.

Based on the average score it is evident that all relationships have a significant rating other than the relationship between transport cost and warehouse cost, which was rated as tangible. Of the nine relationships, four had all aspects (time, cost, quality) within the same range with the balance having at least two aspects within the same range.

Table 49 Relationship rating – Survey average rating
6.5.3. Cost analysis scoring

The cost analysis parameters were determined based on the Table 50 which illustrates the impact of the five scenarios across the elements, as well as the degree of the impact in terms of the absolute average.

Table 50 Cost analysis scoring

<table>
<thead>
<tr>
<th>Element</th>
<th>Model A</th>
<th>Model B</th>
<th>Model A vs B</th>
<th>Relationship Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scenario A1</td>
<td>Scenario A2</td>
<td>Scenario B</td>
<td>Scenario B2</td>
</tr>
<tr>
<td>Transport Cost</td>
<td>39%</td>
<td>28%</td>
<td>22%</td>
<td>69%</td>
</tr>
<tr>
<td>Warehouse Cost</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Temperature Monitoring Cost</td>
<td>4%</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Cold Chain Packaging Cost</td>
<td>48%</td>
<td>11%</td>
<td>48%</td>
<td>11%</td>
</tr>
<tr>
<td>Validation/Qualification Cost</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Non-Conformance Cost</td>
<td>Risk Decreased</td>
<td>Risk Increased</td>
<td>Risk Decreased</td>
<td>Risk Increased</td>
</tr>
</tbody>
</table>

Four of the six elements were impacted by all five scenarios giving them a strong relationship rating. Warehouse cost and temperature monitoring cost were impacted by one and three of the scenarios respectively, giving them a relationship rating of tangible. From an absolute average perspective, three of six cost elements were rated as significant with the two being rated as tangible and non-conformance being not applicable.
6.5.4. Relationship rating and determination

6.5.4.1. Transport cost relationships

Table 51: Relationship rating transport cost

<table>
<thead>
<tr>
<th>Transportation relationship to the element:</th>
<th>Survey scoring</th>
<th>Cost analysis scoring</th>
<th>Overall relationship score (rating)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score (average rating)</td>
<td>Score (consistency across aspects)</td>
<td>Score (impacted by scenario)</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>3 (1.02)</td>
<td>3 (2 in same range)</td>
<td>2 (impacted by 3 of 5)</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>3 (1.33)</td>
<td>4 (all aspects within the same range)</td>
<td>3 (impacted by 4 of 5)</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>3 (1.45)</td>
<td>3 (2 in same range)</td>
<td>4 (impacted by 5 of 5)</td>
</tr>
<tr>
<td>Non-conformance</td>
<td>3 (1.36)</td>
<td>3 (2 in same range)</td>
<td>4 (impacted by 5 of 5)</td>
</tr>
</tbody>
</table>

Score key

<table>
<thead>
<tr>
<th></th>
<th>None (1)</th>
<th>Tangible (2)</th>
<th>Significant (3)</th>
<th>Strong (4)</th>
</tr>
</thead>
</table>

There is a significant relationship between transportation and all elements as shown in Table 51 above.
### 6.5.4.2. Warehouse cost relationships

**Table 52 Relationship rating warehouse cost**

<table>
<thead>
<tr>
<th>Warehousing relationship to the element:</th>
<th>Survey scoring</th>
<th>Cost analysis scoring</th>
<th>Overall relationship score and rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score (average rating)</td>
<td>Score (consistency across aspects)</td>
<td>Score (impacted by scenario)</td>
</tr>
<tr>
<td>Temperature monitoring</td>
<td>3 (1.11)</td>
<td>4 (all aspects within the same range)</td>
<td>2 (impacted by 3 of 5)</td>
</tr>
<tr>
<td>Cold chain packaging</td>
<td>3 (1.03)</td>
<td>4 (all aspects within the same range)</td>
<td>3 (impacted by 4 of 5)</td>
</tr>
<tr>
<td>Validation/qualification</td>
<td>3 (1.19)</td>
<td>4 (all aspects within the same range)</td>
<td>4 (impacted by 5 of 5)</td>
</tr>
<tr>
<td>Non-conformance</td>
<td>3 (1.03)</td>
<td>3 (2 in same range)</td>
<td>4 (impacted by 5 of 5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score key</th>
<th>None (1)</th>
<th>Tangible (2)</th>
<th>Significant (3)</th>
<th>Strong (4)</th>
</tr>
</thead>
</table>

In the case of the relationship between the warehouse cost element and the other cost elements there is a significant relationship as shown in Table 52.
### 6.5.4.3. Transportation and warehousing

**Table 53 Relationship rating transport and warehouse cost**

<table>
<thead>
<tr>
<th>Transportation and warehousing relationship</th>
<th>Survey scoring</th>
<th>Cost analysis scoring</th>
<th>Overall relationship score and rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score (average rating)</td>
<td>Score (consistency across aspects)</td>
<td>Score (impacted by scenario)</td>
</tr>
<tr>
<td>Transportation</td>
<td>2 (0.94)</td>
<td>3 (2 in same range)</td>
<td>4 (impacted by 5 of 5)</td>
</tr>
<tr>
<td>Warehousing</td>
<td>2 (0.94)</td>
<td>3 (2 in same range)</td>
<td>2 (Impacted by 1 of 5)</td>
</tr>
<tr>
<td><strong>Average score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score key</th>
<th>None</th>
<th>Tangible</th>
<th>Significant</th>
<th>Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
<td>(4)</td>
</tr>
</tbody>
</table>

As the relationship between transport and warehouse (shown in Table 53) is common between cost elements, the scores for these two cost elements were averaged to determine that there is a significant relationship between the transport and warehouse cost elements.

### 6.6. Research results and findings

The key outputs from the research thus far consist of the relationship model, key factors and a non-conformance/risk analysis. These form the foundation inputs into the determination of the key challenges, which is the primary objective of this study. Through the identification of the key challenges, it is possible to gain insight into how organisations can balance the regulatory requirements related to quality and SEP to achieve the ultimate objective of quality products delivered to patients in a cost-effective manner.

#### 6.6.1. Relationship model

The outcomes of the research have determined that there is a significant relationship between outbound distribution (transport and warehouse cost) and quality elements of GDP (temperature monitoring, cold chain packaging validation/qualification and non-conformance cost) (see Figure 67). This provides a framework for the identification of key
challenges within the pharmaceutical cold chain, specifically as it relates to the relationship between the outbound distribution elements and the quality elements.

![Figure 67 Relationship model](image)
6.6.2. Key factors

The key factors (see Figure 68) to be considered within each of these elements have been identified in terms of importance. The key factors for each element provide the necessary contextual information for analysis and form part of the inputs into the identification of the key challenges. The key factors will be reviewed for counter priorities and trends, and discussed in detail in the identification of the key challenges.

6.6.3. Non-conformance/risk

The non-conformance element was measured in terms of risk as it was not possible to measure the cost impact of a non-conforming pharmaceutical cold chain. The non-conformance/risk element of pharmaceutical cold chain management must be considered as a key element in assessing challenges between outbound distribution and quality requirements. For this reason, risk inputs from both the survey as well as the cost analysis have been used in order to identify the key challenges in the pharmaceutical cold chain.
6.6.3.1. Survey risk analysis

The risk analysis (see Table 54) indicates that the impact rating is the driver of the overall risk given the average rating of 3.37 (impact) compared to 2.5 (probability). Transport cost stands out as having the highest risk, with temperature monitoring having the lowest risk overall.

Table 54 Risk analysis

<table>
<thead>
<tr>
<th></th>
<th>Probability</th>
<th>Impact</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport Cost</td>
<td>3.20</td>
<td>3.45</td>
<td>3.33</td>
</tr>
<tr>
<td>Warehouse Cost</td>
<td>2.15</td>
<td>3.50</td>
<td>2.83</td>
</tr>
<tr>
<td>Temperature</td>
<td>2.45</td>
<td>2.90</td>
<td>2.68</td>
</tr>
<tr>
<td>Monitoring Cost</td>
<td>2.35</td>
<td>3.35</td>
<td>2.85</td>
</tr>
<tr>
<td>Cold Chain</td>
<td>2.35</td>
<td>3.65</td>
<td>3.00</td>
</tr>
<tr>
<td>Validation/Qualification Cost</td>
<td>2.35</td>
<td>3.65</td>
<td>3.00</td>
</tr>
<tr>
<td>Average</td>
<td>2.5</td>
<td>3.37</td>
<td>2.94</td>
</tr>
</tbody>
</table>

The risk analysis was progressed further to determine the risk between elements by averaging their associated risks. In Table 55 below, it is evident that the highest risk is between transport cost and validation/qualification cost elements at 3.16, while the lowest risk was between warehouse and temperature monitoring cost elements at 2.75.

Table 55 Risk by relationship

<table>
<thead>
<tr>
<th></th>
<th>Relationship Risk Rating</th>
<th>Transportation</th>
<th>Warehousing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport/Warehouse Cost</td>
<td>3.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature Monitoring Cost</td>
<td>3.00</td>
<td>2.75</td>
<td></td>
</tr>
<tr>
<td>Cold Chain Packaging Cost</td>
<td>3.09</td>
<td>2.84</td>
<td></td>
</tr>
<tr>
<td>Validation/Qualification Cost</td>
<td>3.16</td>
<td>2.91</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>3.08</td>
<td>2.83</td>
<td></td>
</tr>
</tbody>
</table>

6.6.3.2. Risks identified in cost analysis

Within the cost analysis it was noted that the reduced service level (i.e. longer transport service level) in Scenario A1/B1, resulted in an increase in risk due to the cold chain parcel spending more time in an uncontrolled environment. The inverse of this is the case in scenario A2/B2 where risk was reduced due to less time being spent in an uncontrolled environment.
In Scenario C there was both an increase and decrease in the risk. There was an increased transportation risk in that there was a need for replenishment shipments, in the case of Model B (decentralised) to the regional distribution centres. In the event of a risk occurrence, for example a vehicle breakdown, the impact would be higher as there would be more stock at risk within the replenishment shipment. The risk at the fine distribution component of the supply chain, i.e. from the distribution centre to the pharmacy/hospital, was lower. This was due to the regional distribution centre reducing the time and distance from the customer; therefore, in the event of a risk occurrence (vehicle breakdown as above), a mitigating response could be actioned in a shorter time.

6.6.4. **Identification of key challenges**

In order to determine the key challenges, both the survey and cost analysis were reviewed and analysed in a holistic manner to identify significant variances, outliers and trends.

Through a structured process of data collection from multiple sources the research has provided an output of key challenges on the basis of relationships between key elements within the pharmaceutical cold chain; risks associated with and between these elements; as well as key factors to consider within these elements. The data generated provided a platform for analysis and interpretation as to what the key challenges within the industry may be, as follows.

1. **Transportation risk**: Transportation represents the highest risk to product across the supply chain. Through the research it is evident that transportation risk as a whole can be considered as one of the key challenges. This is likely due to the lower degrees of control during transportation when compared to warehousing or the other elements, exacerbated by the high level of transportation outsourcing in the pharmaceutical cold chain. This is reflected in the risk rating of transport cost at 3.33. When viewing the relationship between transport cost and the other cost elements in the findings of the research, transport cost (1.17) had a higher average rating than warehouse cost (1.08). Particularly transportation had the highest overall quality rating in its relationship with non-conformance cost (1.56) which supports the high risk rating of 3.33. In the cost analysis, the absolute average impact for the transport cost element was 35%, which was the highest of all cost
elements. This indicates that when transport cost is impacted, the degree of the impact is significant.

2. Shipment volume and weight: Cold chain packaging increases the total shipment volume and weight resulting in higher transport costs. Volume was rated as the most important factor for the transport cost element; conversely weight was rated as the least important factor. This suggests that cold chain shipments typically have a higher volumetric weight compared to the actual weight. The higher volumetric weight is likely due to the cold chain packaging taking up space in the vehicle. Compared to ambient pharmaceutical product, there is a significantly higher packaging-to-product ratio. The importance of the volume factor is likely due to the impact that the volume of the shipment has on transport costs.

3. Transport service level and cold chain packaging duration: Incongruence between the transport service level and the cold chain packaging duration create the possibility of wastage, increased cost and product risk exposure. While the duration to destination was rated as the least important factor with regard to transportation, the duration of the cold chain shipper was rated as the most important factor. Incongruence between the transport service level and the duration that the cold chain packaging remains within specification could result in increased costs through:
   - Increasing the transport service level in order to meet the duration of the cold chain shipper
   - Cold chain shipper durations which far exceed transport service levels, effectively resulting in wastage within the cold chain shipper
   - Increased product write-offs due to cold chain shipper durations which do not meet the transport service level duration.

The cost analysis supports this in that the change to the service level has a significant impact on the cost of cold chain packaging (23% absolute average), with a tangible (12% absolute average) impact on the validation/qualification costs associated with the cold chain packaging.
4. Transportation temperature monitoring: Cost and time associated with temperature monitoring of transportation shipments represent a key challenge compared to warehouse temperature monitoring. The quality relationship between transport and temperature monitoring cost as well as between warehouse and temperature monitoring cost were both rated as higher than the respective cost and time relationship at 1.38. This suggests that there is recognition that temperature monitoring is important to the quality of the product. The time and cost relationships between, transport and temperature monitoring cost was 0.81 and 0.88 while, warehouse and temperature monitoring cost were rated 1.13, 1 respectively. The higher relationship rating of warehousing compared to transportation indicates a potentially higher investment in time and money into the temperature monitoring at the warehousing level. Harvesting, management and analysis of data was ranked as the lowest factor for temperature monitoring.

There is therefore a key challenge in the cost and time required to monitor temperature during transportation of shipments. Issues related to temperature monitoring of transportation could include:

- Costs associated with purchasing and calibrating the required quantity of temperature monitoring devices to monitor many shipments.
- Managing and analysing the data collected from the various shipments across multiple routes.

5. Cold chain packaging: This includes balancing requirements of duration, payload size and cost. Looking at the cold chain packaging cost element, the top three important factors were duration, cost and payload size. These factors however have a direct influence on one another. For example, an increase in the payload size will either increase cost (due to additional thermal requirements) or reduce the duration (due to the increased thermal challenge, i.e. there is more product to keep cool). The relationship between duration, payload size and cost was illustrated in the scenario analysis. In order to increase the duration of cold chain packaging for the longer service level, it was necessary to add additional thermal capacity (i.e. additional gel packs). The net effect of this was an increase in the cold chain
packaging cost as well as a reduction in payload capacity as additional space was required for the gel packs within the polystyrene-insulated container.

6. Transport validation/qualification: The challenge lies in understanding the importance of cold chain packaging validation/qualification. Transport and validation/qualification had the highest risk ratings at 3.45 and 3.65 respectively. The quality relationship between transport and validation/qualification cost was rated as the second highest at 1.50. Despite this relationship, the cold chain shipper qualification was rated as the second least important factor. This is contradictory as qualifying the cold chain shipper would be a key component in ensuring the quality of the product during transportation. The incongruence between the risk and quality relationship of transport and validation/qualification cost indicates a potential misunderstanding in the crucial role validation/qualification has to play in the quality of pharmaceutical product distribution.

6.7. Conclusion
The relationships between elements provide the framework to assess how these elements interact with one another. This has been confirmed by both industry experts through the survey as well as through the cost analysis. The cost analysis provides some specific quantitative examples of how interrelated these cost elements are, understanding that some relationships may be stronger than others. The results of the cost analysis provide the quantitative support to the qualitative views from the survey.

The key factors provide the necessary detail from the industry practitioners to understand what factors within each cost element are considered to be important. Assessing these key factors, trends and counter requirements within these key factors provides guidance as to the key challenges within the pharmaceutical cold chain.

The risk analysis provides the necessary quantitative assessment for the non-conformance cost element of the relationship model. This information is key in terms of understanding the risk to product and in turn patient safety.
Due to the nature of the research it was necessary to have a qualitative departure point such as the survey; however, it was also crucial to provide a quantitative baseline to further reinforce the findings of the survey. The cost analysis provides this quantitative perspective and indeed demonstrates the practical implications of the relationships, key factors and risks identified in the survey.

In every scenario assessed in the cost analysis, transport, validation/qualification and non-conformance were impacted, demonstrating how critical these elements are. In the transportation cost element, the absolute average impact was the highest at 35%, indicating the sensitivity of transport cost to change. Not only does transport cost have the highest absolute average impact (from a pure cost perspective), it also has the highest risk rating at 3.33.

It is this combination of high cost and risk implications that begins to illustrate where the necessary effort is required within the pharmaceutical cold chain. This also aligns with qualitative considerations discussed early in the research, relating to the low levels of control an organisation can affect during transportation. In the case of the pharmaceutical cold chain this is further exacerbated by the fact that 90% of the respondents indicated that there was some degree of outsourcing of transportation in their respective organisations. It is likely that the high level of outsourcing of transportation is in an effort to optimise transportation costs, specifically when one considers the limited ability to pass on costs to the consumer due to SEP. The impact of this level of outsourcing on the non-conformance, and in turn, risk element must be considered in terms of the implications for the other cost elements, particularly cold chain packaging and validation/qualification as indicated by the cost analysis results. The type of vehicle was rated as one of the top key factors to consider relating to the transport cost element. In the context of an outsourced transportation, it may be more difficult to ensure that the vehicle is appropriate for pharmaceutical products. When one considers that for the transport provider to remain competitive it is necessary to consolidate multiple loads from various customers, which may not necessarily be pharmaceutical industry customers, this may make it difficult to enforce pharmaceutical requirements on outsourced transportation providers. Specialised requests for insulated, refrigerated or temperature-controlled vehicles made
with transport providers will likely result in increased transport costs in order for the provider to provide the higher quality standards required by the pharmaceutical cold chain industry. This principle extends further to issues related to validation/qualification of these outsourced vehicles.

On review of the research outcomes, it becomes clear that the key challenges lie primarily in the transportation segment of outbound operations. This is not to say there are no challenges in the warehouse element, but rather that the solutions to the challenges in the warehouse element are better understood and largely already in place. This is likely to be due to the fact that the solutions such as warehouse temperature monitoring and control, cold rooms, generators, etc., can be implemented at a centralised point of control, improving economies of scale. Transportation, by contrast, requires potentially different solutions for each geographic route, due to the many variables in the transportation element.
CHAPTER 7 – CONCLUSION AND RECOMMENDATIONS

7.1. Introduction
Chapter 6 demonstrates the results of the research with the ultimate determination of the key challenges within the pharmaceutical cold chain industry. In chapter 7 the conclusions and recommendations of the research will be discussed linking these back to the objectives as defined in chapter 1. This is crucial to ensure that the research has met that which it set out to achieve. Limitation to the research will be presented as well as opportunities for future research.

7.2. Objectives and outcomes
The research has identified the key challenges in the pharmaceutical cold chain industry by using both qualitative and quantitative data. The research outcomes define the outputs from the research. The outcomes must be assessed against the primary and secondary objectives in order to ensure that the original intention of research has been achieved. The diagram in Figure 69 below summarises the outcomes of the research, linking the specific outcomes to the primary and secondary objectives.
7.2.1. Primary objective

The primary objective was: ‘To identify key challenges between pharmaceutical quality requirements and outbound distribution functions in the pharmaceutical cold chain of the private sector.’

The identification of key challenges was limited to challenges that could be identified between quality and outbound distribution functions. In order to achieve this objective, the relationships between specific elements within these functions were determined. The relationships were determined using both the survey and cost analysis. To provide the required inputs into the achievement of the primary objective, the key factors for each
element as well as the risks related to and across the elements were determined within the survey (see Figure 69).

On analysis of the data generated, six key challenges were identified, primarily related to the relationship between the quality elements and the transport cost element. These key challenges illustrate the need for an integrated approach to decision-making related to transportation, cold chain packaging systems, temperature monitoring and validation/qualification. Based on the identification of these key challenges, the primary objective is considered to have been achieved.

7.2.2. Secondary objectives
Two secondary objectives were identified. These objectives were fundamental to the achievement of the primary objective.

The first of the secondary objectives was: 'To identify the relationships between cost elements within the quality and outbound distribution functions.' The survey defined the degree and nature of relationships between the elements related to quality (non-conformance, validation/qualification, cold chain packaging and temperature monitoring cost) and outbound distribution (transport cost and warehouse cost). The survey provided industry input into the research. The research went further with a cost analysis, which provided a quantitative basis for the verification of the relationships between the cost elements identified. The research determined that there was a significant relationship between the outbound distribution and quality cost elements (see Figure 69). The research provided further granularity in terms of cost, time and quality ratings to these relationships. This granularity provided the necessary detail for further analysis to identify the primary drivers of relationships as an input into the identification of key challenges. A risk analysis provided additional information for the identification of key risk areas and relationships in terms of impact, probability and total risk.

The second of the secondary objectives was: 'To identify the key factors to be considered within each of the relationship elements identified, from highest to lowest priority.' As an output from the survey, key factors for each cost element were determined in order of priority. The prioritised key factors provided further insight into the industry perspective of
what was considered to be important for the various cost elements identified (see Figure 69). The key factors provided specific focus areas to be discussed in the context of the relationships and risks identified in the first component of the secondary objectives.

These two secondary objectives were key inputs into the achievement of the primary objective. Through the combination of the data collected from the survey and cost analysis, further analysis was possible to identify the key challenges and meet the primary objective. As the relationships between elements and key factors were successfully identified, both secondary objectives are considered to have been achieved.

7.3. Conclusion

Within the South African pharmaceutical industry, the highest risk in the pharmaceutical cold chain occurs during transportation, as determined by this research. This was identified as the first key challenge, and the rest of the challenges identified relate to it in some way. From a qualitative point of view this is expected, based on the variable and uncontrolled factors inherent in the transportation process. In order to verify the opinions of the industry experts from the survey, the cost analysis provided a quantitative comparison which demonstrated the relationships inherent between the various elements. The high level of interrelatedness between the elements is what in part creates the challenges within the pharmaceutical cold chain. Through the combination of industry expert opinions and quantitative scenario-based cost analysis, the research has provided detail into specific challenges within the transportation process of cold chain pharmaceutical products. In order to address the risks and challenges within transportation there will likely be an impact on cost that the pharmaceutical industry will need to manage. The research has demonstrated, through the lower level of risk when compared to transportation, that the warehouse processes do not represent a significant challenge to the pharmaceutical cold chain industry at this point.

The primary objective of the research was met through the identification of six key challenges. These key challenges provide guidance as to where the required focus should be within the pharmaceutical cold chain industry.
Through an assessment of the various routes and their respective service levels with outsourced transport providers, organisations can determine the appropriate duration requirements for the cold chain packaging system. This assessment should also be done in terms of product volumes on the various routes, and prioritised appropriately. This would provide the optimal duration while minimising cost, as illustrated by the scenarios tested in the cost analysis.

In order to ensure that the payload volume of the cold chain packaging system is appropriate to an organisation, the cold chain packaging system payload should be appropriate to the typical order size of the organisation. This will ensure an effective cold chain packaging system payload volume and optimise the cost associated with cold chain packaging.

Monitoring during transportation is a particular challenge for cold chain pharmaceuticals as it is not possible to do this in a consolidated manner, i.e. every cold chain parcel is packaged within its own cold chain packaging system, and it is not possible to monitor only the temperature of the vehicle as is possible with ambient product. This makes it difficult to monitor each cold chain parcel, which may have a significant impact on the overall cost of monitoring. As technology improves and the costs of these technologies reduce, it may become more economical to monitor cold chain parcels. A crucial component of temperature monitoring data is to ensure that the data is used for effective decision-making.

Validation/qualification are potentially very powerful tools for the objective management of the outputs required from cold chain equipment and processes. These activities should not be considered as purely regulatory requirements but rather fundamental business processes to manage risk to both patient safety as well as financial risk associated with poor cold chain management. Unfortunately, the benefit is not realised until a risk event occurs that could have been prevented through an effective validation/qualification process. Organisations could benefit through a proactive approach to risk management that is inherent to the validation/qualification process resulting in an ultimate reduction in the non-conformance associated costs.
The challenges and their respective solutions should not be viewed in isolation. Any solution to resolve these challenges should be considered in a border context of the relationships that exist between these various elements.

In order to meet the continually increasing requirements in the pharmaceutical cold chain, practitioners will need to become more innovative about how they meet these requirements. This will require cooperation and collaboration among all parties involved, specifically the operational and quality functions. By sharing knowledge and experiences, industry participants are able to shortcut their problems through the use of solutions already developed by others. The sharing of these solutions should be seen in the context of an industry striving to improve patient safety. Collaboration will require engagement beyond information sharing in terms of effective forums for discussions with government in terms of both the quality and revenue components of regulations.

The fundamental challenge at hand is to balance the increasing quality requirements against the capped cost structure as defined by SEP and the need for business to remain profitable. These two functions and the overall business should focus on an objective of lowest total cost and risk rather than the lowest cost or highest quality levels.

This may require further evolution in the approach to budgeting, performance targeting and incentives to ensure that a collaborative approach is fostered within the organisation, rather than encouraging a silo-oriented mentality. If the appropriate culture can be developed, the next challenge will be to create the awareness of the interrelatedness of the cost elements in order to ensure that when decisions are made, each function considers the potential implications on other functions and the organisation as a whole.

The pharmaceutical cold chain model is intended to provide a framework for analysis as well as the development of awareness within and across organisations. The ultimate objective is to understand that relationships, direct and indirect, exist between the many elements; prior to making any decision, these should be analysed and considered.

It is crucial to view these key challenges in the context of a highly regulated industry both from a quality and cost perspective. While the Pharmacy Council and MCC continue to drive higher quality standards through appropriate validation/qualification, temperature
monitoring and cold chain packaging, SEP means the revenue that can be generated to support these and other core supply chain activities is fundamentally constrained. This is the originating key challenge on which this research was initiated. It may be necessary to review the approach to SEP in such a way as to account for the additional costs associated with the distribution of cold chain pharmaceuticals.

The fundamental objective of good quality medicines to ensure patient safety must at all times be considered in the decisions made. The South African pharmaceutical industry has the challenge of balancing quality of cold chain pharmaceuticals against the cost and access to these crucial healthcare products. This will require regulators, manufacturers, distributors and wholesalers to continue to work together to ensure that the pharmaceutical cold chain continues to deliver to the people of South Africa.

7.4. Recommendations
The key challenges primarily relate to the maintenance of proper quality controls through the transportation process and should be viewed in the context of a cost-sensitive market due to the implications of SEP. In order to resolve these challenges, organisations will need to constantly balance outbound operational requirements against the need for proper quality control. Based on the key challenges of the research the following specific recommendations should be considered:

1. Transportation risk: Transportation represents the highest risk to product across the supply chain.
   
   o Through assessing the risk on the various routes from a time and temperature perspective, appropriate cost-effective solutions can be applied, as opposed a single solution for all routes.
   
   o Standardisation of vehicles (as far as possible): Fewer types (size and design) of vehicles reduce possible variations making validation/qualification of transportation easier and in turn cheaper.

2. Shipment volume and weight: Cold chain packaging increases the total shipment volume and weight resulting in higher transport costs.
When assessing transport cost and efficiency, the impact of the cold chain packaging volume should be considered in conjunction with the duration, payload size and cost.

3. Transport service level and cold chain packaging duration: Incongruence between the transport service level and the cold chain packaging duration creates the possibility of wastage, increased cost and product risk exposure.

   - Alignment of cold chain packaging duration and service transportation service levels: A cost analysis can be done to assess which is more cost effective – shorter transport times resulting in higher transport cost and lower cold chain packaging cost, or longer transport times resulting in lower transport cost with higher cold chain packaging cost.

   - Multiple cold chain packaging system durations: By having multiple packaging system durations, for example, 12 hours, 24 hour and 48 hours, the appropriate cold chain packaging system can be used for the appropriate route, resulting in less wastage on each shipment. This should be considered in the context of additional validation/qualification requirements as well as increased operational complexity during packing.

4. Transportation temperature monitoring: Cost and time associated with temperature monitoring of transportation shipments are to be considered.

   - Sample-based temperature monitoring: Although monitoring of every cold chain shipment is ideal from a quality point of view this may not always be possible. Through a statistically sound sample method, it is possible to monitor the temperature of cold chain shipments more cost effectively. The results of this data can then be used to determine issues within the supply chain or cold chain packaging system, which can then be corrected.

   - Analytical tools and services: The immense amount of data collected through the temperature monitoring process must be effectively managed and analysed. Through the use of specialised computer programs, the data can be managed and analysed, reducing manual effort and allowing for appropriate interpretation of temperature results.
5. Cold chain packaging: Balancing requirements of duration, payload size and cost is necessary.

   o Appropriate payload volume: It is possible that the cold chain packaging system’s payload volume is not appropriate for the average order size of an organisation. This may result in wasted space within the cold chain packaging system as well as in the vehicle that the cold chain packaging system is being shipped in. The transport durations should be considered in this analysis, bearing in mind that longer transport times require increased insulation and thermal capacity which typically result in increased cost.

6. Transport validation/qualification: The importance of cold chain packaging validation/qualification is understated.

   o Education and training: Formal education programmes could be augmented to include more detail of the pharmaceutical cold chain requirements. Furthermore, organisations should invest in the training and development of both quality and operational staff regarding proper cold chain management practices.

   o Outsourcing: Being such a specialised field, validation/qualification activities can be outsourced to specialised service providers who can execute these activities for organisations. It is important, however, that organisations understand what is being done by service providers as the accountability of these activities remains with the organisation.

Based on the outcomes of the research the pharmaceutical cold chain model is recommended as a framework for the analysis of the cost, time and quality impact of decisions in a pharmaceutical cold chain distribution organisation. The model may assist in the assessment of decisions and the impact those decisions could have on the various cost elements, and in turn, the degree to which these decisions could affect the risk to the product.

The key challenges should be investigated on a case-by-case basis within an organisation in order to determine the current risk to product. Resolution of the key
challenges can then be prioritised in terms of risk, assisting the organisation to balance the implementation of quality improvements against the resources available to the organisation, within the context of a total cost approach.

All too often organisations analyse decisions in isolation only to realise after implementation the negative impacts that were not considered at the point of making the decision. This decision could exacerbate other key challenges in the process of trying to correct a specific challenge or issue. Organisations should focus on integrating decision-making related to the cost elements researched in the pharmaceutical cold chain model.

7.5. Limitations of the research
Some key assumptions and parameters were defined for the research. It is therefore important to understand how these assumptions and parameters limit the degree to which this research can be applied.

The following are considered to be the limitations of the research:

- Applicable to South Africa – Although the principle findings are likely to be applicable to other countries in some way, the research, however, cannot confirm this as respondents were limited to South Africa. Furthermore, the regulatory framework in other countries may impact any relationship as defined in this research.
- Outbound distribution – Many overhead costs (such as systems, inventory-carrying costs, etc.) have not been taken into account in this analysis. While all these costs are important and relevant to any organisation, these fall outside of the scope of this research. There are many baseline supply chain considerations that would be applicable to the pharmaceutical cold chain, as in any other supply chain; however, these are not covered within this research.
- Excludes government – As no respondents from any government agency could be recruited, the sample was not representative of government agencies in any way.
- Qualitative guidance – The figures and percentages used during the course of the cost analysis are intended as industry guidelines. These figures would vary from
organisation to organisation depending on the specific processes and infrastructure in the specific organisation. The research findings are intended to provide a framework for internal quantitative investigation to be conducted within a specific organisation.

It should be noted that the above list does not imply that the research is not applicable outside of the assumptions and parameters of the research. Rather this list suggests that it cannot be assumed that the findings of this research are universally applicable, and the findings would need to be verified through further research into any scenario outside of the defined assumptions and parameters.

7.6. Further research
In defining the objectives of the research, it was imperative to define the scope in the appropriate level of detail in order to ensure it would be practically possible to execute the research. Having completed the research there are two potential avenues for further research to be conducted. The subject can be investigated in more depth in terms of the pharmaceutical cold chain.

- The segment of the supply chain could be expanded to include inbound processes. The focus of the research was defined as outbound distribution; the principles and findings, however, may also apply to the upstream supply chain from manufacturer through to fine distribution. This could be further expanded to include the inbound processes for raw materials at the manufacturer.

- A significant challenge to the pharmaceutical industry is that of counterfeit drugs, which present both commercial and patient safety risks. How the industry tackles these challenges could represent a similar challenge to that of cold chain management. In order to address the issue, further challenges are likely to be introduced such as the progression from batch traceability to include serialisation of pharmaceutical products for increased traceability. Part of the challenge with the technological solutions to counterfeiting is that the technologies would need to be validated. There is also a potential auxiliary benefit to serialisation, in that if
temperature monitoring data could be linked to the specific serial numbers, then product temperature exposure could be tracked throughout the supply chain.
LIST OF SOURCES

ABB. (2009). *Best Practice Guide: Pharmaceutical-Chain Temperature Control and Recording*. Available from:

apps.who.int/medicinedocs/documents/s22306en/s22306en.pdf


http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SulfanilamideDisaster/default.htm


Basta, N. (2010). *New Study Sees Double-Digit Growth in Cold-Chain Services for Life Sciences*. Available from:


http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=210&showFR=1

Food and Drug Administration. (2012). *Glossary.* Available from:
http://www.fda.gov/drugs/developmentapprovalprocess/manufacturing/ucm090016.htm


Gavi Alliance. (n.d.). *Glossary.* Available from:
http://www.gavialliance.org/media_centre/glossary/index.php


http://www.gphaonline.org/about-gpha/history


http://www.google.co.za/url?sa=t&rct=j&q=it%20is%20no%20exaggeration%20to%20state%20that%20the%20story%20of%20thalidomide%20is%20the%20story%20of%20the%20modern%20FDA&source=web&cd=1&ved=0CB8QFjAA&url=http%3A%2F%2Fleda.law.harvard.edu%2Fleda%2Fdata%2F389%2FScott_P_Glauberman.rdf&ei=_2VrT8bQlpSjQfP-I2MBw&usg=AFQjCNGL93LQ8JiUeTtVlglg98gLgQT3Q


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ANNEXURE 1 – Survey

Dear Respondent

I am currently a student at the University of Johannesburg (Student Number: 200606630), completing my Masters in Logistics Management. The title of my dissertation is “Pharmaceutical Cold Chain: Determining the Trade Off’s between Quality and Outbound Distribution” I am attempting to determine if there is a relationship between specific elements identified in the management of the pharmaceutical cold chain (for the purposes of the dissertation cold chain refers specifically to product stored and transported at 2°C to 8°C), as well as determine the priority of factors within the identified elements.

Your input into this research will assist in determining if there is indeed a relationship between the elements identified. The questions do not require you to express any company confidential information. The questions are designed to capture your views, opinions and estimate figures based on your experience. Nonetheless all data collected will be kept absolutely confidential. Only aggregated data will be referenced within the dissertation. No company and respondent names will be referenced to, unless with prior consent.

Definitions:

- Outbound Distribution: For the purposes of this survey, outbound distribution is defined as the warehouse and transportation activities and costs associated with moving products to the desired end destination.

- Relationship: The degree to which 2 elements influence one another

- Pharmaceutical Industry: For the purposes of this questionnaire the pharmaceutical industry shall refer to any direct (manufacturer) or indirect (transportation of pharmaceuticals) activities

- Cold Chain: A supply chain requiring products to be distributed under temperature controlled conditions (2°C to 8°C)

- ERP: Enterprise Resource Planning system

Thanking you in advance

Sarantis Kosmas
**General**

**Question 1**

Do you work in the pharmaceutical industry?

- ☐ Yes
- ☐ No

**Question 2**

Which of the following storage temperature ranges do your products require?

- ☐ Ultra-low (below −40 °C)
- ☐ Frozen (−15 °C to −25 °C)
- ☐ Cold (2 °C to 8 °C)
- ☐ Controlled room temperature (15 °C to 25 °C)
- ☐ Other (please specify)

**Question 3**

What is the nature of the organisation?

- ☐ Manufacturer
- ☐ Distributor
- ☐ Wholesaler
- ☐ Retail pharmacy
- ☐ Government agency/department
- ☐ Other (please specify)
Question 4

Does your organisation outsource the warehousing function?

☐ Yes
☐ Some warehousing is outsourced
☐ No
☐ Other (please specify)

Question 5

Does your organisation outsource the majority of the transportation functions?

☐ Yes
☐ Some transportation is outsourced
☐ No
☐ Other (please specify)

Question 6

What is your job title?

☐ Director/executive
☐ Manager
☐ Pharmacist
☐ Supervisor
Question 7
What is the highest level of education you have completed?

- □ Matric
- □ 1 year post matric course (e.g. diploma/certificate)
- □ 3 year post matric course (e.g. diploma/degree)
- □ 4 year post matric course (e.g. Honours degree/B Tech)
- □ Master’s degree or equivalent
- □ Doctorate degree or equivalent
- □ Post-doctorate degree
- □ Other (please specify)

Question 8
Is your job primarily focused on quality or operations?

- □ Quality
- □ Operations

Question 9
How long have you worked in the pharmaceutical industry (years)?

- □ ___ years

Question 10
Rate your knowledge of distribution of temperature-sensitive pharmaceutical products

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Poor (1)</th>
<th>Low (2)</th>
<th>Medium (3)</th>
<th>High (4)</th>
<th>Very good (5)</th>
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</thead>
<tbody>
<tr>
<td>Quality knowledge</td>
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<tr>
<td>Operations knowledge</td>
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</table>
Question 11

What type of vehicles does your company use to distribute?

- Standard bodied
- Insulated bodies
- Refrigerated (cooling only)
- Temperature-controlled (heating and cooling)
- Don’t know
- Other (please specify)

Question 12

Which of the following delivery types do you do?

- Inter DC (distribution centre)/between provinces
- Fine distribution
- Outlying areas
- Temperature-controlled (heating and cooling)
- Don’t know
- Other (please specify)

Question 13

What size vehicles do you make use of?

- Small vehicle (±0.5 ton)
- Light vehicle (±1 ton to 4 tons)
- Medium vehicle (±8 tons)
- Large vehicle (±20-foot container or smaller)
- Very large (inter link/larger than 20-foot container)
- Other (please specify)
Question 14
Have you had to write off product due to failures in the cold chain?

☐ Yes
☐ No

Risk Analysis

Question 15
Rate the probability/ chance of a risk occurrence within the following elements in the cold chain which could result in a product non-conformance:

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Highly improbable (1)</th>
<th>Unlikely (2)</th>
<th>Possible (3)</th>
<th>Likely (4)</th>
<th>Highly probable (5)</th>
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<tbody>
<tr>
<td>Transportation</td>
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<td>Warehouse/ storage</td>
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<td>Temperature monitoring</td>
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<td>Cold chain packaging</td>
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<td>Validation/ qualification</td>
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Question 16
Rate the degree/ impact of a risk occurrence within the following elements in the cold chain which could result in a product non-conformance:

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Negligible impact</th>
<th>Slight impact</th>
<th>Tangible impact</th>
<th>Significant impact</th>
<th>Disastrous impact</th>
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<tbody>
<tr>
<td>Transportation</td>
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<td>Warehouse/ storage</td>
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Estimated cost

The following questions relate to estimated cost in terms of the proportionate spend on cold chain specific distribution. e.g. the proportion of warehousing rent/ cost attributable to cold chain activities.

Question 17

Rank the following cost elements from highest to lowest expense:

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
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<tr>
<td>Transportation</td>
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<td>Warehousing</td>
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<td>Validation/qualification</td>
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Question 18

What percent of total outbound distribution cost do the following elements constitute in your company?

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Less than 5%</th>
<th>10% ±5%</th>
<th>20% ±5%</th>
<th>30% ±5%</th>
<th>40% ±5%</th>
<th>50% ±5%</th>
<th>60% ±5%</th>
<th>70% ±5%</th>
<th>80% ±5%</th>
<th>90% ±5%</th>
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<tbody>
<tr>
<td>Transportation</td>
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<td>Warehousing</td>
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<td>Validation/qualification</td>
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</table>
Key factors

Rate the following factors from highest (1) importance to lowest (5) importance, in the distribution of cold chain pharmaceutical products

Question 19

Non-conformance factors

<table>
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<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<th>5</th>
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<tbody>
<tr>
<td>Direct - e.g. product write-offs</td>
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<td>Remediation - e.g. identification, correction and reporting</td>
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<td>Regulatory - e.g. fines, legal action, recalls and suspended operations</td>
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<tr>
<td>Market share - e.g. lost sales</td>
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<td>Reputational - e.g. negative brand impact</td>
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Question 20

Transport factors

<table>
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<tr>
<th>Answer options</th>
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<th>2</th>
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<tr>
<td>Volume - physical size of the parcel to be transported</td>
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<td>Weight - weight of the parcel to be transported</td>
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<td>Mode of transport (i.e. road, air, sea, rail) - relates to the primary type of transportation e.g. road vehicle, airplane, ship or train</td>
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<tr>
<td>Type of transport equipment - based on the mode of transportation, the type of transport equipment relates to insulation, refrigeration and temperature control equipment</td>
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<td>Duration to destination - the total transportation time from dispatch to receipt at the specified end point</td>
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</table>
Question 21

Warehouse factors

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<th>3</th>
<th>4</th>
<th>5</th>
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</thead>
<tbody>
<tr>
<td><strong>Product storage</strong> (cold room and freezer) - cold room and freezer space required to hold cold chain packaging materials</td>
<td></td>
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<tr>
<td><strong>Packaging storage</strong> (warehouse) - warehouse space required to hold cold chain packaging materials</td>
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<tr>
<td><strong>Electricity consumption</strong> - specifically related to the electricity required to power HVAC, air-conditioning, cold rooms and freezers</td>
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<tr>
<td><strong>Packing of cold chain parcels</strong> - the activity of packaging a cold chain parcel for delivery to the end destination</td>
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</tr>
<tr>
<td><strong>Back-up power requirements</strong> - generators, UPS required to ensure consistent power to warehouse equipment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Question 22

Temperature monitoring factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of equipment</strong> (probes and recording device) used to monitor - the model and specifications of the equipment used to monitor temperature</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of positions monitored</strong> - the number of probes used to monitor temperature</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Alarms and alerts</strong> - alarms that trigger when temperature exceeds predefined temperature limits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Harvesting (collection), management and analysis of data</strong> - the process of collecting and interpreting temperature data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Calibration</strong> of probes - annual testing of probes to ensure they operate within the required accuracy limits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Question 23

Cold chain packaging factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong> capability of cold chain shipper - the time that the cold chain shipper can maintain the temperature within the required temperature range</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Payload size/volume</strong> - the amount of product the cold chain shipper can hold</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complexity</strong> of packaging configuration - the intricacy of the specific instructions used to pack the cold chain shipper</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cost of packaging</strong> - the material cost of the packaging material, i.e. gel packs, insulated box and cardboard shippers, etc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Reusability</strong> of packaging components - the capability and practicality of reusing cold chain shipping material</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Question 24

Validation/qualification factors

<table>
<thead>
<tr>
<th>Answer options</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation of systems (ERP/accounting system and temperature monitoring)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation and temperature Mapping of warehouse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation and temperature Mapping of cold room</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation and temperature Mapping of freezer room</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation and temperature Mapping of cold chain shippers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Relationship between elements

The relationship-based questions were based on the structure shown in Table 3 below, where the underlined elements were swapped until each combination had been asked as follows:

Transportation

Question 25

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between transportation and non-conformance in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Question 26

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between transportation and validation/qualification the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Question 27**

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between transportation and cold chain packaging in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
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<td></td>
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<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Question 28**

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between transportation and temperature monitoring in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Question 29**

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between transportation and warehousing in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Warehousing

Question 30

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between warehousing and non-conformance in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Time</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Question 31

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between warehousing and validation/qualification in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Question 32

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between warehousing and cold chain packaging in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Question 33**

Rate the degree to which you agree/disagree that there is a cost, time or quality relationship between warehousing and temperature monitoring in the distribution of temperature-sensitive products.

<table>
<thead>
<tr>
<th>Answer options</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither disagree or agree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**ANNEXURE 2 – Benchmark Model A cost schedule**

*Note: Blacked out figures are to maintain confidentiality*

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit/ per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transport</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (within province of warehouse) deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 4 156.80</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel - outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 4 860.15</td>
<td>assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel - PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 2 457.38</td>
<td>assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel - JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 4 095.63</td>
<td>assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td><strong>Regional</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Box Size 1 (All Routes)</td>
<td>R 296.50</td>
<td>255</td>
<td>R 75 607.05</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (Durban Outlying)</td>
<td>R 335.13</td>
<td>16</td>
<td>R 5 362.08</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 992.85</td>
<td>98</td>
<td>R 97 299.21</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (Durban Outlying)</td>
<td>R 1 079.49</td>
<td>10</td>
<td>R 10 794.95</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>R 206 255.05</strong></td>
</tr>
<tr>
<td><strong>Warehouse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling equipment</td>
<td>R 2 526.40</td>
<td>1</td>
<td>R 2 526.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Rental (Product storage)</td>
<td>R 5 985.00</td>
<td>1</td>
<td>R 5 985.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square meter</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/ per month</td>
<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------------------</td>
<td>----------</td>
<td>-------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Rental (Packaging storage)</td>
<td>R 1 995.00</td>
<td>1</td>
<td>R 1 995.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square meter</td>
</tr>
<tr>
<td>Generator</td>
<td>R 3 916.67</td>
<td>1</td>
<td>R 3 916.67</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. R235 000 amortised over 5 years</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>3</td>
<td>R 20 784.00</td>
<td>2 pickers/ packers and 1 administrator</td>
</tr>
<tr>
<td>Cold Room</td>
<td>R 6 110.67</td>
<td>1</td>
<td>R 6 110.67</td>
<td>R366 640 amortised over 5 years</td>
</tr>
<tr>
<td>Electrical Consumption</td>
<td>R 9 484.00</td>
<td>1</td>
<td>R 9 484.00</td>
<td>Based on 2 x 13 kW condensers for 20 hours per day</td>
</tr>
<tr>
<td>Freezer Unit</td>
<td>R 88.32</td>
<td>2</td>
<td>R 176.63</td>
<td>R5299 x 2 amortised over 5 years</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>R 50 978.37</td>
<td></td>
</tr>
</tbody>
</table>

**Monitoring**

<table>
<thead>
<tr>
<th>Monitoring System Unit including 11 probes</th>
<th>Cost per unit/ per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 x probes in freezer, 5 x probes in cold room, 2 x probes outside, 2x probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>Ibuttons</td>
<td>R 19.58</td>
<td>48</td>
<td>R 940.00</td>
<td>Monitor inside and out 3 routes daily (therefor 3 x 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (on going calibration)</td>
<td>R 50.00</td>
<td>11</td>
<td>R 550.00</td>
<td>Annual Calibration cost off R600 per ibutton</td>
</tr>
<tr>
<td>Ibuttons (on going calibration)</td>
<td>R 75.00</td>
<td>48</td>
<td>R 3 600.00</td>
<td>Annual Calibration cost off R900 per ibutton</td>
</tr>
<tr>
<td>Time Spent on reviewing and reporting on data</td>
<td>R 6 514.83</td>
<td>1</td>
<td>R 6 514.83</td>
<td>Hourly rate of Responsible Pharmacist x 30 min per data set; (3routes x 5 days’ x 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary to calculate Responsible Pharmacist hourly rate</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>R 13 827.33</td>
<td></td>
</tr>
</tbody>
</table>

**Packaging**

<p>| Box1                                      | R 88.55                  | 945      | R 83 679.75             | NA                                                                          |
| Box 2                                     | R 163.30                 | 287      | R 46 867.10             | NA                                                                          |</p>
<table>
<thead>
<tr>
<th>Description</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>R 130 546.85</td>
<td></td>
</tr>
<tr>
<td>Validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warehouse Validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Cold room validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.</td>
</tr>
<tr>
<td>Freezer Validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.</td>
</tr>
<tr>
<td>ERP Validation</td>
<td></td>
<td></td>
<td></td>
<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Monitoring system Validation</td>
<td></td>
<td></td>
<td></td>
<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Generator Validation</td>
<td></td>
<td></td>
<td></td>
<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 150 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold Room mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Freezer mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Box 1 validation</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Box 2 validation</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Box 1 ongoing validation</td>
<td></td>
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<tr>
<td>Box 2 ongoing validation</td>
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<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>R 31 576.67</td>
<td></td>
</tr>
<tr>
<td>Grand Total</td>
<td></td>
<td></td>
<td>R 433 184.26</td>
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</tbody>
</table>
ANNEXURE 3 – Benchmark Model B cost schedule

*Note: Blacked out figures are to maintain confidentiality

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transport</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Local (within province of warehouse)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 4 156.80</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel - outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 4 860.15</td>
<td>assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel - PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 2 457.38</td>
<td>assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel - JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 4 095.63</td>
<td>assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td><strong>Inter DC</strong></td>
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</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>1</td>
<td>R 1 385.60</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>1</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel - DBN</td>
<td>R 6.30</td>
<td>4800</td>
<td>R 6 048.00</td>
<td>weekly replenishment trip 1200 km per trip</td>
</tr>
<tr>
<td>Fuel - CPT</td>
<td>R 6.30</td>
<td>11200</td>
<td>R 14 112.00</td>
<td>weekly replenishment trip 2800 km per trip</td>
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<td><strong>Regional Distribution</strong></td>
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<tr>
<td>Box Size 1 (all routes)</td>
<td>R 208.80</td>
<td>243</td>
<td>R 50 738.40</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (Durban Outlying)</td>
<td>R 335.13</td>
<td>16</td>
<td>R 5 362.08</td>
<td>NA</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/ per month</td>
<td>Quantity</td>
<td>Cost per unit/ per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
<td>--------------------------</td>
<td>----------</td>
<td>---------------------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Box Size 1 (Cape Town Outlying)</td>
<td>R 296.50</td>
<td>12</td>
<td>R 3 557.98</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 568.98</td>
<td>92</td>
<td>R 52 345.74</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (Durban Outlying)</td>
<td>R 1 079.49</td>
<td>10</td>
<td>R 10 794.95</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (Cape Town Outlying)</td>
<td>R 992.85</td>
<td>6</td>
<td>R 5 957.09</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total R 169 115.39</td>
</tr>
</tbody>
</table>

**Warehouse**

**Gauteng**

- **Handling equipment**: R 2 526.40 | 1 | R 2 526.40 | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume
- **Rental (Product storage)**: R 5 985.00 | 1 | R 5 985.00 | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square meter
- **Rental (Packaging storage)**: R 1 995.00 | 1 | R 1 995.00 | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square meter
- **Generator**: R 3 916.67 | 1 | R 3 916.67 | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. R235 000 amortised over 5 years
- **Staff x 3**: R 20 784.00 | 1 | R 20 784.00 | 2 pickers/packers and 1 administrator
- **Cold room**: R 6 110.67 | 1 | R 6 110.67 | R366 640 amortised over 5 years
- **Electrical consumption**: R 9 484.00 | 1 | R 9 484.00 | Based on 2 x 13 kW condensers for 20 hours per day
- **Freezer unit**: R 88.32 | 2 | R 176.63 | R5299 x 2 amortised over 5 years

**Durban**

- **Rental (product storage)**: R 2 992.50 | 1 | R 2 992.50 | Warehouse space 50% of Gauteng
- **Rental (packaging storage)**: R 997.50 | 1 | R 997.50 | Warehouse space 50% of Gauteng
- **Generator**: R 1 666.67 | 1 | R 1 666.67 | Generator one-third the size of Gauteng
- **Staff x 3**: R 20 784.00 | 1 | R 20 784.00 | 2 pickers still required for redundancy
- **Cold room**: R 2 036.89 | 1 | R 2 036.89 | Cold room one-third the size of Gauteng
- **Electrical consumption**: R 3 129.72 | 1 | R 3 129.72 | Electrical consumption one-third of Gauteng
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit/ per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>1</td>
<td>R 88.32</td>
<td>Only 1 unit required</td>
</tr>
<tr>
<td>Cape Town</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 2 992.50</td>
<td>1</td>
<td>R 2 992.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 997.50</td>
<td>1</td>
<td>R 997.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Generator</td>
<td>R 1 666.67</td>
<td>1</td>
<td>R 1 666.67</td>
<td>Generator one-third the size of Gauteng</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>Cold room one-third the size of Gauteng</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 2 036.89</td>
<td>1</td>
<td>R 2 036.89</td>
<td></td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 3 129.72</td>
<td>1</td>
<td>R 3 129.72</td>
<td>Electrical consumption one-third of Gauteng</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>1</td>
<td>R 88.32</td>
<td>Only 1 unit required</td>
</tr>
<tr>
<td>Total</td>
<td>R 114 369.55</td>
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**Monitoring**

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit/ per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring system unit in including 11 probes</td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 × probes in freezer, 5 × probes in cold room, 2 × probes outside, 2 × probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>Monitoring system unit in including 8 probes</td>
<td>R 2 205.00</td>
<td>1</td>
<td>R 2 205.00</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>Monitoring system unit in including 8 probes</td>
<td>R 2 187.50</td>
<td>1</td>
<td>R 2 187.50</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>Ibuttons</td>
<td>R 19.58</td>
<td>48</td>
<td>R 940.00</td>
<td>Monitor inside and out 3 routes daily (therefor 3 × 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (ongoing calibration)</td>
<td>R 50.00</td>
<td>27</td>
<td>R 1 350.00</td>
<td>Annual calibration cost off R600 per ibutton</td>
</tr>
<tr>
<td>Ibuttons (ongoing calibration)</td>
<td>R 75.00</td>
<td>48</td>
<td>R 3 600.00</td>
<td>Annual calibration cost off R900 per ibutton</td>
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<tr>
<td>Time spent on reviewing and reporting on data</td>
<td>R 7 962.58</td>
<td>1</td>
<td>R 7 962.58</td>
<td>Hourly rate of RP × 30 min per data set; (3 routes × 5 days × 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary for RP hourly rate; add 16 hours for scenario 2</td>
</tr>
<tr>
<td>Total</td>
<td>R 20 467.58</td>
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**Packaging**

---

273
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit/ per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
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</thead>
<tbody>
<tr>
<td>Box 1</td>
<td>R 88.55</td>
<td>945</td>
<td>R 83 679.75</td>
<td>Boxes used for inter DC shipments will be reused at DC of destination</td>
</tr>
<tr>
<td>Box 2</td>
<td>R 163.30</td>
<td>287</td>
<td>R 46 867.10</td>
<td>Boxes used for inter DC shipments will be reused at DC of destination</td>
</tr>
<tr>
<td>Total</td>
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<td>R 130 546.85</td>
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<tr>
<td>Validation</td>
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<tr>
<td>Warehouse validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Cold room validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years</td>
</tr>
<tr>
<td>Freezer validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years</td>
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<tr>
<td>ERP validation</td>
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<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
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<tr>
<td>Monitoring system validation</td>
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<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Generator validation</td>
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<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 150 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Freezer mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Durban</td>
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<tr>
<td>Warehouse validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/ per month</td>
<td>Quantity</td>
<td>Cost per unit/ per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>---------------------------</td>
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<tr>
<td>Cold room validation</td>
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<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Freezer validation</td>
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<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Monitoring validation</td>
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<tr>
<td>Generator validation</td>
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</tr>
<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
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<td>Based on 50 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
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<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Freezer mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cape Town</td>
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<tr>
<td>warehouse Validation</td>
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<td>Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost</td>
</tr>
<tr>
<td>Cold room validation</td>
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<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<tr>
<td>Freezer validation</td>
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<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Monitoring validation</td>
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</tr>
<tr>
<td>Generator validation</td>
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</tr>
<tr>
<td>Warehouse mapping</td>
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<td></td>
<td></td>
<td>Based on 50 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
<td></td>
<td></td>
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<td>Based on 25 probes, cost over 12 months</td>
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<td>Freezer mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Box 1 validation</td>
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<td>Box 2 validation</td>
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<td>Total</td>
<td>R 38 643.33</td>
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<tr>
<td>Grand total</td>
<td>R 473 142.70</td>
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</table>
ANNEXURE 4 – Scenario A1 cost schedule

*Note: Blacked out figures are to maintain confidentiality

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (within province of warehouse) deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 2 771.20</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – Outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 4 860.15</td>
<td>Assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 1 228.69</td>
<td>Assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 2 047.82</td>
<td>Assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Regional</td>
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<td></td>
</tr>
<tr>
<td>Box Size 1 (all routes)</td>
<td>R 197.32</td>
<td>255</td>
<td>R 50 316.42</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (Durban outlying)</td>
<td>R 218.19</td>
<td>16</td>
<td>R 3 491.03</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 533.48</td>
<td>98</td>
<td>R 52 281.11</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (Durban outlying)</td>
<td>R 650.41</td>
<td>10</td>
<td>R 6 504.07</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>R 125 122.28</strong></td>
<td></td>
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</tr>
<tr>
<td>Warehouse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling equipment</td>
<td>R 2 526.40</td>
<td>1</td>
<td>R 2 526.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 5 985.00</td>
<td>1</td>
<td>R 5 985.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square meter</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit per month</td>
<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-------------------------</td>
<td>----------</td>
<td>-------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 1 995.00</td>
<td>1</td>
<td>R 1 995.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre</td>
</tr>
<tr>
<td>Generator</td>
<td>R 3 916.67</td>
<td>1</td>
<td>R 3 916.67</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. R235 000 amortised over 5 years</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>3</td>
<td>R 20 784.00</td>
<td>2 pickers/packers and 1 administrator</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 6 110.67</td>
<td>1</td>
<td>R 6 110.67</td>
<td>R366 640 amortised over 5 years</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 9 484.00</td>
<td>1</td>
<td>R 9 484.00</td>
<td>Based on 2 × 13 kw condensers for 20 hours per day</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>2</td>
<td>R 176.63</td>
<td>R5299 × 2 amortised over 5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Total</strong> R 50 978.37</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring system unit in</td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 × probes in freezer, 5 × probes in cold room, 2 × probes outside, 2 × probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>including 11 probes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibuttons</td>
<td>R 19.58</td>
<td>54</td>
<td>R 1 057.50</td>
<td>Monitor inside and out 3 routes daily (therefore 3 × 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (ongoing calibration)</td>
<td>R 50.00</td>
<td>11</td>
<td>R 550.00</td>
<td>Annual calibration cost of R600 per ibutton</td>
</tr>
<tr>
<td>Ibuttons (ongoing calibration)</td>
<td>R 75.00</td>
<td>54</td>
<td>R 4 050.00</td>
<td>Annual calibration cost of R900 per ibutton</td>
</tr>
<tr>
<td>Time spent on reviewing and</td>
<td>R 6 514.83</td>
<td>1</td>
<td>R 6 514.83</td>
<td>Hourly rate of Responsible Pharmacist × 30 min per data set; (3 routes × 5 days × 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary to calculate Responsible Pharmacist hourly rate</td>
</tr>
<tr>
<td>reporting on data</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td></td>
<td><strong>Total</strong></td>
<td>R 14 394.83</td>
</tr>
<tr>
<td><strong>Packaging</strong></td>
<td></td>
<td></td>
<td></td>
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</table>

277
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Box1</td>
<td>R 97.75</td>
<td>1351.35</td>
<td>R 132 094.46</td>
<td>Addition of 3.2 litres of additional gel packs and reduction of 10% space utilisation</td>
</tr>
<tr>
<td>Box 2</td>
<td>R 181.70</td>
<td>332.92</td>
<td>R 60 491.56</td>
<td>Addition of 4.8 litres of additional gel packs and reduction of 10% space utilisation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total R 192 586.03</td>
</tr>
</tbody>
</table>

**Validation**

- **Warehouse validation**: Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume
- **Cold room validation**: Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years
- **Freezer validation**: Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years
- **ERP validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume
- **Monitoring system validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume
- **Generator validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume
- **Warehouse mapping**: Based on 150 probes, cost over 12 months
- **Cold room mapping**: Based on 25 probes, cost over 12 months
- **Freezer mapping**: Based on 25 probes, cost over 12 months
- **Box 1 validation**: NA
- **Box 2 validation**: NA
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Box 1 ongoing validation</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Box 2 ongoing validation</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>R 34 756.67</td>
<td></td>
</tr>
<tr>
<td>Grand total</td>
<td></td>
<td></td>
<td>R 417 838.18</td>
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</table>
# ANNEXURE 5 – Scenario A2 cost schedule

*Note: Blacked out figures are to maintain confidentiality*

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transport</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (within province of warehouse) deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 5 542.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – Outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 9 720.30</td>
<td>Assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 2 457.38</td>
<td>Assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 4 095.63</td>
<td>Assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td><strong>Regional</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Box Size 1 (all routes)</td>
<td>R 368.53</td>
<td>255</td>
<td>R 93 976.00</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (DBN outlying)</td>
<td>R 419.69</td>
<td>16</td>
<td>R 6 715.06</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 1 280.99</td>
<td>98</td>
<td>R 125 536.97</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (DBN outlying)</td>
<td>R 1 428.19</td>
<td>10</td>
<td>R 14 281.89</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>R 263 947.43</strong></td>
</tr>
</tbody>
</table>

<p>| <strong>Warehouse</strong>                                    |                         |          |                         |                                                                             |
| Handling equipment                               | R 2 526.40              | 1        | R 2 526.40              | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume |
| Rental (product storage)                         | R 5 985.00              | 1        | R 5 985.00              | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre |
| Rental (packaging storage)                       | R 1 995.00              | 1        | R 1 995.00              | Only 20% of the cost is applied, as cold chain constitutes 20% of the volume |</p>
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generator</td>
<td>R 3 916.67</td>
<td>1</td>
<td>R 3 916.67</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. R235 000 amortised over 5 years</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>3</td>
<td>R 20 784.00</td>
<td>2 pickers/packers and 1 administrator</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 6 110.67</td>
<td>1</td>
<td>R 6 110.67</td>
<td>R366 640 amortised over 5 years</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 9 484.00</td>
<td>1</td>
<td>R 9 484.00</td>
<td>Based on 2 × 13 kw condensers for 20 hours per day</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>2</td>
<td>R 176.63</td>
<td>R5299 × 2 amortised over 5 years</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 50 978.37</strong></td>
<td></td>
</tr>
<tr>
<td>Monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring system unit in</td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 × probes in freezer, 5 × probes in cold room, 2 × probes outside, 2 × probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>including 11 probes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibbuttons</td>
<td>R 19.58</td>
<td>48</td>
<td>R 940.00</td>
<td>Monitor inside and out 3 routes daily (therefore 3 × 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (ongoing calibration)</td>
<td>R 50.00</td>
<td>11</td>
<td>R 550.00</td>
<td>Annual calibration cost of R600 per ibutton</td>
</tr>
<tr>
<td>Ibbuttons (ongoing calibration)</td>
<td>R 75.00</td>
<td>48</td>
<td>R 3 600.00</td>
<td>Annual calibration cost of R900 per ibutton</td>
</tr>
<tr>
<td>Time spent on reviewing and</td>
<td>R 6 514.83</td>
<td>1</td>
<td>R 6 514.83</td>
<td>Hourly rate of Responsible Pharmacist × 30 min per data set; (3 routes × 5 days × 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary to calculate Responsible Pharmacist hourly rate</td>
</tr>
<tr>
<td>reporting on data</td>
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<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 13 827.33</strong></td>
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<tr>
<td>Packaging</td>
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</tr>
<tr>
<td>Box 1 18 hour</td>
<td>R 79.35</td>
<td>945</td>
<td>R 74 985.75</td>
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<tr>
<td>Box 2 18 hour</td>
<td>R 144.90</td>
<td>287</td>
<td>R 41 586.30</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
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<td></td>
<td><strong>R 116 572.05</strong></td>
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281
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warehouse validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Cold room validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years</td>
</tr>
<tr>
<td>Freezer validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years</td>
</tr>
<tr>
<td>ERP validation</td>
<td></td>
<td></td>
<td></td>
<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Monitoring system validation</td>
<td></td>
<td></td>
<td></td>
<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Generator validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 150 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Freezer mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Box 1 validation</td>
<td></td>
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<td></td>
<td>Additional validation required for the 18-hour configuration</td>
</tr>
<tr>
<td>Box 2 validation</td>
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<td></td>
<td></td>
<td>Additional validation required for the 18-hour configuration</td>
</tr>
<tr>
<td>Box 1 ongoing validation</td>
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</tr>
<tr>
<td>Box 2 ongoing validation</td>
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<tr>
<td>Total</td>
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<td>R 34 756.67</td>
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<tr>
<td>Grand total</td>
<td></td>
<td></td>
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<td>R 480 081.84</td>
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</table>
### ANNEXURE 6 – Scenario B1 cost schedule

*Note: Blacked out figures are to maintain confidentiality*

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit/per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (within province of warehouse) deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 2 771.20</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – Outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 4 860.15</td>
<td>Assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 1 228.69</td>
<td>Assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 2 047.82</td>
<td>assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Inter DC</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>1</td>
<td>R 1 385.60</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>1</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – DBN</td>
<td>R 6.30</td>
<td>4800</td>
<td>R 6 048.00</td>
<td>Weekly replenishment trip 1200 km per trip</td>
</tr>
<tr>
<td>Fuel – CPT</td>
<td>R 6.30</td>
<td>11200</td>
<td>R 14 112.00</td>
<td>Weekly replenishment trip 2800 km per trip</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/per month</td>
<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-------------------------</td>
<td>----------</td>
<td>-------------------------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Regional – Local distribution</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Box Size 1 (all routes)</td>
<td>R 172.27</td>
<td>243</td>
<td>R 41 860.80</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (DBN outlying)</td>
<td>R 242.21</td>
<td>16</td>
<td>R 3 875.37</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (CPT outlying)</td>
<td>R 197.32</td>
<td>12</td>
<td>R 2 367.83</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 412.38</td>
<td>92</td>
<td>R 37 938.86</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (DBN outlying)</td>
<td>R 650.41</td>
<td>10</td>
<td>R 6 504.07</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (CPT outlying)</td>
<td>R 533.48</td>
<td>6</td>
<td>R 3 200.88</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 131 444.87</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Warehouse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gauteng</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling equipment</td>
<td>R 2 526.40</td>
<td>1</td>
<td>R 2 526.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 5 985.00</td>
<td>1</td>
<td>R 5 985.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 1 995.00</td>
<td>1</td>
<td>R 1 995.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre</td>
</tr>
<tr>
<td>Generator</td>
<td>R 3 916.67</td>
<td>1</td>
<td>R 3 916.67</td>
<td>2 pickers/packers and 1 administrator</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>2 pickers still required for redundancy</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 6 110.67</td>
<td>1</td>
<td>R 6 110.67</td>
<td>R366 640 amortised over 5 years</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 9 484.00</td>
<td>1</td>
<td>R 9 484.00</td>
<td>Based on 2 × 13kw condensers for 20 hours per day</td>
</tr>
<tr>
<td>Freezer Unit</td>
<td>R 88.32</td>
<td>2</td>
<td>R 176.63</td>
<td>R5299 × 2 amortised over 5 years</td>
</tr>
<tr>
<td><strong>Durban</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 2 992.50</td>
<td>1</td>
<td>R 2 992.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 997.50</td>
<td>1</td>
<td>R 997.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Generator</td>
<td>R 1 666.67</td>
<td>1</td>
<td>R 1 666.67</td>
<td>Generator one-third the size of Gauteng</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>2 pickers still required for redundancy</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/per month</td>
<td>Quantity</td>
<td>Cost per unit/per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------------------</td>
<td>----------</td>
<td>-------------------------</td>
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</tr>
<tr>
<td>Cold room</td>
<td>R 2 036.89</td>
<td>1</td>
<td>R 2 036.89</td>
<td>Cold room one-third the size of Gauteng</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 3 129.72</td>
<td>1</td>
<td>R 3 129.72</td>
<td>Electrical consumption one-third of Gauteng</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>1</td>
<td>R 88.32</td>
<td>Only 1 unit required</td>
</tr>
<tr>
<td>Cape Town</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 2 992.50</td>
<td>1</td>
<td>R 2 992.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 997.50</td>
<td>1</td>
<td>R 997.50</td>
<td>Warehouse space 50% of Gauteng</td>
</tr>
<tr>
<td>Generator</td>
<td>R 1 666.67</td>
<td>1</td>
<td>R 1 666.67</td>
<td>Generator one-third the size of Gauteng</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>2 pickers still required for redundancy</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 2 036.89</td>
<td>1</td>
<td>R 2 036.89</td>
<td>Cold Room one-third the size of Gauteng</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 3 129.72</td>
<td>1</td>
<td>R 3 129.72</td>
<td>Electrical consumption one-third of Gauteng</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>1</td>
<td>R 88.32</td>
<td>Only 1 unit required</td>
</tr>
<tr>
<td>Total</td>
<td></td>
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<td>R 114 369.55</td>
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</tr>
<tr>
<td>Monitoring</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Monitoring system unit in</td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 × probes in freezer, 5 × probes in cold room, 2 × probes outside, 2 × probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>including 11 probes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring system unit in</td>
<td>R 2 205.00</td>
<td>1</td>
<td>R 2 205.00</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>including 8 probes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring system unit in</td>
<td>R 2 187.50</td>
<td>1</td>
<td>R 2 187.50</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>including 8 probes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibuttons</td>
<td>R 19.58</td>
<td>54</td>
<td>R 1 057.50</td>
<td>Monitor inside and out 3 routes daily (therefor 3 × 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (ongoing calibration)</td>
<td>R 50.00</td>
<td>27</td>
<td>R 1 350.00</td>
<td>Annual calibration cost of R600 per ibutton</td>
</tr>
<tr>
<td>Ibuttons (ongoing calibration)</td>
<td>R 75.00</td>
<td>54</td>
<td>R 4 050.00</td>
<td>Annual calibration cost of R900 per ibutton</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/per month</td>
<td>Quantity</td>
<td>Cost per unit/per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>-------------------------</td>
<td>----------</td>
<td>-------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Time spent on reviewing and reporting on data</td>
<td>R 7 962.58</td>
<td>1</td>
<td>R 7 962.58</td>
<td>Hourly rate of RP × 30 min per data set; (3 routes × 5 days × 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary for RP hourly rate; add 16 hours for scenario 2</td>
</tr>
<tr>
<td>Total</td>
<td>R 21 035.08</td>
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<td>Packaging</td>
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<tr>
<td>Box 1</td>
<td>R 97.75</td>
<td>1351.35</td>
<td>R 132 094.46</td>
<td>Boxes used for inter-DC shipments will be reused at DC of destination</td>
</tr>
<tr>
<td>Box 2</td>
<td>R 181.70</td>
<td>332.92</td>
<td>R 60 491.56</td>
<td>Boxes used for inter-DC shipments will be reused at DC of destination</td>
</tr>
<tr>
<td>Total</td>
<td>R 192 586.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warehouse validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Cold room validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.</td>
</tr>
<tr>
<td>Freezer validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.</td>
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<tr>
<td>ERP validation</td>
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<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
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<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Generator validation</td>
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<td>Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit/per month</td>
<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
</tr>
<tr>
<td>---------------------------------</td>
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<tr>
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<td>cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Warehouse mapping</td>
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<td>Based on 150 probes, cost over 12 months</td>
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<tr>
<td>Cold room mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Freezer mapping</td>
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<td></td>
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<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Durban</td>
<td></td>
<td></td>
<td></td>
<td>Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost</td>
</tr>
<tr>
<td>Warehouse validation</td>
<td></td>
<td></td>
<td></td>
<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<tr>
<td>Cold room validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<td>Freezer validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<td>Monitoring validation</td>
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<td></td>
</tr>
<tr>
<td>Generator validation</td>
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<td></td>
</tr>
<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 50 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Freezer mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cape Town</td>
<td></td>
<td></td>
<td></td>
<td>Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost</td>
</tr>
<tr>
<td>Warehouse validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<td>Cold room validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<tr>
<td>Freezer validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<tr>
<td>Monitoring validation</td>
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</tr>
<tr>
<td>Generator validation</td>
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<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
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</tr>
<tr>
<td>Warehouse mapping</td>
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<td>Based on 50 probes, cost over 12 months</td>
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<tr>
<td>Cold room mapping</td>
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<td></td>
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<td>Based on 25 probes, cost over 12 months</td>
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<td>Freezer mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<tr>
<td>Box 1 validation</td>
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<tr>
<td>Box 2 validation</td>
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<tr>
<td>Box 1 ongoing validation</td>
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<tr>
<td>Box 2 ongoing validation</td>
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<td></td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 41 823.33</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td></td>
<td></td>
<td><strong>R 501 258.86</strong></td>
<td></td>
</tr>
</tbody>
</table>
## ANNEXURE 7 – Scenario B2 cost schedule

*Note: Blacked out figures are to maintain confidentiality*

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transport</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (within province of warehouse) deliveries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>3</td>
<td>R 5 542.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>3</td>
<td>R 2 162.40</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – Outlying</td>
<td>R 6.30</td>
<td>3857.26</td>
<td>R 9 720.30</td>
<td>Assume daily travel of 178 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – PTA</td>
<td>R 6.30</td>
<td>1950.3</td>
<td>R 2 457.38</td>
<td>Assume daily travel of 90 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td>Fuel – JHB</td>
<td>R 6.30</td>
<td>3250.5</td>
<td>R 4 095.63</td>
<td>Assume daily travel of 150 km; use Road Freight Association (RFA) cost per kilometre (CPK) of 630c, includes maintenance</td>
</tr>
<tr>
<td><strong>Inter DC</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Drivers</td>
<td>R 6 928.00</td>
<td>1</td>
<td>R 1 385.60</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Vehicles</td>
<td>R 2 703.00</td>
<td>1</td>
<td>R 1 621.80</td>
<td>R150 000 per vehicle (9% interest, 72 months). Only 20% of the driver cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Fuel – DBN</td>
<td>R 6.30</td>
<td>4800</td>
<td>R 6 048.00</td>
<td>Weekly replenishment trip 1200 km per trip</td>
</tr>
<tr>
<td>Fuel – CPT</td>
<td>R 6.30</td>
<td>11200</td>
<td>R 14 112.00</td>
<td>Weekly replenishment trip 2800 km per trip</td>
</tr>
<tr>
<td><strong>Regional – Local distribution</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Box Size 1 (all routes)</td>
<td>R 368.53</td>
<td>243</td>
<td>R 89 553.60</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 1 (Durban outlying)</td>
<td>R 419.69</td>
<td>16</td>
<td>R 6 715.06</td>
<td>NA</td>
</tr>
<tr>
<td>Description</td>
<td>Cost per unit per month</td>
<td>Quantity</td>
<td>Cost per unit per month</td>
<td>Assumptions</td>
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<td>------------------------------------------</td>
<td>-------------------------</td>
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<td>-------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Box Size 1 (CPT outlying)</td>
<td>R 197.32</td>
<td>12</td>
<td>R 2 367.83</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (all routes)</td>
<td>R 1 280.99</td>
<td>92</td>
<td>R 117 851.03</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (DBN outlying)</td>
<td>R 1 428.19</td>
<td>10</td>
<td>R 14 281.89</td>
<td>NA</td>
</tr>
<tr>
<td>Box Size 2 (CPT outlying)</td>
<td>R 1 280.99</td>
<td>6</td>
<td>R 7 685.94</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td></td>
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<td>R 285 600.86</td>
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</table>

**Warehouse**

**Gauteng**

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handling equipment</td>
<td>R 2 526.40</td>
<td>1</td>
<td>R 2 526.40</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume</td>
</tr>
<tr>
<td>Rental (product storage)</td>
<td>R 5 985.00</td>
<td>1</td>
<td>R 5 985.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre</td>
</tr>
<tr>
<td>Rental (packaging storage)</td>
<td>R 1 995.00</td>
<td>1</td>
<td>R 1 995.00</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. Based on the cost per square metre</td>
</tr>
<tr>
<td>Generator</td>
<td>R 3 916.67</td>
<td>1</td>
<td>R 3 916.67</td>
<td>Only 20% of the cost is applied, as cold chain constitutes 20% of the volume. R235 000 amortised over 5 years</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>2 pickers/packers and 1 administrator</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 6 110.67</td>
<td>1</td>
<td>R 6 110.67</td>
<td>R366 640 amortised over 5 years</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 9 484.00</td>
<td>1</td>
<td>R 9 484.00</td>
<td>Based on 2 × 13 kw condensers for 20 hours per day</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>2</td>
<td>R 176.63</td>
<td>R5299 × 2 amortised over 5 years</td>
</tr>
</tbody>
</table>

**Durban**

| Rental (product storage)                 | R 2 992.50              | 1        | R 2 992.50              | Warehouse space 50% of Gauteng                                               |
| Rental (packaging storage)               | R 997.50                | 1        | R 997.50                | Warehouse space 50% of Gauteng                                               |
| Generator                                | R 1 666.67              | 1        | R 1 666.67              | Generator one-third the size of Gauteng                                       |
| Staff × 3                                 | R 20 784.00             | 1        | R 20 784.00             | 2 pickers still required for redundancy                                       |
| Cold room                                | R 2 036.89              | 1        | R 2 036.89              | Cold room one-third the size of Gauteng                                       |
| Electrical consumption                    | R 3 129.72              | 1        | R 3 129.72              | Electrical consumption one-third of Gauteng                                   |
| Freezer unit                             | R 88.32                 | 1        | R 88.32                 | Only 1 unit required                                                         |

**Cape Town**
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
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<tr>
<td>Rental (product storage)</td>
<td>R 2 992.50</td>
<td>1</td>
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<td>Generator</td>
<td>R 1 666.67</td>
<td>1</td>
<td>R 1 666.67</td>
<td>Generator one-third the size of Gauteng</td>
</tr>
<tr>
<td>Staff × 3</td>
<td>R 20 784.00</td>
<td>1</td>
<td>R 20 784.00</td>
<td>2 pickers still required for redundancy</td>
</tr>
<tr>
<td>Cold room</td>
<td>R 2 036.89</td>
<td>1</td>
<td>R 2 036.89</td>
<td>Cold room one-third the size of Gauteng</td>
</tr>
<tr>
<td>Electrical consumption</td>
<td>R 3 129.72</td>
<td>1</td>
<td>R 3 129.72</td>
<td>Electrical consumption one-third of Gauteng</td>
</tr>
<tr>
<td>Freezer unit</td>
<td>R 88.32</td>
<td>1</td>
<td>R 88.32</td>
<td>Only 1 unit required</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 114 369.55</strong></td>
<td></td>
</tr>
<tr>
<td>Monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring system unit in including 11 probes</td>
<td>R 2 222.50</td>
<td>1</td>
<td>R 2 222.50</td>
<td>Eurotherm (2 × probes in freezer, 5 × probes in cold room, 2 × probes outside, 2 × probes outside cold room). R133 350 amortised over 5 years</td>
</tr>
<tr>
<td>Monitoring system unit in including 8 probes</td>
<td>R 2 205.00</td>
<td>1</td>
<td>R 2 205.00</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>Monitoring system unit in including 8 probes</td>
<td>R 2 187.50</td>
<td>1</td>
<td>R 2 187.50</td>
<td>As per Gauteng less 3 probes</td>
</tr>
<tr>
<td>Ibuttons</td>
<td>R 19.58</td>
<td>48</td>
<td>R 940.00</td>
<td>Monitor inside and out 3 routes daily (therefor 3 × 8 days) includes time for return; R1 175 per ibutton (R600 for initial calibration; R575 for ibutton). Amortised over 5 years</td>
</tr>
<tr>
<td>PT100 (ongoing calibration)</td>
<td>R 50.00</td>
<td>27</td>
<td>R 1 350.00</td>
<td>Annual calibration cost of R600 per ibutton</td>
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<tr>
<td>Ibuttons (ongoing calibration)</td>
<td>R 75.00</td>
<td>48</td>
<td>R 3 600.00</td>
<td>Annual calibration cost of R900 per ibutton</td>
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<tr>
<td>Time spent on reviewing and reporting on data</td>
<td>R 7 962.58</td>
<td>1</td>
<td>R 7 962.58</td>
<td>Hourly rate of RP × 30 min per data set; (3 routes × 5 days × 4 weeks=60 data sets); 12 data sets for monitoring; 400k annual salary for RP hourly rate; add 16 hours for scenario 2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R 20 467.58</strong></td>
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**Packaging**
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Box 1</td>
<td>R 79.35</td>
<td>945</td>
<td>R 74 985.75</td>
<td>Boxes used for inter-DC shipments will be reused at DC of destination</td>
</tr>
<tr>
<td>Box 2</td>
<td>R 144.90</td>
<td>287</td>
<td>R 41 586.30</td>
<td>Boxes used for inter-DC shipments will be reused at DC of destination</td>
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<td></td>
<td></td>
<td></td>
<td><strong>Total</strong> R 116 572.05</td>
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</tbody>
</table>

**Validation**

- **Warehouse validation**: Based 150 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost. Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.
- **Cold room validation**: Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.
- **Freezer validation**: Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping. Costs amortised over 5 years.
- **ERP validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.
- **Monitoring system validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.
- **Generator validation**: Costs amortised over 5 years. Only 20% of the cost is applied, as cold chain constitutes 20% of the volume.
- **Warehouse mapping**: Based on 150 probes, cost over 12 months.
- **Cold room mapping**: Based on 25 probes, cost over 12 months.
- **Freezer mapping**: Based on 25 probes, cost over 12 months.
- **Durban**: Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost.
<table>
<thead>
<tr>
<th>Description</th>
<th>Cost per unit per month</th>
<th>Quantity</th>
<th>Cost per unit per month</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold room validation</td>
<td></td>
<td></td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Freezer validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Monitoring validation</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Generator validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warehouse mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 50 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td>Freezer mapping</td>
<td></td>
<td></td>
<td></td>
<td>Based on 25 probes, cost over 12 months</td>
</tr>
<tr>
<td><strong>Cape Town</strong></td>
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<tr>
<td>Warehouse validation</td>
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<td>Based 50 probes, IQ, OQ, PQ, PQ mapping for only 1 season, alternate season is included in mapping cost</td>
</tr>
<tr>
<td>Cold room validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
</tr>
<tr>
<td>Freezer validation</td>
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<td>Based 25 probes, IQ, OQ, PQ, PQ mapping excluded as included in annual mapping</td>
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<tr>
<td>Monitoring validation</td>
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</tr>
<tr>
<td>Generator validation</td>
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</tr>
<tr>
<td>Warehouse mapping</td>
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<td>Based on 50 probes, cost over 12 months</td>
</tr>
<tr>
<td>Cold room mapping</td>
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<td>Based on 25 probes, cost over 12 months</td>
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<td>Freezer mapping</td>
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</tr>
<tr>
<td>Box 1 validation</td>
<td>NA</td>
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<tr>
<td>Box 2 validation</td>
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<tr>
<td>Box 1 ongoing validation</td>
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<td><strong>Total</strong></td>
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<td>Description</td>
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<td>Assumptions</td>
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<td>Grand total</td>
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<td>R 578 833.37</td>
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