An Analysis of the Upstream Supply Chain for Second-Line Drugs for Multidrug-Resistant Tuberculosis

by

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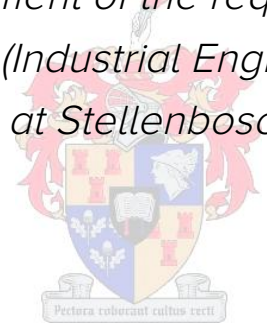
Thesis presented in fulfilment of the requirements for the degree of Master of Engineering (Industrial Engineering) in the Faculty of Engineering at Stellenbosch University



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March 2017

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Abstract

Systematic problems in the supply chain of second-line anti-TB drugs (SLDs) for multi-drug-resistant tuberculosis (MDR-TB) are well documented and contribute significantly to the comprehension of the difficulties preventing successful control of the disease. Though literature contains a wealth of proposed changes to global SLD supply chain policies, there is a significant research gap related to quantitative modelling of the SLD supply chain to accurately predict the expected impact of these proposed changes on the availability of SLDs.

The global SLD supply chain consists of two components: (i) the 'upstream' component which includes all activities from the manufacturing of the active pharmaceutical ingredient through to the warehousing of drugs prior to shipment; and (ii) the 'downstream' component which includes in-country warehousing and delivery of drugs to various healthcare facilities. A prominent problem in the supply chain, is the erratic demand patterns, since these prohibit accurate forecasting and effective planning. Consequently, manufacturers are forced to produce drugs in inefficient batch sizes, causing higher prices and longer, inconsistent lead times. A possible solution to address this problem, is the implementation of a large buffer stockpile directed at (i) preventing stock-outs and treatment interruptions, and (ii) combining and timing orders to permit current manufacturers to produce medicines more efficiently.

The aim of this study is to model a part of the upstream supply chain of MDR-TB SLDs and to evaluate the impact of implementing such a buffer stockpile. The supply chain is modelled using system dynamics and the model is used to evaluate the likely impact of a range of alternative inventory management policies on the supply chain performance. Three different SLD formulations are included in the model to ensure that the recommendations based on this research are robust. These formulations, namely capreomycin, kanamycin and cycloserine, account for approximately 58% of the total procurement costs of the current supply chain.

The modelling results indicate that the inventory policies that will most likely lead to the most significant improvement in the supply chain performance, are the policies that implement a reorder quantity based on an exponential smoothing forecast of previous demand, specifically when a smoothing factor of either 0.1 or 0.5 and a high reorder point are implemented.

This research contributes to the current academic literature by increasing the understanding of the upstream SLD supply chain, by providing a quantitative evaluation of the expected impact of suggested changes to the supply chain, and by presenting an example of an application of the system dynamics modelling approach that is not common in literature.

Opsomming

Sistematiese probleme in die voorsieningsketting van tweede lyn anti-TB-middels (SLDs) vir multi-weerstandbiedende tuberkulose (MDR-TB) is goed gedokumenteer en maak ‘n aansienlike bydrae om die probleme wat die suksesvolle beheer van die siekte voorkom, te verstaan. Alhoewel literatuur 'n rykdom van voorgestelde wysigings aan die globale SLD voorsieningsketting bevat, is daar 'n beduidende navorsing gaping wat verband hou met die kwantitatiewe modellering van die SLD voorsieningsketting om die verwagte impak wat hierdie voorgestelde wysigings aan die beskikbaarheid van SLDs sal hê, akkuraat te voorspel.

Die globale SLD voorsieningsketting bestaan uit twee komponente: (i) die 'stroomop’ komponent wat alle aktiwiteite van die vervaardiging van die aktiewe farmaseutiese bestanddeel, tot die verpakking van die teenmiddels vir distribusie, insluit; en (ii) die ‘stroomaf’ komponent wat die binnelandse (nasionale) pakhuise en die aflewering van teenmiddels na verskeie gesondheidsorg fasiliteite insluit. 'n Prominente probleem in die voorsieningsketting is die dinamiese en wisselvallige aanvraag patrone vir die teenmiddels, aangesien dit akkurate vooruitskatting en effektiewe beplanning verhoed. Gevolglik word vervaardigers gedwing om die teenmiddels in onekonomiese hoeveelhede te vervaardig wat hoër pryse en langer wagtye tot gevolg het. 'n Moontlike oplossing om hierdie probleem aan te spreek, is die implementering van 'n groot buffer voorraad wat gerig is op: (i) die voorkoming van onderbrekings in die behandeling van MDR-TB, deur te verseker dat daar altyd teenmiddels op voorraad is; asook (ii) om beter tydsberekening toe te laat om die verskeie bestellings te kombineer, sodat huidige vervaardigers die teenmiddels meer doeltreffend kan produseer.

Die doel van hierdie navorsing is om 'n deel van die ‘stroomop’ voorsieningsketting van MDR-TB SLDs te modelleer en om die impak wat 'n buffer voorraad op die voorsieningsketting kan hê, te evalueer. Die model is ontwikkel deur ‘n Stelsel Dinamika Modellering benadering en word gebruik om die moontlike impak van 'n verskeidenheid alternatiewe voorraadbestuur beleide op die voorsieningsketting te evalueer. Drie verskillende SLD formulerings is ingesluit in die model om te verseker dat die aanbevelings, op grond van hierdie navorsing, robuus is. Hierdie formulerings, naamlik *capreomycin*, *kanamycin* en *cycloserine*, is verantwoordelik vir ongeveer 58% van die totale aankoopkoste van die huidige voorsieningsketting.

Die resultate van die modellering dui daarop dat die voorraadbestuur beleid wat meer waarskynlik sal lei tot die mees beduidende verbetering in die voorsieningsketting, is die beleide waar die herbestel hoeveelheid bepaal word op grond van 'n eksponensiële ‘gladstryking’ voorspelling van vorige aanvraag, spesifiek wanneer ‘n ‘gladstryking’ faktor van óf 0.1 of 0.5 en 'n hoë herbestelvlak geïmplementeer word.

Hierdie navorsing dra by tot die huidige akademiese literatuur deur die begrip van die stroomop SLD voorsieningsketting te verbeter, deur 'n kwantitatiewe evaluering van die verwagte impak van voorgestelde wysigings aan die voorsieningsketting te verskaf en deur 'n voorbeeld van ‘n Stelsel Dinamika Modellering te verskaf, wat nie algemeen in die literatuur is nie.

Acknowledgments

I am immeasurably grateful to my study leader, Louzanne Bam. Without her dedication, guidance, direction and support this research would not have been possible.

I give a special note of thanks to Prashant Yadav for steering us in the right direction, with regard to data as well as our understanding of the supply chain.

To Adam de Beer, who supported me throughout this thesis more than anyone could realise, I give very special thanks for the constant encouragement and support in the preparation of this final report.

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Nomenclature

Acronyms

API	Active Pharmaceutical Ingredient
BRICS	Brazil, Russian Federation, India, China, South Africa
CLD	Causal Loop Diagram
DES	Discrete-Event Simulation
DOT(S)	Directly Observed Treatment (Short Course)
FLD	First-line Drug
FPP	Finished Pharmaceutical Product
GDF	Global Drug Facility
GLC	Green Light Committee
GPS	Global Positioning System
HBC	High Burden Country
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IOM	Institute of Medicine
K-S test	Kolmogorov-Smirnov Goodness-of-fit Test
LMIC	Low- and Middle Income Country
LTBI	Latent Tuberculosis Infection
MDR-TB	Multidrug Resistant Tuberculosis
M.TB	Mycobacterium tuberculosis
PA	Procurement agent
RIF	Rifampin
SC	Supply Chain
SCM	Supply Chain Management
SD	System Dynamics
SDM	System Dynamics Modelling
SLD	Second-line Drug
TB	Tuberculosis

UNITAID	Not an acronym. Organisation cooperating with other organisations on the WHO millennium goals
USAID	United States Agency for International Development
WHO	World Health Organisation
XDR-TB	Extensively Drug Resistant Tuberculosis

Greek Symbols

α	Exponential smoothing factor $(0 \leq \alpha \leq 1)$
β	Shape parameter or slope
β_S	Exponential smoothing trend factor $(0 \leq \beta \leq 1)$
β_0	Estimate of the intercept
$\beta_{i:}$	Estimate of the slope for variable i
η	Scale parameter or characteristic life
γ	Location parameter or failure free life
γ_S	Seasonality smoothing factor $(0 \leq \gamma \leq 1)$
μ_D	Average demand
μ_{LT}	Average lead time
σ_{mo}	Standard deviation of the order size for each individual order
σ_{os}	Standard deviation of the volume of orders placed per month
σ_D	Standard deviation of the demand
σ_L	Standard deviation of the lead time

Roman Symbols

$\hat{a}_t$	Estimated level at time t
$\hat{b}_t$	Estimated trend at time t
C_H	Holding costs
C_O	Obsolescence costs
C_P	Procurement costs
C_T	Total costs

D	Demand
EOQ	Economic order quantity
e_t	Forecast error for time t
F_t	Multiplicative seasonal index appropriate for period t
n	Number of data points or data entries
P	Number of time periods within the seasonality $\left(\sum_{i=1}^{P} \hat{F}_i = P\right)$
SS	Safety stock
t	Time period
$\hat{x}_{t,t+1}$	Forecast for period $t+1$ made during period t
x_t	Actual demand during time t
x_{t-n}	Actual demand during time $t-n$
Y_i	Demand for variable i
z	Safety stock coverage factor based on the service level

Terminology

Bacilli	A rod-shaped bacterium that causes disease.
Cross-resistance	When resistant mutations to one drug may cause resistance to some of the other members in the same drug family.
Pathogen	A microorganism, such as a bacterium or virus, that can cause disease.
Second-line Drug	Any therapeutic drugs that is not the drug of choice or normally used for treatment.
Subtherapeutic	Not generating a therapeutic effect.
Supply Chain	A network of entities that supply products and/or services from the raw material phase to the end consumers through the flow of information, physical distribution, and finances.
Syndemic	The conversion of two or more epidemics that act together to aggravate the burden of one or more of the diseases.

Chapter 1:
Introduction

"The new numbers revealed what many of us had feared, that the TB epidemic is even bigger than we thought."

- October 2014, Dr Joanne Carter (Vice-chair, STOP TB Partnership)

This study aims to model and analyse the upstream supply chain of second-line drugs for multi-drug resistant tuberculosis, through the use of data gathering, simulation, correlational analysis and statistical analysis. The intended goal of the model is to identify operational changes that will improve the management of the supply chain and to quantify the potential impact that these changes will have.

This chapter serves as an introduction to the study. Background information on the underlying themes of the topic is shortly discussed and is followed by the formulation of the problem statement, objectives, expected contributions and the boundaries and limitations. Thereafter, the research process is explained through a detailed description of the research design and methodology, as well as the timeframe and scope of the study.

1.1 Background information

Tuberculosis (TB) is an airborne disease and is a foremost cause of death, disease and disability, especially in developing countries (Fraser *et al.*, 2013). A report delivered by the World Health Organisation (WHO) in 2015, stressed that "TB now ranks alongside HIV as a leading cause of death worldwide" (World Health Organization, 2015a). According to the report, approximately 9.6 million cases of TB were reported in 2014 and the death toll for that year was near 1.5 million.

Efforts towards reducing the global occurrence of drug-susceptible TB have had a minor positive impact (Gandhi *et al.*, 2010). The rate by which new infections are falling on a

global scale, is 1,5% each year. There is no concrete evidence to suggest that this rate will improve in the near future (Senthilingam, 2014). The main challenge is the global control from the standpoint of diagnosis, treatment and the detection of drug-resistance (Wilson, 2011).

Multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis have emerged over the last few decades and threaten to deteriorate any advances towards stabilising the TB epidemic (Gandhi *et al.*, 2010). In 2013, an estimated 190,000 people died from MDR-TB, according to the aforementioned 2015 WHO report. It is believed that 75% of people carrying MDR-TB remain undetected and unreported (World Health Organization, 2015a). Finally, the increase of antimicrobial resistance places the global health risk posed by MDR-TB in even more stark light. According to Furin *et al.* (2016), "estimates indicate that unless the management of MDR TB changes radically, it will be one of the main drivers of antimicrobial resistance, which could kill more persons than cancer by 2050".

The management of MDR-TB is much more complex, costly, time-consuming and less effective than drug-susceptible TB (Gandhi *et al.*, 2010). The treatment generally spans over a two-year period with complex and often toxic drug regiments (Fraser *et al.*, 2013). It is therefore vital to exert all efforts in preventing the spread thereof. MDR-TB can be caused by the incorrect completion of TB treatment, poor adherence, poor drug quality, or transmission from one person to another (Gandhi *et al.*, 2010). In most cases, a patient becomes drug-resistant due to TB treatment failures. Treatment failures are mostly ascribed to the lack of sufficient supplies, especially in poorer nations (De Lucia, 2014).

APICS, The Association for Operations Management, defines a supply chain as: "The global network used to deliver products and services from raw materials to end customers through an engineered flow of information, physical distribution, and cash" ('APICS Dictionary 10th Edition', 2002). Disruptions and problems within the supply chain (especially with financing, production, supply and quality) are a main reason for the unavailability of the drugs. As previously stated, this contributes to the development of drug resistance. Even if patients are adhering to the treatment, problems within the supply chain, such as the absence of quality monitoring and maintenance, can cause the treatment to be sub-therapeutic (Gandhi *et al.*, 2010).

In the supply chains of critical medications, such as TB- and MDR-TB treatment drugs, there are severe risks attached to lengthy and slow-moving logistics, especially during the shipment from warehousing to various countries. This portion of the supply chain is defined as the 'upstream' segment of the supply chain by the Institute of Medicine (Nicholson *et al.*, 2013).

MDR-TB is a manmade occurrence, developed due to the inadequate treatment of TB. Recorded cases of drug resistance are increasing almost as fast as drugs come to the

market (Chang and Yew, 2012). The prospect of MDR strains becoming the leading form of TB will remain, unless the detection and treatment of drug-resistant cases is intensified (Gandhi *et al.*, 2010).

1.2 Problem statement

Systemic problems in the supply chain for second-line drugs (SLDs) for MDR-TB are well documented and contribute significantly to the difficulties preventing successful control of the disease. Although literature contains a wealth of proposed changes to the management of the global SLD supply chain, there is a significant research gap related to quantitative modelling of the supply chain to accurately predict the expected impact of these proposed changes on the availability and delivery of SLDs. In this research, a model of a segment of the upstream MDR-TB SLD supply chain will be developed. This model will be used to evaluate the likely impact of some alternative approaches to managing and operating the supply chain.

1.3 Aim and objectives

The aim of this thesis is: (i) to model the upstream supply chain of MDR-TB SLD, and (ii) to use this model to identify potential improvements and quantify the expected impact of these improvements on the performance of the supply chain on a global scale.

Achieving each of the two parts of the aim (i and ii) will demand different approaches throughout the research. To simplify the execution and understanding of the research approach, the aforementioned parts of the aim will from hereon be referred to as Phase A and Phase B, respectively.

Each phase is associated with a separate set of objectives. For Phase A, the objectives are to:

- provide accurate descriptions of the different supply chain aspects in all of their complexity;
- define the limitations (that will be considered in this research) of the upstream environment in which the supply chain operates;
- identify the prominent factors or variables within this environment and their relevance to the research; and
- develop a descriptive model that accurately portrays the upstream supply chain.

The objectives for Phase B are to:

- simulate the model of the upstream MDR-TB SLD supply chain;
- identify problems and opportunities for improvement, and make associated recommendations to address these;
- quantify the likely performance of the supply chain, using the simulation model, to measure the expected impact of certain improvements; and
- make conclusions and recommendations on which changes will contribute most to the strengthening of this supply chain.

1.4 Boundaries and limitations

Boundaries are the result of specific decisions made and the deliberate exclusion and inclusion of certain aspects and elements. As stated in the title of this study, only the upstream component of the supply chain will be investigated. This research complements a similar study by Coetzee (2015) of the downstream component of the supply chain.

Furthermore, the study will only consider the supply chain of MDR-TB drugs, and not that of drug-susceptible TB or XDR-TB drugs. The systematic problems in the MDR-TB SLD supply chain as well as suggestions for improvement have previously been discussed in literature, but the expected impact of these improvements are yet to be quantified. This study will aim to fill this gap in the MDR-TB research area. Additional boundaries of the study can be derived from Section 1.2 and Section 1.3, where problem statement and research objectives are provided, respectively.

Limitations are effects, shortcomings or conditions that flow from implicit features of the chosen method and design. The availability of and access to data is the most prevailing limitation of this research. Only data that is publically available or provided by research partners and organisations can be used. As with any qualitative study, the validity and reliability of the study is a limitation. To try and uphold the external reliability, which is defined as “the degree to which a study can be replicated” (Bryman *et al.*, 2014), the research approach will be carefully defined and described (see Section 1.6) and all the steps and actions taken during the progression of the study will be recorded in detail (Bryman *et al.*, 2014). Another limitation of the study arises with the correlational analyses (see Section 1.6.4). This type of analysis merely demonstrates that two variables are associated with each other. There can, however, be other variables that have an influence on this association. Another reason for the association can be the situation or circumstance under which the correlation was analysed. Therefore, there is some uncertainty about the generalisability of the correlation.

1.5 Expected contributions

The documentation of the upstream supply chain for MDR-TB SLDs can prove to be beneficial to further studies in this field. The expected contributions of this study are threefold:

i. This study forms part of a larger project that incorporates both the upstream and downstream components of the MDR-TB SLD supply chain. This global project can be used to aid companies and organizations (that are a part of the supply chain) in their decision making process and contribute to the sustainability of the supply chain.
ii. The impacts of the various solutions suggested by professionals for improving the operation of the upstream supply chain have not been quantitatively analysed or evaluated to date. Therefore, another contribution of this study is the quantification of the likely impact of one or more of these suggestions, to aid in the strengthening of the global MDR-TB SLD supply chain.
iii. Lastly, the identification and modelling of the dynamic relations and associations in the supply chain can provide support for decision making in other medical and drug supply chains.

1.6 Research design

The research design of this study will differ for each of the two phases of the aim, as defined in Section 1.3, and the designs will be discussed separately in subsequent subsections. A summary of the research design is given in Table 1.1 for clarification and to illustrate how the design differs for the two phases.

Table 1.1: Summary of the research design.

	Phase A		Phase B
Research Purpose	Exploratory	Descriptive	Explanatory
Research Category	Basic Research		Applied Research
Research Methodology	Mostly Qualitative, Inductive Study		Mostly Quantitative, Deductive Study

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Data Acquisition	Data, Documents (text, numerical, speech), Graphical modelling		Previous studies, experiment with simulation and modelling
Data Analysis	Thematic Data Analysis	Conceptual Description	Statistical Analysis

1.6.1 Research category

For the modelling of the supply chain (Phase A) the purpose is to obtain new knowledge about and deepen understanding of the resources, manufacturers, suppliers, distributors etc. Their properties, structures and relationships need to be determined and analysed. The research will be carried out with the prospect of forming the basis of the next phase. The research category of the modelling phase is therefore oriented basic research.

For the analysis and evaluation of the supply chain (Phase B), further research is carried out to build on the findings of the basic research in the previous phase. The research is directed primarily towards the specific aims and objectives as set out in Section 1.3, thus it falls into the category of applied research.

1.6.2 Research purpose

Due to the lack of existing research on the upstream supply chain for MDR-TB medication, an exploratory research approach will initially be followed. During this stage of the research, the key issues and variables will be identified. Thereafter, the research will follow a descriptive approach where an accurate and valid representation of the upstream supply chain will be provided.

For the evaluation of the supply chain model, an explanatory research approach will be followed to identify any links between factors and variables. During this phase of the research, the effect that different changes have on the supply chain will be determined and assessed.

1.6.3 Data acquisition

The fundamental data to be used in Phase A will be obtained from research partners and publically available databases, such as the database of the Global Fund to Fight Aids, Malaria and TB. Any additional data will be acquired through documents (text, numerical or speech) and through explanation building.

The evaluation of the supply chain (Phase B) will make use of simulation and modelling to experiment with changes made to the supply chain. These changes entail possible

improvements that were identified in the first phase of the study. The independent variable(s) will be manipulated, according to the improvements, to observe the effect on the dependent variable(s).

1.6.4 Data analysis

For both phases, the data analysis is an iterative process as the process can be adjusted to adapt to the outcomes. Constant comparison will be done to lead the process from analysis to results and back again. During the exploratory research, a thematic data analysis will be done. Any fundamental or underlying topics and patterns observed in the literature and data will be identified. Coding will be used to define connections between different topics and patterns, and to attempt to develop networks between the patterns, processes and activities. The descriptive part of the research will involve a conceptual/thematic description that will comprise of the presentation of the networks and concepts developed during the exploratory research. This will form the foundation of the graphical model of the supply chain. During the explanatory phase of the research, recommended improvements and operational changes will be evaluated with simulation and modelling. The obtained results will be used to perform a statistical analysis to describe the effects of the improvements on the supply chain and to expand on the outcomes of the improvements.

1.7 Research methodology

As with the research design, the research methodology will be distinctive for every phase. The first phase of the study will involve qualitative research and follow an inductive approach. It will aim to provide an in-depth and thorough model of the upstream supply chain. For the second and final phase of the study, the contextual framework (within which the research will be conducted) will be much clearer. Therefore, it will follow a deductive approach and primarily consist of quantitative research. The procedure to be followed is based on the abovementioned approaches and can be seen in Figure 1.1. The tools to be used with each of the steps are also provided in the figure.

The procedure highlights the different steps and processes associated with each of the two phases mentioned in Section 1.3. As can be seen in the figure, both phases start with a literature review. Throughout the literature review process, the validity of the study is ensured by performing a critical analysis on each source before making assertions and conclusions based thereon. The evaluation method as laid out by Jonathan Paulo in the Madison Research Essentials Toolkit (Paulo, 2014) as well as the Critical Appraisal and Analysis technique from the Cornell University Library (Engle,

2015) were combined to develop a checklist, illustrated in Appendix A, which is used to analyse each source. Sources include electronic as well as printed resources.

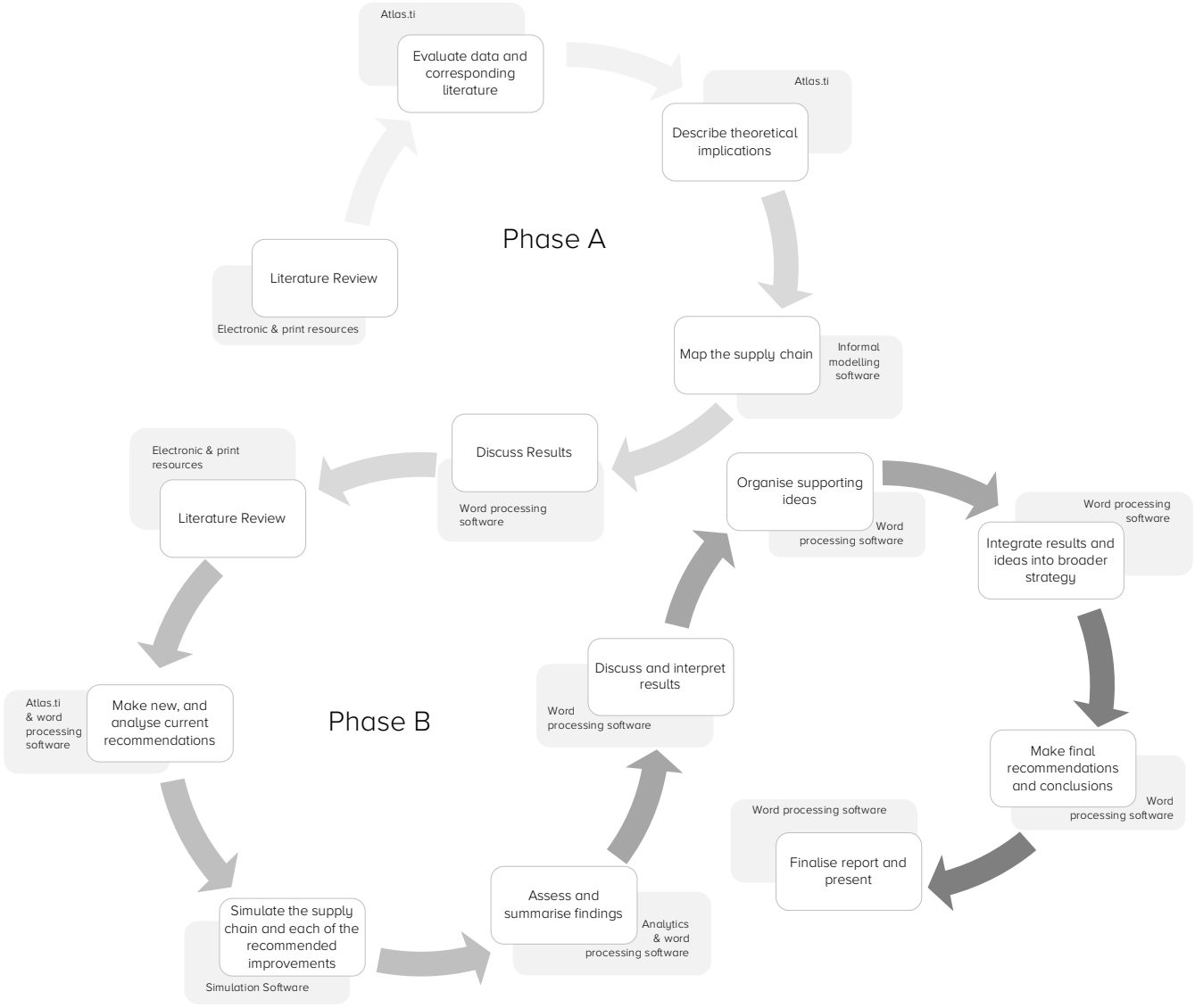

Figure 1.1: Research process and tools.

After a source has been analysed and approved, it is imported into the ATLAS.ti software package. Various codes and code groups are created in ATLAS.ti and relevant information in the sources are coded. As indicated in Section 1.6.4, coding is used to define connections between the sources and to identify relevant themes that are used to develop descriptions and/or concepts.

For the mapping of the supply chain, informal modelling software will be used. This step is limited to a graphical representation, software such as Microsoft Visio or PowerPoint can therefore be used. The simulation model of the supply chain will make use of software specific to the chosen technique. Similarly, analytics software such as SPSS and Microsoft Excel will be used for the assessment of the simulation results.

1.8 Structure of the report

The scope of the study is summarised in the structure in Figure 1.2. The different chapters of the study can be grouped in three main research phases, namely the research orientation, research body and research outcomes, which will be discussed separately below.

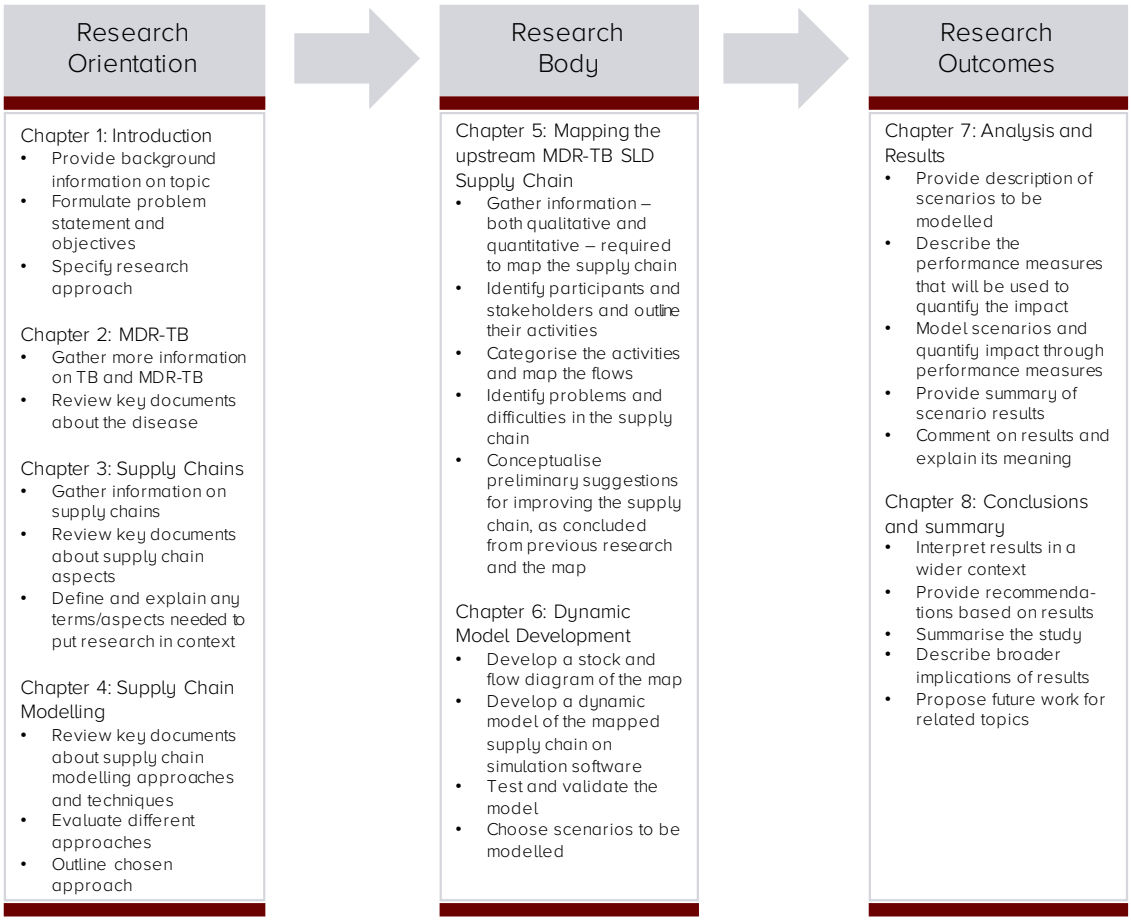

Figure 1.2: Breakdown of the study's scope.

The first four chapters form part of the research orientation. These chapters serve to acquire direction and become familiar with topics and themes relevant to the problem statement and objectives. This first chapter provides an introduction to the study by providing background information, the problem statement, objectives, expected contributions and the boundaries and limitations. The research process to be followed in the study is also given in this chapter.

Chapter 2 provides an overview of the real-world problem through a discussion of the relevant aspects regarding TB and MDR-TB, such as (i) the advancement of the disease to its current status; (ii) the diagnosis and treatment of TB and MDR-TB; (iii) other factors, such as diabetes and HIV, fuelling the disease; (iv) the main areas of infection; and (v) funding for responding to the disease.

In Chapter 3, selected aspects of a supply chain will be defined and discussed. This includes the levels of supply chain management related to decision making and measuring the performance of the supply chain. Furthermore, certain methods for demand forecasting and inventory management are also discussed.

Chapter 4, the final chapter for research orientation, is concerned with supply chain modelling and determining the most appropriate modelling method for this study. A taxonomy of supply chain modelling approaches and techniques is provided and discussed, after which an overview of the chosen method is provided.

Chapter 5 and 6 form part of the research body; the central part of the study. In Chapter 5, a representation of the supply chain for SLDs for MDR-TB is provided, by describing some of the unique characteristics of the supply chain and the initiatives developed to address TB and MDR-TB. The supply chain flows (information flow, product flow and financial flow) are also discussed. The concepts are combined to map and describe the supply chain through a theoretical model, followed by a summary of the difficulties and challenges in the supply chain as well as recommendations to improve the supply chain. Chapter 6 presents the dynamic model of the supply chain and the modelling process followed to build the model. This includes a description of the available data, as well as the limitations and boundaries thereof. After the discussion of the models that were developed, the models are validated through various validation techniques.

The final two chapters, contain the research outcomes. Chapter 7 present the analysis and results of the models and scenarios. It also includes a discussion of the results as well as general findings that were concluded from the results. Chapter 8 is the final chapter of the document and provides a summary of the research as well as recommendations to the stakeholders, the research contributions and opportunities for further research.

These chapters and their sections are meant to be sequential, however, in some cases it will be necessary to revisit previous sections, as they are dependent on one another.

1.9 Conclusion: Introduction

This chapter served as an introduction to the research project by providing background information on the MDR-TB epidemic and problems faced in the supply of SLDs. The problem statement together with the aims and objectives for this project were provided, as well as the research design and methodology that will be followed in order to reach these objectives. This chapter also included a summary of how the project is structured. In Chapter 2, a more detailed description of TB and MDR-TB is provided.

Chapter 2:
Overview of MDR-TB

"This threat has to be prevented and when it does occur, extraordinary measures must be put in place. It's a real threat and has to be taken extremely seriously."

- 2014, Mario Raviglione (Director, WHO Global Tuberculosis Program)

In the previous chapter, which served as an introduction to the research project, a short account of the TB and MDR-TB epidemic were provided. This chapter provides background to the project by providing more information on TB with the focus on MDR-TB. The following topics will be discussed:

1. The causes and advancement of TB and MDR-TB;
2. The diagnosis and treatment of the disease;
3. Other factors, such as Diabetes and HIV, fuelling the disease;
4. The main areas of infection; and
5. Funding for countering the epidemic.

2.1 An introduction to TB and MDR-TB

TB is an infectious and airborne disease, spread easily through simple actions such as coughing, sneezing, laughing or talking. A person with the disease will most likely infect other people that are in contact with him/her for extended periods of time. Consequently, TB has long been associated with poverty, where the majority of the infected resides in informal settlements (En, 2014).

The primary cause of TB is the pathogen Mycobacterium tuberculosis (M.TB). The two critical anti-TB drugs, isoniazid (INH) and rifampin (RIF), are essential in the effective

treatment for TB, since most M.TB strains are sensitive to these drugs (Rodwell, 2010). MDR-TB occurs when the M.TB strain is resistant to at least both INH and RIF and can be due to the incorrect completion of TB treatment or it can be transmitted from one person to another (Fraser *et al.*, 2013). More specifically, drug resistance is a result of tubercle bacillus mutations. When the predominant bacilli are exposed to a single effective anti-TB drug and is sensitive to that drug, it is killed. The few drug resistant mutants are left to multiply freely (New Jersey Medical Shcool: Global Tuberculosis Institute, 2015). Genetic resistance to anti-TB drugs is a natural occurrence, resulting from chromosomal mutations that accompany mycobacterial replication (Chang and Yew, 2012).

The treatment of a single case of TB spans over, at least, a six-month period of daily drug therapy. MDR-TB, on the other hand, can take two years or more to treat. Since none of the SLDs used to treat MDR-TB are as effective as INH and RIF, MDR-TB has a substantial impact on the course and outcome of the TB disease. As previously mentioned, the treatment of MDR-TB is also much more complex as SLDs are costlier and more toxic than first-line drugs (FLDs) (Atun *et al.*, 2010).

A study done by the University of Cape Town found that in South Africa, even though the MDR-TB cases comprised of only 2.2% of the case burden, it consumed 32% of the total estimated 2011 national TB budget. (Pooran *et al.*, 2013). The high costs associated with the treatment of drug-resistant TB can drain much needed resources required for global TB control. Difficult drug-resistant TB can cripple all TB control efforts if preventative- and management strategies are not implemented timeously and effectively (Chang and Yew, 2012).

2.2 Advancement of MDR-TB

Drug-resistance began to develop over the last 100 years. When it was first discovered, there was no strategy that included a means of testing for this new strain of TB and no drugs were provided to countries for the treatment thereof. Consequently, MDR-TB began to spread across the globe (Wexlar, Rockwood and Childress, 2014).

Over the last four to five decades, the MDR-TB burden has become worse. In 2007, a WHO global laboratory surveillance network revealed that the global caseload of MDR-TB increased from approximately 274,000 cases in 2000 to over half a million cases in 2007 (Dheda *et al.*, 2010). Although these figures have recently declined to about 480,000 cases in 2014, it is estimated that only about a quarter (123,000) of these were detected and reported (World Health Organization, 2015a). The global epidemic of drug-resistant TB can be attributed to inadequate treatment, aggravated by a delay in diagnosis and by environments that increase the probability of transmission, infection and development of the disease (Chang and Yew, 2012).

Currently, the conditions for MDR-TB look promising. For the first time in more than four decades, two new drugs have been registered for MDR-TB - bedaquiline and delamanid (Burki, 2014). Furthermore, the global rate at which new cases of MDR-TB are being reported, remains stable at 3,5% (World Health Organization, 2014). These aspects might seem optimistic, but on closer inspection, the data is incomplete (Brigden, 2015). Several areas across the globe are dealing with a severe and increasing MDR-TB crisis. For example, in Belarus, Kyrgyzstan and Kazakhstan, more than 70% of patients that have been treated for TB, are now drug-resistant. Furthermore, 35% of people diagnosed with TB for the first time are already drug-resistant (Brigden, 2015). With a cure rate of only 50%, MDR-TB is a major threat to these areas, which run the risk of having MDR-TB being the predominant diagnosis (Brigden, 2015).

The new drugs for treating MDR-TB, bedaquiline and delamanid, are not yet being distributed to the areas that require them the most (Brigden, 2015), even though they were approved for use in 2012 and 2013 respectively (Burki, 2014). Since the approval of bedaquiline by the Food and Drug Administration on 31 December 2012 (Field, 2013), only one thousand patients have had access to the drug as of March 2015 (Brigden, 2015). Similarly, by December 2014 fewer than 10 patients had, had access to delamanid outside of clinical trials (Brigden, 2015), after its conditional approval by the European Medicines Agency in 2013 (Burki, 2014; Lessem, 2014).

Delamanid has only been granted conditional approval, thus further studies need to be conducted to maintain the approval. Although this approval gives the manufacturer Otsuka permission to market delamanid in all European Union countries, they have only distributed the drugs in the United Kingdom and Germany, as of 2015. The drug has not been submitted for registration in any of the high burden countries and it is unclear whether Otsuka has sufficient drug supply to meet the high demand (Lessem, 2014). The country has recently announced a targeted access initiative, details have not yet been announced (Rustomjee and Zumla, 2015).

The Johnson and Johnson affiliate, Janssen Therapeutics, has been more proactive in the registration of their drug, bedaquiline. However, despite a tiered pricing structure, there are concerns regarding the affordability for several high-burden countries (Brigden, 2015). In December 2014, Janssen signed a Memorandum of Understanding in an attempt to lift the price barrier, under which they will provide 30,000 treatment courses of bedaquiline over a 4-year period (Liden *et al.*, 2014). This is unfortunately not a comprehensive solution, as only a portion of the global need will be fulfilled for a limited time (Brigden, 2015).

2.3 Diagnosis of TB and MDR-TB

Correctly diagnosing a patient with TB is the critical first step towards a successful TB programme. The process starts with the bacteriological confirmation of TB, whereafter it is determined whether the patient is drug resistant (World Health Organization, 2014). A detailed description of various diagnosis methods, including their drawbacks and benefits, have been provided elsewhere (Unitaid, 2012; World Health Organization, 2015b) and will not be repeated here.

Although it is not recommended by WHO due to current insufficient evidence, Sputum smear microscopy, which was developed over 100 years ago, is the general method used to diagnose TB worldwide. In this method, a sputum sample is collected from the patient to observe bacteria under a microscope. The use of rapid molecular tests to diagnose TB and DR-TB, however, is continuing to increase in popularity (World Health Organization, 2014).

According to the Global Tuberculosis Report 2015, of the 5.2 million patients that were diagnosed, only 58% were bacteriologically confirmed according to a WHO-recommended diagnostic, while the remaining 42% were diagnosed clinically, i.e. based on symptoms, chest X-ray abnormalities or suggestive histology. Since X-ray screening has poor specificity and the symptoms associated with TB are fairly common (fatigue, coughing, weight loss, fever), false diagnosis is a strong possibility (World Health Organization, 2015a).

Once the diagnosis confirms that the patient has TB, further investigation is required to determine whether the patient is drug-resistant (Fraser *et al.*, 2013). The diagnostics for drug-resistance can be done through conventional culture-based methods, liquid culture-based methods, rapid phenotypic methods or rapid molecular methods (McNerney *et al.*, 2015). Failure to test the patient for drug resistance can result in prescribing the wrong treatment plan and can cause further spread and development of the drug-resistant strains (World Health Organization, 2014).

2.4 Treatment of TB and MDR-TB

As previously mentioned, the treatment of TB spans over several months (typically six months for TB and up to 20 months for DR-TB) and often requires supervised treatment for maximum cure rates, reduced incidence and to minimise chances of developing drug resistance (Wells *et al.*, 2011). The first effective drug treatments for TB, were developed in the 1940s, while rifampicin, the most effective first-line drug to date, became available in the 1960s. Success rates of approximately 85% are reported for the treatment of drug-susceptible TB (World Health Organization, 2014). the success rate for MDR-TB is significantly lower at 50% globally (World Health Organization, 2015a).

The seven essential drugs in treatment policies of drug-susceptible TB are isoniazid (H/Inh), rifampicin/rifampin (R/Rif), pyrazinamide (Z/Pza), ethambutol (E/Emb), rifapentine (P/Rpt), rifabutin (Rfb) and streptomycin (S/Stm) (World Health Organization, 2010, 2015c). For the majority of the public sector, policies for the treatment for TB are based on WHO recommendations. For example, a typical first-line treatment adhered by most countries, is a 6-month regime denoted as 2HRZE/4HR. This translates to a treatment consisting of two months of isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E), followed by four months of isoniazid (H) and rifampicin (R). The Global Drug Facility (GDF), more detail in Section 5.2.3, supports the WHO recommendations by facilitating the purchase of TB treatment in these dosages (Wells *et al.*, 2011).

In countries with a high TB burden, the average cost of treatment for a patient with drug-susceptible TB in 2014 was approximately US$100 – US$500, while for MDR-TB it varied between US$5,000 and US$10,000 per patient, with an average price of US$6,826 in low-income countries and US$21,265 in upper middle-income countries (World Health Organization, 2015a). As shown in Table 2.1, the drugs for MDR-TB are grouped according to their efficacy, experience of use and drug class, with Group 1 containing the most potent and best tolerated drugs – unless the bacillus have become resistant to these drugs (World Health Organization, 2010).

Table 2.1: Groups of drugs to treat MDR-TB (Adapted from Caminero et al., 2010 and World Health Organization, 2011).

Group		Drugs
1	First-line oral agents	Pyrazinamide (Z/Pza) Rifabutin (Rfb) Ethambutol (E/Emb)
2	Second-line parenteral agent (injectable anti-tuberculosis drugs)	Kanamycin (Km) Amikacin (Am) Capreomycin (Cm) Streptomycin (S/Stm)
3	Fluoroquinolones	Ofloxacin (Ofx) Levofloxacin (Lfx) Moxifloxacin (Mfx) Gatifloxacin (Gfx)
4	Oral bacteriostatic second-line agents	Ethionamide (Eto) Prothionamide (Pto) Cycloserine (Cs) Terizidone (Trd) Para-aminosalicylic acid (PAS)

Continued on next page

Continued from previous page

5	Agents with unclear role in treatment of DR-TB	Clofazimine (Cfz) Linezolid (Lzd) Amoxicillin/Clavulanate (Amx/Clv) Imipenem (Ipm) Thiocetazone (Thz) High-dose Isoniazid (High-dose H) Clarithromycin (Clr)

The WHO (World Health Organization, 2010, 2011) provides principles and guidelines for the management and planning of MDR-TB treatments. At least four drugs, to which the M.TB isolate is likely to be susceptible and for which effectiveness is certain, should be included in a hierarchical order from Groups 1-5, although more than four drugs might be necessary (Caminero *et al.*, 2010). In general, one drug from Group 1, 2 and 3 should be included if susceptibility is documented or suspected, or the agent is thought to have efficacy and drugs from Group 4 are used to complete the regimen, to have at least four effective drugs. Group 5 drugs are not recommended due to their unclear influence on the efficacy of multidrug regimens and should only be included in cases where the design of adequate regimens was impossible. The typical regimen to treat patients with MDR-TB, includes the following:

1. pyrazinamide from Group 1;
2. an injectable parenteral agent from Group 2;
3. a fluoroquinolone from Group 3;
4. ethionamide or prothionamide from Group 4; and
5. cycloserine or PAS (only if cycloserine cannot be used) from Group 4.

From the Group 2 formulations, kanamycin or amikacin is often the first choice for an injectable agent since they are inexpensive and have been widely used in the treatment of drug- resistant TB. However, kanamycin and amikacin are very similar and therefore have a high frequency of cross-resistance. Cross-resistance is when resistant mutations (in M.TB bacteria) to one of the anti-TB drugs may cause resistance to some of the other members in the drug family (World Health Organization, 2010). If drug resistance surveillance data indicates high prevalence of resistance to amikacin and kanamycin, capreomycin should be used instead. Avoiding the use of streptomycin is highly recommended, even if a DST shows susceptibility, due to the high amount of cases reporting resistance with DR-TB strains (World Health Organization, 2011). Ethionamide or protionamide (Group 4) is frequently added to the regimen since it is inexpensive. If cost is not a limitation, PAS may be added first, because it is relatively well tolerated and there is no cross-resistance to other agents. If two formulations are required from Group 4, cycloserine should be used instead of PAS, as a combination of ethionamide

or protionamide and PAS can cause gastrointestinal side-effects and hypothyroidism. PAS, cycloserine and ethionamide or protionamide should only be used together when three Group 4 drugs are required (World Health Organization, 2010).

The chosen formulations should be based on treatment history and drug susceptibility testing, although the reliability and clinical value of drug susceptibility testing for drugs in Group 4 and 5 have not been entirely documented. Drugs that are commonly used in the country and the prevalence of resistance to specific FLDs and SLDs should also be taken into consideration (World Medical Association, 2008). Any drug for which there is a possibility of cross-resistance or that is not safe to use due to, for example, unknown quality, should not be considered (World Health Organization, 2010). The total treatment lasts between 18 and 20 months and most regimens are divided into two phases, an initial intensive phase, followed by a continuation phase. The intensive phase lasts at least 6 months and at least four drugs, including the parental agent, and pyrazinamide are included in the treatment. The exact length of the intensive phase is guided by smear and culture conversion, since the injectable agent should be continued for at least 4 months after the patient becomes and remains smear- or culture-negative. If the susceptibility pattern is unknown or the effectiveness of an agent is questionable, the injectable agent is continued for a longer period. In the continuation phase, the patient takes at least four oral drugs for 12 months or more. During both of the phases the drugs are taken daily (Caminero *et al.*, 2010) and it is therefore recommended that each dose is given as a directly observed treatment (DOT) (World Health Organization, 2010).

In May 2016, WHO released a conditional recommendation on the use of a shorter MDR-TB regimen. The shorter regimen lasts less than 12 months and has been used in clinical trials in a number of countries, including Cameroon, DR Congo, Guinea, Niger, Uzbekistan and Bangladesh. The new recommendation is anticipated to help MDR-TB patients worldwide, but the resistance could be worsened if not used appropriately (World Health Organization, 2016b). **Figure 2.1** demonstrates the flow chart, adapted from WHO's recommendation, outlining the selection of patients for the shorter regimen.

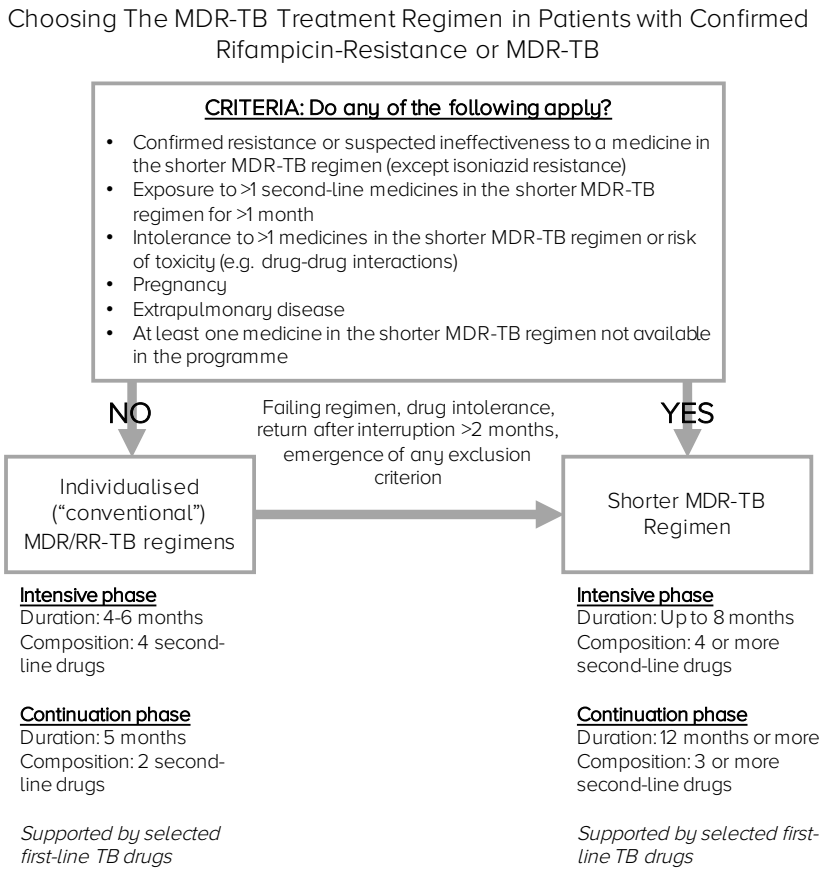

Figure 2.1: Flowchart of the selection of patients for the shorter treatment regimen (Adapted from World Health Organization, 2016b).

2.4.1 Directly Observed Therapy Short Course

DOT is a constituent of the wider WHO strategy called Directly Observed Therapy Short Course (DOTS) (Karumbi and Garner, 2015). The DOTS treatment strategy was introduced in the 1990s by WHO (Nicholson *et al.*, 2013), and incorporates five components (Nicholson *et al.*, 2013; World Health Organization, 2015a): (i) political commitment to improve TB programmes with increased financing; (ii) case detection through quality-assured bacteriology; (iii) standardised treatment with supervision; (iv) an effective drug supply and management system; and (v) impact measurement and a monitoring system. The DOT constituent is part of an effort to improve patient adherence by actively monitoring and logging the consumption of all drugs by a suitable observer (Karumbi and Garner, 2015).

The DOTS strategy was, however, specifically designed for the treatment of drug-susceptible TB (Nicholson *et al.*, 2013). While DOTS treatment requires the collection of data on patient admission, follow-up and smear results, MDR-TB requires considerably more detailed data on the drug regimens, laboratory results, treatment side-effects and treatment difficulties (Fraser *et al.*, 2013). To address the rising epidemic of MDR-TB, the DOTS-Plus framework was developed to include treatment of MDR-TB with SLDs (Nicholson *et al.*, 2013).

2.5 Other factors fuelling the disease

TB skin test data suggest that more than two billion individuals are infected with latent TB (Field, 2013). Latent tuberculosis infection (LTBI) is a condition that occurs when the immune system stabilises M.TB infection inside the macrophages of healthy patients (Shi and Sugawara, 2010). This means that almost one third of the global population runs the risk of developing the active disease (Field, 2013). The lifetime risk of a person with LTBI progressing to active TB is approximately 10% (Horsburgh, 2004).

In LTBI, treatment is difficult, since the hypoxic intracellular environment inhibits the M.TB metabolism (Stover *et al.*, 2000). The diagnoses and treatment of LTBI is vital for TB prevention strategies. Once diagnosed, the risk of developing the active disease can be reduced with preventative drugs and treatment (Field, 2013). The risk of progressing from LTBI to active TB is greater in children younger than 5 years, patients previously cured of TB and patients that are underweight, have had a gastrectomy or have a history of renal failure or silicosis. The two conditions that increase the risk of developing active TB the most are diabetes and HIV (Field, 2013), these are discussed in more detail in the subsequent subsections.

2.5.1 Diabetes

Diabetes used to be associated with high-income groups as one of the principal causes of the disease is diets that are high in fat and sugar. This is, however, not the situation today (Senthilingam, 2014). According to the International Diabetes Federation diabetes atlas (International Diabetes Federation, 2013), eighty percent of diabetics live in low- and middle-income countries (LMICs), as can be concluded from Figure 2.2.

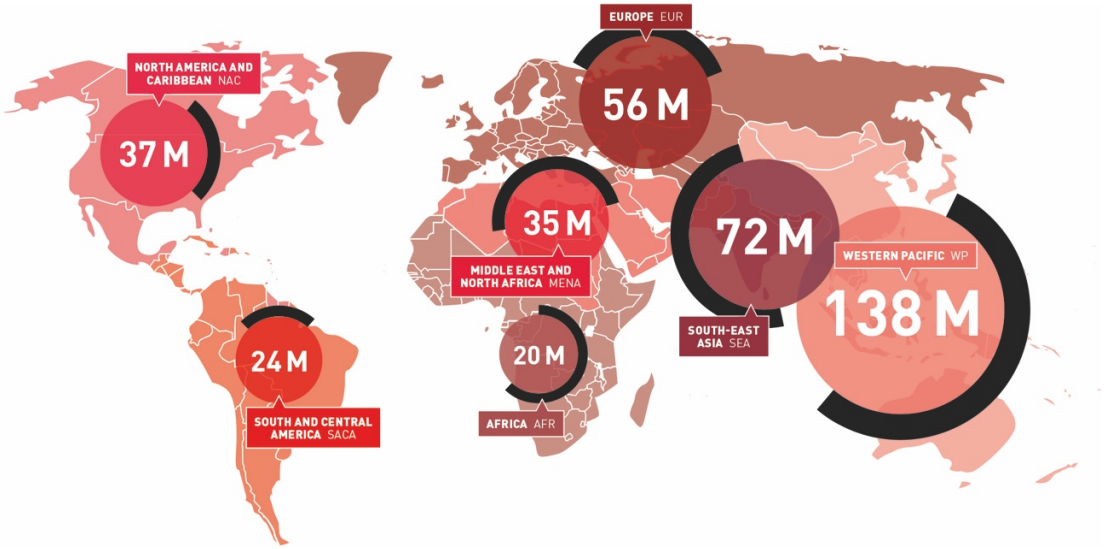

Figure 2.2: Number of people with diabetes per region in 2013 (Reproduced from Aguiree *et al.*, 2013, p. 11).

Diabetes decreases the body's ability to produce insulin and absorb glucose from the bloodstream (Senthilingam, 2014). This triples the risk of developing TB (International Diabetes Federation, 2013). As of 2014, approximately 387 million people have diabetes, and the International Diabetes Federation predicts that this will increase to 592 million people by 2035 (International Diabetes Federation, 2013).

The high percentage of people with latent TB is already a cause for alarm. When considering the global increase in diabetes, it is immediately evident that there is a serious risk (Senthilingam, 2014). In some areas, such as Kerala in India, almost fifty percent of people diagnosed with TB suffer from diabetes as well (International Diabetes Federation, 2013). The cost of treating patients with diabetes in countries with high TB cases could be significant, especially when taking the unfaltering levels of TB drug-resistance into account (Senthilingam, 2014).

2.5.2 Human Immunodeficiency Virus (HIV)

A serious constraint in the effective control of the TB epidemic is the lethal co-infection of TB and HIV (Zhang and Yew, 2009). In 2013, more than 12% of people infected with TB, were also HIV positive (World Health Organization, 2014). In countries with high HIV prevalence, the rate of TB infection can increase up to four times, as HIV weakens the immune system (Senthilingam, 2014) and results in a patient being 29 times more likely to develop TB (World Health Organization, 2014). Additionally, there is also a high mortality rate in MDR-TB and HIV co-infected patients, especially in low-income areas (Gandhi *et al.*, 2010).

The association between HIV and drug resistant TB is complex. The HIV infection does not cause the drug-resistant mutants to multiply more rapidly, but it potentially accelerates the prevalence of drug-resistant TB (Selwyn *et al.*, 1989). More specifically, it can cause the number of people that have a high-probability to develop drug resistance to increase (Gandhi *et al.*, 2010).

A recent meta-analysis of observational data in LMICs, led by WHO, found that antiretroviral therapy decreases tuberculosis incidence by 65% (Suthar *et al.*, 2012). The earlier delivery of antiretroviral therapy and drug resistance treatment to co-infected patients, may play a significant role in improving and controlling the HIV-associated TB syndemic (Gandhi *et al.*, 2010; Chang and Yew, 2012).

2.6 Areas of infection

More than 95% of tuberculosis mortality occurs in LMICs. In 2013, South East Asia and the Western Pacific Regions carried the largest number of new TB cases (56% of new cases globally). The greatest proportion of new cases per population, also in 2013,

occurred in Africa where 280 out of every 100,000 people were diagnosed with TB (Smith, 2015).

Since 1998, twenty-two countries have been prioritised on a global level due to their high TB prevalence and mortality (*TB Statistics | Global, regional, high burden & MDR*, 2013). These countries are known as high burden countries (HBCs) and account for approximately 80% of the global TB burden (Wells *et al.*, 2011). These 22 countries, in alphabetical order, are: Afghanistan, Bangladesh, Brazil, Cambodia, China, DR Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, Philippines, Russian Federation, South Africa, Thailand, Uganda, UR Tanzania, Vietnam and Zimbabwe.

Recently, the WHO defined three new HBC lists for the period 2016 to 2020. There is now a separate list for TB, MDR-TB and for TB/HIV, with 30 countries on each list. Twenty of the countries are defined as the top 20 in terms of absolute numbers of cases, while the remaining 10 countries are those with the highest burden in terms of incidence rates per capita, namely 10 000 cases per year for TB and 1 000 cases per year for MDR-TB and TB/HIV. The 30 countries on the list account for 87% to 92% of the global burden, almost exclusively accounted for by the top 20 countries (World Health Organization, 2016a). The countries in each list are summarised in Table 2.2.

Table 2.2: List of the HBCs for TB, TB/HIV and MDR-TB (Adapted from World Health Organization, 2016a).

TB HBC List		TB/HIV HBC List		MDR-TB HBC List	
Top 20	Additional 10	Top 20	Additional 10	Top 20	Additional 10
– Angola – Bangladesh – Brazil – China – DPR Korea – DR Congo – Ethiopia – India – Indonesia – Kenya – Mozambique – Myanmar – Nigeria – Pakistan – Philippines – Russian Federation – South Africa – Thailand – UR Tanzania – Viet Nam	– Cambodia – Central African Republic – Congo – Lesotho – Liberia – Namibia – Papua New Guinea – Sierra Leone – Zambia – Zimbabwe	– Angola – Brazil – Cameroon – China – DR Congo – Ethiopia – India – Indonesia – Kenya – Lesotho – Malawi – Mozambique – Myanmar – Nigeria – South Africa – Thailand – Uganda – UR Tanzania – Zambia – Zimbabwe	– Botswana – Central African Republic – Chad – Congo – Ghana – Guinea-Bissau – Liberia – Namibia – Papua New Guinea – Swaziland	– Bangladesh – China – DPR Korea – DR Congo – Ethiopia – India – Kazakhstan – Kenya – Indonesia – Mozambique – Myanmar – Nigeria – Pakistan – Philippines – Russian Federation – South Africa – Thailand – Ukraine – Uzbekistan – Viet Nam	– Angola – Azerbaijan – Belarus – Kyrgyzstan – Papua New Guinea – Peru – Republic of – Moldova – Somalia – Tajikistan – Zimbabwe

From the table, it is clear that several countries appear on more than one of the lists. Figure 2.3 illustrates this overlap among the three lists.

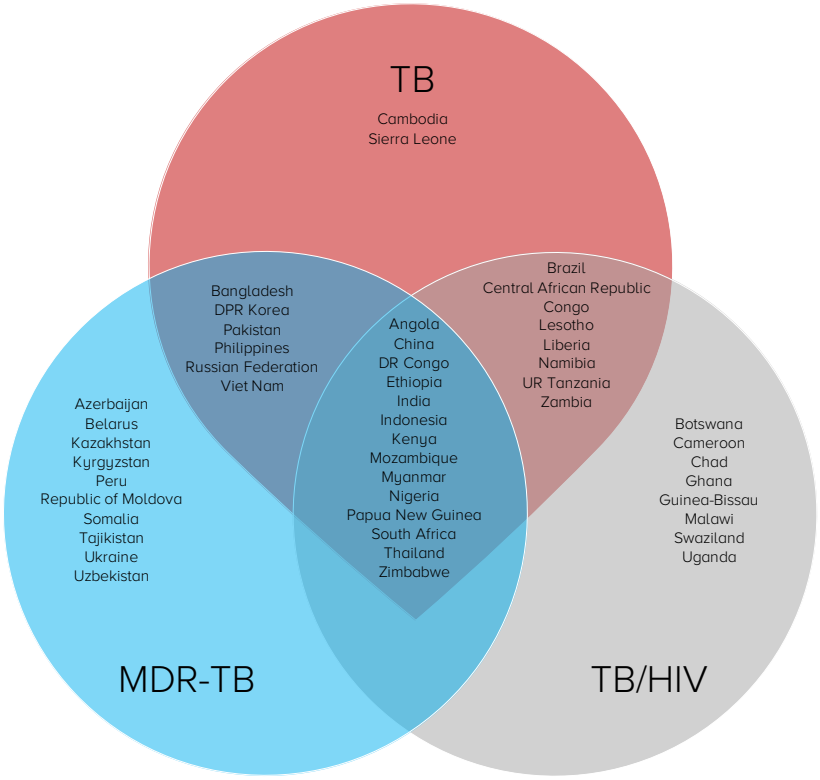

Figure 2.3: Overlap of HBC lists (Adapted from World Health Organization, 2016a).

2.7 Funding for TB and MDR-TB

It is estimated that approximately US$ 8 billion, divided into four spending categories as shown in **Figure 2.4**, is required per year to fund a full response to the TB epidemic in LMICs (World Health Organization, 2015a). This amount excludes the US$ 2 billion per year necessary for research and development (for new TB vaccines and diagnostics), as laid out in the Global Plan (Frick, 2014).

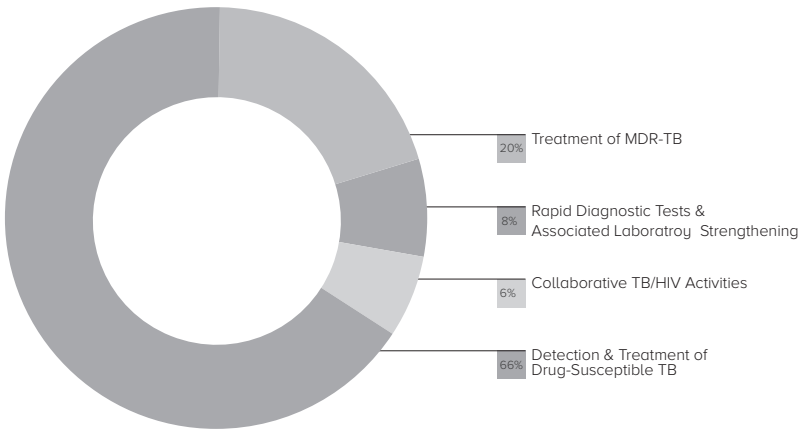

Figure 2.4: Spending categories for a full TB response (Adapted from World Health Organization, 2015a).

According to projections made in 2013, the WHO recommends that US$6 billion could be obtained from domestic sources, while the remaining US$2 billion would most likely need to be obtained through international donors (World Health Organization, 2015a). The BRICS countries (Brazil, Russian Federation, India, China and South Africa) collectively make up 50% of the global TB cases, yet most of them (India being the exception) are able to obtain the majority or all of their necessary funding from domestic sources (World Health Organization, 2016a). In 2016, 84% of the available US$6.6 for TB care and prevention in LMICs, were domestically sourced. International donors, however, remain the main source of funding in most of the low income HBCs. In Afghanistan, Bangladesh, the Democratic Republic of the Congo and Mozambique more than 90% of the available funding in 2015 was from international donors (World Health Organization, 2015a).

2.8 Conclusion: Overview of MDR-TB

This chapter provided background information on the TB and MDR-TB epidemic. The primary causes of TB and MDR-TB were discussed, as well as the advancement of MDR-TB over the last 100 years. The steps involved with the diagnosis were summarised, as well as the treatment regimens for both TB and MDR-TB. The risk of developing active TB due to diabetes or HIV were also discussed. A summary of the HBCs and the funding required to respond to the epidemic were provided.

Chapter 3 will provide further background information for this research, focussing on supply chains and their importance in controlling the TB epidemic.

Chapter 3:

Supply chains

"No supply chain exists in isolation. Many supply chains are integrated and a disruption at one point could have knock on effects for other entities."

- Evan Bloom (Founder and managing partner of Root Change)

The previous chapter provided background information on TB with the focus on MDR-TB. This chapter includes a description of applicable topics and themes, related to supply chains, that would help put the research in context. Topics that will be discussed include the levels of supply chains, measuring the performance of the supply chain with measures and metrics, demand forecasting, push and pull systems, and inventory management policies.

3.1 Defining supply chains and supply chain management

Adding to the definition provided in Section 1.1, a supply chain is a collection of facilities, materials, clients, products and procedures to manage inventory, procurement, and distribution (Sabri and Beamon, 2000). In a supply chain, goods flow through numerous echelons as they progress from supplier to customer, where each of these echelons may consist of more than one facility (Sabri and Beamon, 2000). In an effective and operational supply chain, each unit is treated as a customer by its predecessor, with the focus always on providing the best possible service to the end user (Holmstrom, Jr and Louhiluoto, 2012).

Supply chain management (SCM) involves the services associated with the set of activities involved in moving products from the supplier to customer (Dowling, 2011). APICS ('APICS Dictionary 10th Edition', 2002) defines SCM as "the design, planning, execution, control, and monitoring of supply chain activities with the objective of

creating net value, building a competitive infrastructure, leveraging worldwide logistics, synchronising supply with demand, and measuring performance globally."

A common theme in defining a supply chain and SCM is that it takes place among a connected series of echelons and facilities (Scannell, Vickery and Dröge, 2000) that operate at various levels within a country (Dowling, 2011). Furthermore, there can be a number of different supply chains that operate vertically within a country. These supply chains usually have many points where they overlap and a diverse set of participants. It is essential to link all functions and components of the supply chain to ensure that supply can meet demand (Dowling, 2011).

Medical supply chains, such as for MDR-TB SLDs, require agile procurement mechanisms that are able to deliver high quality drugs at the lowest possible cost. More funds and support are being provided to the various initiatives that aim to aid in the development and strengthening of this type of procurement. Such initiatives include the Global Fund's Voluntary Pooled Procurement Mechanism and the Global Drug Facility, as will be discussed in Section 5.2.3 (Dowling, 2011).

3.2 Levels of supply chain management decision making

Supply chain management includes all of the decisions made in the supply chain process and covers various decision areas (Biswas and Narahari, 2004). Over time, a certain factor in one decision area can influence a factor in another. To understand the relationships and influences of the different decision areas, it is necessary to comprehend the three levels of SCM decision making (Thierry, Bel and Thomas, 2010), namely the strategic, operational and tactical levels. These levels are best explained when represented as a pyramid, refer to Figure 3.1, since it illustrates the hierarchy which governs the control over the supply chain as well as the development and arrangement of guidelines and policies.

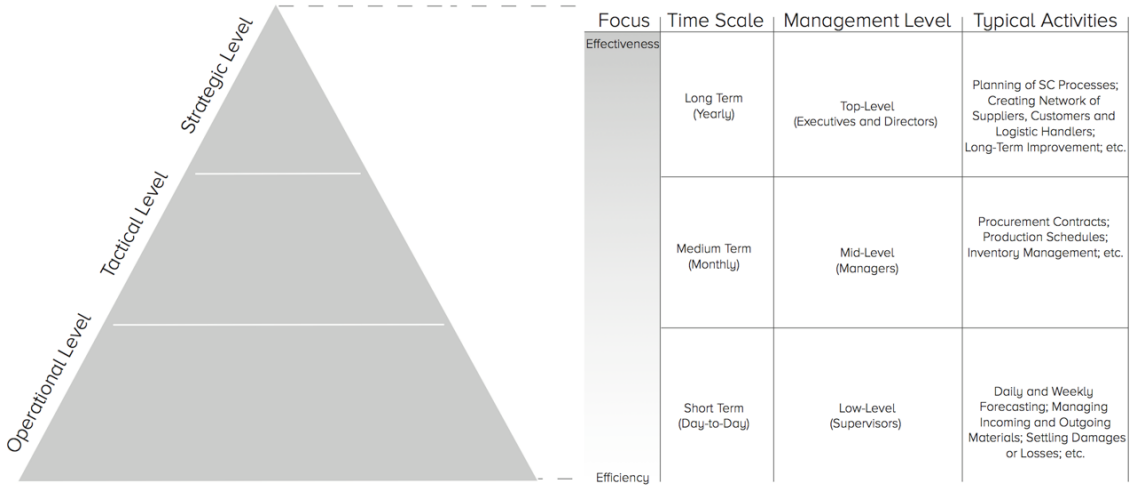

Figure 3.1: Levels of supply chain management decision making.

This hierarchy is based on factors such as the time horizon for activities and the relevance of decisions to the different levels of management. When moving down from the strategic to operational level, the focus shifts from improving the effectiveness of the supply chain to improving its efficiency (Gunasekaran, Patel and McGaughey, 2004).

3.2.1 Strategic level

The strategic level involves long-term decisions and is influenced by top-level management. At this level, the basis of the entire supply chain process is planned, the organisational goals are set and broad based policies are determined (Gunasekaran, Patel and McGaughey, 2004). Usually decisions at a strategic level will need revision after one or several years, depending on the design of the supply chain network, since it involves long-range choices such as the locations and number of warehouses, factories, distribution centres, and so forth (Thierry, Bel and Thomas, 2010).

3.2.2 Tactical level

The tactical level involves medium-term decisions, usually covering approximately six to twelve months. These decisions involve cost control and risk management, logistics planning, fleet management and storage management, among others, and are limited by the strategic decisions. Although the supply chain processes are planned at the strategic level, they are outlined at the tactical level. Performance measurements are taken to evaluate whether the goals, set at the strategic level, have been met. This provides valuable feedback to mid-level management (Gunasekaran, Patel and McGaughey, 2004).

3.2.3 Operational level

The operational level involves short-term decisions that take place on a weekly, daily or hourly basis. Accurate data is an essential requirement on this level since it entails the day-to-day decisions required for the effective functioning of the supply chain (Thierry, Bel and Thomas, 2010). Operational level activities include monitoring, production processes and communicating with suppliers and customers. Operational objectives are set by low-level management in order to achieve the tactical objectives. Strong strategic and tactical decisions will contribute to the effectiveness of the operational processes (Gunasekaran, Patel and McGaughey, 2004).

3.3 Importance of supply chains

Although there are several variables that influence the availability of drugs and access to drugs, a principal constraint is the capacity of supply chains to forecast, procure and deliver the drugs and health supplies that are crucial in the treatment of TB (Dowling, 2011). This constraint is strongly related to the quality of information-, product- and

financial flow management. Many LMICs do not initially consider the critical role of the supply chain in effective management of TB and this can drive the aforementioned constraint (Riungu, 2011).

Inadequate supply chain management and weak procurement systems lead to poor drug quality and treatment interruptions (Atun *et al.*, 2010). This can lead to the development of drug-resistant TB, as discussed in Section 2.1. More than 10 million lives could be saved, per year, through improved access to drugs and treatment (Frick, 2014). Furthermore, disruptions in the supply can result in multiple additional problems, such as inefficiency, waste, stock-outs, and poor service (Holmstrom, Jr and Louhiluoto, 2012). These disruptions can be reduced and prevented by paying the necessary attention to the operations and management of the supply chain (Holmstrom, Jr and Louhiluoto, 2012). By incorporating the supply chain in the overall disease management strategy, efforts towards controlling the TB epidemic can be enhanced through the effective utilisation of available assets and recourses. This is, however, becoming increasingly difficult due to the participation of an increasing number of organisations and stakeholders on both a national and international level (Riungu, 2011).

The positive effect that SCM can have on a country's health system is evident in the Hashemite Kingdom of Jordan in the Middle East. Two years after a new management system for contraceptives was implemented, the number of stock-outs in health centres was reduced by 75% (Holmstrom, Jr and Louhiluoto, 2012). Other than reduced stock-outs, an effective supply chain can also increase response time, flexibility and drug utilisation, reduce waste and possibly decrease the chances of medication errors (Riungu, 2011).

3.4 Measuring supply chain performance

A supply chain analysis involves studying how products move from forecasting and procurement to the final delivery to the consumer. It entails assessing the performance of all the entities and processes involved during the entire supply chain (Unicef, 2009). In this research, the supply chain's performance will be measured under the different circumstances of the modelling scenarios and then compared with one another in order to make recommendations for the strengthening of the supply chain.

3.4.1 Measures and metrics

Measures and metrics are required to test the feasibility and sustainability of strategies and support the development of clear improvement goals (Gunasekaran, Patel and Tirtiroglu, 2001). A performance measure can be described as a selection of metrics that is used to quantify and subsequently measure the effectiveness and/or efficiency of a process, action or entity (Mandal, 2012a). In this sense, effectiveness typically refers to

meeting the customer's requirements and efficiency measures the utilisation of resources (Mandal, 2012b). The metric typically includes the measure's definition, the calculation method and the data source (Mandal, 2012a). With this in mind, all metrics can ultimately be grouped into either (i) utilisation, (ii) productivity, or (iii) effectiveness metrics. Utilisation is a measure of input usage and is typically a ratio of an actual amount and a norm value. For example, a ratio of the number of hours a machine was used and the number of hours the machine is available. Productivity (or efficiency) compares inputs with outputs and is typically a ratio of the actual output and the actual inputs that were consumed. For example, a ratio of the amount of orders that were processed and the number of hours it took. Lastly, effectiveness measures the quality of the output and is typically a ratio of the actual output and a norm output. For example, a ratio of the amount of orders fulfilled and the amount of orders received.

A challenging aspect of performance measurement, is identifying the key performance indicators (KPIs) that will add the most value to the supply chain analysis (Mandal, 2012a, 2012b). Having several metrics measuring all the aspects of the supply chain will waste time and is often unnecessary. Therefore, the metrics used in performance measurement and improvement should be chosen carefully and only be used if they capture a necessary aspect of the supply chain performance (Gunasekaran, Patel and McGaughey, 2004). Metrics can be assessed according to several criteria, namely (i) robustness, (ii) validity, (iii) usefulness, and (iv) integration (Caplice, 2016b). A robust metric is timeless, comparable across locations and organisations and is repeatable. Valid metrics accurately represent the processes measured and take outside influences into account. Useful metrics are easy to comprehend and deliver a sensible description of the measured process. An integrative metric includes all of the significant factors and influences of the measured process and encourages coordination across the entire supply chain. The metrics will typically have trade-offs between these criteria. For example, a metric that is exceptionally integrative, will typically be less useful and valid. This is why it is best for a system to have a set of metrics.

The goals of the measurement system should represent the goals of the organisation and, in this case, the goals of the research as well. This is often reflected in the way that the metrics and measurement system is grouped. In previous studies, metrics and measurement systems have been grouped according to the type of information or data they provide, i.e. whether they are quantitative or qualitative (Chan *et al.*, 2003) or according to their tactical, operational or strategic focus (Gunasekaran, Patel and Tirtiroglu, 2001; Gunasekaran, Patel and McGaughey, 2004). Furthermore, they have also been grouped according to the process, activity or tier in the SC that they relate to most (Lambert and Pohlen, 2001), or at what link they influence the performance across the entire supply chain (Lockamy and McCormack, 2004). Combinations of the above-mentioned groupings can be used, such as grouping the metrics according to their level

of focus and then subgrouping them according to their related SC process. In a global supply chain, such as the one being investigated in this study, the metrics that monitor the supply chain can be said to be on either a global-, regional-, or country-level (Unicef, 2009). Regardless of the grouping used, it is best that the metrics comprise of both financial and non-financial measures (Biswas and Narahari, 2004; Gunasekaran, Patel and McGaughey, 2004).

3.4.2 Supply Chain Operations Reference (SCOR)

The Supply Chain Operations Reference (SCOR®) was developed by the Supply Chain Council in 1996 and has since become the world's leading management tool for supply chain decision making. The SCOR framework provides a unique supply chain framework that links people, practices, processes and performance metrics. For this study, the focus will be on performance metrics.

The performance metrics section of SCOR is divided into two types of elements, namely metrics and performance attributes. A metric measures the capability of a supply chain to achieve a certain strategy, while a performance attribute is described as a set of metrics that represent the strategy. SCOR distinguishes between three levels of metrics. The overall wellbeing of the supply chain is described by Level 1 metrics and helps to ascertain supply chain targets and goals. These metrics are characterised by Level 2 metrics, which aim to identify causes of performance gaps in the Level 1 metrics. Likewise, Level 2 metrics are characterised by Level 3 metrics. Furthermore, there are five core performance attributes identified by SCOR, namely (i) reliability, (ii) responsiveness, (iii) agility, (iv) costs and (v) assets. Each of these five attributes are described in Table 3.1.

Table 3.1: Description of SCOR attributes.

Attribute	Description
Reliability	• Addresses the capability to execute and complete expected tasks. • Centred around the predictability of process outcomes. • Customer-oriented attribute. • Level 1 metric is Perfect Order Fulfilment.
Responsiveness	• Describes the rate at which tasks are executed. • Customer-oriented attribute. • Level 1 metric is Order Fulfilment Cycle Time.
Agility	• Describes the capability to respond and adapt to outside influences, such as unexpected changes in demand, suppliers leaving the market, labor issues, etc. • Customer-oriented attribute. • Level 1 metric is Upside Supply Chain Flexibility.

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Costs	• Describes the costs of the processes. • Covers all supply chain spend, including labour costs, material costs, transportation costs, supply chain management cost etc. • Internally-oriented attribute. • Level 1 metric is Supply Chain Management Cost.
Assets	• Describes the proficiency of asset utilisation. • Strategies include inventory reduction, outsourcing vs. insourcing, etc. • Internally-oriented attribute. • Level 1 metric is Cash-to-Cash Cycle Time.

3.5 Demand Forecasting

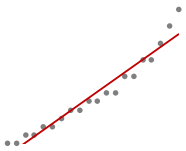
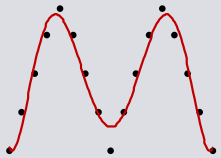
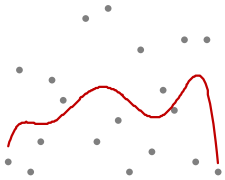
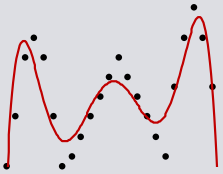
Demand forecasting refers to the prediction of the likely demand for a product or a service based on historical events and present trends. There are three levels within the demand forecasting component, related to the forecast's time horizon and purpose. These levels are associated with the supply chain levels discussed in Section 3.2, namely strategic forecasts, tactical forecasts and operational forecasts.

There are several forecasting methods, each with their own advantages and limitations. The methods can be divided into two groups, namely subjective and objective. Subjective methods can be further divided into judgemental methods (such as sales force surveys or expert opinions) or experimental methods (such as customer surveys or focus groups). Objective methods can also be subdivided into two groups, namely, causal methods (such as regression analysis) and time series methods (such as exponential smoothing). Subjective methods are mostly applied by marketing and sales, while objective methods are mostly applied for production and inventory planning). For the purpose of this study, some of the more common objective methods will be discussed further.

3.5.1 Time series

Time series is essentially used to identify patterns or trends in the data distributed over time. To be able to identify and capture the patterns, historical data or records of demand for several time periods are required. There are five aspects associated with time series, namely (i) level, (ii) trend, (iii) seasonality, (iv) random variabilities and (v) cyclical movements. Each of these components are described shortly in Table 3.2.

Table 3.2: Five components of time series.

Aspect	Description	Graphical Example
Level	• The demand remains approximately the same with small variations. • In the absence of other patterns, the demand remains a constant value.	
Trend	• The demand either grows or declines over time; i.e. it moves in one direction. • Trends are typically linear, but can be exponential, quadratic etc.	
Seasonality	• Demand follows a repeated cycle related to a known and fixed time period (hourly, weekly, monthly, etc.). • This can be due to natural (winter vs summer) or man-made (school holidays, sporting events) forces.	
Random Variabilities	• Demand is irregular and unpredictable.	
Cyclical Movements	• Similar to seasonality, but the time period is not fixed. • The duration of the cycle can be different every time.	

The forecasting procedure for time series can be described in four steps:

1. Select a suitable model of the demand pattern;
2. Estimate and regulate values for the model parameters;
3. Forecast the future demand with the selected model and parameters; and
4. Review the model's performance and adjust the parameters if necessary.

Three common time series models are the cumulative forecast model, the naive forecast model and the moving average forecast model. In a cumulative forecast model, all the history matters equally and therefore all of the data is included. These forecasts often change very slowly over time and are more constant than responsive. The equation for a cumulative forecasting model is

$$\hat{x}_{t,t+1} = \frac{\sum_{i=1}^{t} x_i}{t} \tag{3.1}$$

where:

$\hat{x}_{t,t+1}$ represents the forecast for period $t+1$ made during period t, and

x_t represents the actual demand in period t.

In a naive forecast model, only the latest data point affects the system. These forecasts are typically more volatile and can alter rapidly and dramatically making it more responsive than stable. The equation for a naive forecasting model is

$$\hat{x}_{t,t+1} = x_t. \tag{3.2}$$

In a moving average forecast model, the amount of data to use (the last M periods) can be altered. The equation for a moving average forecasting model is

$$\hat{x}_{t,t+1} = \frac{\sum_{i=t+1-M}^{t} x_i}{M}. \tag{3.3}$$

All of three of these model examples assume stationary demand. Therefore, if there is any trend or seasonality present in the data, the forecast will be lagging. Furthermore, the models also apply equal importance to each of the historical data points. A fourth model, the exponential smoothing forecasting model, treats data points differently depending on their age. The basic principle of exponential smoothing is that the weight of a data point decreases over time to ensure that the more recent observations have a greater effect on the forecast. The weights that data points carry, decrease exponentially as they age. The equation for a simple exponential smoothing forecasting model is

$$\hat{x}_{t,t+1} = \alpha(1-\alpha)^0 x_t + \alpha(1-\alpha)^1 x_{t-1} + \alpha(1-\alpha)^2 x_{t-2} + \cdots + \alpha(1-\alpha)^n x_{t-n} \tag{3.4}$$

where:

$\hat{x}_{t,t+1}$ is the forecast for time $t+1$ made during time t,

α is the exponential smoothing factor $(0 \leq \alpha \leq 1)$,

x_t is the actual demand during time t, and

x_{t-n} is the actual demand during time $t-n$.

As with the previous three models, this model also assumes stationary demand; however, the equation can be altered to assume a level, trend and seasonality. This model is also known as the Holt-Winter Method. The equation is given by

$$\hat{x}_{t,t+\tau} = (\hat{a}_t + \tau\hat{b}_t)\hat{F}_{t+\tau-P}, \tag{3.5}$$

where $\hat{a}_t$ and $\hat{b}_t$ is the estimated level and trend at time t, respectively, and $\hat{F}_t$ is the multiplicative seasonal index appropriate for period t calculated by

$$\hat{a}_t = \alpha\left(\frac{x_t}{\hat{F}_{t-P}}\right) + (1-\alpha)(\hat{a}_{t-1} + \hat{b}_{t-1}), \tag{3.7}$$

$$\hat{b}_t = \beta_S(\hat{a}_t + \hat{a}_{t-1}) + (1-\beta_S)\hat{b}_{t-1}, \text{ and} \tag{3.6}$$

$$\hat{F}_t = \gamma_S \left(\frac{x_t}{\hat{a}_t}\right) + (1 - \gamma_S)\hat{F}_{t-P} \tag{3.8}$$

where:

β_S represents the exponential smoothing trend factor $(0 \leq \beta_S \leq 1)$,

γ_S the seasonality smoothing factor $(0 \leq \gamma_S \leq 1)$, and

P the number of time periods within the seasonality $\left(\sum_{i=1}^{P} \hat{F}_i = P\right)$.

3.5.2 Causal analysis

Causal analysis is used when the demand is correlated with some known and measurable factors. The demand (Y) is the dependent variable, and is given as a function of one or several independent variables $(x_1, x_2, \dots, x_n)$. The equation for linear regression is:

$$Y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \cdots + \beta_i x_{ni} \;\; for\; i = 1,2, \dots n, \tag{3.9}$$

where:

β_0 is the estimate of the intercept, and

$\beta_{i:}$ is the estimate of the slope for variable i.

3.5.3 Forecasting quality

Irrespective of the chosen forecasting method, the quality of the forecast remains an important consideration. There are two dimensions significant to forecasting quality, namely bias and accuracy. Bias is the persistent tendency to over- or under-forecast, while accuracy refers to the forecast's closeness to the actual data. Since no single metric can accurately capture both of these dimensions, it is best to use multiple metrics. The most common metrics used for accuracy are the mean absolute percent error and the root mean squared error, while the most common metric used for bias is the mean percent error.

The root mean squared error ($RMSE$), mean absolute percent error ($MAPE$) and mean percent error (MPE) is given by:

$$RMSE = \sqrt{\frac{\sum_{t=1}^{n} e_t^2}{n}}, \tag{3.10}$$

$$MAPE = \frac{\sum_{t=1}^{n} \frac{|e_t|}{A_t}}{n}, \text{ and} \tag{3.12}$$

$$MPE = \frac{\sum_{t=1}^{n} \frac{e_t}{A_t}}{n}, \tag{3.11}$$

where e_t is the forecast error for time t and is calculated as the difference between the actual demand and forecasted demand for time t.

3.6 Push and pull systems

A system where the forecasted demand, instead of the actual demand, is used during planning and operations is referred to as a push system. In contrast, a pull system is where planning and operations are only initiated in response to an order, when the exact demand is known for certain. Push systems are known to have faster response times, since stock is already on hand, but can sometimes result in either excess stock or a shortage of stock. In contrast, pull systems rarely have any excess stock or stock shortages, since the actual demand is used; however, it is accompanied by longer response times.

Although push systems are more common, nearly all supply chains implement a push-pull hybrid, which is combination of both a push and a pull system. The point in the supply chain where it changes from a push system to a pull system is typically referred to as the decoupling point or customer order decoupling point. A common strategy is to implement a push system in the upstream segment of the supply chain and a pull system in the downstream segment. A simple example is illustrated in Figure 3.2. The demand is forecasted, orders are placed to manufactures and stock is kept at a central warehouse or distribution centre. When a customer places an order it is pulled from the warehouse or DC. This strategy combines the benefits of having a product ready on demand (push system) and of fast customisable services (pull system).

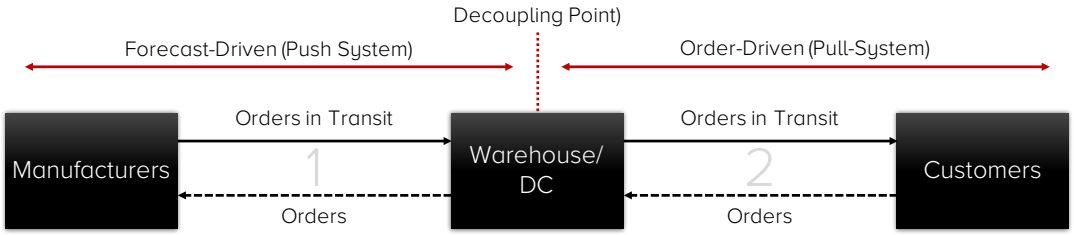


Figure 3.2: Example of a push-pull hybrid system.

3.7 Inventory management

Inventory management involves the administration and monitoring of the order, storage and use of the items or products that a company sells. Where applicable, it also involves the management of the raw materials used to produce the products or items. Inventory is kept to use as a safeguard against uncertainties in the demand, supply, distribution or manufacturing. It alleviates the need to manufacture a product from scratch for each individual order. Inventory is the result of a push system where the forecast regulates the amount of inventory that is required.

It is important to determine the amount of inventory that will reduce the probability of having excess inventory and consequently possible spoilage or obsolescence. To do

this, inventory decisions are made across all three supply chain levels. Strategic inventory decisions cover the implications of the design (of the product and network), such as the capacity of warehouses and distributions, implementing a centralised or decentralised network, etc. Tactical inventory decisions cover the details of the distribution process, such as what products to keep in stock and where. Lastly, operational decisions cover the replenishment policies of inventories, such as the safety stock level, reorder periods, etc. The operational decisions are critical to establish how the supply chain is set up. Some of the inventory policies related to operational decisions will be discussed in the remainder of this section.

3.7.1 Single period inventory models

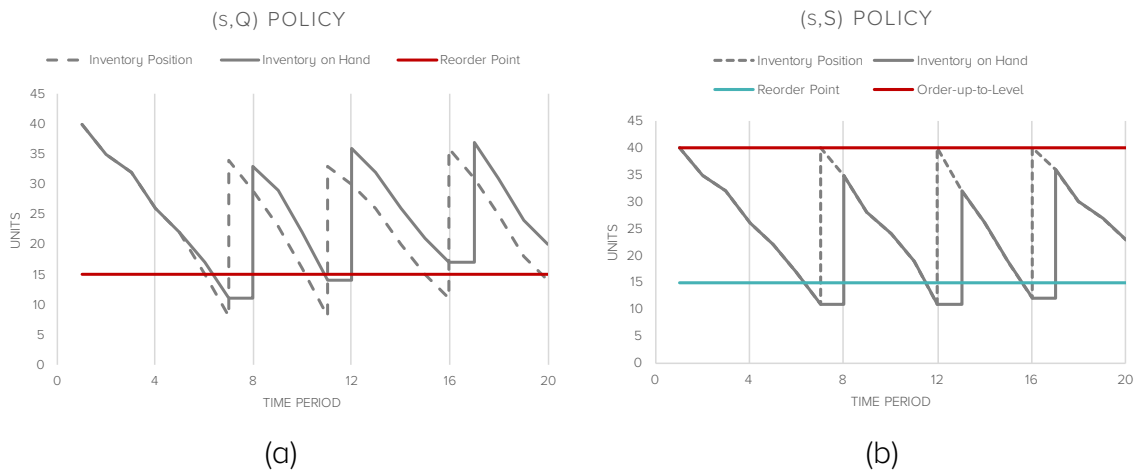
A single period inventory model, also known as the newsvendor problem, permits variable and stochastic demand and assumes only a single time period. Only a single order can be placed at the beginning of the time period and no replenishment orders can take place during the period. Any excess inventory at the end of the time period is discarded and any unmet demand is lost.

3.7.2 Base stock policy

The base stock policy determines a base stock for each item. If an order is placed for that item, an order of the same size is placed to replenish the inventory to the base stock level. Therefore, the inventory position will always equal the base stock. The inventory position is given as the sum of the stock on hand and the orders placed, subtracted by backorders (if applicable). The base stock is typically set at a level to meet the estimated demand during the lead time. Furthermore, the model assumes that any excess inventory can be used at a later time period and it is not discarded.

3.7.3 Continuous review policies

A continuous review policy allows inventory replenishment at any time. There are two common continuous review policies used, namely: the order-point, order quantity (s, Q); and the order-point, order-up-to-level (s, S) policy. With the (s, Q) policy, Q units are ordered when the inventory position is less than or equal to the replenishment point s, while with the (s, S) policy, a maximum of S units can be ordered. The latter policy is especially useful in cases where there is a capacity or budget constraint. The order size of the (s, S) policy is typically the difference between the inventory position and S. Both of these policies are illustrated with an example in Figure 3.3, where a lead time of one period is applied.



(a) (b)

Figure 3.3: (a) Example of an order-point, order quantity (s,Q) policy, (b) example of an order-point, order-up-to-level (s,S) policy.

In the (s, Q) policy example, the same amount (Q) is ordered every time the inventory position falls below the replenishment point s, while in the (s, S) policy, the amounts being ordered differ, since these depend on the inventory position at the time of the order placement.

3.7.4 Periodic review policy

A periodic review policy allows inventory replenishment only at certain time periods. For example, with an order-up-to-level policy (R, S), a maximum of S units are ordered every R time periods. This is illustrated in Figure 3.4, where an order is placed every four periods and there is a lead time of one period. The order size differs depending on the inventory position at the time of the order placement.

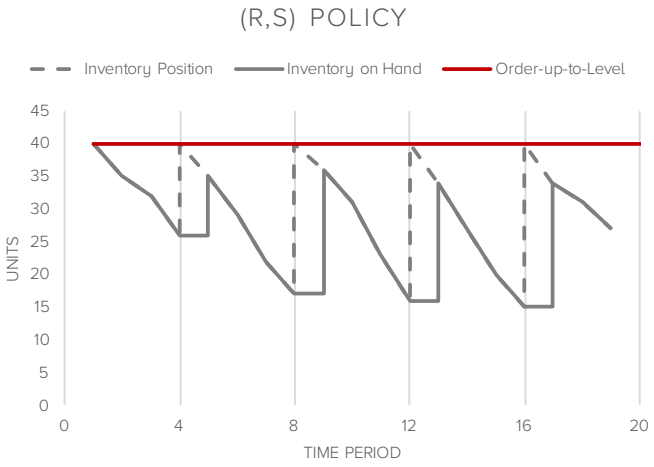


Figure 3.4: Example of an order-up-to-level (R,S) policy.

The different inventory policies can also be combined to form a hybrid policy, for example, an (R, s, Q) policy indicates that every R periods, Q units should be ordered, only if the inventory position is less than s. Another popular hybrid is a (R, s, S) policy

where every R time periods, a maximum of S units should be ordered, only if the inventory position is less than s.

3.8 Conclusion: Supply chains

This chapter provided a brief introduction to supply chains and a description of the applicable topics and themes in more detail. The importance of the MDR-TB supply chain for SLDs was also discussed. The following chapter will present typical approaches to model supply chains, before identifying and describing the approach that will be applied in this study.

Chapter 4:

Supply chain modelling

"What gets measured gets improved."

- Peter F. Drucker (described as the “founding father of modern management”)

The previous two chapters aimed to provide background information on the two main themes of the study, namely TB and supply chains. This chapter will continue to put the research in context by describing the approaches and techniques that are typically applied to model supply chains. A taxonomy of supply chain modelling approaches and techniques will be provided and discussed, after which the discussion will move on to the selection of an approach that will be applied to this study. The selected approach and important concepts related to it, will be described in detail.

4.1 Supply chain modelling and analysis

Modelling implies ‘mapping’ the system, in some shape or form, so that it represents the real system. The analysis of these models can lead to significant contributions to the improvement of organisations and product or service delivery. Supply chains are modelled for multiple reasons, such as optimising the supply chain activities and processes or to merely gain an understanding of the cause-and-effect relationships in the supply chain (Kleijnen and Smits, 2003).

In this section, the perspective from which a supply chain can be modelled is discussed, after which a taxonomy of supply chain modelling approaches and techniques will be presented.

4.1.1 Supply chain perspectives

When modelling a supply chain, it is necessary to determine which (of two) potential perspectives will be applied. The perspectives are: (i) the supply chain is of a single given organisation, or (ii) the supply chain comprises of a network of organisations and the focus of the study is on the entire system and not on a specific organisation in the network (Thierry, Bel and Thomas, 2010).

In the first perspective, the supply chain can be further divided into the internal and external supply chain. The internal supply chain focuses on functional processes, material flow and information flow. The external supply chain focuses on the integration and cooperation between the organisation, the suppliers, the suppliers' suppliers, the customers and the customers' customers (Thierry, Bel and Thomas, 2010).

In the second perspective, the network of supply chains is linked through upstream and downstream segments. These segments connect all the organisations and actors that are involved in the various processes and activities that contribute to the delivery of the product or service to the end consumer. The focus is on the relationship and cooperation between the organisations and actors in the supply chain (Thierry, Bel and Thomas, 2010).

4.1.2 Classification of modelling approaches and techniques

As already mentioned, a supply change involves various stages. To model the multi-stage supply chain as a whole, there are various modelling techniques to consider. These techniques are grouped or categorised into different modelling approaches. There has been some discrepancy in the literature as to how the modelling approaches should be categorised.

Beamon (1998) defines four categories of modelling approaches and discusses various modelling techniques associated with each. The approach categories are: (i) deterministic analytical models, (ii) stochastic analytical models, (iii) economic models, and (iv) simulation models. Most of the techniques leads to static models, with average performance or steady state conditions used as input variables (Sarimveis *et al.*, 2008).

When modelling supply chains, it is necessary to take into account aspects such as fluctuations in demand, sales forecasting, delays in delivery and procurement, etc., all which add to the dynamic complexity of a supply chain. The static models, however, do not sufficiently describe and analyse problems in the supply chain (Sarimveis *et al.*, 2008), since they are ineffective in modelling the complex dynamics of the supply chain as a whole (Manzini *et al.*, 2005). Furthermore, the static models do not allow easy adjustments and any changes typically require additional computing time (Manzini *et al.*, 2005).

Riddalls, Bennett and Tipi (2000) propose an alternative categorisation of approaches for modelling the dynamics of supply chains: (i) continuous time differential equation models, (ii) discrete time difference equation models, (iii) discrete event simulation models, and (iv) classical operational research methods.

Both of the aforementioned groupings are largely based on mathematical techniques. For this study, a more general classification is desired. Biswas and Narahari (2003) categorised the various modelling techniques into three approaches, namely (i) optimisation models, (ii) analytical performance models, and (iii) simulation models. Two of the three approaches defined by Thierry, Bel and Thomas (2010), labelled as analytical methods, and simulation and emulation, align to Biswas and Narahari's (2003) categories (ii) and (iii). Thierry et al.'s third category, however, is physical experimentation and they omit to categorise optimisation models as a separate approach.

The different approaches, as defined in the literature, were compared and combined in order to determine a classification of the approaches that would encompass most (if not all) of the applicable modelling techniques. The three modelling approaches, used in this study's supply chain modelling taxonomy, are categorised and defined below.

1. Analytical measures and modelling

Analytical models primarily use mathematical models to define the system. Equations and mathematical functions are used to describe the environment of the system and the changes made to it. This approach encompasses numerous techniques that are subdivided as (i) optimisation models or operations research, (ii) statistical models, and (iii) supply chain analytics. These subcategories were determined by comparing the different techniques and analytical models described in the literature.

2. Physical experiments

This approach is used to improve the design of certain processes by changing the actual process and evaluating the results. Physical experiments, such as industrial pilot implementations, are rarely used in supply chain management today. This is mainly due to the technical- and cost-related limitations associated with physical experiments (Mandal, 2012b), especially when modelling large-scale improvements. Using this approach to evaluate an entire supply chain will be particularly difficult if not impossible.

3. Simulation and emulation

As with the modelling approaches, there is also some discrepancy in the literature as to how the simulation and emulation techniques should be categorised. Kleijnen and Smits (2003) categorised the different simulation techniques as (i) spreadsheet simulation, (ii) system dynamics, (iii) discrete-event dynamic system simulation, and (iv)

business game simulation. Kersten and Saeed (2013) defined similar categories, with the exceptions that they defined a fifth category, namely agent-based simulation, and that the third category (discrete-event dynamic system simulation) is instead merely labelled discrete-event simulation.

The difference between discrete-event dynamic system simulation and discrete-event simulation is made clear by Thierry, Bel and Thomas (2010). They define two categories of simulation techniques, namely continuous simulation and discrete event simulation. The latter is further divided into being either event-driven or time bucket-driven. Discrete-event dynamic system simulation is an example of event-driven DES, whereas time bucket-driven DES is alternatively referred to as spreadsheet simulation. System dynamics, as mentioned in the other sources, is an example of continuous simulation.

Hybrid simulation is also important to consider as a modelling technique. White and Ingalls (2009) acknowledge hybrid models as one of five categories, which is given as (i) continuous system simulation, (ii) Monte Carlo simulation, (iii) discrete-event simulation, (iv) hybrid simulation, and (iv) agent-based simulation.

After reviewing the techniques and their categorisation as discussed in the literature, the techniques associated with this approach will be classified in the taxonomy as (i) discrete-event simulation, (ii) business games, (iii) agent-based simulation, (iv) continuous simulation, and (v) hybrid simulation. The taxonomy of supply chain modelling approaches and techniques is illustrated in Figure 4.1, with one or more examples of selected techniques. Since physical experimentation will be infeasible for this study, only the two alternative approaches ('Analytical Measures & Modelling' and 'Simulation & Emulation') will be further discussed in more detail.

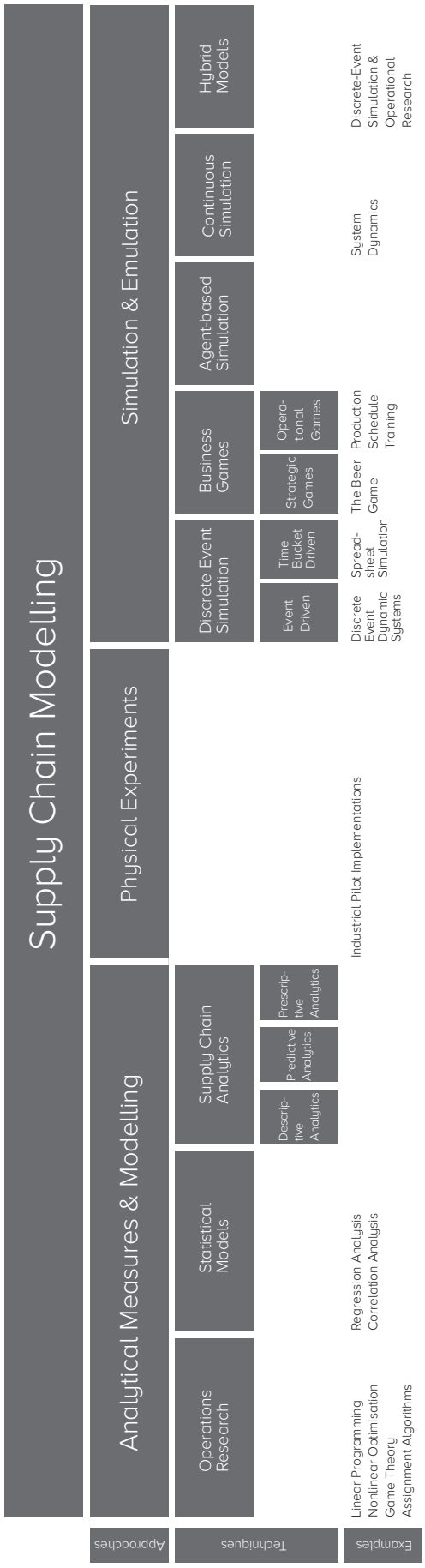


Figure 4.1: Taxonomy of supply chain modelling approaches and techniques.

4.1.3 Operations research

Operations research (OR) is a branch of knowledge concerned with the application of analytical methods to aid in decision-making (Mielczarek and Uzialko-Mydlikowska, 2010). OR is commonly used in industry, even though it is not technically considered a modelling technique. Well-known examples of OR include linear programming, game theory and nonlinear optimisation. OR is usually associated with a computational burden and typically requires the estimation of many of the model's parameters. When using OR, a comprehensive understanding of the model is required and the models are often validated through the use of discrete event simulation (Riddalls, Bennett and Tipi, 2000). In most cases, however, OR techniques fail to explain the dynamics of the system (Riddalls, Bennett and Tipi, 2000).

The technique describes the different processes and corresponding activities of a system using mathematical models (Ahmadi, 2012). A systematic problem solving approach is followed (Ahmadi, 2012) to reach an optimal or near-optimal solution (Mielczarek and Uzialko-Mydlikowska, 2010). Traditionally, an optimisation model involves the minimisation or maximisation of a certain function, under constraints. In supply chain optimisation models, algorithms and data structures, that are capable of achieving large-scale systems integration, are developed (Biswas and Narahari, 2004). One of the major focus areas of this type of modelling is to optimise specific aspects of the supply chain, such as the optimal amount and location of warehouses or facilities (Biswas and Narahari, 2004), the optimal distribution methods, etc.

4.1.4 Statistical models

Statistical modelling and analysis embodies families of probability distributions and aims to represent the assumptions of the real-world situation. For the modelling to be successful, data and patterns that are subject to statistical analysis are required. These patterns are not always available in practice; consequently, estimates have to be determined and used instead. This often leads to limited success when using this technique to model large, complex systems (Luke and Stamatakis, 2012). Nonetheless, statistical modelling essentially attempts to reduce complex data to less complex terms, focusing primarily on individual aspects (such as parameter estimates, links and interactions) in the supply chain (Luke and Stamatakis, 2012).

4.1.5 Supply chain analytics

Supply chain analytics involves the application of organisational procedures and tools in combination with various techniques from statistical analysis and operations research (Trkman *et al.*, 2010). It is used to gain and analyse information that will allow better decision-making with regard to the product-, finance-, and information flows (Souza, 2014) and to predict the results of changes to the supply chain (Trkman *et al.*, 2010). A

foremost unique characteristic of this technique is that it is a proactive model used to continually sense changes and that it therefore allows immediate response (O'Dwyer *et al.*, 2011). It allows proven techniques and algorithms (such as data mining, stochastic modelling and regression analysis) to be applied to large, ever-expanding sets of data (O'Dwyer *et al.*, 2011). The technique comprises of three types of analytics: (i) descriptive, (ii) predictive and (iii) prescriptive , all of which work in parallel for optimal results (Souza, 2014).

Descriptive analytics uses modern day data sources, such as global positioning system (GPS) data of transportation vehicles containing inventories, and radio frequency identification data from tags in pallets, to derive real-time information. With data visualisation, this information allows the organisation to see where schedule adjustments need to take place, whether emergency orders will be required and so forth. The acquired information is also used in the predictive analytics, where demand forecasts are derived. In prescriptive analytics, statistical techniques and optimisation models are applied to the real-time information and forecasts (from the previous categories). Recommendations for improvement are derived from these model conclusions (Souza, 2014).

4.1.6 Analytical measures and modelling: verdict

For the global upstream supply chain being investigated in this study, the techniques associated with the analytical measures and modelling approach will be impractical due to the simplifications (of real-world factors) that are required to analyse such models (Kersten and Saeed, 2013).

In order to understand and analyse the behaviour of an entire supply chain, the system should be studied as a whole and not as individual parts (Luke and Stamatakis, 2012). This implies that for this study, an analytical approach would not suffice as the required mathematical models would be too large and complex to solve (Thierry, Bel and Thomas, 2010).

4.2 Computer simulation

Simulation involves experimenting with a computer model of a real world system (Kersten and Saeed, 2013). With simulation, it is easy to investigate the effects of certain changes in order to determine the configuration that would benefit the system the most (Thierry, Bel and Thomas, 2010). Simulation aims to model the complex and dynamic behaviour of a real world system and to increase the understanding and knowledge of this system through observations of the effects of model configuration (Mielczarek and Uzialko-Mydlikowska, 2010). Therefore, simulation is used in industry to aid decision makers in the design and improvement of supply chain operations since the dynamic

behaviours of the supply chain can be studied and better understood (Kersten and Saeed, 2013).

4.2.1 Discrete-event simulation

These techniques involve the flow of physical entities between resources. For example, in the MDR-TB SLD supply chain, the entities will start as raw materials that progresses through manufacturing processes (resources), at which point their attributes are changed and they emerge as drugs for treatment. As previously mentioned, discrete-event simulation (DES) techniques are either classified as time bucket-driven or event-driven. They are classified according to the time advance process of the technique (Kasaie, Dowdy and David Kelton, 2013). The time bucket-driven technique is often referred to as spreadsheet simulation. In this technique, refer to Figure 4.2, time is divided into buckets (periods of a given length) and incremented step by step within a given bucket. An activity causes the system to move from one step to the next. After every step, an event occurs that changes the state of the system, requiring the calculation of the new state using the model equations (Thierry, Bel and Thomas, 2010).

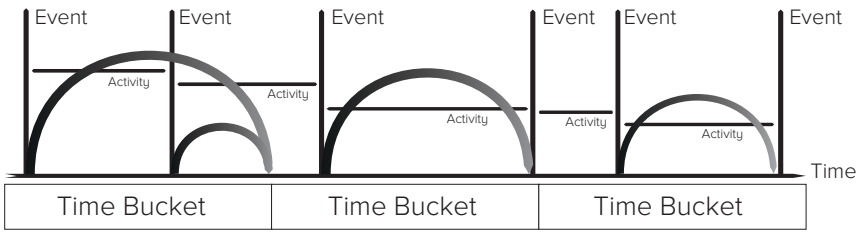


Figure 4.2: Time bucket-driven discrete-event simulation (Adapted from Thierry, Bel and Thomas, 2010).

This technique allows the development of a simple time slice model, however, attempting to model an entire complex system will prove difficult (Kersten and Saeed, 2013).

The event-driven technique works similarly to the time bucket driven technique, except that it omits time buckets. Instead, it focuses only on event times, which are the moments at which the model's state undergoes a change. This is illustrated in Figure 4.3.

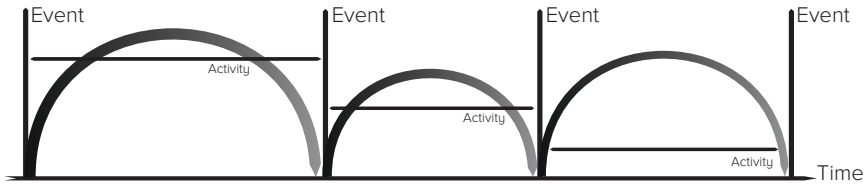


Figure 4.3: Event-driven discrete-event simulation (Adapted from Thierry, Bel and Thomas, 2010).

When using this technique to model large and complex supply chains, some difficulties might occur due to the size of the supply chain. The flow of each individual actor or entity in the supply chain can create an excessively large number of events, which

could make the model infeasible. In some cases, however, this risk can be reduced with the use of model reduction techniques (Thierry, Bel and Thomas, 2010).

4.2.2 Business games

Supply chain modelling provides members of the chain with the opportunity to understand and visualise their own network and integration of activities. By using corresponding business games with the model, it can serve as a beneficial tool for the discussion and validation of possible changes to the real-world supply chain network (Holweg and Bicheno, 2002). By letting managers and essential partners operate within the simulation of the supply chain, their human behaviour can also be modelled. It is difficult to model the human behaviour aspect with other simulation techniques (Kersten and Saeed, 2013). Although business games can be accomplished without computers, this study only considers business games that rely on computers, classifying them as a type of computer simulation.

Business games are further classified as being either strategic or operational. Strategic games consist of several teams, each representing an organisation or partner of the supply chain network, competing with each other in the simulation for numerous rounds. The game is usually modelled to illustrate a specific cause-effect relationship (Kleijnen, 2005). In operational games, only a single team interacts with the simulated world, also for numerous rounds. The team consists of one or several players (Kersten and Saeed, 2013). The games are against nature, such as games for training in production scheduling (Kleijnen, 2005). Business games take advantage of every individual participant's knowledge of their area of expertise. The participants are more open for improvements to the way in which they make decisions as they have personally experienced the potential effects of their behaviour in the simulation (Holweg and Bicheno, 2002).

4.2.3 Agent-based simulation

Agent-based modelling is used to study complex systems by outlining characteristics and rules of the different individual elements (agents) of the system. Agents can either be a real or virtual entity. For example, agents can represent different supply chain activities (virtual entity) and their interactions. Agents are active, independent and responsive and therefore interact with one another. The simulation examines the system environment and how the agents behave and interact as a function of their characteristics and rules. Histories that explain the emergent behaviour and properties of the system are generated in order to obtain solutions for the improvement of the system. Many agent-based simulations allow the system behaviour to be viewed in real-time, which is an important attraction of this technique (Luke and Stamatakis, 2012).

4.2.4 Continuous simulation

Models of this technique often use mathematical equations that fit the assumptions of the system under investigation. Similar to the time-bucket driven approach in Section 4.2.1, time advances in equal periods. After every period, the model equations and values are recalculated (Ahmadi, 2012). The state of the system therefore changes continuously (Kleijnen, 2005). One of the predominant continuous simulation techniques is system dynamics, which focuses on the dynamic behaviour of complete systems (Thierry, Bel and Thomas, 2010). In system dynamics, organisations and supply chains are seen as complex systems with various distinctive flows. The system also has stocks or levels that, over time, integrate with each other according to the flow variations (Thierry, Bel and Thomas, 2010).

4.2.5 Hybrid simulation

For several systems, the use of a single simulation technique will not be the most effective or efficient approach. In these cases, hybrid simulation can be used to improve the modelling process. Hybrid simulation involves the combination of a simulation technique with another technique from either the same, or a different approach.

A popular combination is discrete-event simulation and operations research. As previously stated, discrete-event simulation is often used to validate operations research models. Another reason for this combination is when the input variables for the optimisation model are unknown. A discrete-event simulation model is run to provide estimates to be used in the optimisation model. The decision rules for the discrete-event simulation are restructured based on the solution of the optimisation model. The process is repeated until both models provide approximately the same solutions (Almeder, Preusser and Hartl, 2009). A hybrid simulation can also consist of two computer simulation techniques such as discrete-event simulation and system dynamics. In this combination, DES are used to model decisions for selected divisions of the network, while system dynamics are used to model the long term effects of the decisions on the entire network (Tako and Robinson, 2012).

4.2.6 Computer simulation: verdict

Computer simulation is often used in the industry and appears to be the better approach when it comes to the modelling and analysis of supply chain performance (Kleijnen, 2005; Kersten and Saeed, 2013). Simulation is an ideal tool for replicating the behaviour of complex systems for decision-making, since the implications of the changes can be evaluated before being applied to the real system (Kersten and Saeed, 2013). With simulation, problems can be diagnosed, operations can be optimised and cause-effect relationships can be studied, all without interrupting or disturbing the real system (Mandal, 2012b; Kersten and Saeed, 2013).

The best computer simulation technique to be applied depends on the type of problem to be solved (Kleijnen, 2005; Thierry, Bel and Thomas, 2010; Kersten and Saeed, 2013). Kersten and Saeed (2013) did a study on the use of simulation in SCM. Included in their conclusions is a summary of the main simulation techniques that support a certain SCOR-based SCM process, as discussed in Section 3.4. The chart in Figure 4.4 illustrates the application of simulation techniques when modelling more than one of the SCOR processes, as is the case with this study.

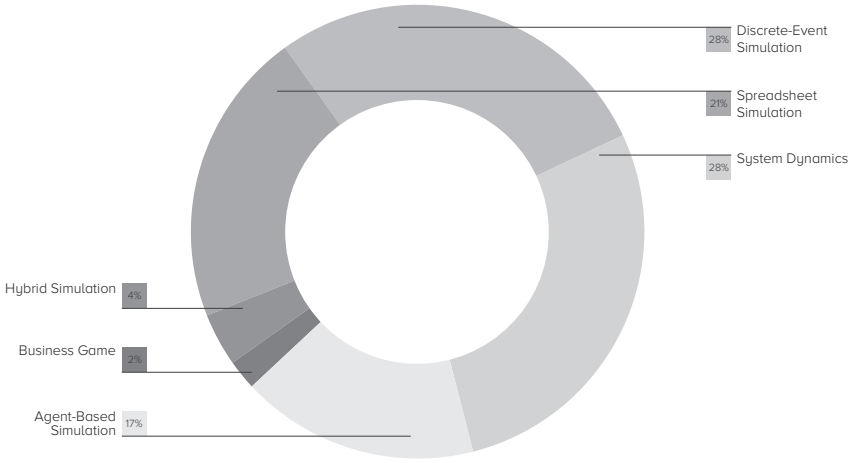


Figure 4.4: Application of simulation techniques for modelling more than one SCOR process (Adapted from Kersten and Saeed, 2013).

As can be concluded from the figure, the most widely used techniques when modelling more than one process are system dynamics (a type of continuous simulation) and discrete event simulation (a type of discrete, event-driven simulation). In order to determine which of these two techniques will be the better choice for modelling the MDR-TB SLD upstream supply chain, a comparison of the two techniques will be done. From this point forward, when referring to discrete-event simulation, it will imply that it is event-driven. It is important to note that though this research will employ a computer simulation approach, techniques from the analytical measures and modelling approach will also be incorporated where appropriate. As mentioned in Section 1.6, this study will potentially make use of correlational analysis and statistical analysis, which are all techniques that fall under the analytical measures and modelling approach. These techniques will not necessarily be used to model the supply chain, but it will aid in the analysis process.

4.3 Selection of modelling approach

This section will provide a comparison of system dynamics (SD) and discrete-event simulation (DES). The origin of SD dates back to 1961, where Jay Wright Forrester introduced a methodology for simulating dynamic models in his book Industrial Dynamics (Campuzano and Mula, 2011). The key points of DES were first discussed in

an article published in 1959 by Richard W. Conway, William L. Maxwell and Louis W. Miller, believed by many to be the introduction to DES (Goldsman, Nance and Wilson, 2010). Even though both these techniques were developed around the late 1950s, minimal attention was devoted to comparing the two fields. In recent years, however, there has been a significant amount of interest in their comparison (Tako and Robinson, 2010). The majority of literature on the subject is based on personal opinions of authors and often biased towards their field of expertise (Tako and Robinson, 2010).

In the remainder of this section, an overview of the general principles of each technique will be given and compared in order to determine which technique will potentially model the upstream MDR-TB SLD supply chain more effectively.

4.3.1 Structure

The different elements (entities, resources, activities, etc.) and the relationships between these elements are referred to as the structure of the system. In SD, an essential concept is that structure regulates performance. A clear understanding of the system structure is therefore required to be able to effectively improve the performance. To illustrate this concept, the relationships or links between the elements should leave no room for confusion (Sweetser, 2009). Feedback loops are used to model these links, which causes the variables that are linked to be interdependent. As the entities advance through the system the variables will change, consequently causing the behaviour of the system to change. It is these changes throughout the system that causes SD models to be dynamic (Sweetser, 2009).

Although structure is also important in DES, it is not as essential as in SD. Less emphasis is placed on the structure and instead the focus is placed on ensuring statistical validity. To successfully populate the model, accurate historical data or estimates are required. Therefore, a considerable amount of time is spent on data analysis and determining the distribution that fits the data best in order to ensure statistically valid outputs (Sweetser, 2009).

4.3.2 General procedure

As stated in the previous section, SD is best suited for modelling continuous systems and primarily focuses on the study of the entire system. Although SD can be used to model discrete changes in systems, it performs best when applied to continuous processes where dynamic changes in the system behaviour are observed (Sweetser, 2009). DES, on the other hand, largely models only specific processes (instead of whole systems). DES can model both continuous and discrete processes, yet its focus is on discrete processes. This is due to the technique's capability to model discrete changes in the behaviour of the process and to deliver a comprehensive analysis of linear processes (Sweetser, 2009).

With SD, the modelling process begins with the identification of the basic structure of the system and its relationships. The relationships are defined by assigning functions and values to them. After the system is entirely described, the model is simulated to investigate whether the outputs accurately reflect the initial perception of the system. This process is iterative and is only complete once the modeller(s) is satisfied with the model's output. The model can help to increase the modeller's knowledge and comprehension of the system and how its performance is dependent on the system structure (Sweetser, 2009).

DES modelling follows a similar procedure, but with some alterations. As discussed in Section 4.2.1, DES represents individual events which cause the state of the system to change (Kersten and Saeed, 2013). The events can be scheduled, such as a change of a shift, or unscheduled, such as the failure of a resource, and occur at discrete points in time (Sweetser, 2009). The model follows individual entities as they partake in processes and consume resources (Mielczarek and Uzialko-Mydlikowska, 2010). The model can provide an animation of the system in which icons or images represent the entities as they move through the system. This graphical representation can improve understanding of the process. However, in complex processes with a larger amount of entities, the animation is often hard to follow and make sense of (Sweetser, 2009).

4.3.3 Underlying principles

Both DES and SD models are developed to improve the understanding of the system behaviour and to analyse what effect different conditions will have on its performance. There are, however, some differences related to the underlying principles of the techniques (Tako and Robinson, 2012). In SD, the system is modelled as a set of stock and flows where the state changes continuously over time. The entities are viewed as a continuous quantity with a fixed rate by which they move in and out of processes. Even though the state changes are continuous, the differential equations in the model, transfer time (which is continuous) into a discrete counterpart using a time-slicing approach (Brailsford and Hilton, 2001). With DES, on the other hand, the system is modelled as a network of queues and activities where the state changes at irregular discrete points in time (Tako and Robinson, 2012). The time duration that an individual entity spends in a process, is sampled from probability distributions as determined by the modeller (Brailsford and Hilton, 2001).

4.3.4 Mapping of systems

Often when organisations use SD to model a system, the individuals that contribute to a specific process have their own unique interpretation and understanding of the system. They each envision a 'mental model' in their head. A key step in the SD modelling process is to develop an accurate representation of the system in a casual-

loop diagram (CLD). This mapping process is iterative and participants continue to add or modify the diagram until it incorporates everyone's mental model (Sweetser, 2009).

DES models are instead often built from an activity diagram, flow chart or process map, which allows clarification of the important decisions, relationships and processes in the system. In DES models, defining the system with diagrammatic representations tend to be easier since the systems being modelled typically have a narrower focus (than those modelled using SD). In SD, obtaining a CLD that everyone is satisfied with can prove to be a difficult task. This is mainly due to the exceptionally complex networks that are typically modelled with SD (Sweetser, 2009).

4.3.5 Validity

In SD, models are built from CLD, as discussed in the previous section. Therefore, they are considered to be based on a single group's interpretation of the system at that specific point in time. The captured representation could quickly become out-dated due to changes caused by the dynamic behaviour of the real system. Furthermore, human behaviour, which often plays a vital role in SD, is extremely challenging to quantify (Sweetser, 2009).

As previously mentioned, in DES historical data is analysed and used to populate the model. When historical data is absent, estimates are determined and the model's users approve the assumptions before implementation. This gives DES a stronger empirical basis compared to SD, especially since the processes modelled with DES are usually specific and observable. Unfortunately, the ability of DES models to adapt and predict changes of system behaviour decline over time (Sweetser, 2009).

4.3.6 Application to supply chain levels

To answer specific questions on an operational or tactical level, DES is typically the preferred modelling technique (Tako and Robinson, 2012). SD has a strong focus on structure, as discussed in Section 4.3.1, and can model both qualitative and quantitative data. Therefore, it is most often used at a more strategic level since it can be used to increase the understanding of the different relationships and links between the different elements of the system (Brailsford and Hilton, 2001). However, SD has been effectively used to model operational systems as well. It can be concluded that each modelling technique may have a different outlook of the same problem and therefore emphasise different aspects of the problem (Tako and Robinson, 2012).

4.3.7 Comparison conclusion

DES is beneficial due to its flexibility and capability to incorporate uncertainty, such as customers arriving at different points in time. Apart from being used to design new systems, DES permits easy assessment of the system efficiency and the ability to

analyse what-if scenarios (Mielczarek and Uzialko-Mydlikowska, 2010). One drawback of DES, is that clients can have difficulty understanding certain aspects of the DES models, especially the underlying statistics, such as the probability distributions and sampling, especially if they do not have a statistical background (Brailsford and Hilton, 2001). Since SD models can incorporate both quantitative and qualitative variables, they can normally enhance the client's understanding of large and complex systems (Mielczarek and Uzialko-Mydlikowska, 2010).

Although SD can effectively model relationships within the system, the output is normally limited to graphs, numerical displays and data outputs that can be analysed. The output of DES, in addition to graphs, numerical displays and data outputs, also includes an animation of the system (Sweetser, 2009).

Both approaches clearly have distinctive advantages and limitations. The choice of which technique to use, is therefore dependent on the type of system that has to be modelled and the type of information that is desired (Sweetser, 2009). To conclude the comparison, a summary of the criteria that will be taken into consideration during the selection was created and is given in Table 4.1.

Table 4.1: Criteria for comparing system dynamics and discrete-event simulation.

	System Dynamics	Discrete-Event Simulation
Purpose	Policy making: gaining understanding	Decisions: optimisation, prediction and comparison
Performance Dependency	Structure (Relationships)	Statistical (Validity)
Scope	Strategic level	Tactical, Operational level
Control	Rates (Stocks and flows)	Holding (Queues and activities)
Relative Timescale	Long	Short
Perspective	Holistic, emphasis on dynamic complexity	Analytic, emphasis on detail complexity
Resolution	Homogenised entities, continuous policy pressures and emergent behaviour	Individual entities, attributes, decisions and events
Time Increments	Continuous	Discrete
Outputs	Understanding of structural source of behaviour modes	Point predictions, performance measures

The MDR-TB SLD supply chain has various elements, both quantitative and qualitative, that play an important role in understanding the dynamics of the supply chain as well as the effects of decisions. The model will be used to quantify the impacts of strategic improvements and to analyse the cause-and-effect relationships in the supply chain. To effectively analyse the impact of these improvements, it is necessary to model the supply chain over a longer timescale.

After comparing these requirements with the criteria in Table 4.1, SD was selected as the more appropriate modelling technique to use in this study.

4.4 Overview of system dynamics

In several cases, the policies and decisions implemented to improve the supply chain do not necessarily accomplish the anticipated goals, but instead instigate unforeseen and unwanted consequences (Atun, 2012b). In order to prevent this, it is necessary to understand the behaviour of the supply chain as well as the nonlinear dynamics and feedback enclosed within the chain (Sterman, 2001).

SD is a computer aided, graphical (Kumar and Kumar, 2014) and analytical modelling technique (Brailsford and Hilton, 2001) that can be accredited to Professor Jay Wright Forrester and his students at the Massachusetts Institute of Technology (Brailsford and Hilton, 2001; Kumar and Kumar, 2014). He presented the first published work on the application of SD on Supply chain management in the book *Industrial Dynamics: A major breakthrough for decision makers* (Angerhofer and Angelides, 2000).

The technique provides a theoretical framework to model, analyse and understand the behaviour of complex systems over time (Luke and Stamatakis, 2012). SD models are capable of incorporating numerical data as well as descriptive data, making it possible to combine qualitative and quantitative aspects in order to enhance the understanding of the total system and its environment, elements and variables as well as the relationships between them (Brailsford and Hilton, 2001). This contributes to the broader boundaries that SD models permit, compared to other types of models (Luke and Stamatakis, 2012).

The aim of SD is not necessarily optimisation or point prediction, but rather to enhance the comprehension of the dynamics, behaviour and feedback loops of complex systems by providing both quantitative and qualitative output measures (Brailsford and Hilton, 2001). This section provides an overview of the SD modelling technique by defining important concepts.

4.4.1 Policy resistance

Policy resistance stems from the inability to comprehend the full network of functioning feedbacks in a system. In order to solve problems, well-intentioned solutions are applied and often cause unexpected consequences and reactions. These attempts to prevent or alter problems in the system are overcome by the system's response to the attempt (Sterman, 2001).

When it comes to systems that are dynamic, interrelated and always changing, decisions are usually based on the mental models of users. These mental models normally fail to capture the full network (Sterman, 2001) and reduce the complexity by overlooking the non-linearities, feedback structures and time-delays of the system (Atun, 2012b). This is due to the incapability of the human mind to fully comprehend complexity and to understand the effects of our choices. Normally the mental models only consider actions that will address the short-term and immediate concerns, which often causes adverse effects in the future (Sterman, 2001). An example of policy resistance, relevant to this study, is the evolution of drug-resistant pathogens. This is illustrated in **Figure 4.5**.

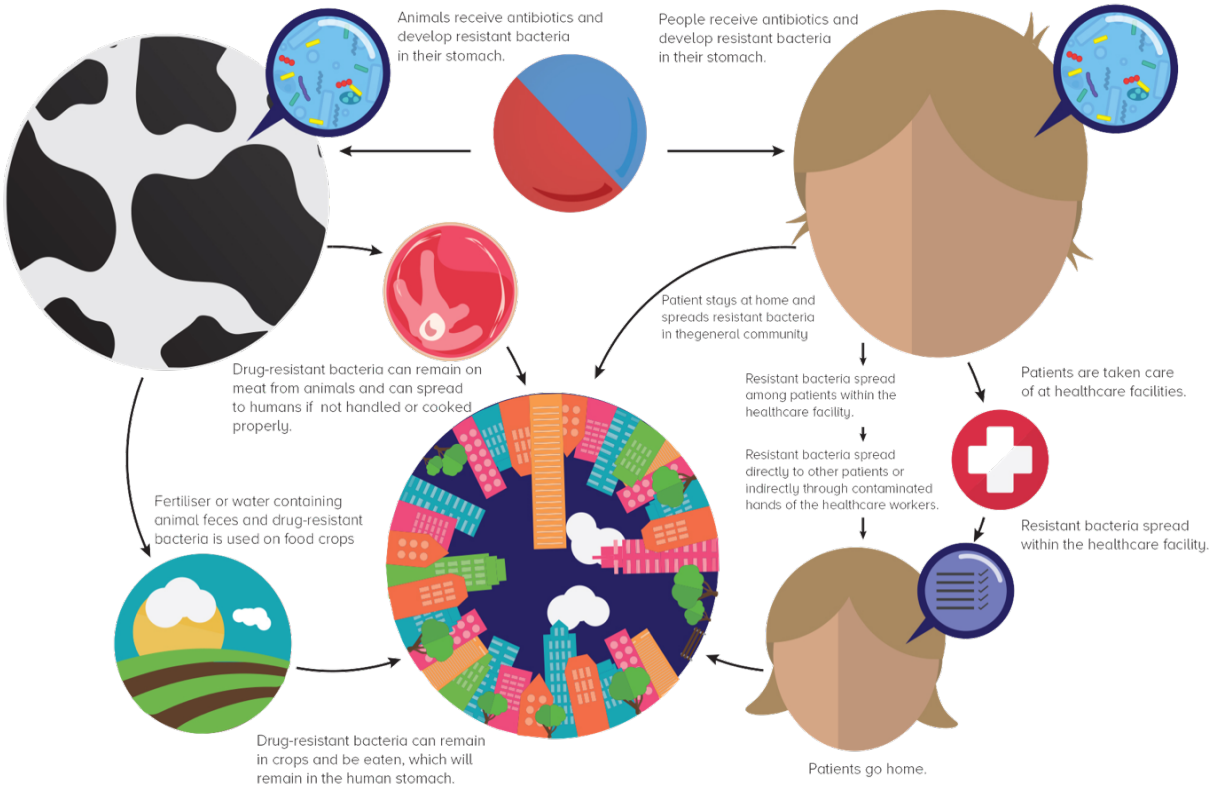


Figure 4.5: Example of policy resistance - evolution of drug-resistant pathogens (Adapted from U.S. Department of Health and Human Services, 2013).

To comprehend the cause and effects of policy resistance, it is necessary to assume a holistic view of the system and all of its complexity (Sterman, 2001). An important concept in understanding this is dynamic complexity.

4.4.2 Dynamic complexity

A system can be defined as a set of elements, such as procedures and events, functioning in conjunction as parts of an integrated network. When a system contains properties that cannot be entirely described through an understanding of the parts, it is said to be a complex system. The main differences between complex systems and traditional systems is summarised in Table 4.2.

Table 4.2: Main differences between complex systems and traditional systems (Adapted from Luke and Stamatakis, 2012).

Domain	Traditional Systems Assume:	Complex Systems Assume:
Functional Form	Linearity	Non-Linearity
Common Distributions	Normality	Non-Normality
Characteristics of Actors	Homogeneity	Heterogeneity
Level-of-Analysis	Single Level	Multiple Levels
Temporality	Static, or Discretely Longitudinal	Dynamic, with Feedback
Fundamental Relationship	Among Variables	Interaction of Actors
Perspective	Reductionist	Holistic

Complex systems are characterised by non-linearity and dynamic behaviour while traditional analytic techniques typically assume linear relationships where changes in dependent variables causes changes in independent variables. Normal distributions are commonly used in analytical modelling, which provides an unlikely description of reality. Complex systems, on the other hand, typically assume power laws resulting in scale-free distributions. Traditional analytical modelling tends to takes a reductionist perspective, focusing only on individual parameters, interactions and links. Complex systems, in contrast, consider the whole system and its complex behaviour (Luke and Stamatakis, 2012). Complex systems incorporate a large number of diverse interconnected and interdepended elements that form part of a widespread network of feedback loops. The different elements interact with each other, causing a system response or 'effect' (Atun, 2012b). Over time, the effects will cause the system environment to change, which can influence the elements and the way that they interact with each another (Luke and Stamatakis, 2012). These effects often behave differently than anticipated, which leads to dynamic complexity (Sterman, 2001).

Dynamic complexity is when: (i) the short term and long term effect, caused by the same element or interaction, is noticeably different; (ii) the effect, caused by the same element

or interaction, is distinctively different on two different parts of the system; and (iii) clear actions lead to different unintended results (Atun, 2012b). Examples of system characteristics that can lead to dynamic complexity as discussed by Sterman (2001) are provided in Appendix B.

As mentioned previously, the mental models and tools we use to analyse relationships and links omit important elements of dynamic complexity. Therefore, tools and approaches that are able to accurately capture the various sources of dynamic complexity are required to understand how these sources create the dynamics of a system. Among the sources of dynamic complexity are feedback, stocks and flows and time delays. The tools that can be used to evaluate these sources include causal-loop diagrams and the simulation of these diagrams (Swanson, 2002). These aspects will be discussed in the remainder of this section.

4.4.3 Systems thinking

Systems thinking is the ability to view a system and its environment as a complex whole of interrelated parts instead of separate entities, symptoms and event sequences (Atun, 2012b; Porsteinsson, 2015). It involves the understanding that every individual element in the system is connected to every other element. Identifying the links and relationships that results in events is eminent in systems thinking (Porsteinsson, 2015) since it can help to predict events and therefore better prepare for unfolding problems and challenges (Atun, 2012b). Although it is important to view the system as a whole, systems thinking includes the ability to define and communicate boundaries of the system under study (Porsteinsson, 2015).

The systemic perspective implied with systems thinking, supports the decision making process by ensuring that the decisions are not only beneficial for the short-term requirements, but also for the long-term requirements of the elements and the system as a whole (Sterman, 2000). In order to fully comprehend the system as a whole, however, it is necessary to deconstruct the system. This is referred to as systems analysis and helps to create an understanding of the cause-and-effect relationships, structural arrangement and stocks-and-flows of the system (Porsteinsson, 2015). Systems analysis allows the user to learn more of the system by questioning certain occurrences observed in the model. The results of the system analysis are used to reconstruct the system to further expand the knowledge of the system and forms part of the SD process.

4.4.4 Causal-loop diagrams

A causal-loop diagram (CLD) is a significant tool in SD modelling. The CLD captures the causalities, feedback structures (Porsteinsson, 2015) and the factors that influence the system behaviour (Sweetser, 2009). The links and relationships between the individual

elements of the system, as well as those between the system and its functional environment are illustrated in the diagram (Sweetser, 2009). The qualitative analysis of constructing CLDs alone can prove to be significantly useful as it provides a better understanding of the whole system and its behaviour (Brailsford and Hilton, 2001). Additionally, CLDs are used to effectively capture theories about the causes of the system's dynamics and to illustrate the collective mental models of the system participants (Porsteinsson, 2015).

In order to construct a CLD, it is first necessary to determine linkages that associates the system elements with each other. These links are represented by a set of directed arrows, as shown in Figure 4.6 (Brailsford and Hilton, 2001). The system's structure is explained by the link polarities – it does not explain the variable behaviour, but rather the effects that will result from a change in the system (Porsteinsson, 2015). A positive link (+ sign) signifies that the effect is positively related to the cause (Sterman, 2003). Referring to Figure 4.6 (a), if X increases, then Y increases and if X decreases, Y decreases. In contrast, a negative link (- sign) signifies that the effect is negatively related to the cause. Thus, as illustrated in Figure 4.6 (B), if X increases, Y decreases and if X decreases, Y increases (Porsteinsson, 2015).

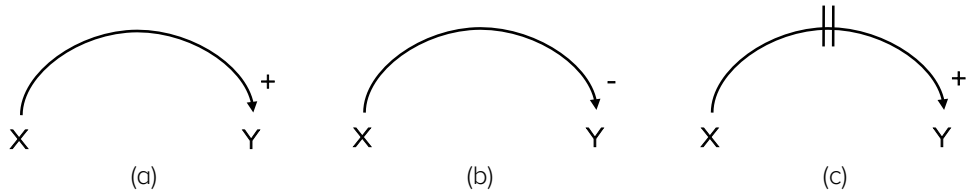


Figure 4.6: (a) Positive link between variables, (b) negative link between variables, (c) time delay between variables.

Another critical aspect in SD is delays. Naturally, time will pass between a decision and its effect on the system. These delays cause unpredictability and increase the probability of oscillations in the system, which are necessary for a realistic representation of the system. Decision makers tend to assume an event-based view of causality and continue to interfere with the system in an attempt to correct the differences between the desired and actual state of the system. The disregard of time delays can lead to over estimation and uncertainty (Sterman, 2001; Swanson, 2002).

A simple example of a CLD is depicted in Figure 4.7.

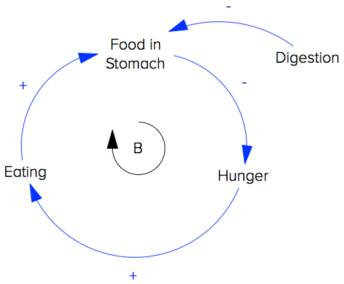


Figure 4.7: Example of a causal-loop diagram (Adapted from Brailsford and Hilton, 2001).

4.4.5 Feedback thinking

As previously mentioned, a cause of policy resistance is the misconception of the collection of feedbacks in the system. An event-based view of a system, refer to Figure 4.8 for an example, omits apparent feedback loops in the real system. Real systems react to actions causing additional effects through the feedback loops (Sterman, 2001).

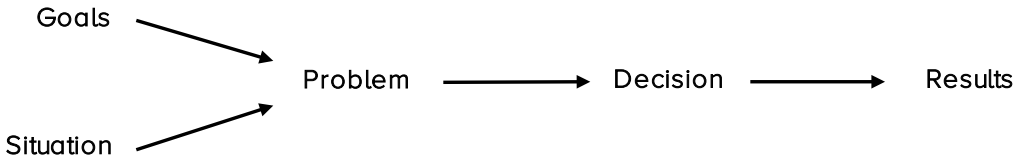


Figure 4.8: Example of an event-based view of a system (Adapted from Sterman, 2001).

With an event-based perspective of systems, the emerging problems that result as a consequence of the feedback processes will be interpreted as confirmation that the system is unstable, irregular and unmanageable. The use of feedback loops, as depicted in Figure 4.9, will improve the understanding of the feedback processes and consequently the perception of the system will be less deceiving (Sterman, 2001).

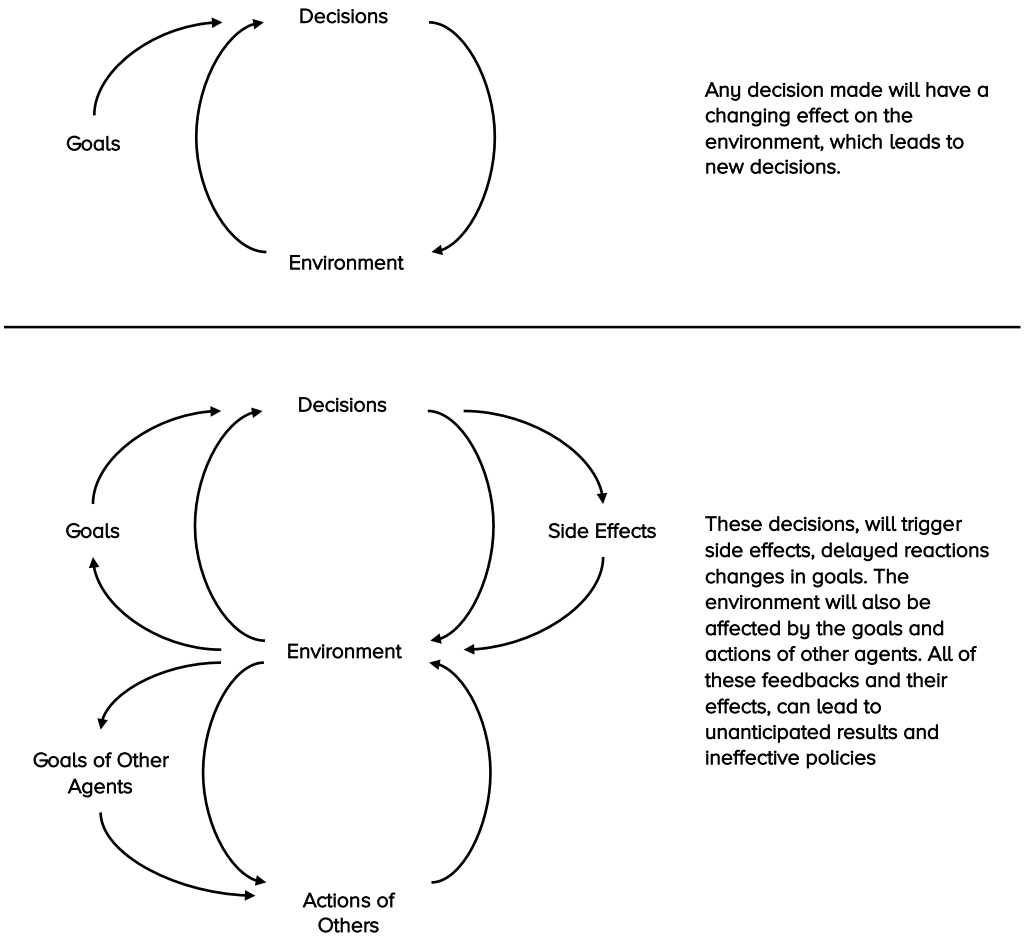


Figure 4.9: Example of a system with feedback (Adapted from Sterman, 2001).

Feedback loops involve the flow of information generated by an action through several variables until it returns back to its origin, affecting the functioning of the entire system in the process. The relationships between the variables and constants determine the nature of the information. A feedback loop, similar to the directed arrows that illustrate linkages, either has a positive or negative polarity that can be determined by multiplying the polarity of all the arrows in the loop (Kumar and Kumar, 2014).

Positive feedback loops are self-stimulating and generate their own growth or decline, which is why they are often termed reinforcing loops and denoted by an R symbol, as illustrated in Figure 4.10 (Sterman, 2000). These loops pursue exponential growth, but since no quantity can increase indefinitely, the growth must be limited (Porsteinsson, 2015). Negative feedback loops are described as self-limiting and cause balance and stability. They are therefore often referred to as balancing loop and denoted by a B symbol, also depicted in Figure 4.10. Where positive feedback loops reinforce and amplify (Sterman, 2001; Swanson, 2002), the negative feedback loops attempt to achieve balance by counteracting and opposing in order to achieve a specified goal (Kumar and Kumar, 2014).

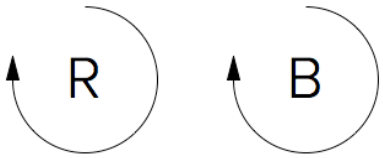


Figure 4.10: Reinforcing (R) and balancing (B) loop.

A complex system typically contains numerous feedback loops of both types that are connected through delays, nonlinearities and accumulations. The interactions of these feedbacks are the foundation of the dynamics of systems. Although it is possible to explain the dynamics of isolated loops, it is nearly impossible to do so when multiple loops interact. This is why the CLDs have to be modelled with computer simulation (Sterman, 2000).

4.4.6 Stocks and flows

To model the CLD with computer simulation it is beneficial to first clarify the important stocks and flows. Stocks and flows are fundamental in the dynamics of complex systems (Sterman, 2001). A simple example of a stocks and flow system is a bathtub, as illustrated in Figure 4.11. In this case the stock would be the water in the tub, which is filled by the inflow of water from the tap and drained by the outflow of water through the drain (Sterman, 2003).

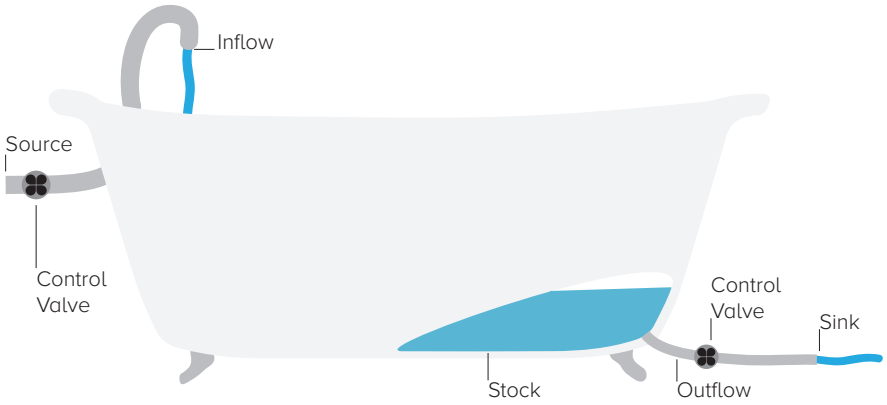


Figure 4.11: Example of a stocks and flows system (Adapted from Sterman, 2001).

Normally state variables and stocks are represented by rectangles; pipe-like arrows represents the flows and flow rates (Sterman, 2001); curved arrows represents the linkages/connectors (Kumar and Kumar, 2014); and the remaining elements are the auxiliary variables and constants. This is illustrated in Figure 4.12, which is the flow diagram of the CLD in Figure 4.7. In this example, the stock is food that is increased by eating (inflow) and decreased due to digestion (outflow). The amount of food in the stomach affects the hunger variable, which influences the eating rate (Brailsford and Hilton, 2001).

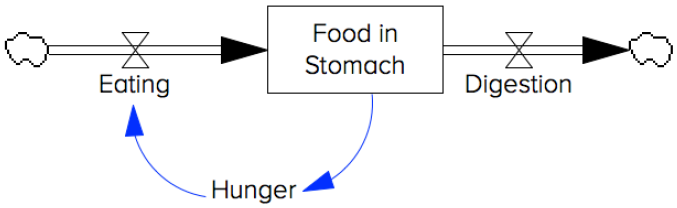


Figure 4.12: Example of a stock and flow diagram (Adapted from Brailsford and Hilton, 2001).

4.4.7 Modelling procedure

The procedure followed when building a model with system dynamics can be described in five steps. The five steps that will be followed in this study are summarised in Figure 4.13, with a more comprehensive description provided in Appendix C. These steps and sub steps were determined by comparing the modelling processes laid out by Sterman (2003); Campuzano and Mula (2011); and Maani and Cavana (2012) with one another.

Since modelling is an iterative process and will go through constant testing and modification, the steps are not necessarily sequential, but rather an iterative cycle. As illustrated in Figure 4.13, the output of one step can change the current understanding of the system and therefore require revision of an earlier step.

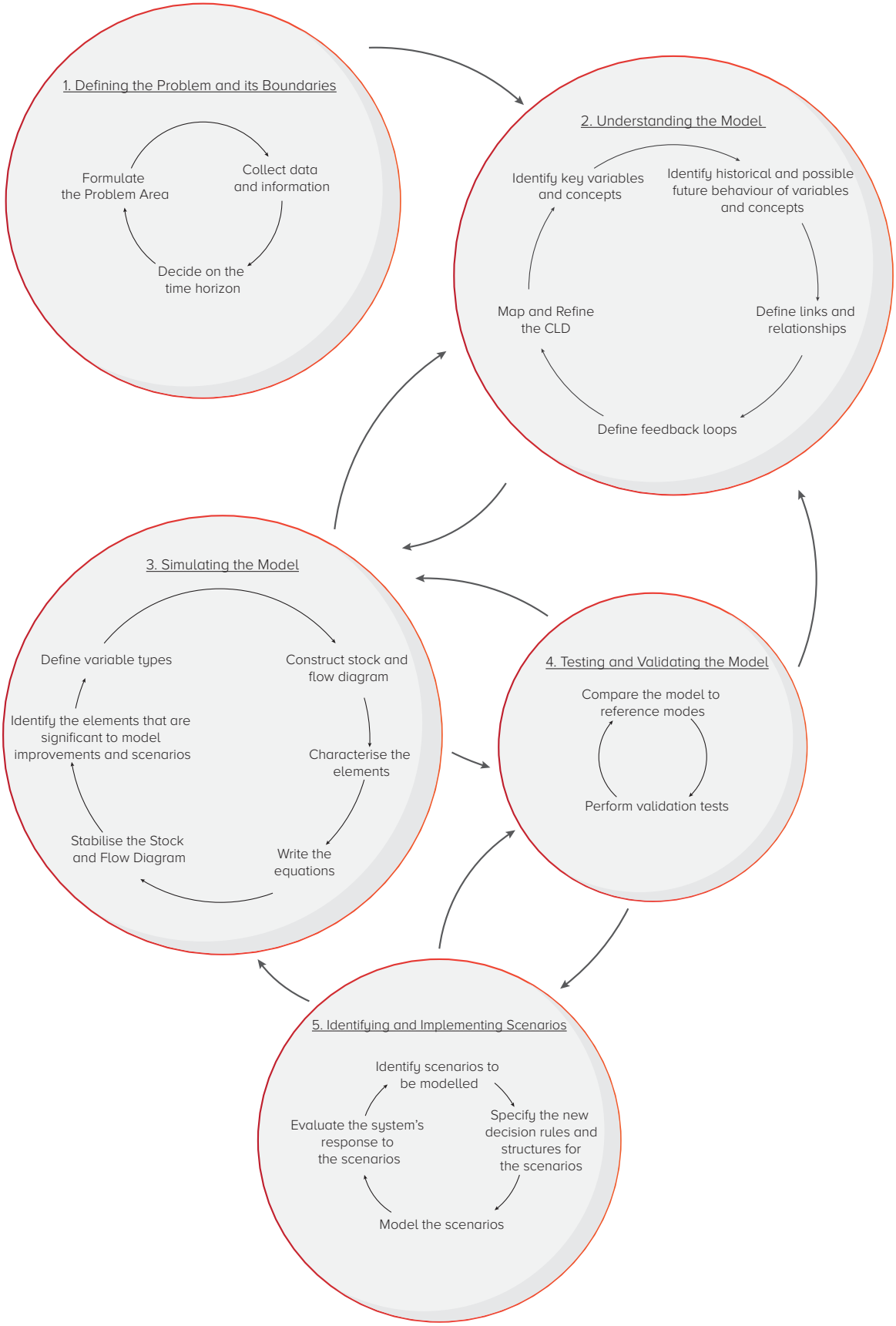


Figure 4.13: System dynamics modelling procedure.

Simulation models are built from mental models and are based on information of the real world system. When the aspects of the real world are captured and tested in the model, the mental models and interpretation of the system can change, leading to the redesign or adaption of the current model. Therefore, modelling is said to be a continuing process of switching between the model and the real world.

4.4.8 Conclusion: System dynamics

In SD, simulations are constructed as a series of equations that monitor the accumulations of stocks that are established by the flows, feedback loops and time delays in the system (Luke and Stamatakis, 2012). With SD modelling, the behaviour of systems with a high level of unpredictability, fluctuation, structural complexity and different types of delays, can be easily described and analysed (Peng, Chen and Zhou, 2014). SD improves the understanding of complex systems by allowing the adjustment of parameters and variables, rearrangement of system elements and adding of new links and feedback loops. This also enhances the decision-maker's ability to model different scenarios and analyse how the scenarios will impact the system (Sweetser, 2009). Furthermore, a SD model provides a visualisation of the system that increases the understanding of the structure and the interaction between the different elements (Piewthongngam *et al.*, 2014).

4.5 Conclusion: Supply chain modelling

This chapter provided an introduction to the different techniques and approaches used to model supply chains. The characteristics of two widely applied techniques, namely system dynamics and discrete event simulation, were compared and system dynamics was chosen as the more suitable approach for this study.

The next chapter will aim to provide an accurate and valid description of the MDR-TB supply chain for SLDs.

Chapter 5:
Mapping the upstream MDR-TB SLD supply chain

"We have known how to cure TB for many years. What we have lacked is the will and the resources to quickly diagnose people and get them the treatment they need"

- July 2004, Nelson Mandela

The previous chapter was the last to provide background information to the research, by introducing different supply chain modelling approaches, comparing the characteristics of two widely applied techniques, and selecting and discussing the chosen approach for this study.

This chapter aims to present an accurate and valid representation of the supply chain for SLDs for MDR-TB, by providing a description of: (i) unique characteristics of the supply chain; (ii) the initiatives developed to address TB and MDR-TB; (iii) the flow of information, finances and products in the supply chain; (iv) other important concepts and entities related to the upstream supply chain. The described concepts will be combined to map and describe the supply chain through a theoretical model, followed by a summary of the difficulties and challenges in the supply chain as well as recommendations to improve the supply chain.

5.1 Unique characteristics of the supply chain

The MDR-TB SLD supply chain is donor-funded. Donor-funded supply chains have a number of characteristics that distinguish them from commercial supply chains and that

should be taken into consideration when studying the dynamics of these supply chains. During the course of this study, a paper on the distinguishing features of donor-funded supply chains was written and published as a conference proceeding. Table 5.1 summarises the most prominent distinguishing features.

Table 5.1: Summary of characteristics for commercial and donor funded supply chains (Reproduced from: Lingervelder, Bam and Bam, 2016).

Characteristics		Commercial SC	DFSC (general)
Structure & Components		Upstream (global) segment and downstream (domestic) segment primarily managed as two coupled segments by primary stakeholders	Upstream (global) segment and downstream (domestic) segment are ordinarily decoupled from one another
Stakeholders	Primary Stakeholders	Shareholders (that guide the organisation's policies, goals and decisions)	Host Government and some NGOs
	Other Stakeholders	Several stakeholders with different needs – rarely conflicts with shareholders' interests	Stakeholders have different, often conflicting, goals, missions, interests, capacity and constraints with different perspectives and approaches
Trust		Spend time and resources to build lasting relationships with their partners	There is often not enough time or resources to enable the building of trust
Goals & Objectives	Main Goal	To make profits and provide financial returns to shareholders	To produce value for money, be efficient and effective, ensure fair competition between suppliers, ensure accountability, and ensure procedures are done ethically
	Objectives	'Owners' of the supply chain share the organisations policies, goals and decisions	Each organisation involved in the supply chain strives to achieve its own purpose and mission
Finances	As an objective	Strategic objectives are based on the financial returns paid out to the shareholders and the value created through delivering high quality goods and services to the consumers	Finances are seen as a constraint rather than an objective
	Revenue	Income earned from the sale of goods and services	Government funding and donations from individuals and organisations
	Financial Supply Chain	Manages payment transactions and orders collectively	Often has a separate chain for international flows and domestic flows
Customer Service & Marketing	Customer characteristics	Any individual or organisation that buys and receives the product or service	Often seen as the end-consumers that receive the intended aid, but some view the donors as the customers
	Choice of product	End-consumer can analyse the market and choose which product, out of several options, to buy	End-consumers often do not have a choice of product

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Customer Service & Marketing	Target	Market their product to the customer	Targets donors and convince them to provide some contribution
	Market segmentation	Large amounts of time and money is allocated towards market segmentation – in most cases dedicated departments are assigned to segment the consumers and market the product/service according to the segments.	Doesn't spend time and money to market product differently to market segments – since the consumers are in need of the product, the goal is to provide supplies and services to populations in need.
Research & Development (R&D)		Financial resources are typically allocated to both strategic and operational activities with large amounts of time and money allocated for R&D	Typically, funding is provided specifically for operational activities and not R&D. Instead, they have to rely on global initiatives for their R&D.
Demand & Forecasting	Stability	Relatively stable and predictable demand	Irregular amounts at irregular intervals
	Demand Pattern	Occurs from recognised locations in fixed quantities at consistent time intervals	Often unpredictable and occurs in irregular amounts and time intervals
Procurement		Often build a lasting relationship with their partners and set up long-term agreements and contracts	Often use a competitive bidding process and short-term contracts or agreements are set up
Manufacturing	Processes	Processes can be forecast-driven due to the relatively stable demand patterns	Processes are mostly order-driven due to the unpredictable demand
	Volume	Typically uses economic batch sizes and order quantities. One manufacturer often has several customers and can produce larger volumes.	Supplies are manufactured in smaller batch sizes that are not cost effective, since the limited actual demand and lack of accurate forecasting weakens the manufacturers' confidence to produce large volumes of supplies.
	Market & competition	Manufacturers rarely have a monopoly in the market	The difficult nature of products and lack of incentives leads to a restricted market structure and lack of competition.
Logistics	Definition	Process of managing flows from source to the final customers	Process of managing flows from the donors to the affected populations
	Collaboration	Often implements horizontal collaboration, to create a distribution pool	Unpredictable demand patterns makes collaboration difficult
Agility		A key strategy that allows them to compete in the global market by improving delivery rates	Used in managing different relationships between donors and actors, evaluating impacts of distributed supplies and monitoring various ongoing activities

In the remainder of this section, the following four of these distinguishing characteristics are discussed in the context of the supply chain for SLDs for MDR-TB: (i) structure and

components, (ii) price and demand elasticity, (iii) demand and forecasting, and (iv) market constraints.

5.1.1 Structure and components

As mentioned in the previous section, a supply chain comprises of various functions. Figure 5.1 summarises the basic steps in a drug supply chain. It involves the continuous flow of products from supplier to consumer. Typically the flow of materials is forward and the flow of information backward (Sarimveis *et al.*, 2008).

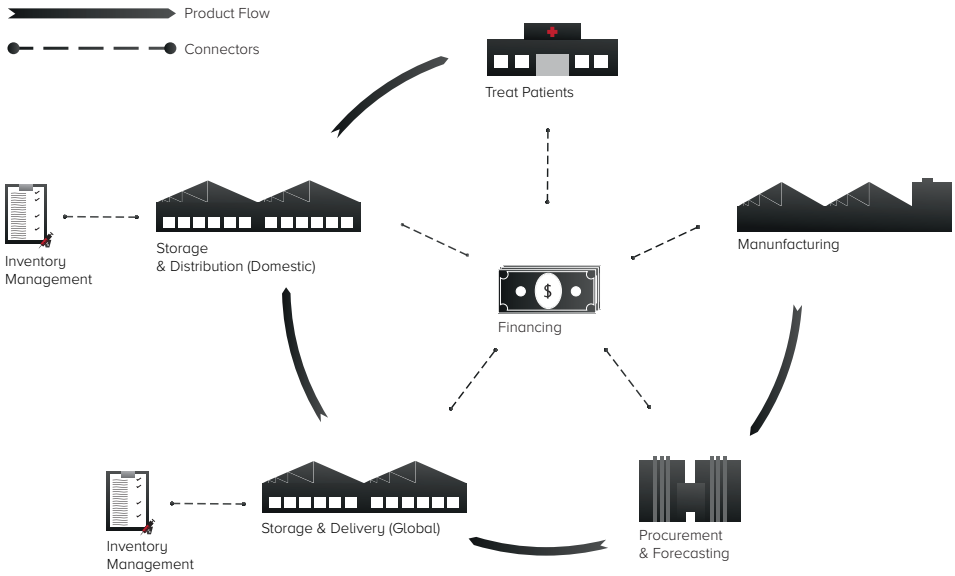

Figure 5.1: Basic steps in a drug supply chain.

All of the various steps and activities involved with the different processes in Figure 5.1, cooperate with one another to form an integrated supply chain (Beamon, 1998). As can be seen from Figure 5.1, financing is a key component of the supply chain, as it is associated with every process. The procurement and distribution of supplies are dependent on the availability of funds (Dowling, 2011). However, even with enough domestic and donor funding, and a selection of new treatments, problems and flaws in the supply chain will continue to restrict access to the required drugs (Riungu, 2011).

The manufacturing process includes sub-processes such as scheduling for the acquisition of raw materials, the design and scheduling of manufacturing processes and the control of materials (Beamon, 1998). The storage and delivery (global) process determines how the drugs and health supplies are transported from storage to the in-country suppliers. Similarly, the storage and distribution (domestic) process determines how it is transported from storage to the organisation(s) and facilities that treat the patients (Beamon, 1998). At a domestic level, drugs for treatment are primarily distributed through three organisation types, namely (i) public or government-run systems, (ii) private not-for-profit systems, and (iii) private commercial systems (Dowling, 2011). This is especially the case in LMICs. A vital sub-process of both of the storage and

delivery/distribution processes is inventory management, as illustrated in Figure 5.1. Inventory management and control encompasses the design and management of policies and procedures for any type of inventory (Beamon, 1998).

Furthermore, the MDR-TB SLD supply chain is divided into two components, namely the 'upstream' component and the 'downstream' component, also known as the global- and domestic segments. This is the case for most donor-funded supply chains. A key characteristic of these types of supply chains is that the two components are decoupled from one another (Nicholson *et al.*, 2013). This is illustrated in Figure 5.2.

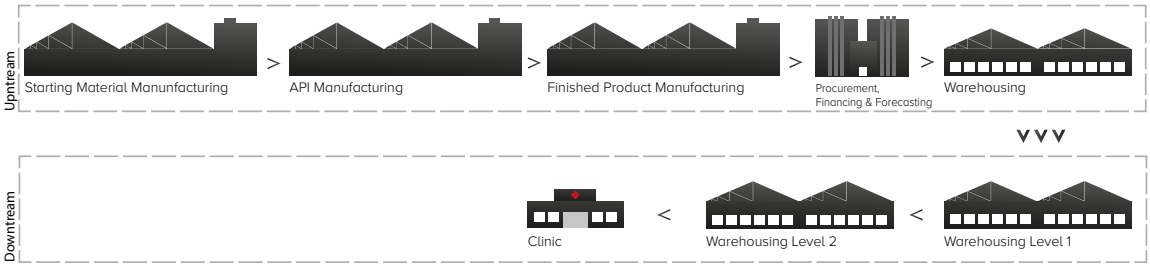

Figure 5.2: Upstream and downstream components (Adapted from Yadav, 2012).

The structure of the upstream component of the supply chain entails the (i) manufacturing, (ii) procurement, (iii) financing, (iv) forecasting, and (v) storage (warehousing) of the drugs. The manufacturing includes the manufacture of the starting material, the active pharmaceutical ingredient (API), and the finished pharmaceutical product (FPP). The warehousing of the upstream component only involves the storage of drugs prior to its shipment to other countries (Nicholson *et al.*, 2013). The downstream component includes the (i) in-country warehousing, (ii) distribution of drugs, and (iii) the treatment of patients (Nicholson *et al.*, 2013). It is important to note that a single upstream component can be connected to more than one downstream component, i.e. a global manufacturer can distribute the drugs and medication to more than one country.

5.1.2 Price and demand elasticity

The MDR-TB SLDs supply chain has two separate financial supply chains, an international chain financed by one or more global funds and a domestically financed chain within a given country (Nicholson *et al.*, 2013). This corresponds with the previously mentioned upstream and downstream segments of the supply chain that are decoupled from one another. The decoupled financial supply chain results in a unique situation with regard to price and demand elasticity. Demand in the internationally financed supply chain is ordinarily inelastic to small changes in price, when compared to the domestically financed portion. The demand starts out flat and unresponsive to large changes in volume or small changes in price (international), but the volume drastically increases when the price falls below a certain threshold (domestic) (Nicholson *et al.*, 2013).

5.1.3 Demand and forecasting

A principle difference between the MDR-TB SLDs supply chain and a commercial supply chain is the demand. For most commercial supply chains, demand is steady and can be predicted (Afshar, 2009), due to the fact that the demand typically occurs from known locations and the orders are placed for the same quantities, in constant time intervals and from fixed suppliers (Beamon and Balcik, 2008; Afshar, 2009). In the MDR-TB SLDs supply chain, however, the demand is unpredictable and occurs in irregular amounts and time intervals (Giffin and Robinson, 2009; Nicholson *et al.*, 2013).

The irregular demand makes accurate forecasting very difficult, which weakens manufacturers' confidence to work with large volumes. Instead, they make use of small batch sizes that are not cost effective. Consequently, several manufacturers choose to instead start the production process only once an order has been received, causing long delivery lead times. Countries are often pressured to place orders months or even years in advance. In many cases, the inaccurate forecasting leads to either shortages, when needs are forecasted too low, or destruction of expired goods, when needs are forecasted too high (Nicholson *et al.*, 2013).

5.1.4 Market constraints

The MDR-TB SLDs supply chain is faced with some unique market constraints. The poorest and most susceptible populations are often in areas that are difficult to distribute to, which causes distribution costs to rise even more (Nwuneli *et al.*, 2014). Another market constraint for the supply chain is the weak visibility into the market due to inconsistent demand and lack of data, as discussed previously. The weak market visibility is one of several reasons for a third market constraint, namely, a lack of manufacturers. The lack of competition in the manufacturing of some the drugs, results in a monopoly – with only a single supplier of the drug (Nicholson et al., 2013).

5.2 Initiatives to address TB and MDR-TB

This section provides short descriptions of initiatives, relevant to this study, that have been developed to address TB and MDR-TB.

5.2.1 The Green Light Committee

The Green Light Committee (GLC) was founded between 1998 and 2000, as a multi-institutional partnership, composed of global stakeholders, to respond to the emerging threat of MDR-TB. The GLC was designed with the intention that it would act as a pilot project mechanism for DOTS-Plus projects, by providing affordable SLDs exclusively to DOTS-Plus pilot projects and to gather data about these projects in order to determine recommended MDR-TB treatment policies (Nicholson *et al.*, 2013). During its

development, the GLC's multi-institutional partnership was hosted by WHO's TB department, but was transferred to the Stop TB partnership when it was founded in 2001. Since 2007, following the increasing number of approved projects, the GLC merged with the GDF (see Section 5.2.3) to share responsibility.

5.2.2 The Global Partnership to Stop TB

On 24 March 2000, the first World TB Day, ministerial representatives from 20 HBCs came together at The Ministerial Conference on Tuberculosis and Sustainable Development to develop the 'Amsterdam Declaration to Stop TB' (Amsterdam Declaration to Stop TB, 2000). The declaration urged the necessity for drastic action in HBCs and called for the development of the Global Partnership to Stop TB to organise and manage these exertions, together with WHO. This global partnership, ultimately founded in 2001, aims to (i) identify and fund innovative diagnostic and treatment approaches; (ii) aid in the procurement of drugs and diagnostics; (iii) help with forecasting and preventing stock-outs; and (iv) assist the Global Fund to Fight Aids, Malaria and TB (*The Stop TB Partnership: Leading the Fight Against TB*, 2015).

5.2.3 The Global Drug Facility

On 24 March 2001, a year after the Amsterdam Declaration to Stop TB was developed, the Global Drug Facility (GDF) was launched as an initiative of the Global Partnership (Kumaresan *et al.*, 2004). The main donors of the GDF includes the World Bank, the Government of the Netherlands (Kumaresan *et al.*, 2004), the Canadian International Development Agency and the United States Agency for International Development (USAID) (Kumaresan *et al.*, 2004; De Lucia, 2014). It also has projects supported by UNITAID and the Kuwait Fund (De Lucia, 2014). The reason for establishing the GDF, was to support the Global Partnership by contributing to the development and improvement of (i) procurement management by operating a direct procurement system to attain quality-assured drugs at low prices; and (ii) supply chain management of countries in need by offering in-country assistance on SCM (Atun *et al.*, 2010; De Lucia, 2014). The GDF mainly provides two services, one being a grant service and the other a direct procurement service. Through the grant service, the GDF serves countries in need of resources for the procurement of quality assured adult and paediatric FLDs and supports the expansion and sustainability of DOTS. The direct procurement service permits countries or agencies to procure quality-assured drugs and equipment at reduced prices. Countries usually place orders with donor funding, typically from the Global Fund or from their national government budgets.

5.2.4 The Global Fund to Fight Aids, Malaria and TB

The Global Fund to Fight Aids, Malaria and TB (Global Fund), founded in 2002, is the largest international donor for TB and provides more than 80% of TB funding worldwide

(Stop TB Partnership, 2015). It is described as a "partnership between governments, civil society, the private sector and people affected by the disease". Almost US$4 billion is raised and invested every year to support programs to fight TB, Malaria and HIV in countries in need (The Global Fund, 2016)

5.2.5 UNITAID

UNITAID was launched in September 2006 through a partnership of countries (Brazil, Chile, France, Norway and the United Kingdom) as an international drug purchase facility to provide funding for SLDs against MDR-TB. What makes UNITAID unique, is their innovative financing – the 'air ticket levy' that is used to fund the programme. The ten participating countries (Cameroon, Chile, Congo, France, Guinea, Madagascar, Mali, Mauritius, Niger and the Republic of Korea) decides on an amount to add to an existing airport tax, usually ranging from US$ 1 for economy-class tickets to approximately US$ 40 for business and first class tickets (UNITAID, 2016a).

5.2.6 Relationship between the different initiatives

Today, the above-mentioned organisations and foundations can be seen as an inter-connected system that has collectively taken responsibility for the execution of MDR-TB projects in countries. The GLC is responsible for approving MDR-TB projects in countries, which permits the Global Fund or UNITAID to release funds to a project. The Stop TB Partnership provides technical assistance by facilitating effective management of the projects, planning and, if necessary, site visits.

A country can procure SLDs through the open market and/or state procurement mechanisms, with the drugs often being of unknown quality. Another option is to procure quality-assured drugs, often at reduced prices, from the GDF under supervision of WHO's GLC. If a country is funded by the Global Fund or UNITAID they are required to procure through GDF. A country can apply to the GLC through their website, the GLC then reviews the application form and approves a number of patients for treatment. The country/project will be monitored and regularly evaluated by GLC consultants to assess whether and when scale-up is required. The only responsibility of the GLC is to ensure that the approved projects deliver quality-assured drugs under the program conditions described in WHO's *Guidelines for the programmatic management of drug-resistant tuberculosis*. The procurement of these drugs falls under the responsibility of the GDF and their contracted procurement agent (PA). Furthermore, the GDF tracks orders and monitors the performance of the PA, while the PA oversees SLD purchases and solicits agreements with manufacturers at reduced prices for approved projects.

5.3 MDR-TB SLD supply chain flows

This section aims to provide a description of the application process for grants from the GF, financing, application for procurement from the GDF, the ordering process of the GDF and the physical flow of the SLDs by investigating the flows in the supply chain.

5.3.1 Information flow

Information flow plays a particularly important role in the MDR-TB SLDs supply chain, since it warrants more effective use of drugs and treatments, which are often in short supply (Ballou-Aares *et al.*, 2008). Information flow can have a powerful effect on the efficiency and effectiveness of the activities in a supply chain, since it helps to maintain a balance between supply and demand and provides a basis for good planning (Unicef, 2009). Stakeholders can greatly benefit from an established information flow that can enable them to adjust their activities in order to improve their performance, but only if it is timely, reliable and provides actionable data.

The basic information flow diagram of the supply chain for MDR-TB for SLDs is depicted in Figure 5.3. Initially, a country has to apply to the GLC to approve one or more projects. On approval, the GLC Secretariat will send a letter to notify the country of the approval. Additionally, GLC sends a letter of agreement (LoA) to countries whose projects are in accordance with WHO's *Guidelines for the programmatic management of drug-resistant tuberculosis.* The country has to accept the conditions of the letter of agreement by returning a countersigned original of the letter – no SLDs can be ordered until the letter is received by the GLC (World Health Organization, 2008).

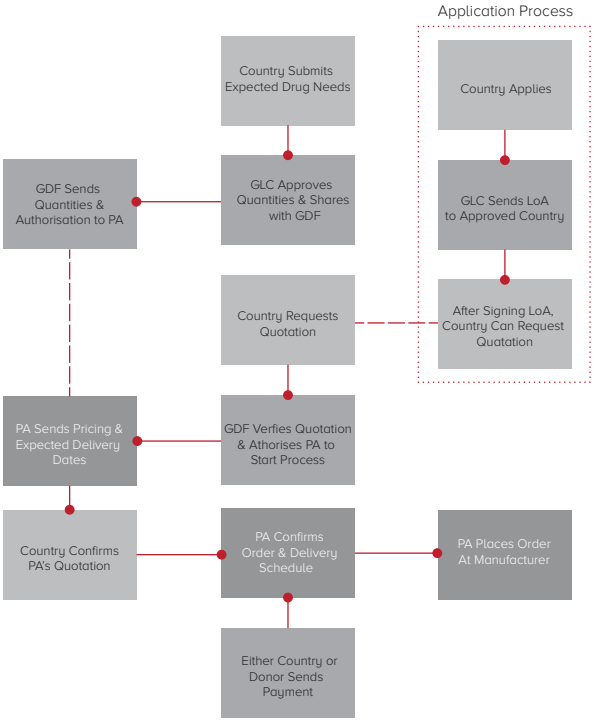

Figure 5.3: Information flow diagram of the supply chain.

All GLC-approved projects submit an estimation of their SLD needs for a full 2 year course of treatment for their patient regimens. The GLC has to review and approve these quantities before they share it with the GDF. Once the GDF receives the approved quantities they forward a letter of authorization with the drug needs to the PA. Only then is the PA allowed to sell the required drugs, up to the approved quantity, to the project (Nicholson *et al.*, 2013). For a project to place an order, they have to complete a procurement form and send it to the GDF who has to verify the information regarding regimens, quantities, consignee details, documents needed for importation or status of drugs registration in the country (World Health Organization, 2008). Once reviewed and validated the PA is requested to initiate the procurement process for the project. After the PA has received (i) a letter of authorisation with the total approved quantity, (ii) the quotation request from a project site, and (iii) an official request to initiate the procurement process from the GDF, will they respond to the project with a quotation containing pricing information and expected delivery dates. After a quotation is received, reviewed and accepted by the project, they confirm by sending a purchase order and transferring payment, if applicable. Once the order is confirmed and paid for, the PA communicates with the manufacturer to begin production and deliver the drugs to its facility. The PA will allocate the drugs to the project sites and contact them when delivery is arranged (World Health Organization, 2008; Giffin and Robinson, 2009).

5.3.2 Financial flow

The lifeblood of the supply chain is its finances, since regular and effective financial flows are essential for the accurate functioning of the supply chain. An apparent difference in a donor funded supply chain such as this one, is the source of revenue. Where commercial supply chains rely on customers that purchase goods and services for their own benefit (Moore, 2000), the MDR-TB supply chain relies on government funding (Menzies *et al.*, 2012) and charitable donations from individuals and organisations (Beamon and Balcik, 2008). Well-timed financial flows between the different stages of the supply chain will assist in ensuring a maintainable system with a continuous product flow (Ballou-Aares *et al.*, 2008). The timing and reliability of available funding has a strong impact on the production and distribution schedule of the SLDs. A delay in funding could lead to a delay in treatment, which can cause resistance to some of the SLDs.

Figure 5.4 illustrates the basic financial flow diagram of the supply chain for MDR-TB for SLDs. The diagram also includes the information flows directly associated with finances, such as grant application process. The process begins when the GF issues an “open call for proposals”. The country coordinating mechanism (CCM) prepares and submits a proposal on behalf of the country. If accepted, the CCM is also responsible for identifying the principle recipients in the country and to oversee implementation.

Typically, representatives from both the public and private sectors can serve on the CCM, such as the government, NGOs, private businesses, academic institutions, etc. The Global Fund Secretariat assesses whether the proposal meets the eligibility criteria, after which the Technical Review Panel assesses the technical merit of the proposal. Finally, it is up to the board to decide whether the proposal is approved or declined.

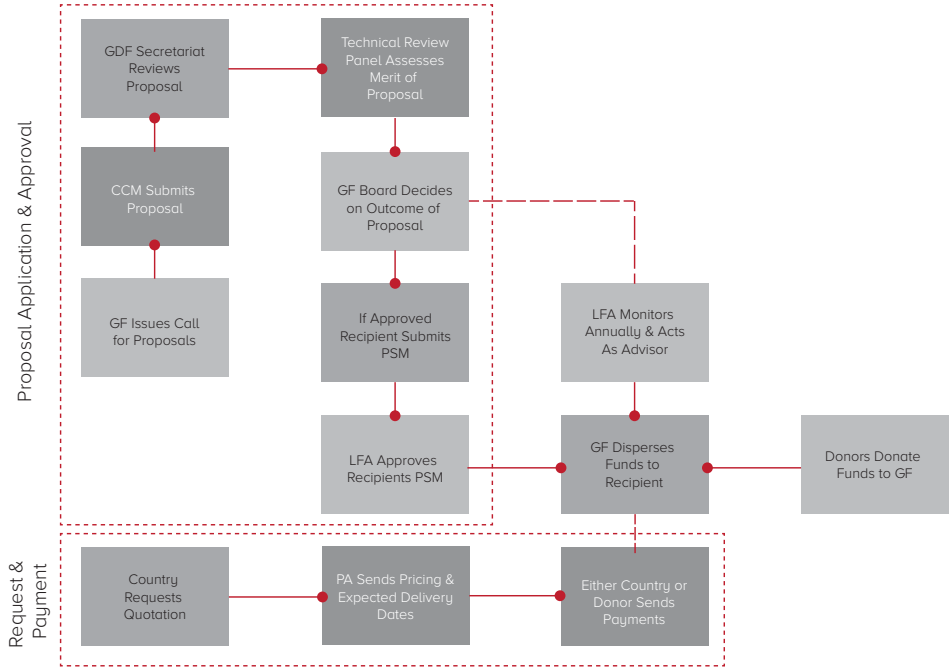

Figure 5.4: Financial flow diagram of the supply chain.

To ensure that procurement is done in accordance with the Global Fund, WHO guidelines and national and international laws, the principle recipients of the grant has to submit a detailed procurement and supply management plan (PSM). The PSM is assessed based on the financial management and administrative capacity of the recipient by local funding agents. Once the PSM is approved by the local funding agents, the funds can be disbursed. The agents also monitor the principal recipients on an annual basis and serves as advisor to the Global Fund.

5.3.3 Product flow

The product flow facet of a supply chain involves the system that is used for moving supplies between the different entities of the chain. In general, the product flow is a linear and forward-moving process that forms the backbone of the supply chain. The product flow process relies on the integrated activities of the different entities and has a great influence on the strength and effectiveness of the entire supply chain. One of the longest and more variable steps in in a supply chain is transportation. Various factors can cause long transportation time and high variability. On a local level, causes can include seasonal weather problems, road weight restrictions or waiting for

shipments of multiple supplies (not just SLDs for MDR-TB) to be prepared. On a global level, delays and variability often take place at the port of departure, point of transhipment and port of arrival due to congestion, regulatory paperwork and loading and unloading of containers.

The basic product flow diagram of the supply chain for MDR-TB for SLDs is depicted in Figure 5.5. The process is initiated once the PA places an order at the manufacturer. The production of SLDs involves several steps as illustrated in the Figure. A starting material has to be manufactured from raw materials before the active pharmaceutical ingredient can be manufactured. These first two steps can be complicated, dangerous and expensive due to the often toxic nature of the chemicals and the crystallisation steps required (Nicholson *et al.*, 2013).

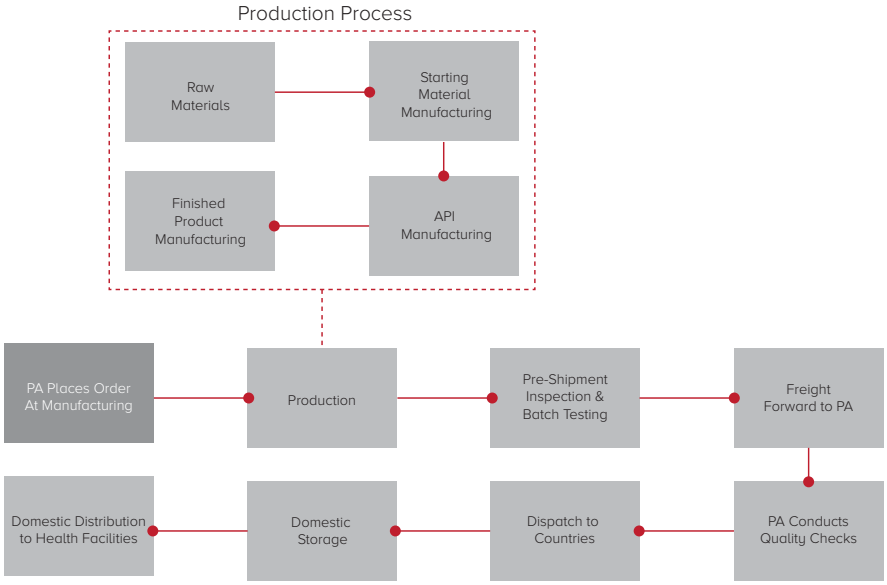

Figure 5.5: Product flow diagram of the supply chain.

If the SLDs delivered to the PA is not up to quality standards, it can be seen as a violation of their contract. Therefore, manufacturers perform pre-shipment inspections and batch testing to ensure that the shipment will be approved by the PA (IDA Foundation, 2016). When the order is received by the PA, they conduct their own assessment to ensure the product meets quality standards. This includes checking the product packaging and labelling as well as batch testing (TB Alliance, 2006). Once the order has cleared the PA's quality assessment, it is shipped from their warehouse directly to a pre-specified location in the destined country. Hereafter, the project and country is responsible for the distribution of the SLDs (TB Alliance, 2006; Giffin and Robinson, 2009).

5.4 Other important concepts and entities in the MDR-TB SLD supply chain

This section provides a description of some concepts and entities, in addition to those introduced in the previous sections, that are important for understanding the global MDR-TB SLD supply chain.

5.4.1 The price and quality reporting tool

Principal recipients of grants from the Global Fund are required to report all purchases of key pharmaceutical and health products that were procured with funds from the grant, by entering procurement information in the online Price and Quality Reporting (PQR) Tool. The recipients enter the data only when receiving the goods in the country, based on the best available documentation at that time. The recipient also has to select whether goods were purchased directly from the manufacturer or via a third-party intermediary such as the GDF (The Global Fund, 2014).

To properly fill out the PQR form, a recipient will need:

- The invoice(s) from the manufacturer;
- The invoice(s) or cost estimate(s) of the third party intermediary (where applicable);
- The scheduled and actual delivery dates; and
- The purchase order date and number. This specifies the first date on which a price was secured from a manufacturer or third party intermediary.

5.4.2 Manufacturers

For a manufacturer to be eligible to supply SLDs to the GDF, their product and manufacturing site must comply with the GDF quality assurance criteria. The criteria require all of the products to be authorized by the relevant national medicines regulatory authority in the country of use as well as either one of the following (Global Drug Facility, 2016):

i. The product is pre-qualified by WHO under the WHO Prequalification of Medicines Program; or
ii. The product is approved by the relevant Stringent National Medicines Regulatory Authority; or
iii. The product is found acceptable through an assessment process involving an independent expert review panel.

Newly approved manufacturers can qualify for long-term agreements (LTAs) through a competitive bidding process managed by the GDF's PA. Up to 4 LTAs are rewarded per product, with an established market share of the potential orders based on the

manufacturers' ranking following the bidding process. The ranking is done according to the manufacturers' score (with a maximum score of 100) from the evaluation criteria. The evaluation criteria and the corresponding maximum points are provided in **Table 5.2** (IDA Foundation, 2016).

Table 5.2: Evaluation criteria for manufacturers (Adapted from IDA Foundation, 2016).

Criteria	Max Points
Price (lowest)	50
Supplier performance on delivery lead time (highest)	15
Shelf life (longest)	20
Production lead time (shortest)	5
MOQ (lowest)	5
Product registration in HBCs and LMICs	5

A primary, secondary, tertiary and auxiliary status is awarded to the manufacturers according to their rank following the bid. The market share allocation is executed per product formulation and the estimated total orders for that formulation as follows (IDA Foundation, 2016):

- For 1 LTA – 100% for the sole manufacturer;
- For 2 LTAs – 55% for the primary and 45% for the secondary manufacturer; and
- For 3 LTAs – 50% for the primary, 30% for the secondary and 20% for the tertiary manufacturer.

When more manufacturers enter the market, the total production capacities increase, creating more competition within the market. This can have a positive impact on the prices of drugs, since manufacturers can reduce prices to compete in the market (Lunte, 2012).

5.4.3 The strategic rotating stockpile

The TB market remains small and divided with more than 40 different regimens being offered by various different suppliers/agents. Manufacturers have few incentives to invest and innovate for new medicines, demand is difficult to pool in order to negotiate price reductions, and forecasting to plan production and avoid product shortages is difficult (UNITAID, 2014).

UNITAID's solution for the prevention of stock-outs is the Strategic Rotating Stockpile (SRS), implemented by the STOP TB Partnership through its GDF. The stockpile consists of SLDs for MDR-TB which is accessible by countries in emergencies, i.e. when they require drugs at short notice to prevent a stock-out and possible treatment interruptions

(UNITAID, 2016b). The procurement of the SLDs for the SRS began in November 2007 with the aim of having enough drugs for up to 800 patients or treatments (Giffin and Robinson, 2009). Currently, the SRS has enough SLDs for 5,800 MDR-TB treatments (UNITAID, 2016b).

5.4.4 Projects outside the GLC initiative

Most countries require MDR-TB treatment as part of their TB-program and need access to an expanded supply of SLDs. For most SLDs available through the GLC mechanism, there is only one eligible manufacturer that is quality assured. The insufficient drug supply and logistical problems result in long delays for countries procuring through the GLC initiatives. A procurement mechanism with inadequate supplies and long lead times will provide little incentive to countries to seek endorsement from the mechanism. Therefore, several countries with a large MDR-TB burden that are not obliged to procure through the GLC, avoid procuring through the GLC and GDF (Giffin and Robinson, 2009). Additionally, some countries, such as Korea and the BRICS representatives, have local manufacturers and national markets for SLDs, so they have no reason to procure through the GLC or GDF (Giffin and Robinson, 2009). For examples, refer to Coetzee (2015) for a study of a section of South Africa's downstream supply chain or Giffin and Robinson (2009) for a country profile of Brazil.

5.5 Map of the MDR-TB SLD supply chain

In this section, the complete global supply chain for MDR-TB SLDs will be mapped and described by providing a theoretical model that combines the discussed characteristics, actors, flows, entities and concepts.

The complete supply chain, including both the upstream and downstream segments, is illustrated in Figure 5.6. The supply chain begins with the extraction of raw materials and the manufacturing of the starting material. The active pharmaceutical ingredient(s) is then manufactured from the raw materials and starting materials through both chemical and physical means. Once a formulation has been manufactured (through finished product manufacturing), there are three alternative paths it can take, namely:

i. to the GDF and its procurement agent or the GDF stockpile, who then distributes it to the applicable countries;
ii. directly to the country, if the country ordered directly from the manufacturer; or
iii. to a supplier or agent acting on behalf of a country, this is the case for projects outside the GLC initiative.

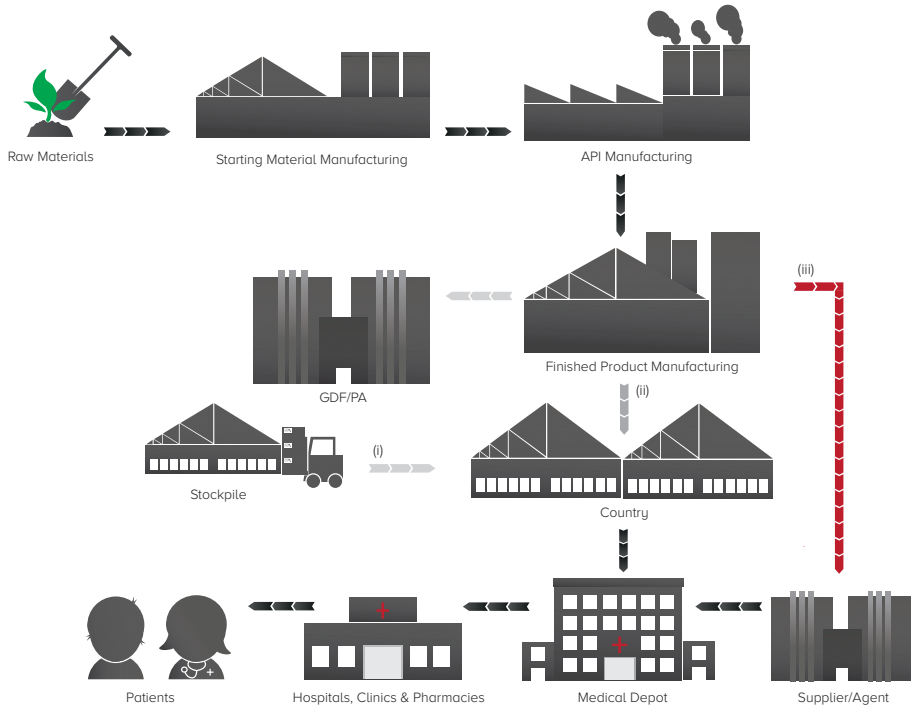

Figure 5.6: Map of the supply chain for SLDs for MDR-TB.

5.6 Challenges in the supply chain

In this section, the key difficulties and challenges in the upstream segment of the supply chain (up and till drugs reaches the country, as illustrated in Figure 5.6) will be discussed, these constitute the primary focus of this study. Table 5.3 provides a summary of the predominant difficulties and challenges in the upstream segment of the supply chain as given by Giffin and Robinson, (2009); Nicholson *et al.*, (2013); de Lucia, (2014); Keravec, (2014); Olson, English and Claiborne, (2014); and Coetzee, (2015).

Table 5.3: Summary of difficulties and challenges.

Aspect	Related Difficulties and Challenges
Demand and Forecasting	• There is a high degree of uncertainty in the procurement process due to the limited demand and lack of accurate forecasting, • Most of the current demand forecasting techniques do not fully or accurately capture patients' needs for SLDs, thus the forecasted demand is most likely lower than the actual demand, and • The inconsistent and unpredictable demand patterns prevent manufacturers from implementing optimal production processes, resulting in backlogs, delays, and high prices.
Market	• The general SLD market is comparatively small due to the restricted diagnostic capacity at country level, and • Visibility into the SLD markets are limited and doubtful, with high barriers to entry that often discourage current manufacturers and prevent new manufacturers from entering the market.

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Financial Challenges	• SLDs carry high prices when compared with FLDs, • Ineffective and inefficient management of funding coming from several sources, • Financial limitations making access to drugs difficult for patients, and • Some countries struggle with managing the complex global financing architecture.
Lead Times	• The arrival of drugs into countries procured directly from manufactures or through the GLC-mechanism can be delayed for months, during which time patients are transmitting DR-TB, and • The timely delivery of high-quality SLDs is part of a complex health care challenge that includes several steps, such as testing, diagnosis, treatment protocols, drug manufacturing, delivery and initiation and completion of treatment.
Other Challenges	• Most SLDs have a short shelf life compared with FLDs, • Some countries struggle with the procurement processes and mechanisms, • Strict regulatory processes and quality standards often creates barriers to suppliers entering the SLD market, and • Low volumes of active pharmaceutical ingredients and finished pharmaceutical products.

According to Mostaghim, (2012) high prices (listed under “financial challenges” in Table 5.3) and the limited availability of quality assured SLDs (listed under “market” and “other challenges” in Table 5.3), are the two leading challenges faced by the upstream segment of the supply chain. These are discussed in more detail in the following subsections. The section is concluded with a short discussion of the causes of challenges facing the supply chain.

5.6.1 High prices

There are four elements that affect the pricing of SLDs, namely (i) monopoly premium, (ii) risk premium, (iii) cost of sub-scale manufacturing, and (iv) the true cost of manufacturing (Mostaghim, 2012). A monopoly premium refers to the premium that manufacturers charge due to the lack of competition among manufacturers. The risk premium is driven by the poor market visibility, which causes manufacturers to charge a premium based on the risk of investing in the SLD market. Sub-scale manufacturing costs are associated with suboptimal batch sizes and production policies that manufacturers have to implement due to the limited actual demand and lack of accurate demand forecasting. The true cost of manufacturing refers to the actual cost of producing the drugs, such as raw material and labour (Nicholson *et al.*, 2013). By increasing volumes and creating competition between manufacturers, the non-essential price elements (monopoly premium, risk premium and sub-scale manufacturing costs) can be drastically decreased or even eliminated (Kimerling, 2012), which would contribute to the affordability of SLDs.

5.6.2 Limited availability of quality assured SLDs

For most second-line drugs procured through the GLC mechanism, there are only one or a few quality assured manufactures. Inadequate drug supplies, that can be at least partially attributed to the small number of suppliers, frequently cause delays. Several manufacturers have worthwhile contracts in place with the national TB programs in their countries where they are situated, in some cases, this can limit their motivation for joining the GLC initiative (Giffin and Robinson, 2009; Lunte, 2012). Some of these manufacturers do not have the required quality control and assurance measures in place to meet the WHO prequalification. Since the steps for prequalification are considered laborious by some manufactures, they require significant financial incentive to participate. The high production costs and irregular demand provide little motivation for manufacturers to join the GLC initiative (Lunte, 2012). According to industry interviews, adapting and using manufacturing facilities for the production of SLDs does not maximise profit generation (Nicholson *et al.*, 2013).

It is worth noting that several of the countries outside the GLC Initiative have government-run or other quality assured programs that provide appropriate treatment and quality assured drugs. However, approximately 90% of patients with DR-TB are receiving their treatment from sources outside of these government-run and quality assured programs (Nicholson *et al.*, 2013). In a recent study, Arinaminpathy *et al.* (2016) concluded that the suspected number of TB cases in India is two to three times more than was previously estimated. This is due to the fact that several patients in India use private medical programs instead of the government-run or quality assured programs. The private system comprises of several providers and is essentially unregulated with most cases of TB not being reported to public health officials. The patients are given drugs, but do not receive the appropriate education and support. Consequently, patients stop treatment as soon as they feel better, instead of completing the full treatment therapy (Arinaminpathy *et al.*, 2016). Interrupted treatments, as previously mentioned, is a primary cause of DR-TB.

5.6.3 Causes of difficulties and challenges

The difficulties and challenges are predominantly a result of (i) the unpredictable demand patterns, as discussed in Section 5.1.3; (ii) the restricted market structure, as introduced in Section 5.1.4; and (iii) the low volumes of active pharmaceutical ingredients (APIs) and finished pharmaceutical products (FPPs) (Mostaghim, 2012). The production of APIs is restricted to only a few manufacturers. As with the final product manufacturing, there are few incentives to invest and innovate for new medicines, the demand is difficult to pool, and forecasting to plan production and avoid product shortages is difficult. As previously mentioned, the lack of competition (monopoly premium) and the unstable demand patterns (risk premium) add to the total cost of the APIs. It is estimated that the

costs of APIs are responsible for a 30% to 60% variability in the cost of FPPs (Keravec, 2014).

Furthermore, the limited demand and lack of accurate forecasting weakens the manufacturers' confidence to produce large volumes of supplies. Therefore, they are forced to implement suboptimal manufacturing processes and manufacture the supplies in smaller batch sizes that are not cost effective. China is the world's leading provider of APIs for TB drugs, both FLDs and SLDs, holding more than 85% of the market (Olson, English and Claiborne, 2014). The manufacturers in China, however, have not been pre-qualified by WHO to sell the drugs globally, which has a major influence over the availability of SLDs (Nicholson *et al.*, 2013; Olson, English and Claiborne, 2014).

5.7 Improving the MDR-TB SLD supply chain

Between 2008 and 2013, experts on the prevention, diagnosis, treatment and management of drug-resistant TB came together to discuss and investigate ways to improve the effectiveness of the MDR-TB SLD supply chain. This discussion took the form of a series of workshops, held by the Institute of Medicine's (IOM) Forum on Drug Discovery, Development and Translation, and took place in Washington, Pretoria, Moscow, New Delhi and Beijing. A workshop summary, put together by the IOM, summarised the conclusions and recommendations from the workshops, which included participants from the World Health Organisation, Harvard Medical School, Stop TB partnership, the World Bank, the Bill & Melinda Gates Foundation and Médecins sans Frontières, among others.

The suggestions and possible solutions derived from these workshops, were arranged in three categories, namely (i) mechanisms of purchase and supply; (ii) logistics, supply and demand; and (iii) innovative financing. Table 5.4 summarises some of these suggestions that are applicable to the upstream segment of the supply chain.

Table 5.4: Summary of recommendations to improve the upstream segment of the supply chain.

Mechanisms of purchase and supply
– Restructuring of the current organisational and institutional formation to align the interests of all the partners in the system in order to possibly improve the current internal politics among key partners of the supply chain (Keshavjee, 2012).
– Provide clearer guidelines to manufacturers on how to enter to SLD market, to potentially encourage the entry of new suppliers to the market (Mostaghim, 2012).
– Applying a tiered pricing strategy according to the country's ability to pay. However, high income groups in poor populations should pay the same prices as high income groups in developed countries. Therefore, the tiered pricing strategy should also investigate the possible application of market segmentation within the countries to ensure suitable price differences for all lower-income markets, regardless of the country's income group (Yadav, 2012; Nicholson *et al.*, 2013).

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- Improving the current information systems in the supply chain, for example developing a universal bar coding system for the drugs and diagnostics, combined with mobile information technology that will allow the tracking of drug supply and stock-outs (Bloom, 2013). The sharing of this data between countries and projects could improve forecasting for manufacturers (Giffin and Robinson, 2009)

Logistics, supply and demand

- Providing incentives for manufacturers of SLDs that would encourage them to manufacture the drugs according to a set of quality standards. This could potentially include the support of local manufacturers as well. International donors should not allow the procurement of drugs that are not quality assured with their funds (Nicholson *et al.*, 2013).
- Reducing procurement barriers of the GDF to allow countries to procure drugs from local quality assured suppliers (Giffin and Robinson, 2009)
- Developing and implementing smooth, reliable and accurate forecasting methods to reduce the large differences between actual and forecasted needs. It is important to improve communication with and between manufacturers in order to share the knowledge of the whole supply chain, i.e. to forecast the donor-driven and non-donor-driven markets together and not in isolation (Yadav, 2012; Nicholson *et al.*, 2013).
- Developing public-private partnerships (Bloom, 2013).
- The development of a buffer inventory to fulfil orders of countries, while smoothing orders placed to the manufactures. This could possibly improve batch sizes and reduce costs associated with set-up and changeovers (Yadav, 2012).

Innovative financing

- Implementing a pooled financing system from which countries could withdraw funding at the appropriate time to pay for procurement, instead of providing funds to countries in advance, when their needs might still be uncertain due to inaccurate forecasting. WHO could then incorporate their data to monitor the pooled finances to ensure that drugs are procured and used at the appropriate times and countries (Bloom, 2013).
- Implementing push and pull financing strategies. Push strategies will be used to create incentives to new manufacturers to enter the market, such as providing research and development credits or fast-tracking regulatory approval. Pull strategies will be used to create demand, by expanding health insurances or risk insurance to cover MDR-TB, and encourage current manufacturers to stay in the market, by providing long-term partnerships and providing funds for the development of new SLDs (Atun, 2012a).
- Implementing new long-term contract structures to manufactures that allows quantities to be flexible (if the actual demand is slightly different than what was forecasted) and/or volume-price arrangements that would, for example, guarantee the manufacturer a certain percentage increase in orders every year, in return for a mutual percentage decrease in price over the same period (Yadav, 2012; Nicholson *et al.*, 2013).

One of the recommendations included in the table is the development of a buffer inventory. By smoothing the orders placed to manufactures, this buffer inventory could possibly resolve several problems associated with the erratic and inconsistent demand for SLDs, such as batch sizing and costs. Yadav (2012) suggested that this buffer

inventory could aid in implementing a push-pull boundary, as depicted in Figure 5.7. Refer to Section 3.6 for a description of this type of push-pull hybrid system. In the current supply chain, processes such as substance manufacturing, formulating and packaging, pre-delivery inspection and transport are predominantly order-driven due to the erratic demand. Manufacturers apply suboptimal batch sizes and production policies which results in longer lead times and higher costs. With the buffer inventory, a lean manufacturing approach could be applied upstream, while simultaneously ensuring that the stockpile is agile and capable of delivering drugs to the unpredictable marketplace, as illustrated in Figure 5.7. This would enable manufacturers to forecast more accurately and plan ahead, which would allow improved inventory management and batch sizes to be implemented. Furthermore, the implementation of such a buffer inventory could, in time, also address problems associated with lead times, demand and forecasting; consequently making the SLD market more attractive to potential manufacturers (Nicholson *et al.*, 2013).

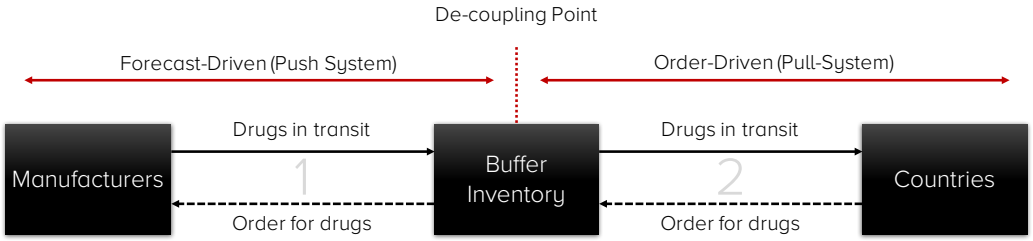

Figure 5.7: Implementation of a buffer inventory (Adapted from Yadav, 2012).

To evaluate the impact of such a buffer inventory, a model will be designed where the current SRS, with an increased capacity, is used to fulfil all orders placed through the GDF, as opposed to it being used only for emergency orders. This will be explored in more detail in the next chapter.

5.8 Conclusion: Mapping the upstream MDR-TB SLD supply chain

This chapter provided a description of the supply chain for SLDs for MDR-TB by providing background on the characteristics, flows and entities of the supply chain. A map of the supply chain was provided, followed by a summary of problems and difficulties experienced in the chain. Some of the recommendations to improve the supply chain were summarised and the idea of implementing a buffer inventory was discussed in more detail.

The following chapter will provide a description of the modelling process that was followed.

Chapter 6:
Dynamic model development

"The good thing about computers is that they do what you tell them to do. The bad news is that they do what you tell them to do."

- Ted Nelson (American pioneer of information technology)

The previous chapter provided background information, as well as a map (conceptual model) of the supply chain for SLDs for MDR-TB. This chapter will focus on the modelling process used to simulate the applicable segment of the supply chain as well as the scenarios to be implemented.

The chapter is divided into five sections, each related to the five main steps in the modelling process provided in Appendix C, namely (i) defining the problem and its boundaries, (ii) understanding the model, (iii) simulating the model, (iv) testing and validating the model, and (v) identifying and implementing scenarios.

6.1 Defining the problem and its boundaries

This section aims to clearly define the purpose of the model and discuss the boundaries and limitations associated with the data and information. It is divided into three subsections, namely (i) problem area, (ii) data and information, and (iii) time horizon.

6.1.1 Problem area

The problem area will be clarified by providing the reason for developing the model, summarising the stakeholders and considering the objectives of both the SRS and the model.

6.1.1.1 Reasons for developing a dynamic model

Many parts of the world experience serious and frequent drug shortages. In most cases, this can lead to treatment failures and cause the patient to become drug-resistant. Patients with MDR-TB who fail to adhere to treatment due to drug shortages, are at risk to develop XDR-TB. The cost of curing a single XDR-TB patient is equal to the cost of curing 200 non-resistant TB patients (Nugent, 2010).

Although several recommendations towards improving the global SLD supply chain has been documented, there are almost no evidence of quantitative models of the supply chain that can be used to accurately predict the expected impact of these recommendations on the supply chain performance.

6.1.1.2 Stakeholders

The majority of the stakeholders that are involved in the supply chain were described in Sections 5.2 and 5.4. The central entity in the model is the GDF, who is responsible for ordering the drugs from the suppliers and manufacturers on behalf of countries and delivering these drugs to countries. They also govern the SRS on behalf of the Stop TB Partnership and UNITAID. Funding for the SRS and other activities is received from several donors, though UNITAID and the Global Fund are the main funders.

6.1.1.3 Model objectives

To comprehend the main objectives of the model, it is useful to consider the motives for having a SRS. The SRS was mainly developed to be used as a safety stock for emergency orders in order to prevent stock-outs. Other than preventing treatment interruptions, it was also intended to combine and time orders – permitting current manufacturers to produce medicines more efficiently and increases market attractiveness to draw in new manufacturers (UNITAID, 2016b). However, a retrospective analysis done by Yadav (2015) for the GDF, concluded that although the SRS was successfully used as a buffer inventory for emergency orders, it was not effectively used to consolidate and time orders to optimize production for manufacturers.

With the right data scenarios can be modelled in an attempt to identify changes to the operation of the SRS that would allow it to satisfy both of these goals. The model can also simulate design changes that can support consistent access and reduced lead times whilst making the market more attractive for manufacturers. With this in mind, the main goal of the simulation model is to measure:

1. the impact of certain changes to operational policies on the variability of the demand to the suppliers and the availability of stock for clients; and
2. the combination of changes to operational policies that achieve the best outcome in terms of the variability of the demand to the suppliers and the availability of stock for clients.

In addition to two aforementioned metrics (variability of demand to suppliers and availability of stock for clients), the impact of operational changes on the cost of operating the supply chain, must of course also be taken into consideration. The extent to which these questions can be answered or discussed will depend on the boundaries, limitations and level of detail of the model.

6.1.2 Data and information

To substantiate and clarify the scope of the problem statement, the boundaries and limitations will be discussed and a conceptual model provided to illustrate the fragment of the supply chain that falls within these boundaries. Furthermore, the available data and accompanying limitations will be examined.

6.1.2.1 Boundaries, limitations and conceptual model

As initially mentioned in Section 1.4, two boundaries of the project are that (i) only the upstream segment of the supply chain will be considered, i.e. only up and till the point that the drugs are dispatched and delivered to the country; and (ii) it will only include the flow of SLDs for MDR-TB and not any FLDs. Since there is a lack of reliable data for the processes and activities that precedes the finished product manufacturing (i.e. API manufacturing, starting material manufacturing and raw materials), these steps will not be included in the simulation model. Furthermore, since the procurement data for projects outside of the GLC and GDF are not included in the main source of data for this report, the PQR database, their associated activities will be omitted from the model. By way of explanation, the map of the supply chain presented in the previous chapter in Figure 5.6 is repeated in Figure 6.1, with emphasis on the fragment of the supply chain that falls within the abovementioned boundaries and limitations.

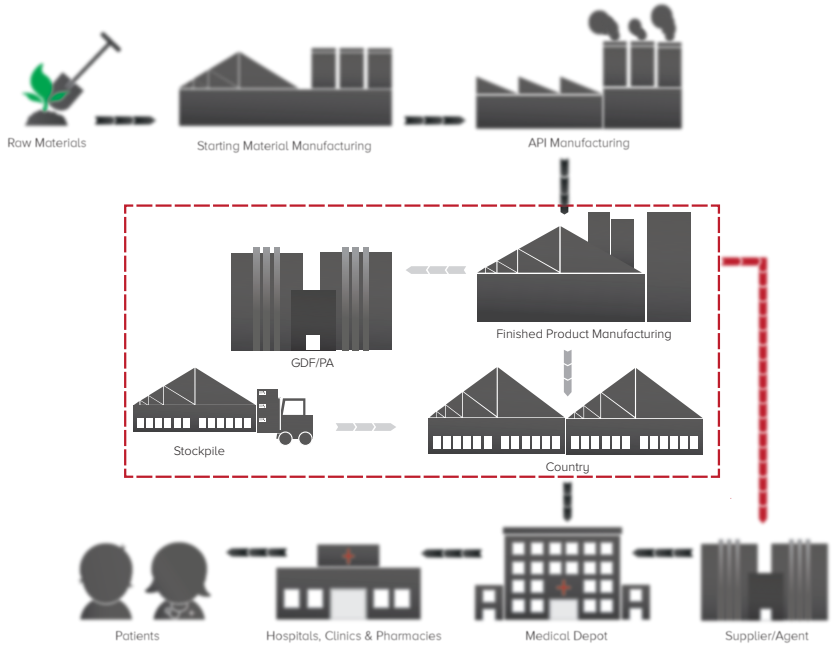

Figure 6.1: Fragment of the supply chain that falls within boundaries and limitations.

A conceptual model was developed to clarify the steps and pathways in the fragment of the supply chain that will be modelled. The conceptual model, depicted in Figure 6.2, is centred around the GDF and its PA who manages the warehouse, DC and SRS. As shown in Figure 6.2, there are currently four main 'pathways', namely (i) normal, 'everyday' orders; (ii) emergency orders; (iii) orders to replenish the stockpile; and (iv) orders from countries directly to the manufacturer. Each of these pathways will be discussed shortly.

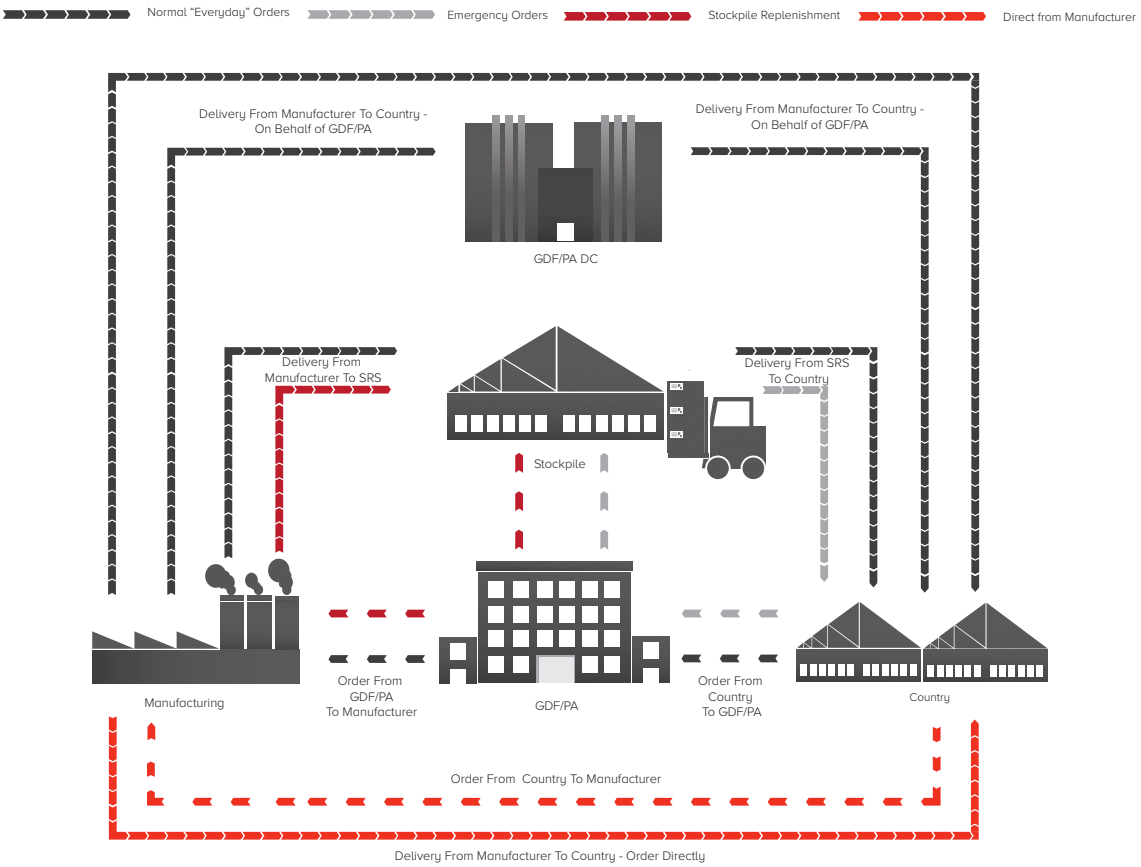

Figure 6.2: Conceptual model of the fragment of the supply chain to be modelled.

Pathways i and ii: Normal, 'everyday' orders and Emergency orders

It is important to note that the steps in the information flow, described in Section 5.3.1, still applies to pathways i and ii, even if some steps are not explicitly mentioned in the descriptions that follow. In this research, a normal, everyday order is understood to be those orders placed by a country in accordance with the expected drug needs that they submitted to the GLC and GDF. Emergency orders, on the other hand, are orders that are urgently required, at reduced lead times, to prevent a stock-out and treatment interruptions.

The process for normal, everyday orders is:

1. A country puts in a requisition of a certain size, required by a certain date.

2. The GDF considers the country's laboratory capacity, clinics, patients registered for treatment etc. and enters into negotiation with the country. Ultimately the GDF has the final say on the size of the order; however, there is usually no or only a small difference from the original requisition amount. The GDF confirms the order and forwards it to the PA.
3. The PA creates a firm purchase order based on the country requisition and places this to the various manufacturers. Drugs can also be dispatched from the SRS instead of the manufacturer to assist with stock rotation in the SRS.
4. The manufacturer(s) produces the order and dispatches it to the DC. In some cases, the GDF/PA can request that the manufacturer dispatch the drugs directly to the country, instead of the DC.
5. The PA does inspection at the DC and dispatches the drugs to the countries.

The process for emergency orders is:

1. A country places an emergency order through the GDF.
2. The GDF considers the country's laboratory capacity, clinics, patients registered for treatment etc. and enters into negotiation with the country.
3. The GDF creates a firm purchase order based on the country requisition and places this to the PA who makes necessary arrangements with the SRS.
4. The drugs are dispatched from the SRS to the country, typically within 30 to 55 days.

Pathway iii: Orders to Replenish the Stockpile

There are two flows of drugs out of the stockpile, namely (i) drugs dispatched for emergency orders, and (ii) drugs of a certain age that are dispatched as a part of stock rotation to ensure drugs do not become obsolete. The stockpile, however, is set to always have a certain number of drugs on hand for emergency orders. The exact process for stockpile replenishment is unknown due to the lack of data or information available on the inventory and ordering policies currently applied by the PA for the SRS. For the purpose of this research, the process for stockpile replenishment is assumed to be as follows:

1. The PA places an order to manufacturers; and
2. The manufacturer(s) produces the order and dispatches it to the SRS.

Pathway iv: Orders from Countries Directly to the Manufacturer

In some cases, a country decides to rather order directly from a manufacturer instead of ordering through the GDF. There are three typical reasons for this decision, namely (i) a country doesn't want to create a dependency on the GDF; (ii) countries that order

large volumes are often able to negotiate better prices themselves when ordering directly from the manufacturer; and (iii) some countries (this is debatable and there is no data to prove this) believe there are unnecessary steps when ordering from the GDF. This was confirmed by a Subject Matter Expert (SME) who has made several notable contributions to the development and research of the MDR-TB SLD supply chain, (SDL supply chain SME, Personal communication, 16 February 2016). The process for these orders is rather simple:

1. A country places an order directly to the manufacturer; and
2. The manufacturer dispatches the drugs to the country after production is completed.

Since there is no authority or control over a country's decision to order directly from the manufacturers, this path will be omitted from the model as no operational policy will directly affect their decision.

6.1.2.2 Available Data

As previously mentioned, the main source of data for the model is the PQR database, discussed in Section 5.4.1. The data from this database, however, comes with some constraints and limitations, as summarised in Table 6.1.

Table 6.1: Limitations and constraints of the database (Adapted from The Global Fund, 2005).

Constraint	Description
Misreporting	There is a large number of principal recipients that enter data into the database, increasing the chances for data entry errors to occur. The most frequent entry to be misreported is the order quantity or size and the currency.
Costs	As preferred by the PQR, some principal recipients report the unit costs without the freight, insurance, in-country distribution and handling fees. However, since it is not standard practice in the industry to report costs separately, many invoices and tender documents do not have the separate unit cost. Therefore, some principal recipients are unable to report the unit costs and includes other costs in their data entry.
Currency	A principal recipient has to specify the date on which the order was placed and report data in the currency specified on the invoice. The PQR then converts the amount into USD based on what the exchange rate was on the date that the order was placed. If a recipient misreports the order date, the converted cost will not accurately represent the manufacturer's price. The fluctuating exchange rates can also lead to variability in the converted prices.
Data integrity	Other errors and issues, such as the duplication of orders, have been reported in the past.

The purchase order information included in the PQR database is:

- the country/territory and their grant number;
- the supplier/agent;
- the manufacturer;
- the formulation and description of thereof;
- the product pack, pack quantity and pack cost (in USD);
- the purchase order date;
- the scheduled delivery date; and
- the actual delivery date.

The limited available data provides several additional limitations. The database doesn't provide any lead times, however, the time between the 'purchase order date' and 'actual delivery date' can be derived from the data. The 'actual delivery date' is the date that the drugs arrives in the country. There are, however, several separate steps in the ordering and manufacturing processes that constitutes this lead time. Thus none of these steps (described in Section 5.3) can be modelled separately. Furthermore, the entries made in the database do not state whether the order is normal or urgent. It could be argued that the emergency order classification can be derived from the data by looking at orders with a shorter lead time; however, the orders that are dispatched from the SRS as a part of stock rotation will also have a shorter lead time. Therefore, there is no way to confidently distinguish between normal orders, emergency orders and orders fulfilled due to stock rotation. Additionally, no information or data regarding the replenishment process of the SRS are available. Since the time between when the drugs are manufactured and delivered to the SRS is not specified, it would be difficult to determine the age of the drugs. Consequently, determining the number of drugs available for stock rotation or the number of drugs that exceeds their shelf life (and becomes obsolete) becomes problematic. The data regarding the manufacturers' batch sizes, minimum order quantity, lead times etc. is not publically available, making it impossible to model the manufacturers and their processes in detail.

6.1.2.3 Formulations to include in the model

An analysis of the GDF's expenditure on SLDs in 2012 and 2013 (Stop TB Partnership, 2013) indicated that 10 formulations are accountable for 92% of the total cost for SLDs. Figure 6.3 illustrates the 10 formulations and their procurement value in $US millions. These values are the total unit costs, and excludes costs associated with freight, insurance, procurement administration, handling, quality control or inspections.

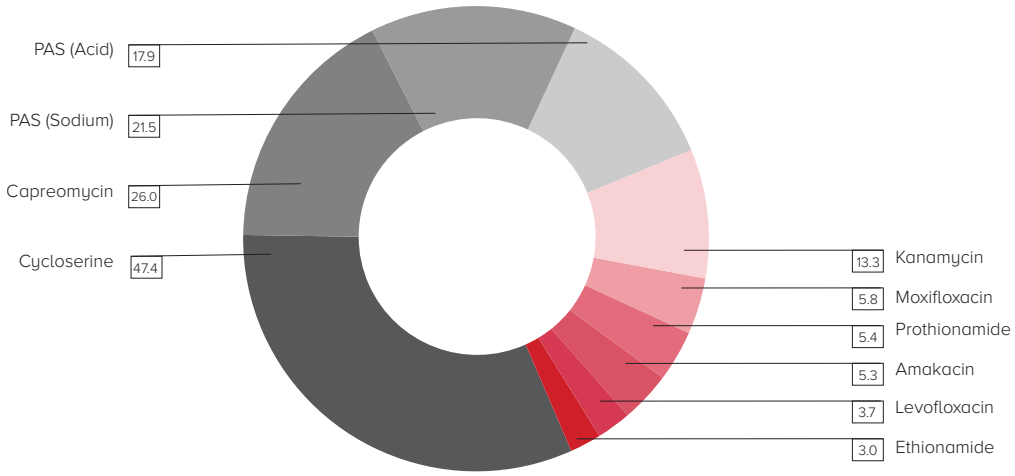

Figure 6.3: Top 10 SLDs based on procurement values from 2012 and 2013 (Adapted from Stop TB Partnership, 2013).

To ensure that the recommendations based on this research are robust, three different formulations will be included in the model. After an initial analysis of the formulations in **Figure 6.3**, it was decided to include (i) capreomycin, (ii) kanamycin, and (iii) cycloserine. These three formulations account for approximately 58% of the total procurement costs. Both kanamycin and capreomycin are from Group 2, the second-line parenteral agent (injectable anti-tuberculosis drugs). As mentioned in Section 2.4, kanamycin or amikacin is often the first choice from the Group 2 formulations; however, if drug resistance surveillance data indicates high prevalence of resistance to amikacin and kanamycin, capreomycin should be used instead. Cycloserine is from Group 4, the oral bacteriostatic second-line agents, and is a preferred choice from the group (World Health Organization, 2010)

Although PAS (acid) and PAS (sodium) account for a large percentage of the total cost, it will not be included in the model. PAS (acid) cannot be included since there is no recorded data entries in the PQR database, while PAS (sodium) will not be included due to a drastic decrease in the amount of orders placed from 2010 to 2014. For example, in 2014 only 19 orders for PAS (sodium) were placed throughout the entire year. The reasons behind the decline in PAS (sodium) could possibly be ascribed to the recent increase in the use of PAS (acid), although this cannot be proven by the available historical data from the PQR database. While the first PAS compound to be used was acid salt, PAS sodium became increasingly common during the 1950s and 1960s. It was the compound used in most countries from the 1970s until 2000 (Caminero *et al.*, 2010). The demand for PAS sodium continued to increase from 2000 to 2010, due to its effectiveness in the treatment of MDR-TB. To manage this high demand, PAS acid was reintroduced in the form of enteric-coated aminosalicylic acid granules (Peloquin *et al.*, 1994). Since then, the acid formulation has steadily replaced PAS sodium, while some countries still use it due its proven effectiveness (Caminero *et al.*, 2010).

It should also be noted that cycloserine, accountable for almost a third (32%) of the procurement costs, is available in both a 250mg tablet and 250mg capsule. It is unclear whether the percentage in Figure 6.3 covers tablets, capsules or both. From an examination of the data, orders for cycloserine capsules increased significantly from 2010 to 2014 whilst there was a corresponding decrease in orders placed for cycloserine tablets, see Figure 6.4. As reported on the Stop TB partnership's list of available products, only cycloserine capsules are currently available for purchase from the GDF. This could explain the drastic decrease in orders placed for the tablets, as it has progressively been replaced by capsules.

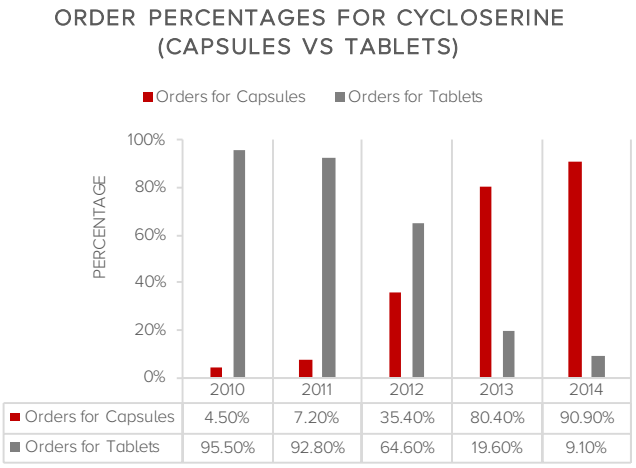

Figure 6.4: Annual order percentages of cycloserine tablets and capsules.

For practical purposes, the orders for both capsules and tablets from 2010 to 2014 can be used in the model to represent the demand for cycloserine. To ensure that this option is valid, a Mann-Whitney U test was performed to compare differences between the tablet and capsule samples. The Mann-Whitney U-test is a non-paracontinuous-level test, that does not assume any properties regarding the distribution of the variables. The data was arranged to meet the assumptions of the test, with the order size (of both dosage forms) as the dependent variable at a continuous level and dosage form as the independent variable represented by two categorical, independent groups, namely tablets and capsules. The test was performed on the SPSS software and returned a p=value of 0.159. As the computed p-value is greater than the significance level $\alpha = 0.05$, there is no compelling evidence that the two samples differ. Therefore, the total demand for cycloserine in the model developed in this research will comprise of orders for both capsules and tablets.

6.1.3 Time horizon

The PQR database contains the purchase order information for MDR-TB SLDs from 2007; however, only data from 2010 to 2014 will be used to ensure that the data relates only to steady state operation of the supply chain, and therefore excludes the initial build-up and growth phases from 2007 to 2009.

When deciding which time step (hours, days, weeks, etc.) to use in the simulation model, it is important to consider how it will affect both the level of detail and the practicality of the model. For this model, using a daily time step will provide a high level of detail, but the orders placed per day are too irregular and will result in an unnecessarily high amount of 'empty' outputs. For example, in 2010 orders were placed on only 92 days of the year, i.e. there were 268 'empty' days. This is illustrated in Figure 6.5. A weekly time step combines an acceptable level of detail with significantly fewer empty entries (refer to Figure 6.5). Although a monthly time step has no empty entries, the level of detail it provides is not as high as a weekly time step. Therefore, a weekly time step will be used in the model.

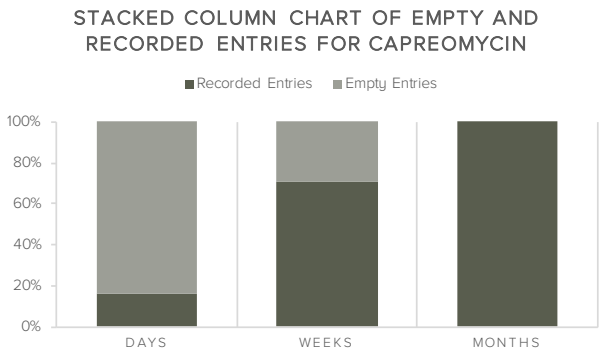

Figure 6.5: Comparison of data entries for different time steps.

For the validation and verification, the model will be run for a time horizon of 5 years in order to compare the results with the historical data (from the PQR database) from 2010 to 2014. When experimenting with the operational policies, the time horizon will be much longer to ensure that the effects and changes in system behaviour can be identified and analysed.

As suggested by Law (2004), a warm-up period will be implemented. The warm-up time is a specified number of time cycles that the simulation runs for before collecting data. The purpose of a warm-up period is to allow the parameters and queues to stabilise before measurements commence. From a graphical evaluation, it was concluded that the parameters and queues stabilise after approximately 40-45 weeks. Therefore, data will only be collected after a warm-up period of 52 weeks (one year). The impact of the various scenarios will therefore effectively be evaluated over a period of four years.

6.2 Understanding the model

This section aims to illustrate the system and its environment by identifying and describing the elements relevant to the system and by providing a CLD that reveals the links, relationships and feedbacks between the elements. The three subsections are (i) key variables and concepts, (ii) historical and possible future behaviour of variables and concepts, and (iii) the CLD.

6.2.1 Key variables and concepts

The key variables and concepts can be derived from the sections discussed in Chapter 5. The chief variables to be included in the model are centred around the conceptual model in Figure 6.2. There are also several associated variables that, as discussed in the previous section, will be consciously excluded from the model. All of the possible variables associated with the conceptual model, regardless of whether data for the variable is available, are listed in Table E.1, in Appendix E, classified as either: endogenous variables (determined by other variables), exogenous variables (independent of the other variables), or omitted variables.

It is important to note that these variables and concepts can still be modified during the remainder of the modelling process. Some of the variables might be removed or replaced and additional variables can be added.

6.2.2 Historical and possible future behaviour

This section will investigate the current behaviour by evaluating the descriptive statistics of the data and attempting to identify patterns through correlation analyses and inspection of graphs.

6.2.2.1 Demand and order size

The main input of the model is the country demand. Probability distribution functions will be used to feed random values to the model. Each week will comprise of up to four separate orders to enable more detailed modelling thereby replicating the behaviour of the real-world supply chain more closely. The size of these orders will be acquired from the distribution. For each of the three formulations, a frequency chart was generated to visualise the data. The charts for capreomycin, kanamycin and cycloserine are given in Figure 6.6 – 6.8. Each of the charts also include a polynomial trendline to indicate the general tendency of the data.

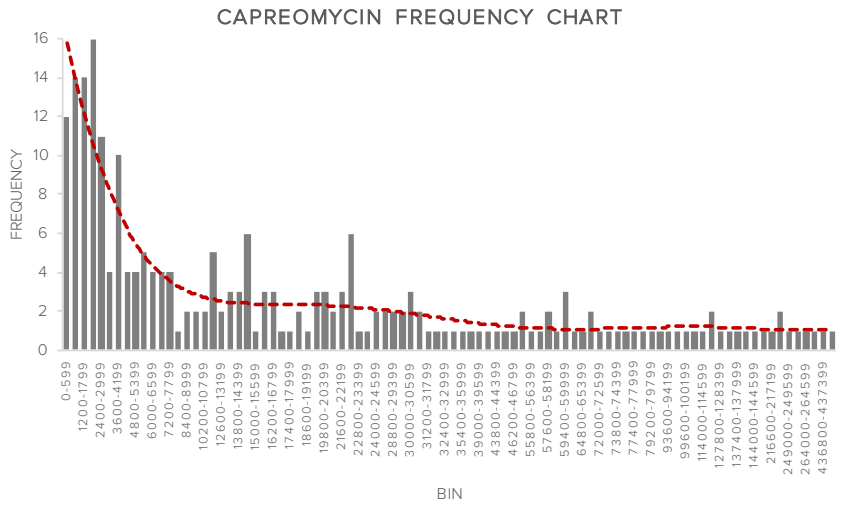

Figure 6.6: Frequency diagram of capreomycin.

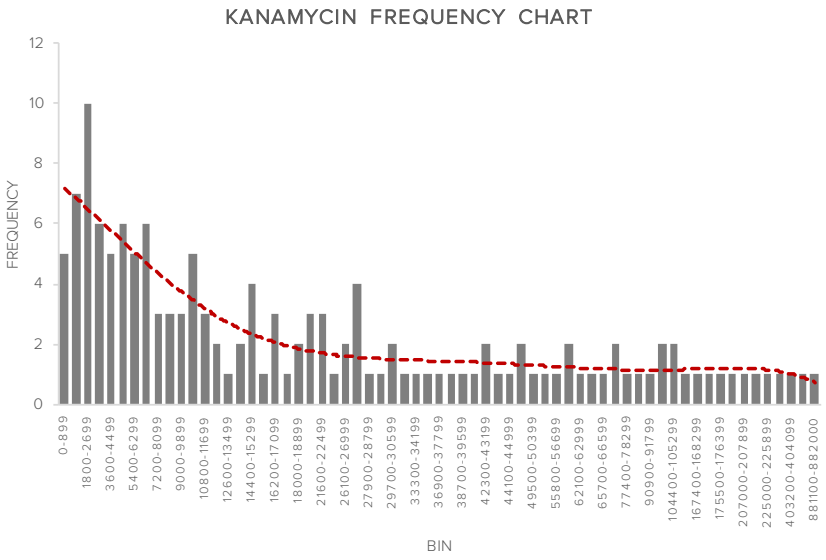

Figure 6.7: Frequency diagram of kanamycin.

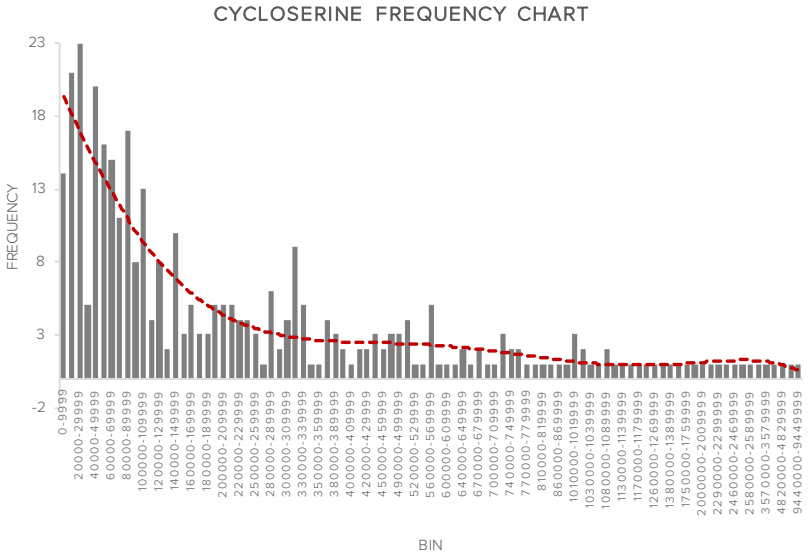

Figure 6.8: Frequency diagram of cycloserine.

Since the main objectives of the model is to evaluate the impact of changes to operational policies, it is expected that the exact value of the order sizes will not negatively affect the system. For example, even though an order of 91.34 tablets is unrealistic, it would not influence the outcomes of modelling scenarios concerning changes to the operational policies. Furthermore, if continuous variables do cause difficulties, the model can be coded to round the generated values to integers. For this reason, both discrete and continuous distributions will be considered, expanding the list of available distributions to fit to the data. A graphical evaluation of the demand for each formulation makes it clear that the data is asymmetric and has mostly positive outliers. From Figure 6.9 it was therefore concluded that the distribution that will best represent the data is either a Negative Binominal distribution (discrete) or a Gamma, Weibull or Lognormal distribution (continuous).

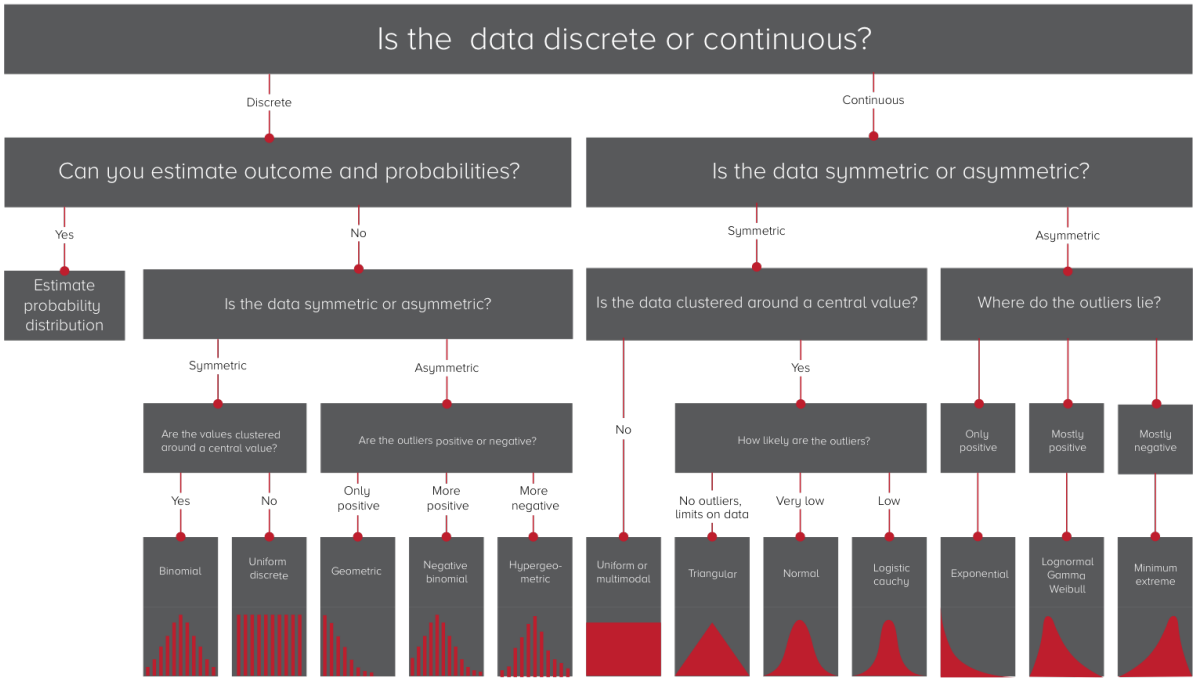

Figure 6.9: Distributional choices (Adapted from Damodaran, 2016).

Because Vensim does not support the Lognormal distribution, only the Negative Binominal, Gamma and Weibull distributions will be considered for further analysis. Distribution fitting tests were performed using the CrystalBall, EasyFit and ModelRisk software. All three tests established that, for all three formulations, the Weibull distribution is more suitable than the Gamma and Negative Binominal distributions.

A Weibull distribution can be classified as being a one-parameter (1P) Weibull, a two-parameter (2P) Weibull or a three-parameter (3P) Weibull. The three obtainable parameters are (i) the location parameter or failure-free life, symbolised by γ; (ii) the shape parameter or slope, symbolised by β; and (iii) the scale parameter or characteristic life, symbolised by η.

The 1P Weibull probability distribution function assumes $\gamma = 0$ and $\beta = k$, where k is some assumed constant value. The scale parameter (η) is the only known parameter. The probability distribution function for the 1P Weibull is therefore given by

$$f(t) = \frac{k}{\eta}\left(\frac{t}{\eta}\right)^{k-1} e^{-\left(\frac{t}{\eta}\right)^{k}}, \tag{6.1}$$

where:

$f(t) \geq 0$,

$t \geq 0$, and

$\eta > 0$.

For the 2P Weibull pdf, $\gamma = 0$ and the scale and shape parameter is known. The probability distribution function is similar to (6.1) with the constant k being replaced by β:

$$f(t) = \frac{\beta}{\eta}\left(\frac{t}{\eta}\right)^{\beta-1} e^{-\left(\frac{t}{\eta}\right)^{\beta}}, \tag{6.2}$$

where:

$f(t) \geq 0$,

$t \geq 0$,

$\eta > 0$, and

$\beta > 0$.

With all parameters known, the 3P Weibull pdf is given by

$$f(t) = \frac{\beta}{\eta}\left(\frac{t-\gamma}{\eta}\right)^{\beta-1} e^{-\left(\frac{t-\gamma}{\eta}\right)^{\beta}}, \tag{6.3}$$

where:

$f(t) \geq 0$,

$t \geq 0$ *or* $\gamma, \eta > 0$,

$\beta > 0$, and

$-\infty < \gamma < +\infty$.

The Weibull distribution recommended by the software is either: (i) a two-parameter (2P) Weibull distribution, as computed by the ModelRisk software; (ii) a three-parameter (3P) Weibull distribution, as computed by the CrystalBall software; or (iii) both a 2P and 3P Weibull distribution, as computed by the EasyFit software. A summary of the results can be seen in Table 6.2. A Kolmogorov-Smirnov goodness of fit test (K-S test) was performed to assess how well all the proposed Weibull distribution functions fit the data. The K-S test statistic (D_n) for each set of parameters is also provided in Table 6.2.

Since the location, scale, and shape parameters were estimated from the data, the critical region of the Kolmogorov-Smirnov test might be invalid. Therefore, the selection of a single 'best' parameter set, based solely on the best D_n value, will be avoided. Instead, each of the suggested set of parameters in Table 6.2, will be experimented with to determine a new set that generates a more accurate representation of the historical data. This is discussed in more detail in Section 6.3.3.2.

Table 6.2: Weibull parameters determined by distribution fitting software.

	Software	Weibull Parameters			K-S Test
		Location	Shape	Scale	D_n
Capreomycin	CrystalBall	78	0.7571	21 477.19	0.0743
	EasyFit	78	0.6183	21 462.00	0.0494
		0	0.7081	20 557.00	0.0792
	ModelRisk	0	0.6224	21 999.67	0.0542
Kanamycin	CrystalBall	450	0.5100	28 840.68	0.0813
	EasyFit	450	0.5879	23 752.00	0.0918
		0	0.7859	27 186.00	0.0855
	ModelRisk	0	0.6525	29 773.15	0.0893
Cycloserine	CrystalBall	1500	0.6832	278 210.51	0.0730
	EasyFit	1500	0.6755	280 090	0.0628
		0	0.8161	262 280	0.0830
	ModelRisk	0	0.7236	284 342.11	0.0799

It is important to note that all of the calculations in this section only considered the weeks in which at least one order was placed and ignored the weeks where there were zero orders. When weeks where no orders were placed were included in the data, the software used for distribution fitting concluded that there are no valid distributions that represents the data. To compensate for this in the model, the input variable for demand will either generate a 0 value, with x probability, or a value from the appropriate Weibull distribution with $1 - x$ probability. To determine these probabilities, the proportion of weeks where orders were placed and where no orders were placed, for each year, was calculated from the data. Similarly, the probabilities that more than one, two and three orders are placed were also calculated. The calculations for probabilities from 2010 to 2014 are summarised in Appendix E, Section E.2.2.2. It could be argued that the probabilities could be determined in more detail to have, for example, a different probability for every week of the year; however, the unpredictability of the demand makes such an approach unsuitable. The appropriateness of this approach to generating the demand data for the model was validated through consultation with a SME from the Centre for Statistical Consultation at Stellenbosch University. Furthermore, if there are any difficulties or anomalies, these will be identified during the validation and verification phase.

6.2.2.2 Descriptive Statistics

The descriptive statistics of the order size will be used to provide background on the behaviour of the orders placed. The descriptive statistics are summarised in Table 6.3 for each of the three formulations.

Table 6.3: Descriptive statistics of order size.

Statistic	Capreomycin	Kanamycin	Cycloserine
Mean	33 323	43 808	381 362
Standard Error	4 146	8 124	43 073
Median	12 150	13 900	129 600
Mode	3 600 (5)	1 800 (5)	54 000 (9)
Q1	2 400	5 200	52 925
Q3	30 346	40 787.5	381 900
Standard Deviation	63 012	96 813	803 512
Minimum	78	450	1 500
Maximum	448 000	882 000	9 449 100
Sum	7 697 603	6 220 780	132 714 100
Count	231	142	348

A noticeable difference between the different formulations is the much higher values for cycloserine. This can be ascribed to the use of the formulations in treatments. Capreomycin or kanamycin is used only during the intensive phase of treatment and approximately 210 units (for both formulations) is required on average per patient course. Cycloserine, on the other hand, is used during both the intensive and continuation phase of treatment and requires about 1560 units on average per patient course (Lunte, 2012).

The standard deviations for all of the formulations are exceptionally high, approximately double the size of the mean. A high standard deviation is expected since the order sizes will vary from country to country. For example, a high-burden country with a large population will most likely place a significantly larger order than a low-burden country with a small population. This, combined with the inconsistent and unpredictable demand patterns, leads to the high standard deviations depicted in the table. Further proof of the inconsistent demand is found when comparing the mean and the median. The median is roughly three times smaller than the mean, which indicates that half of the orders placed are smaller than the average order size.

The next section will investigate possible correlations between the variables in the data that could be linked to the order size (demand) and lead times.

6.2.2.3 Correlation analysis

For each of the three formulations, both the demand (order size) and lead time were tested for correlations with the (i) day of the week, (ii) day of the month, (iii) month of the year, (iv) week of the year, and (v) region. Additionally, an analysis was conducted to determine whether the two variables were correlated with each other and whether the

lead time had any correlation with the manufacturer. Table 6.4 provides a summary of the correlation results and provides both the value of the correlation coefficient (CC) and the p-value.

All of the correlations were determined using a Spearman Rank Correlation Test. The Spearman Correlation was selected as it is a paracontinuous-level test which does not make the assumption that the variables follow a multivariate normal distribution. The choice of correlation test was validated as appropriate by an SME from the Centre for Statistical Consultation at Stellenbosch University. As revealed in Table 6.4, there are only five significant correlations (with a p-value < 0.005), however, for three of these the correlation coefficients are small enough (<0.2) to be considered negligible (CC < 0.2) and for the remaining two, the correlations are very weak (CC < 0.3). For this reason, these correlations will not be considered during the modelling process.

Table 6.4: Correlation tests results.

	Capreomycin		Kanamycin		Cycloserine	
	CC	P-value	CC	P-value	CC	P-value
Demand and Lead Time	0.215	0.000	0.128	0.002	0.084	0.048
Demand and Day of the Week	-0.027	0.642	-0.015	0.839	0.053	0.216
Demand and Day of the Month	-0.050	0.392	-0.009	0.877	0.064	0.133
Demand and Month of the Year	0.013	0.824	0.099	0.179	0.029	0.490
Demand and Week of the Year	0.011	0.856	0.095	0.198	0.031	0.461
Demand and Region	0.019	0.743	0.219	0.003	0.024	0.580
Lead Time and Day of the Week	-0.082	0.161	-0.011	0.881	-0.180	0.000
Lead Time and Day of the Month	-0.109	0.060	-0.001	0.988	-0.176	0.000
Lead Time and Month of the Year	-0.006	0.914	0.047	0.520	0.055	0.199
Lead Time and Week of the Year	-0.014	0.806	0.047	0.527	0.042	0.324
Lead Time and Region	0.094	0.108	0.023	0.756	0.066	0.119
Lead Time and Manufacturer	-0.073	0.209	N/A		0.058	0.176

6.2.2.4 Visual assessments of the data

This section will provide visual assessments of the available data following a similar approach as applied by Yadav (2015) in his analysis of the SRS for the GDF. Only the analysis for capreomycin is provided in this section, while the graphs and analysis for kanamycin and cycloserine are provided in Appendix D. Figure 6.10 depicts the weekly purchase order quantity as a percentage of the annual order quantity, plotted by week for each of the five years. This provides a visual assessment of any possible trends in the order timing from one year to the next. The figure clearly illustrates the dynamic nature of the data and that there is no trend in the time of year when orders are placed.

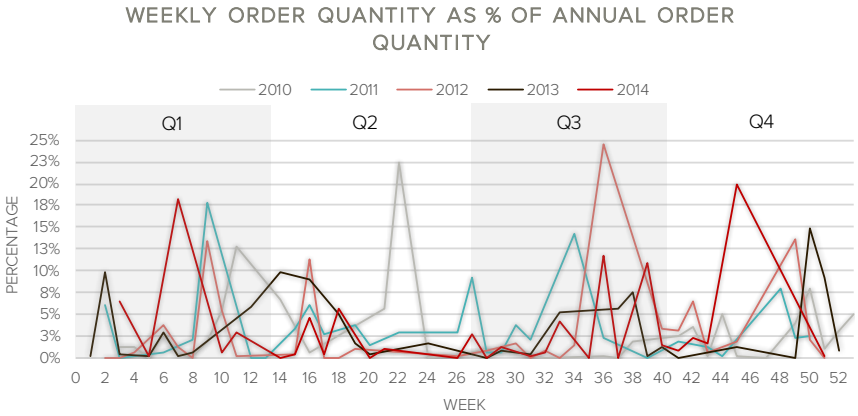

Figure 6.10: Visual assessment of trends in order timing for capreomycin.

Figure 6.11 illustrates the average weekly order size as well as the average lead time for the orders placed in that week over the last five years. This is to enable a visual assessment of how the lead time and demand fluctuates and whether any correlation between order size and lead time possibly exists. The figure clearly demonstrates the inconsistency of both the demand and lead time. The intuitive conclusion from the figure also corresponds with the results from the correlation analysis presented in Section 6.2.2.3 - there is no correlation between the order size and lead time.

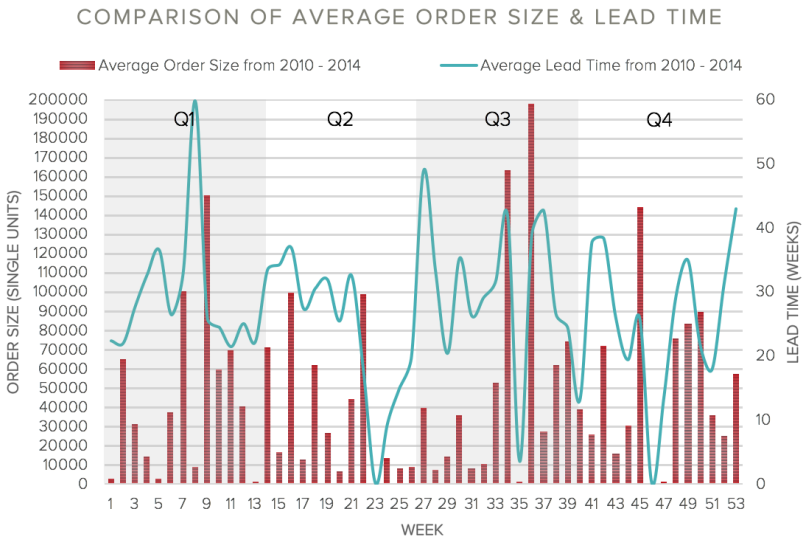

Figure 6.11: Visual assessment of the average lead times and order sizes for capreomycin.

Figure 6.12 provides a plot of the weekly lead time against the purchase order dates over the five-year period. The lead time is calculated as the difference (in weeks) between the purchase order date and the order delivery date. This is to enable a visual assessment of whether any changes in the lead time occurred over the last five years. A linear regression analysis of the lead time was performed and no statistically significant relationships were observed, this is consistent with the graphic representation in the figure, which illustrates a relatively stable trend.

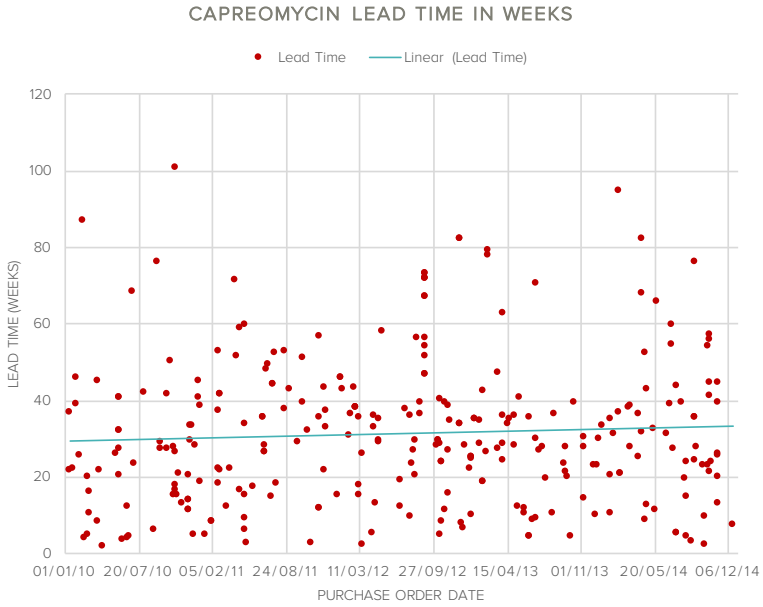

Figure 6.12: Visual assessment of changes in lead time for capreomycin.

6.2.3 Causal-loop diagram

This section will capture the theories about the causes of the supply chain's dynamics in order to provide a better understanding of the whole system and its behaviour. To do this a CLD will be developed to illustrate the causalities, feedback structures and the factors that influence the system behaviour.

6.2.3.1 Links and relationships

Figure 6.13 depicts the CLD of the upstream MDR-TB supply chain. As described in Section 4.4.4, a positive link (+ sign) signifies that the elements are positively related, while a negative link (- sign) signifies that the elements are negatively related. This CLD includes (i) variables that influence or have some effect on the upstream segment of the supply chain, as well as (ii) some variables that are influenced or affected by the supply chain.

There are loops in the CLD, denoted by either a 'B' or an 'R', that illustrate the balancing and reinforcing processes in the supply chain. The remainder of this section will provide a description for each of the balancing and reinforcing loops in order to illustrate the relationships between the associated variables.

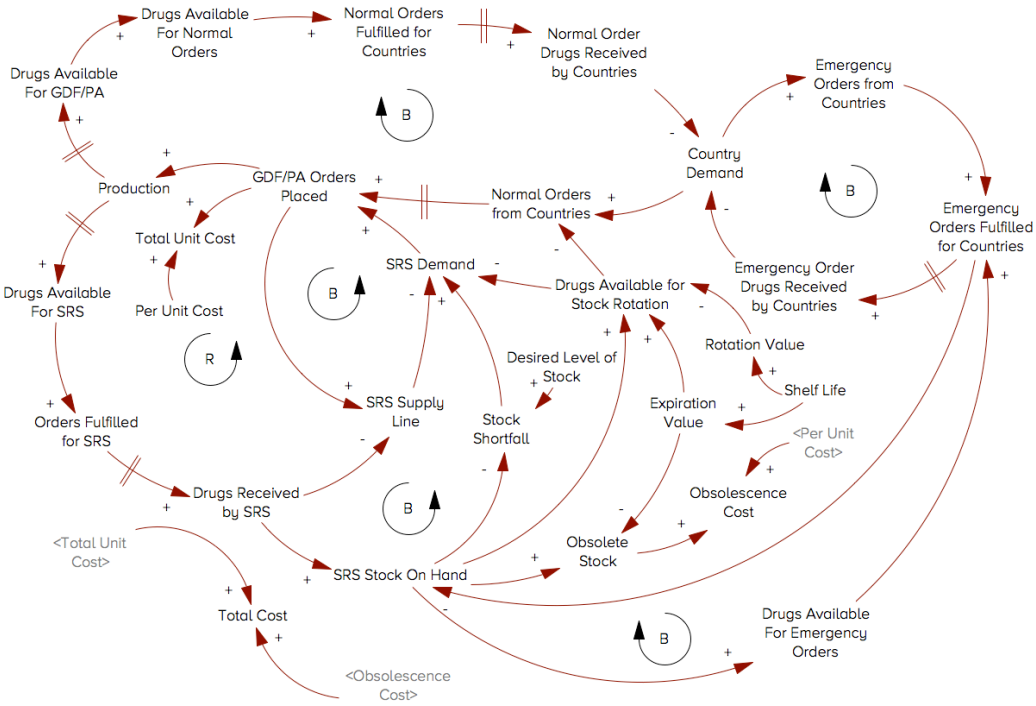

Figure 6.13: Causal-loop diagram of the upstream supply chain.

6.2.3.2 Feedback loops

The balancing loops illustrated in Figure 6.14, involves the counteracting and opposing effects that the 'SRS stock on hand' will have on some of the variables. An increase of the 'GDF/PA orders placed', will increase the 'production' consequently increasing the 'drugs available for SRS', after a delay (production and dispatch lead time). This will lead to an increase in the 'orders fulfilled for SRS', which causes the amount of 'drugs received by SRS' to increase, after a delay (distribution lead time). This results in an increase of the 'SRS stock on hand'. As depicted in Figure 6.14 (a), this decreases the 'stock shortfall' and, in turn, decreases the 'SRS demand', causing the 'GDF/PA orders placed' to decrease. In Figure 6.14 (b), an increased 'SRS stock on hand' will increase the amount of 'drugs available for stock rotation', consequently decreasing the 'normal orders from countries'. This leads to a decrease in the 'GDF/PA orders placed'.

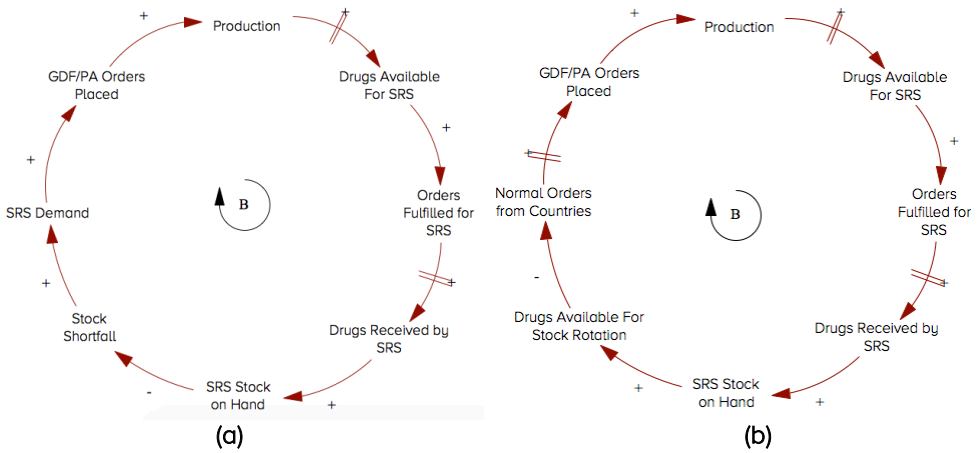

Figure 6.14: Two balancing loops of the SRS stock on hand.

Figure 6.15 depicts both a balancing and reinforcing loop related to the 'SRS Demand' and the 'SRS Supply Line'. In the balancing loop, an increase in the 'SRS Demand' will cause the 'GDF/PA Orders Placed' to increase, consequently increasing the 'SRS Supply Line'. This increase of the 'SRS Supply Line', however, will cause a decrease in the 'SRS Demand'. In the reinforcing loop, the increase in the 'SRS Demand' and 'GDF/PA Orders Placed', will cause an increase of 'Production', the 'Drugs Available for SRS', 'Orders Fulfilled for SRS' and 'Drugs Received by SRS', similar to the balancing loop in Figure 6.14. The increase in 'Drugs Received by SRS', however, will cause the 'SRS Supply Line' to decrease, which results in an increase of the 'SRS Demand'.

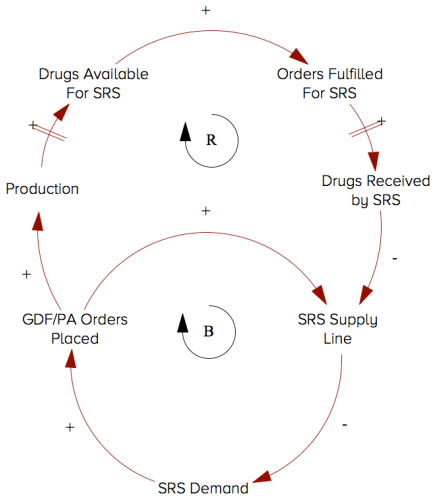

Figure 6.15: Balancing and reinforcing loop of SRS demand and supply line.

A balancing loop associated with the normal orders, is depicted in Figure 6.16. An increase in the 'Country Demand', will result in more 'Normal Orders from Countries' causing more 'GDF/PA Orders Placed', after a delay (order processing). As with the previous balancing loops, this causes an increase in the 'Production', 'Drugs Available for GDF/PA' and 'Drugs Available for Normal Orders'. With more drugs available, the 'Normal Orders Fulfilled for Countries' will increase, which will increase the 'Normal Order Drugs Received by Countries', after a delay (distribution lead time). When the countries receive drugs, their 'Country Demand' will decrease.

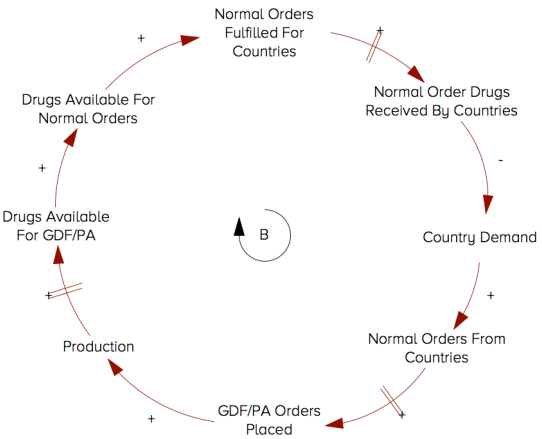

Figure 6.16: Balancing loop of normal orders.

The last two balancing loops, depicted in Figure 6.17, involves the emergency orders. As illustrated in Figure 6.17 (a), if the 'Country Demand' increases, the 'Emergency Orders from Countries' will increase as well, resulting in more 'Emergency Orders Fulfilled for Countries'. This causes the number of 'Emergency Order Drugs Received by Countries' to increase, reducing the 'Country Demand'. As illustrated in Figure 6.17 (b), on the other hand, an increase of the 'Emergency Orders Fulfilled for Countries' will cause the 'SRS Stock on Hand' to decrease, resulting in a decrease of the 'Drugs Available for Emergency Orders'.

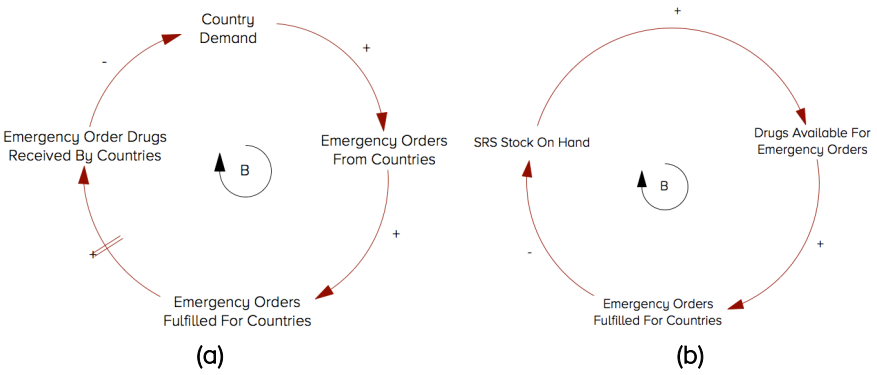

Figure 6.17: Balancing loops of emergency orders.

6.3 Simulating the model

In this section, the CLD will be expanded to develop the more detailed stock and flow diagram to clearly define the physical structure of the model. The process of building the stock and flow diagram and simulating the model using the chosen software will also be described. The process includes several steps and the subsections of this section are divided to follow these steps chronologically. The first subsections are (i) selecting the modelling software, (ii) level of detail, and (iii) variable types. This will be followed by sections dedicated to describing the different models that were built. For each model, the following will be discussed: (i) stock and flow diagram, (ii) characteristics and equations of the elements, and (iii) assumptions of the model.

6.3.1 Modelling software

The majority of SD software, such as Stella, Vensim, Powersim etc. have a great deal in common. A number of factors influence the choice of software for this model, namely price of the software, the available support, and whether it has the required tools and features. For this model, Vensim (from Ventana Systems incorporated) will be used as it is the less expensive software and the preferred SD software by many other students at the Industrial Engineering Department, meaning support is readily available. The Vensim software is also expected to be sufficient for the model in terms of capacity, performance, functionality, speed and optimization capabilities. As stated by Ventana

Systems, the sensitivity analysis is fast and powerful and has no limits on the size of the model.

6.3.2 Level of detail

This subsection includes a discussion of the level of detail for certain variables in the model. These detailing decisions corresponds with the limitations and boundaries that were discussed in Section 1.4 as well as the limitations associated with the available data, as discussed in Sections 6.1.2.1 and 6.1.2.2.

6.3.2.1 Countries

More than 70 countries are included in the data set, each placing between one and five orders a year for each of the formulations. To ensure that the recommendations based on the output of the data is robust, stochastic input data is required. However, with the available data, it will be impossible to generate stochastic input data based on only the few orders placed per country per year. Instead, the countries will be treated as a single entity representing the total demand of all the countries. This approach is sufficiently detailed to evaluate the impact of changes to various operational policies on the performance of the supply chain, thus it is sufficiently detailed to achieve the objective of the modelling exercise.

6.3.2.2 Formulations

A ‘formulation’ subscript will be used to include each of the three formulations, namely capreomycin, kanamycin and cycloserine. Although a weekly time step will be used in the model, each week will contain up to four orders to enable more detailed modelling of orders. To achieve this, an additional ‘order’ subscript will be used to represent the four possible orders per week.

6.3.2.3 Manufacturers

As with countries, there are two options regarding the level of detail in which to model manufacturers. The first option is to treat manufacturers as unique entities, where each manufacturing company has their own batch sizes and ordering policies and will only be able to produce one or more of the formulation types. The GDF/PA places orders at different manufacturers according to the formulation. In order to effectively model manufacturers in this amount of detail, additional data is required, such as the batch sizes and policies regarding batches and production, production rates etc. of each manufacturing organisation. Since this data is not publically available, the second modelling option will be applied instead. This (second) modelling option entails treating the manufacturers as a single entity, where all the orders from the GDF/PA (for each formulation) are placed to the same manufacturing entity. This entity will have the same ordering policy for all orders and be able to produce all formulations. This level of detail is sufficient to achieve the objective of the modelling exercise.

6.3.3 Model A

To evaluate the impact of different scenarios, it would be beneficial to compare the performance of the scenarios with the current system. It is, therefore, necessary to develop a 'base case' model that illustrates the current system. The variables and concepts identified in Section 6.2.1, were examined to determine a potential model that can be supported by the available historical data obtained from the PQR database. This model will be referred to as Model A. Model A is an initial model that is intended to define a physical structure of the aspects of the supply chain segment to be modelled, that can be supported and validated by the available data. It is intended to serve as a valid and reliable starting point from which to expand and add more elements and detail necessary to evaluate alternative modes of operating the supply chain.

6.3.3.1 Model A: Stock and flow diagram

The complete stock and flow diagram for Model A consists of two parts, namely (i) the main model, and (ii) the costs section. These are illustrated in Figures 6.18 and 6.19 respectively. The cost section is an expansion of the main model, and is necessary to assess the effects of different operational policies on cost.

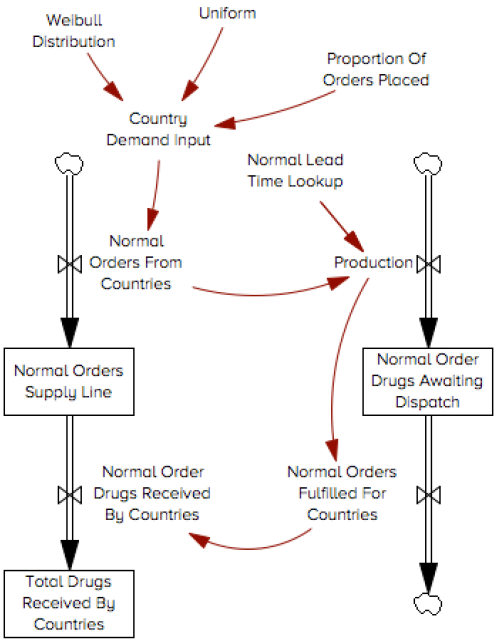

Figure 6.18: Stock and flow diagram of the main section of Model A.

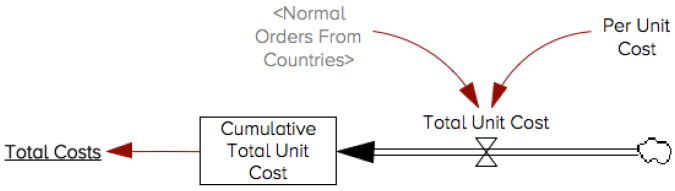

Figure 6.19: Stock and flow diagram of the cost section of Model A.

6.3.3.2 Model A: Characteristics and equations of elements

The complete modelling details for Model A, including the list of variables that were used and the details and equations of each element, are provided in Appendix E. This section will highlight some of the aspects that proved challenging during the development of Model A.

As discussed in Section 6.2.2.1, the input demand will follow a Weibull distribution with a location, shape and scale parameter. Each of the suggested set of parameters provided in Section 6.2.2.1 were experimented with in the model and the output analysed. Through a process of trial and error, the set of parameters that generate the most accurate representation of the historical data for each formulation was identified. The parameters are summarised in Table 6.5.

Table 6.5: Final parameters for the demand input.

	Location	Shape	Scale
Capreomycin	78	0.6161	32 500
Kanamycin	450	0.4525	50 000
Cycloserine	1 500	0.4755	420 000

As mentioned in Section 6.3.2.2, each week will comprise of up to four orders to provide more detail. With this in mind, it is important to note the following prerequisites:

- a second order can only be placed if a first order has been placed;
- a third order can only be placed if a second order has been placed; and
- a fourth order can only be placed if a third order has been placed.

Therefore, during the time steps that no (first) order is placed, there cannot be any second, third, or fourth orders. The probability of a second, third and fourth order being placed each week had to be calculated from the data. Refer to Appendix E, Section E.2 for details on the calculations and results. To incorporate this in the model, a uniform variable was added, as suggested by a Vensim 'super administrator'. The uniform variable generates a value between 0 and 1 at every time step and if it is smaller than the probability (of an order being placed) the model generates an order value; otherwise it returns zero, indicating that no orders are placed that week. This is described in more detail in the appendix.

6.3.3.3 Model A: Assumptions

The assumptions made with regard to the entities in Model A are discussed in this subsection.

Assumptions about Manufacturers:

It is assumed that:

- the manufacturers have no additional orders other than that of the GDF and their PA. In reality, they might have orders waiting from other companies (that are not reported in the PQR database used for this research) which would potentially cause additional delays in the supply chain.
- second-line anti-TB drugs are not kept in stock by any of the drug manufacturers. Thus it is assumed that once production is completed, drugs are immediately dispatched to the GDF and their PA's DC.

Assumptions about Countries:

It is assumed that:

- no delays or other problems related to patent registrations or restrictions can delay an order. This is assumption is viewed as reasonable since countries requesting drugs are responsible for ensuring that the drugs comply with the country's legislation on patent registration or restrictions.
- countries place an order to cover drug needs and include a buffer stock in their procurement order (to cover drug consumption for the whole expected delivery time).

Assumptions about the GDF, Distribution Centre and Stockpile:

It is assumed that:

- drugs are dispatched from the stockpile based on a first-in-first-out basis.
- the distribution centre is only used as a buffer area, intended to dispatch all incoming stock to the countries as soon as possible. Thus it is assumed that there is no permanent stock in the distribution centre.

6.3.4 Stabilising Model A

As can be derived from the different supply chain flows discussed in Section 5.3, there are several separate steps in the ordering and manufacturing processes that constitute the lead time. All of these steps can be summarised in three major steps, namely (i) the ordering process of the GDF and their PA, (ii) the production of the drugs and its dispatch from manufacturers to the GDF and their PA's distribution centre, and (iii) the quality checks (QC's) at the distribution centre and the dispatch of the drugs from the distribution centre to the countries.

The diagram in Figure 6.20 demonstrates the three major steps, their associated activities and an approximation of their lead times, as obtained from WHO (2008); Giffin

and Robinson (2009); Lunte (2012); Nicholson *et al.* (2013); Keravec (2014); and Muzafarova (2015). These lead times were derived either from country case studies, averages or estimates that were provided in the sources mentioned above.

Figure 6.20: The three major steps that summarises the ordering and manufacturing processes.

The abovementioned steps can be incorporated into Model A with 'orders ready for production' and 'orders available for dispatch' as the stock variables and 'order processing', 'production and dispatch to GDF/PA' and 'QC's and dispatch to countries' as the flow variables. If used in the model, the time between when the drugs are manufactured and delivered to the GDF/PA can be assumed, consequently making it possible to determine the age of the drugs. This will enable the number of drugs available for stock rotation and the number of drugs that exceed their shelf life (and become obsolete) to be calculated, although more assumptions about the stock rotation policies will have to be made.

6.3.5 Model B

Model A was developed to serve as a dependable model that could be entirely validated with historical data; therefore, several elements had to be omitted from the model due to the lack of available data to validate these elements. As previously mentioned, it would be beneficial to compare the performance of possible scenarios with the current system; however, Model A alone does not accurately represent the current system in its entirety and does not provide enough elements to allow the effective evaluation of the performance. A second model (Model B) was built, by expanding Model A, to incorporate aspects that would allow the current system to be evaluated and compared with potential scenarios. These aspects include separate lead times, stock rotation, obsolete stock, and emergency orders. Where accurate historical data were unavailable, certain assumptions were made to implement the new aspects in the model.

6.3.5.1 Model B: Stock and flow diagram

The complete stock and flow diagram for Model B consists of two parts, namely (i) the main model, and (ii) the costs section. Both of these are illustrated in Figure 6.21 and Figure 6.22, respectively. As depicted in Figure 6.21, the main model is larger and more complex than Model A. As discussed, this additional complexity is required to enable a comparison of the performance of the stock pile in its current mode of operation with that of the stockpile under various alternative supply chain management approaches.

Large sections of this model are based on assumptions due to the lack of historical data.

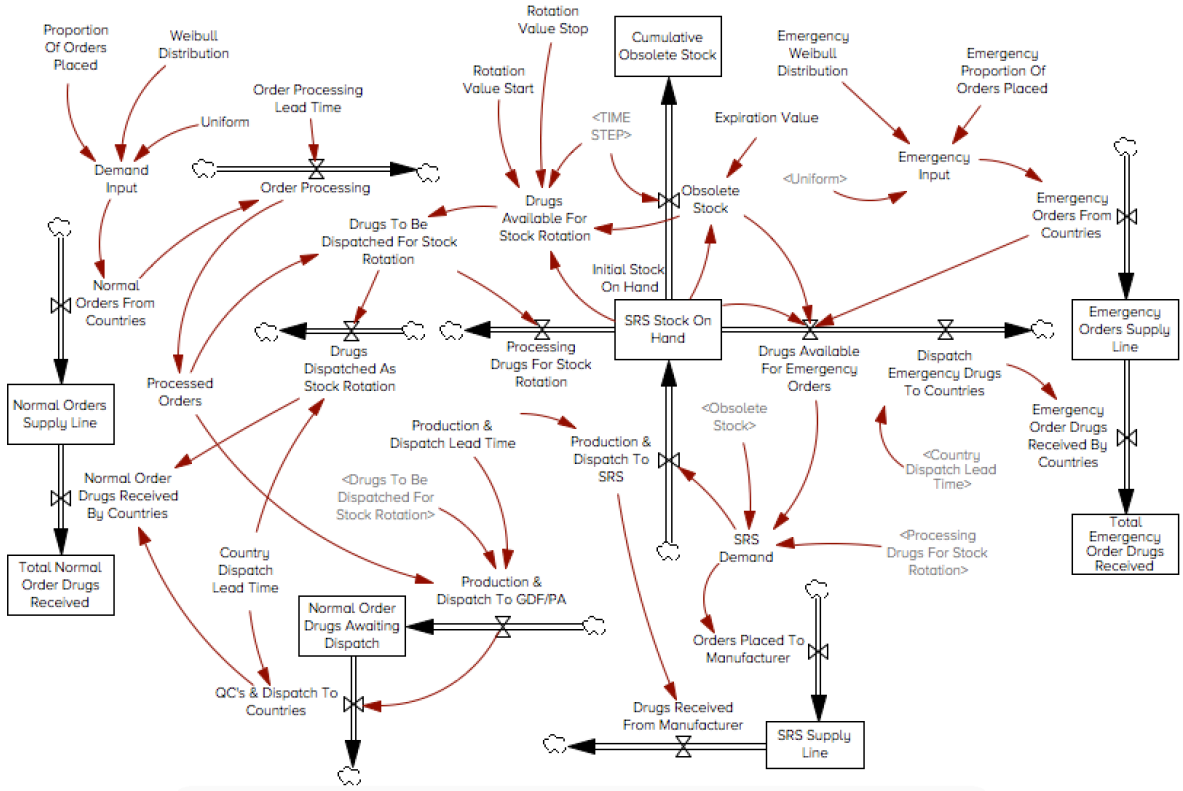

Figure 6.21: Stock and flow diagram of the main section of Model B.

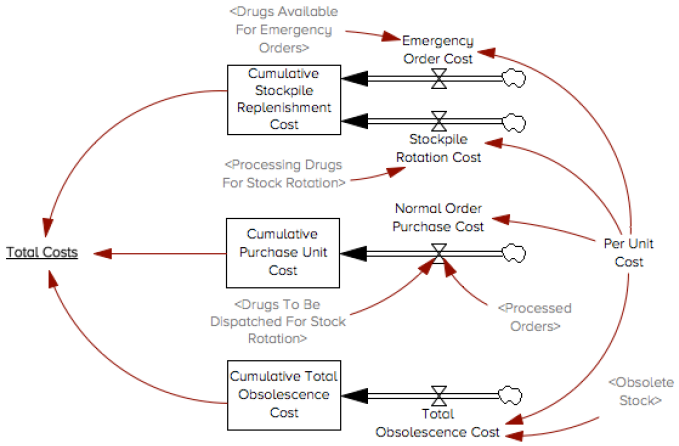

Figure 6.22: Stock and flow diagram of the cost section of Model B.

6.3.5.2 Model B: Characteristics and equations of elements

This section will summarise some of the challenging aspects of the modelling process of Model B. The complete modelling details for Model B, such as the list of variables that were used and the details and equations of each element, are provided in Appendix E, Section E.3.

The only information on the lead times that could be derived from the sources mentioned in Section 6.3.4 is the minimum, maximum and average waiting time for the

processes. Therefore, a triangular distribution was used to generate input values for the lead time. Additional minimum and maximum constraints were added to control the range of the output. Through a process of trial and error, these maximum and minimum values, as well as the parameters of the triangular distribution were adjusted until the summation of the separate lead times accurately represented the lead times in the historical data. More details are provided in the validation in Section 6.4 as well as in Appendix E, Section E.3.2.1.

Since the age of every individual unit cannot be tracked with system dynamics, the shelf life of the drugs is when they reach the stockpile from manufacturers is unknown in the model. However, with the use of a discrete queue function, the age of the drugs can be tracked once they are in the stockpile. The function also ensures that the stockpile functions on a first in, first out basis, meaning that the 'oldest' drugs are utilised first. This function is used to determine when drugs are considered obsolete and when drugs become eligible for rotation. It is assumed that when the drugs arrive at the stockpile they have a remaining shelf life of 22 months for capreomycin and cyclosorine and 34 months for kanamycin. Equations were applied to variables to ensure the following stockpile 'rules' with regard to emergency orders and stock rotation orders are implemented in the model:

- For capreomycin and cyloserine – if a drug has been in the stockpile for 4 months, it becomes eligible for stock rotation. However, to ensure that drugs have at least 10 months of shelf life remaining when reaching a country (as part of stock rotation), any drugs that have been in the stockpile for 9 months or longer, are no longer eligible for stock rotation. All of the drugs in the stockpile are eligible for emergency orders at all times, but a drug is considered obsolete after it has been in the stockpile for 13 months or longer. This is to ensure that the drugs dispatched as an emergency order, will have at least 6 months of shelf life remaining when it reaches the country.
- For kanamycin – if a drug has been in the stockpile for 10 months, it becomes eligible for stock rotation. However, to ensure that drugs have at least 10 months of shelf life remaining when reaching a country (as part of stock rotation), any drugs that have been in the stockpile for 21 months or longer, are no longer eligible for stock rotation. All of the drugs in the stockpile are eligible for emergency orders at all times, but a drug is considered obsolete after it has been in the stockpile for 25 months or longer. This is to ensure that the drugs dispatched as an emergency order, will have at least 6 months of shelf life remaining when it reaches the country.

To calculate the initial stock on hand, it was assumed that there are enough drugs for 5800 treatments and that the treatments entail several regimens (UNITAID, 2016b). The data from the PQR database was used to analyse each of the different SLD groups (refer to Table 2.1) in order to determine what proportion the formulations included in

the model represent in each group. It was found that 18.32% and 15.33% of all the Group 2 drugs, were for capreomycin and kanamycin, respectively, while 34% of the Group 4 drugs were for cycloserine. This would mean that of the 5800 available treatment courses for group 2, there are 1063 (18.32%) courses using capreomycin and 889 (15.33%) courses using kanamycin. Similarly, of the 5800 available treatment courses for Group 4, there are 1972 (34%) courses that includes the use of cycloserine. The average number of units that a patient will use for each of the formulations during a treatment course is 208 for capreomycin and kanamycin and 1560 for cycloserine (Lunte, 2012). Thus, it can be assumed that the stock on hand (in units) for the formulations is:

- 221 018 units of capreomycin (1063 x 208)
- 184 984 units of kanamycin (889 x 208)
- 3 076 643 units of cycloserine (1972 x 1560)

6.3.5.3 Model B: Assumptions

All of the assumptions for Model A, also apply to Model B. This subsection provides a summary of the new assumptions that were made with regard to the entities in Model B.

Assumptions about Manufacturers:

It is assumed that

- the manufacturer is one entity that fulfils both orders to replenish the stockpile and orders placed on behalf of countries. To enable the separate analysis of the orders placed on behalf of countries and the orders placed to replenish the stockpile, these are modelled as two separate processes.

Assumptions about Orders:

It is assumed that:

- emergency orders receive preference over orders for stock rotation.
- if an emergency order cannot be delivered in full, the stockpile will dispatch all of the available stock to the country, but the 'outstanding' drugs will not be put on backorder. Instead, it is assumed that the country will make other arrangements and the order is considered lost.
- for stock rotation, normal orders will only be dispatched via the SRS if the entire order can be fulfilled with the available stock.

Assumptions about the GDF and Stockpile:

It is assumed that:

- a base stock policy is currently applied at the SRS. An assumption is necessary as no information on the current operational policies of the SRS is available. Based on a base stock policy, it is assumed that if drugs are dispatched or removed from the stockpile (due to emergency orders, stock rotation or obsolescence), an order of identical size is placed to the manufacturers.

Assumptions about Costs

It is assumed that:

- the obsolescence costs are equal to the procurement cost (Li, Lim and Rodrigues, 2009).

Assumptions about Lead Times

It is assumed that:

- the lead time components, namely (i) order processing lead time, (ii) production and dispatch lead time, and (iii) country dispatch lead time, are the same for all three formulations.

6.3.6 Model C

Model B has been developed to represent the current system at a sufficient level of detail to allow for the evaluation of its performance. However, to quantify the impact of a buffer inventory as described in Section 5.7 the model will have to be adapted. Therefore, a new model (Model C) was developed by making adjustments to Model B to simulate the potential performance of a larger stockpile that is used to fulfil all of the demand from countries, instead of being used solely to fulfil emergency orders. Different inventory management policies can be applied to the model in order to determine which policy or policies are more effectively able to satisfy the demand and consolidate and time the orders for stockpile replenishment to smooth the demand to manufactures.

6.3.6.1 Model C: Stock and flow diagram

The complete stock and flow diagram for Model C also consists of two parts, namely (i) the main model, and (ii) the costs section. Both of these are illustrated in Figure 6.23 and Figure 6.24, respectively.

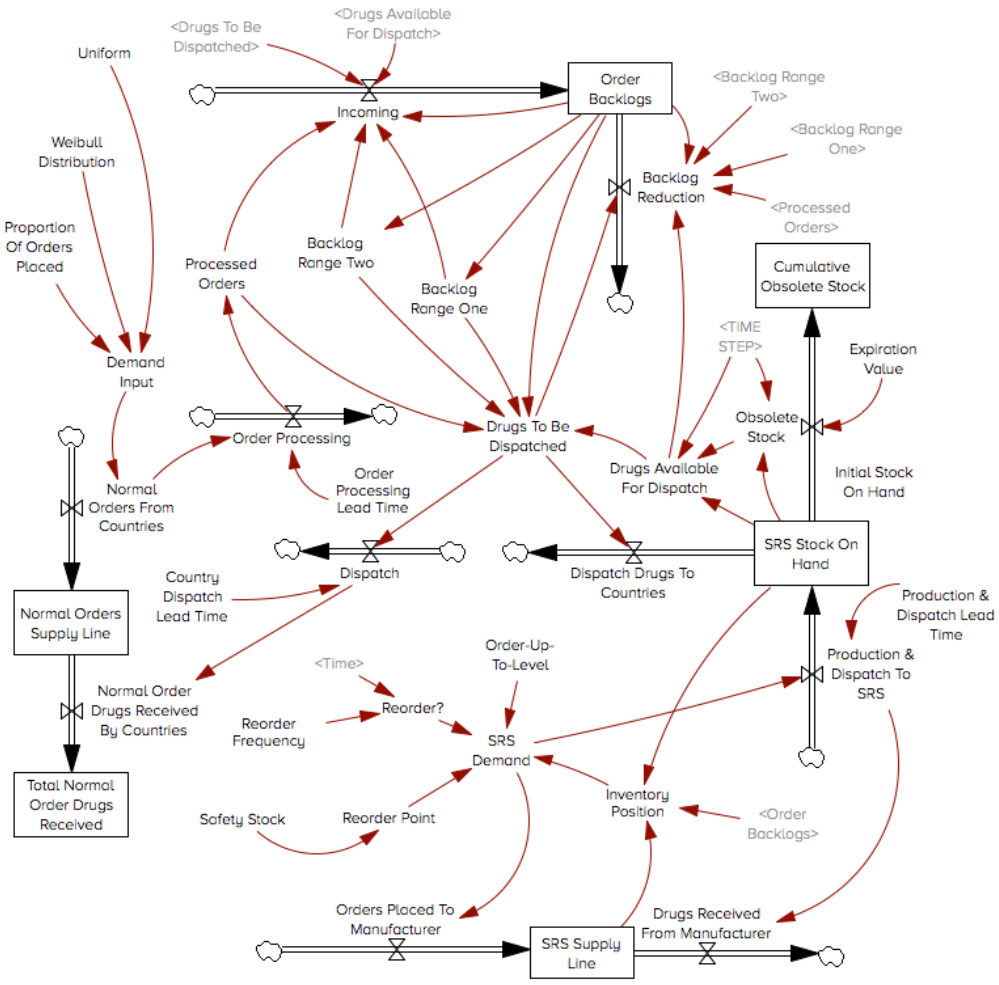

Figure 6.23: Stock and flow diagram of the main section of Model C.

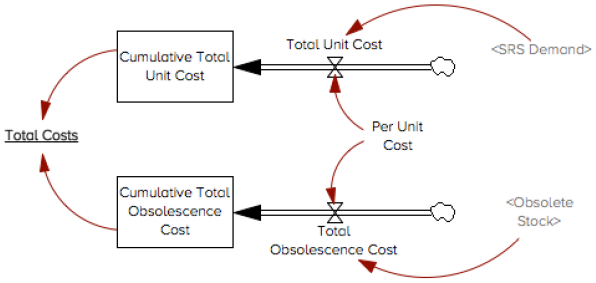

Figure 6.24: Stock and flow diagram of the cost section of Model C.

6.3.6.2 Model C: Characteristics and equations of elements

The complete modelling details for Model C, such as the list of variables that were used and the details and equations of each element, are provided in Appendix E, Section E.4. This section will highlight some of the aspects that proved challenging during the building process of Model C.

The biggest differences between Models B and C are:

- In Model C, all of the orders are fulfilled by the stockpile,
- emergency orders and stock rotation have been removed in Model C,

- backorders have been added in Model C, and
- in Model C, the SRS no longer follows a base stock policy. Instead, different inventory policies are experimented with.

Since all of the orders are fulfilled by the stockpile, it is assumed that there will no longer be emergency orders and stock rotation orders will longer be necessary. In Model B, when a country places a normal order, the GDF places an order of the exact size to manufacturers on behalf of the countries. Since all of the normal demand is always completely fulfilled, there are no backorders. Emergency orders, on the other hand, are fulfilled through the stockpile. If the order cannot be fulfilled by the stock-on-hand, it is not put on backorder, since an emergency situation requires that the drugs be delivered as soon as possible. It is assumed that if an emergency order cannot be fulfilled immediately through the stockpile, the country will make other arrangements and the order is considered lost (SDL supply chain SME, Personal communication, 16 February 2016). In Model C, on the other hand, all of the orders go through the stockpile and backlogs are now included for orders that cannot be fulfilled immediately.

System dynamics cannot track the individual orders that are added to the backlog separately, but instead pools these together. However, to overcome this modelling limitation, the backlogs are implemented as follows:

- The discrete queue function is used to track the age of incoming orders,
- a variable, ‘backlog range one’, is added to track the oldest backlogged units in the queue, and
- a second variable, ‘backlog range two’, is added to track the group of backlogged. units that are half the age of the oldest backlogged units,

This enables the model to keep track of two groups of units that have been backlogged the longest and second longest, respectively. This method was confirmed by a Vensim super administrator to be a suitable representation of backlogs for a system dynamics model. For a more accurate implementation of backlogged order tracking, a discrete-event simulation should be used instead.

6.3.6.3 Model C: Assumptions

Not all of the assumptions for Model A and B apply to Model C. Therefore, for the sake of completeness, the applicable assumptions of previous models and the new assumptions that were made with regard to the entities in Model C will be summarised below.

Assumptions about Manufacturers:

It is assumed that:

- the manufacturers have no additional orders other than that of the GDF and their PA. In reality, they may have orders waiting from other companies (that are not reported in the PQR database used for this research) which would cause additional delays in the supply chain.
- second-line anti-TB drugs are not kept in stock by any of the drug manufacturers. Thus it is assumed that once production is completed, manufacturers immediately dispatch the drugs to the GDF and their PA's DC.

Assumptions about Orders:

It is assumed that

- there will be no emergency orders, since the lead time between placing an order and receiving an order is reduced. The time that a country will have to wait now consists only of the order processing time and the dispatch time from the stockpile.
- all of the country demand is being fulfilled by the stockpile. Thus it is assumed that stock rotation will no longer be implemented to fulfil some of the normal orders.
- backlogged orders will receive preference over new incoming orders.
- if there is not sufficient stock to fulfil the backlogged order(s), but there is sufficient stock for the incoming order, the incoming order will be fulfilled.

Assumptions about Countries:

It is assumed that:

- no delays or other problems related to patent registrations or restrictions can delay an order. This is assumption is viewed as reasonable since countries requesting drugs are responsible for ensuring that the drugs comply with the country's legislation on patent registration or restrictions.
- countries place an order to cover drug needs and include a buffer stock in their procurement order (to cover drug consumption for the whole expected delivery time).

Assumptions about the GDF, Distribution Centre and Stockpile:

It is assumed that:

- drugs are dispatched from the stockpile based on a first-in-first-out basis.
- Since the stockpile does not currently function like depicted in Model C, different operational policies will be experimented with.

Assumptions about Costs

It is assumed that:

- the obsolescence costs are equal to the procurement cost (Li, Lim and Rodrigues, 2009).

Assumptions about Lead Times

It is assumed that:

- the lead time components, namely (i) order processing lead time, (ii) production and dispatch lead time, and (iii) country dispatch lead time, are the same for all three formulations.

6.4 Testing and validating the models

The aim of testing and validating the model, is to ensure that the model is accurate with regard to the purpose of the model. To assess the accuracy of the model, some of the most significant validation tests, as summarised by Sterman (2003), are applied. The eight tests that are applied are: (i) CLD Validity, (ii) parameter assessment, (iii) dimensional consistency, (iv) boundary adequacy, (v) structure assessment, (vi) behavioural reproduction, (vii) extreme conditions, and (viii) sensitivity analysis.

Additionally, a System Dynamics Modelling (SDM) document is provided, for each of the three models, in Appendix I. The SDM document provides a summary of each variable and equation and can therefore be used to understand the models, as well as to reproduce and expand the models.

6.4.1 CLD validity

The first validity test entails evaluating the CLD, since it is the first diagram to be constructed and is used as a baseline to construct the stock and flow diagrams. The constructed CLD is considered valid if it accurately represents the real-life system and can be used to support the execution of the aim and objectives. As previously mentioned, the key aim of this study is to evaluate the performance of the upstream segment of the supply chain and to measure the impact of certain changes to operational policies on this performance. The CLDs includes all the necessary parameters of the supply chain as well as the links and relationships between them, required to carry out the aim and objectives.

6.4.2 Parameter assessment

Parameter assessment refers to whether the values that are assigned to the parameters, both constants and variables, are consistent with the applicable data and information of the system. To ensure better results, there are two recommended

approaches to estimate the parameter values Sterman (2003), namely (i) statistical methods using numerical data; or, in cases where no data is available, (ii) judgment gained from literature, experience, interviews, etc. Both of these approaches can be used collectively by initially estimating a credible range based on knowledge of the system (judgemental) followed by statistical estimation to confirm the estimated range.

As illustrated throughout the modelling details of Model A, B and C in Appendix E, statistical methods were applied to the available historical data to assign values to constants, such as the shelf life, and estimate values for variables, such as the demand. Due to the lack of data, not all of the values could be determined through statistical estimation. The majority of the parameter values in Models B and C were estimated from what was gleaned from literature or derived from the available data. Possible correlations between different parameters were investigated and it was concluded that no correlations exist (Section 6.2.2.3). Despite these tests, however, it is possible that there are other unknown parameters (for example, the weather) that have an influence on the correlations, but that have been inadvertently omitted from the model. This is a typical limitation of a correlation analysis.

6.4.3 Dimensional consistency

Dimensional consistency entails the investigation of the links and relationships between the variables in the model by identifying their primary dimensions (for example, time) and their units of measure (for example, days or weeks) and tracing these dimensions as equations are constructed throughout the model.

To ensure dimensional consistency, each of the variables and equations in the models are subjected to Vensim's 'unit-check' function, that confirms whether the units on the equation's right-hand side are consistent with the units on the left-hand side. Vensim indicated no errors regarding the dimensions and units of both Model A and B. Furthermore, each equation was analysed separately to identify any factors that could discredit the dimensional consistency.

6.4.4 Boundary adequacy

Boundary adequacy involves the assessment of the model boundaries and whether these are suitable for the purpose of the study. The model boundaries were discussed in Section 6.1.2.1 and illustrated in Figure 6.2. To assess the adequacy of the boundaries, some of the feedbacks that were omitted from the models were investigated to assess the potential impact these could have on the model. Since there are several omitted feedbacks, only those that could be significant to the aim of the model were investigated.

Some of the upstream stages such as raw material sourcing, starting material manufacturing and API manufacturing were omitted due to a lack of data. Including

these stages in the models could perhaps alter the dynamics of the models. For example, since the finished product manufacturers for SLDs are typically order-driven, they only order the APIs once an order for drugs has been received. The API manufacturers therefore have a direct impact on how long a country has to wait for an order to be fulfilled. Therefore, if the omitted upstream stages were represented separately in the model, the different lead times of each stage could provide a more dynamic and realistic model. Nonetheless, the lead times used in the models, represent the total time between placing an order and receiving an order, and include the delay caused by API manufacturers. Therefore, although the individual stages are not represented in the models through stocks, flows and variables, they are incorporated to some extent through the lead time of the finished product manufacturers.

Furthermore, there are various concepts related to the manufacturers and manufacturing process that were omitted, such as batch sizes, manufacturing capacity, economic order size, etc. Feedback loops associated with these concepts could impact the dynamics of the models. However, as discussed in Section 6.1.2.2, the lack of data on manufacturers prevents the inclusion of these details in the model.

6.4.5 Structure assessment

Structure assessment refers to whether the model corresponds with the knowledge of the real-world system, relevant to the aim of the model. This includes aspects such as the model conformance to physical realities such as the conservation of flows, the accumulation and decrease of stocks, and the practicality of decision rules.

A thorough investigation of the stocks and flows confirms that all of the model inputs are balanced with outputs. All of the demand from countries integrated into the models are accounted for by being fulfilled by manufacturers or the stockpile. Applicable variables, for example stock and costs, were monitored to ensure that they remain positive throughout the simulation, and that the outflows from all stocks approach zero as the stock approaches zero. The number of drugs received by countries is no more than the amount ordered. The number of drugs produced by the manufacturers is no more than what was ordered and the number of drugs dispatched from the stockpile is no more than what was required.

6.4.6 Behaviour reproduction

The goal of behaviour reproduction is to identify errors and flaws in the model and to determine whether they will affect the aim of the model. It is important to note that all models are simplified representations of the real-world system and therefore differ from the real-world system in several ways. Since the SLD supply chain is exceptionally dynamic, the models will not be able to reproduce the behaviour of the real system with 100% accuracy. To determine whether the models behave similarly to the real-world

system, the following aspects were analysed: (i) Demand; (ii) Number of orders placed per week; (iii) Lead time; and (iv) Costs

6.4.6.1 Demand

Sterman (2003) and Robinson (1997) state that the most common methods to assess the behaviour reproduction are to compare the descriptive statistics of historical data and the model data, as well as to visually compare the distribution of the data sets. The comparisons for each formulation are provided in Appendix F, Section F.1. In addition to the comparisons, a Mann-Whitney U test was performed, for each of the formulations, to determine whether there are statistically significant differences between the historical and modelled data sets. From the test results it can be concluded that all differences are too small to be statistically significant and that the modelled data accurately represents the historical data.

6.4.6.2 Number of orders placed per week

The number of orders placed per week (for the weeks where an order was in fact placed) during the five-year simulation was compared to the historical data. The results are summarised in Table 6.6.

The results show that the number of orders placed per week in the simulation, are very similar to the historical data.

Table 6.6: Number of orders placed per week for model output and historical data.

	Number of Orders placed	Probability from Data	Probability from Model Output
Capreomycin	1 order	0.5736	0.5736
	2 orders	0.2226	0.2151
	3 orders	0.0566	0.0943
	4 orders	0.0151	0.0377
Kanamycin	1 order	0.4189	0.4491
	2 orders	0.0792	0.0792
	3 orders	0.0226	0.0264
	4 orders	0.0113	0.0075
Cycloserine	1 order	0.7210	0.7472
	2 orders	0.3360	0.3962
	3 orders	0.1510	0.1358
	4 orders	0.0450	0.0528

6.4.6.3 Lead time

As previously mentioned, there are several limitations associated with the modelling of the lead time. Since the lead time in Model B and C is separated into three parts, there is no historical data available to compare the modelled data with. Therefore, there is

no accurate way to assess whether it replicates the behaviour of the real system. Although the separate lead times cannot be analysed, the summation of the separate lead times could be compared with the historical data to demonstrate whether the total lead time replicates the real-world behaviour.

Another limitation of the lead time is that there are several outliers in the historical data that are not present in the models. This is evident in the comparison of the descriptive statistics for the historical data and modelled data, as summarised in Table 6.7. As can be derived from the table, the outliers lead to a large difference between the maximum and minimum values. When disregarding the outliers, the modelled data represents the historical data more accurately, as depicted in the last columns of the table. This is also visually illustrated in Figure 6.25.

Table 6.7: Total lead time for model output and historical data.

Statistic	Model Output	Hist. Data	% Diff	Hist. Data (No outliers)	% Diff
Mean	40.21	36.24	10.97%	39.93	-0.69%
Standard Error	0.56	0.69	-18.36%	0.57	2.14%
Median	36.43	32.29	12.84%	36.14	-0.79%
Standard Deviation	14.89	21.19	-29.73%	15.21	2.14%
Minimum	12.85	8.14	57.82%	13.43	4.51%
Maximum	81.22	159.00	-48.92%	82.14	1.13%
Sum	28 149.44	34 245.29	-17.80%	27954.43	-0.69%

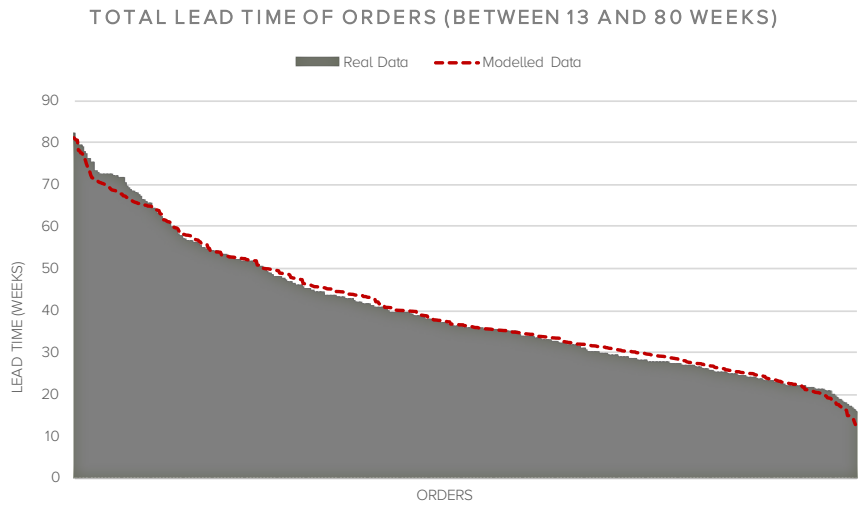

Figure 6.25: Graph comparing the lead time of model output and historical data.

6.4.6.4 Costs

Cycloserine has the highest costs with 57% of the total expenses, while kanamycin has the least with 14% of the total expenses. The ratio of the costs for the formulations is

illustrated in Figure 6.26. This is similar to that of the real-world procurement values in 2012 and 2013, as discussed in Section 6.1.2.3.

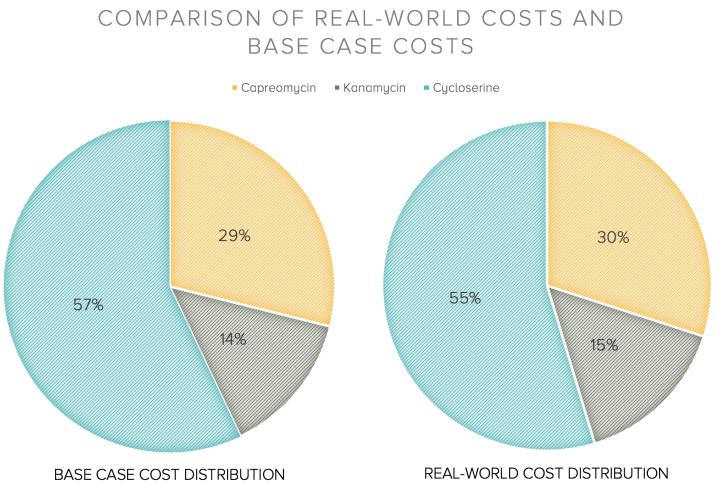

Figure 6.26: Comparison of the distribution of real-wold costs and base case costs.

6.4.6.5 Plausibility

The models behave as they expected to and exhibit the same difficult behaviour as the real-world system, including long lead times and demand that occurs in irregular amounts and at unpredictable time intervals.

6.4.7 Extreme conditions

To assess whether the models and their equations respond as expected, extreme values were assigned to some of the parameters. A sudden increase and sudden decrease of both the demand and lead times were implemented both separately and in combination, while monitoring the behaviour of the models. The models behaved as expected, for example a sudden decrease in the emergency order demand caused the stockpile to deplete faster while a decrease in overall demand caused high levels of obsolete stock. Furthermore, the test confirms that the reinforcing and balancing loops works as they should, since the model returned to base conditions after the shock of sudden increases or decreases in parameters.

6.4.8 Sensitivity analysis

A sensitivity analysis is conducted to identify the most sensitive parameters. If a parameter is found to be particularly sensitive, the maximum feasible effort is put into ensuring its accurate estimation. Additionally, parameters to which they are particularly sensitive should be highlighted during the reporting of results. Only the most important parameters, namely the demand and the lead time will be assessed. The parameters will be adjusted by approximately 10% to measure the impact that such small changes will have on the system. The results of the sensitivity analysis for Model B, capreomycin are summarised in Table 6.8, while the full set of results for all models and formulations

can be found in Appendix F, Section F.2. For each of the adjusted cases (increase or decrease in demand and lead time), the following values over the five-year simulation are compared with the base case values:

i. the total obsolete stock,
ii. the total number of drugs received from manufacturers for normal orders,
iii. the total number of drugs delivered stock rotation orders received,
iv. the total number of drugs delivered for emergency orders, and
v. the stock on hand at the end of the simulation period.

For the base case, a base stock policy is assumed. (I.e. it is assumed that if drugs are removed from the SRS due to obsolescence, stock rotation or emergency orders, an order of the same size is placed to the manufacturers to replenish the inventory to the desired level.) The percentage that the value differ from the base case is given in brackets below each value.

Table 6.8: Sensitivity analysis results for Model B, capreomycin.

Capreomycin (Model B)	Total obsolete stock	Total drugs received from manufacturers	Total drugs received from SRS	Total emergency order drugs delivered	Total stock on hand
Base Case	0	6 603 560	1 295 330	406 100	88 510
Increase demand	0 (0%)	7 032 000 (6%)	1 222 000 (-6%)	432 800 (7%)	95 200 (8%)
Decrease demand	0 (0%)	6 781 000 (3%)	1 304 000 (1%)	395 000 (-3%)	96 300 (9%)
Increase lead times	0 (0%)	6 734 000 (2%)	1 213 000 (-6%)	388 600 (-4%)	97 400 (10%)
Decrease lead times	0 (0%)	6 665 000 (1%)	1 306 000 (1%)	401 300 (-1%)	87 880 (-1%)

As depicted in table, an increase in the demand and lead time has the most significant effect on the variables. Furthermore, the variable that is affected the most by the changes, is the stock on hand. These findings apply to all three formulations and all the models.

6.5 Identifying and implementing scenarios

Model B will be evaluated to quantify the performance of the current system, while scenario modelling will be applied to Model C. The goal of the scenario modelling is to determine what policies should be implemented to allow the prevention of stock-outs at countries and to combine and time orders to decrease order variability to

manufactures. The scenarios will consist of various inventory policies that will be applied to the model

The identified scenarios, as well as the implementation and results will be described in more detail in Chapter 7.

6.6 Conclusion: Dynamic model development

The chapter provided a description of the modelling process that was followed to build three models. The problem and its boundaries were defined, followed by an analysis of the data to provide a better understanding of the system. After CLDs were developed, the stock and flow diagrams, assumptions and important characteristics of each of the three models were presented. The models were validated by performing various validation tests. Finally, the reasoning behind the scenario testing to be implemented using Model C was briefly discussed.

The next chapter will provide a more detailed description of the scenarios that will be implemented and the measures and metrics that will be used to evaluate the performance. The analysis methodology and results are also presented, followed by a discussion of the general research findings.

Chapter 7:
Analysis and results

"We call things we don't understand complex, but that means we haven't found a good way of thinking about them."

- Tsutomu Shimomura (Scientist and computer security expert)

The previous chapter included a discussion of the modelling process that was followed to build the system dynamics simulation models. This chapter will present the analysis and results of the current system (the base case) as well as several alternative stockpile scenarios. The evaluation criteria that will be used to measure performance is described, followed by the evaluation of the base case. After a summary of the scenarios to be analysed, the results of the scenario modelling are discussed and general findings concluded from the results are provided.

7.1 Evaluation criteria

Evaluation criteria are used to determine to what extent alternative scenarios or solutions meet the required standards or objectives by comparing their trade-offs, strengths and weaknesses (Maani and Cavana, 2012). The evaluation criteria comprise of a set of performance measures and metrics that will be used to communicate the results of the scenario modelling and the insights that stem from this.

As discussed in Section 6.1.1, one of the main objectives of the modelling is to assess the impact that changes to the operational policies will have on the availability of stock for countries and the variability of the demand to the manufacturers. Therefore, the first two performance measures are stock performance and order variability performance. Furthermore, since cost is an important aspect in any supply chain, a third performance measure is also added to measure the impact on costs.

7.1.1 Stock performance

A significant aspect of stock performance, applicable to this study, is how well the stock is being used to satisfy customer demand. To evaluate this, the fraction of the total demand that was not fulfilled immediately will be measured. The metrics for stock performance will therefore include:

i. the fraction of orders that were backlogged;
ii. the total volume of orders that were backlogged; and
iii. the average and maximum time duration that an order is backlogged for.

7.1.2 Order variability performance

The order variability performance metrics will be used to evaluate whether the scenarios will benefit the manufacturers in terms of decreasing order variability. Two metrics will be utilised:

i. the standard deviation of the order size for each individual order (σ_{os}); and
ii. the standard deviation of the volume of orders placed per month (σ_{mo}).

It is beneficial to manufacturers if both these deviations are low. For example, individual order sizes that are the same size, will not benefit the manufacturer if they are placed at irregular time intervals.

7.1.3 Cost performance

The MDR-TB SLD supply chain is predominantly a donor-funded supply chain where funding is used to benefit populations and patients in need. The more funds that are available, the more people can benefit from treatment. Therefore, cost performance is an important part of the evaluation criteria. There are several aspects contributing to costs, including holding costs, logistical costs, shortage costs, procurement costs and obsolescence costs. These are discussed in the following subsections.

7.1.3.1 Holding costs

In the base case, the stockpile receives funding to be kept at the same level, which causes the holding costs (C_H) to remain constant. Therefore, the holding costs are seen as a fixed cost and typically does not play an important role when measuring the cost performance of the current stockpile (SDL supply chain SME, Personal communication, 16 February 2016).

For the implementation of a large buffer inventory, however, holding costs will be taken into consideration. The holding costs will be calculated on a monthly basis and will be assumed to be 25% of the value of the average inventory on hand in that month (Hou, 2013; Vermorel, 2013).

7.1.3.2 Logistical costs

Although logistical costs are an important factor, these cannot be included in the model since the countries are grouped into a single entity, as discussed in Section 6.3.2. The individual locations of the countries and their distance from the stockpile are not taken into account, making the inclusion of logistical costs infeasible. This restriction is not considered to pose a significant limitation on the usefulness of the modelling results as it is unlikely that the various inventory management policies that are being evaluated will have a significant impact on these logistical costs.

7.1.3.3 Shortage costs

Although stock-outs can occur at the stockpile, the GDF assumes that the country should prepare for this probability and therefore have their own safety stock. Therefore, there are no shortage costs or backorder costs (SDL supply chain SME, Personal communication, 16 February 2016).

7.1.3.4 Procurement costs

The procurement costs (C_p) are, as the name implies, the costs related to the purchasing of the drugs from manufacturers. In Model B, the procurement costs will comprise of the costs of drugs purchased for normal orders placed by the GDF on behalf of countries and for orders placed to replenish the stockpile. In Model C, all orders go through the SRS and the only procurement cost will be for the orders made to replenish the stockpile.

7.1.3.5 Obsolescence costs

Obsolescence costs (C_O), are the cost of stock that is 'lost' due to the shelf life being exceeded. An excessively large stockpile will be able to fulfil all orders at any time, but is likely to lead to high levels of excess stock that will become obsolete. It is therefore important to consider obsolescence costs.

7.1.3.6 Total costs

In summary, the only costs to be included are the procurement costs, holding costs and obsolescence costs. The total cost is therefore given by:

$$C_T = C_P + C_H + C_O \tag{7.1}$$

7.2 Performance of base case

Before any scenarios can be implemented and analysed, the performance of the base case (Model B) will be analysed. The stock performance, order variability performance and cost performance will be discussed separately. For ease of reference, the results of the base case will be repeated in each of the tables that summarise the results of different scenarios.

7.2.1 Stock performance

As previously mentioned, there are no backorders in Model B; therefore, the fraction of orders that were backlogged as well as the average and maximum time that an order is backlogged cannot be measured. Instead, the amount of emergency orders that were not fulfilled in full will be considered. During the five-year simulation, all of the emergency orders for kanamycin and cycloserine were 100% fulfilled. For capreomycin there was only one emergency order which could not be fulfilled completely, however, 51% of that order quantity was dispatched.

7.2.2 Order variability performance

In the base case model, there are two types of orders that are placed to manufacturers, namely normal orders placed by the GDF on behalf of countries and orders placed to replenish the stockpile. The order variability performance metrics for both order types, as well as for the total orders placed to manufacturers are provided in Table 7.1.

Table 7.1: Order variability performance of base case.

		Capreomycin	Kanamycin	Cycloserine
σ_{os}	Normal Orders	58 647	87 424	958 925
	Stockpile Orders	11 916	7 412	173 176
	All Orders	**59 466**	**88 219**	**976 715**
σ_{mo}	Normal Orders	129 050	172 988	1 780 729
	Stockpile Orders	23 389	13 287	362 617
	All Orders	**132 118**	**173 929**	**1 865 129**

Both the standard deviation of the order size for each individual order (σ_{os}) and the standard deviation of the volume of orders placed per month (σ_{mo}) are exceptionally high. The reason for the high variation in order sizes, is ascribed to the fact that orders are placed from different countries, each with different demand. For example, a high-burden country with a large population will undoubtedly place a larger order than a low-burden country with a small population. The high value of the standard deviation of the volume of orders placed per month (σ_{mo}) indicates that, regardless of the separate order types, the total order quantities per month vary considerably. This is also clear from the graphical illustration, in Figure 7.1 to Figure 7.3, of the total quantity of each drug ordered per month.

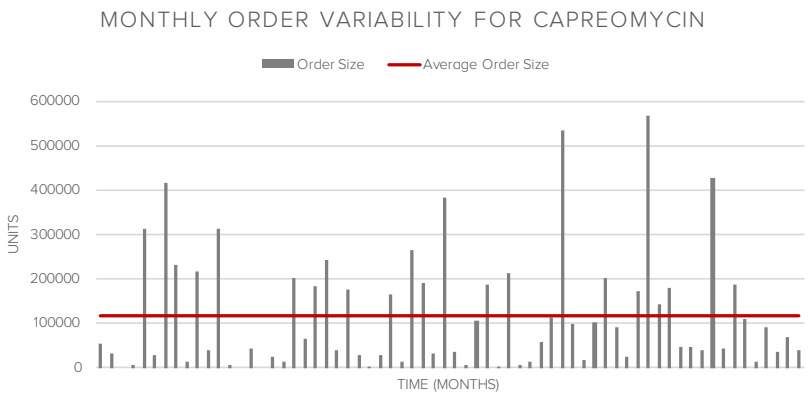

Figure 7.1: Base case order variability of capreomycin.

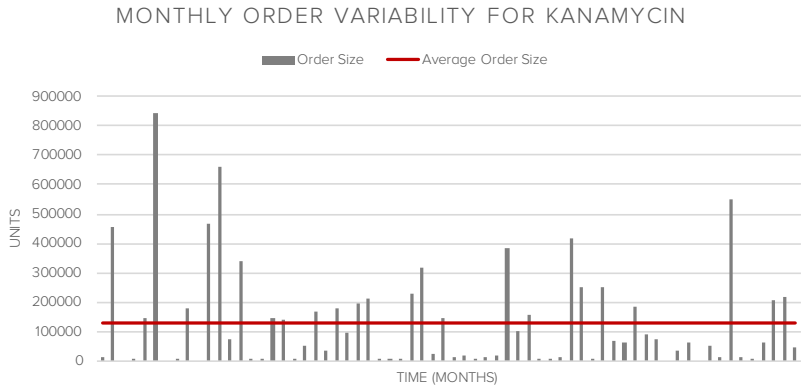

Figure 7.2: Base case order variability of kanamycin.

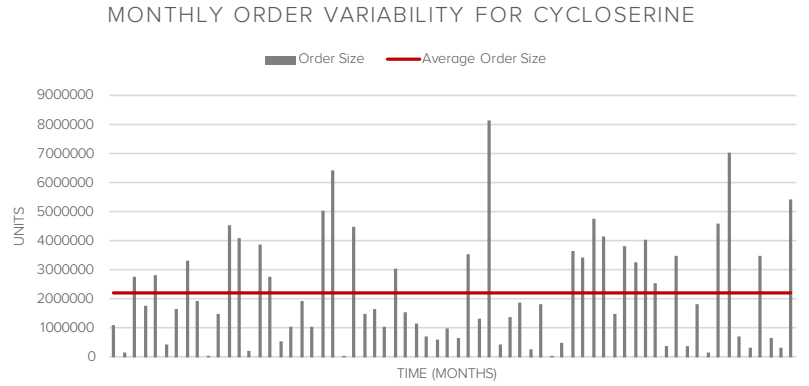

Figure 7.3: Base case order variability of cycloserine.

7.2.3 Cost performance

For the base case, the procurement costs consist of the cost to manufacture drugs for normal orders, which are not fulfilled through stock rotation, as well as the cost to replenish the stockpile due to the outgoing orders for emergencies and stock rotation. In order to compare the total cost of the scenarios with the total cost of the base case, a holding cost for the base case will be calculated based on the assumption that the holding cost remain constant, as discussed in Section 7.1.3.1. All of the costs are provided

in Table 7.2. As shown in the table, there are no obsolescence costs with the base case, as all of the stock were rotated well before they reached their expiration date.

Table 7.2: Cost performance of base case during a five-year simulation.

	Capreomycin	Kanamycin	Cycloserine
Emergency Order Costs	$2 332 182	$389 984	$4 277 763
Stockpile Rotation Costs	$5 782 832	$1 349 844	$7 273 228
Normal Order Costs	$35 026 266	$19 266 897	$73 649 431
Obsolescence Costs	$0.00	$0.00	$0.00
Holding Costs	$18 764 428	$7 186 628	$25 382 280
Total Costs	**$61 905 708**	**$28 193 353**	**$110 582 702**

7.3 Scenario planning and modelling

Scenario planning can be seen as the process of visualising what future conditions are possible and what the consequences of these conditions will be. This section provides a description of the scenarios that are formulated and evaluated. The scenarios will consist of various inventory policies that will be applied to Model C, in order to determine the likely impact of each policy on the variability of the demand to the suppliers and the availability of stock for countries.

7.3.1 Inventory policies

In a typical commercial supply chain, an organisation wants to satisfy customer demand in the shortest possible time. When an order is placed by the organisation to the manufacturers, there is a time delay (lead time) between placing the order and receiving the goods that were ordered. For an organisation to be able to satisfy incoming demand during this lead time, on-hand inventory is required.

An inventory policy is a set of boundaries and guidelines that serve as a framework when making decisions regarding inventory and inventory management, such as when to order, how regularly to order, how much to order, the level of safety stock, etc. Two factors that have a large influence on the amount of inventory that is required, are lead time variability and demand variability. The greater the variability, the greater the amount of inventory required.

As previously mentioned, the MDR-TB SLD supply chain experiences high variability in terms of both demand and lead time. Therefore, different inventory policies will be applied and evaluated to determine how they perform based on the evaluation criteria discussed in Section 7.1. The remainder of this section will discuss the concepts associated with inventory policies, namely (i) the reorder point, s; (ii) the order-up-to-

level, S; (iii) the reorder frequency, R; and (iv) the reorder quantity, Q. A summary of the alternative values for each concept will be provided at the end of the section. The inventory policy scenarios will be applied to Model C, where the SRS is used to fulfil all of the orders for SLDs. Each of the policies' performance will evaluated individually, compared with each other and compared with the base case. The scenarios will consist of the following inventory policies:

- (s, S) policy;
- (R, S) policy;
- (R, s, S) policy;
- (s, Q) policy; and
- (R, s, Q) policy.

7.3.1.1 Reorder point

The reorder point is the stock level at which a new order should be placed to the manufacturer to replenish the stock. The equation for calculating the reorder point (s) is (Jacobs and Chase, 2014):

$$s = (\mu_D \times \mu_{LT}) + SS\,, \tag{7.2}$$

where μ_D is the average demand, μ_{LT} the average lead time, and SS the safety stock.

Safety stock is a level of extra stock that is held to mitigate the risk of stock-outs caused by factors such as unpredictable demand, inaccurate forecasting and inconsistent lead times. There are several methods to determine the required level of safety stock, each with its own benefits and drawbacks. It can be determined from time-based calculations (such as the percentage growth in demand over a time period) or from statistical and mathematical calculations using the theory of probability. It can also be set at a fixed level based purely on managerial judgment, usually informed by forecasted stock levels.

For the purpose of this study, four alternatives for safety stock will be evaluated. The first three alternatives will be a fixed value based on the very basic safety stock equation shown in (7.3) (Jacobs and Chase, 2014). In this method, a safety factor (SF) is added to the average demand to cope with the variations of the manufacturer lead time and country demand. A typical safety factor is 1.5; however, with the high variations in this study, a larger safety factor is required. Consequently, a safety factor of 3, 4.5 and 6 will be evaluated.

$$SS = \mu_D \times SF \tag{7.3}$$

The fourth alternative will be based on a desired service level and the fact that the consumption and lead time pattern both have large fluctuations. The equation is given as (King, 2011):

$$SS = z\sqrt{(\mu_D + \sigma_L)^2 + (\mu_{LT} + \sigma_D^2)}\,, \tag{7.4}$$

where z is the safety stock coverage factor based on the service level, σ_L is the standard deviation of the lead time and σ_D the standard deviation of the demand. Since the stockpile aims to never have a stock-out, a service level of 100% is desired. The value of z for a service level of 99.99% is 3.72.

7.3.1.2 Order-up-to-level (reorder maximum)

The order-up-to-level (S) is the maximum inventory position that is allowed and can be seen as the target level of stock to have on hand. The inventory position is dependent on the inventory on hand, backlogs and the inventory on order, which is defined as the total drugs that have been ordered from manufacturers, but not yet received. The formula for inventory position (IP) is given as (Caplice, 2016a):

$$IP = Inventory\ On\ Order + Inventory\ On\ Hand - Backlogs \tag{7.5}$$

The order-up-to-level and inventory position determines how much should be ordered from the manufacturer. The formula for the order quantity is (Caplice, 2016a):

$$Order\ quantity = S - IP \tag{7.6}$$

The order-up-to-level is typically calculated by multiplying the average demand and average lead time and adding some safety amount. For the purpose of this study, two alternatives for the order-up-to-level will be evaluated. The first alternative is based on a basic formula for the order-up-to-level, given by (Jacobs and Chase, 2014):

$$S = (\mu_D \times \mu_{LT}) \times SF \tag{7.7}$$

In this formula the product of the average demand and average lead time is multiplied with a safety factor. For this study, a safety factor of 2.5 is chosen, based on the high variability of the demand and lead time. The second alternative to calculate the order-up-to-level, is based on a desired service level, similar to (7.4) for safety stock. The formula is (Jacobs and Chase, 2014):

$$S = (\mu_D \times \mu_{LT}) + z \times \sigma_D \times \sqrt{\mu_{LT}} \tag{7.8}$$

Here the safety amount is based on the desired service level and the deviation of the demand over the average lead time. As with the safety stock equation, a z value of 3.72 will be used, corresponding to a service level of 99.99%.

7.3.1.3 Reorder frequency

Reorder frequency refers to the regularity of review periods to determine whether or not to place an order to manufacturers. There are two groups of inventory control policies based on the reorder frequency, namely continuous review policies and periodic review policies. With continuous review policies, an order can be placed at any

time, usually when the inventory level reaches some threshold. In contrast, periodic review policies are time-based and orders are only placed every R time periods.

Four alternative reorder frequencies will be evaluated in the scenarios, including every week, two weeks, three weeks and four weeks. It should be noted, that since the model follows a weekly time step, an R value of one week will function the same as a continuous review policy. For example, in the model, a continuous (s, S) policy will generate the same results as an (R, s, S) policy if $R = 1$.

7.3.1.4 Reorder quantity

In this model, the SRS demand is analogous to the reorder quantity (Q). A common method for calculating the reorder quantity is by determining the economic order quantity (EOQ):

$$EOQ = \sqrt{\frac{2 \times D \times C_O}{C_H}}\ , \tag{7.9}$$

where D is the demand, C_O the ordering costs and C_H the holding costs. The EOQ is used to calculate the order quantity that will minimise the total holding and ordering costs. It is based on the assumption that the ordering cost is constant, the demand rate is evenly dispersed and known, and the lead time is known and fixed. These assumptions do not hold for the supply chain being analysed in this study and will therefore not be considered as a valid value for the reorder quantity.

Another method to calculate the reorder quantity, is to base the amount to be ordered on a forecast of the demand. Since no trend or seasonality is present in the model, the best method of forecasting to use is simple exponential smoothing, as discussed in Section 3.5. Exponential smoothing is calculated as:

$$Q = \alpha(1-\alpha)^0 x_t + \alpha(1-\alpha)^1 x_{t-1} + \alpha(1-\alpha)^2 x_{t-2} + \cdots + \alpha(1-\alpha)^n x_{t-n} \tag{7.10}$$

where α is the smoothing factor, which determines the weight that is assigned to the latest data. As $\alpha \to 1$, the latest data has a greater impact and the forecast becomes more volatile. In contrast, as $\alpha \to 0$, the latest data has less of an impact and the forecast is more cumulative and smooth. Therefore, three alternative smoothing factors will be evaluated during the scenario modelling, namely 0.1, 0.5 and 0.9, as suggested by Coetzee (2015) and Caplice (2016a).

In the (s, S), (R, S) and (R, s, S) policies, the reorder quantity will be calculated with (7.6), as stated in the previous section.

7.3.2 Summary of inventory policy scenarios

Table 7.3 provides a summary of the alternative equations that will be used for the reorder point, order-up-to-level, reorder frequency and reorder quantity.

Table 7.3: Summary of equations for inventory policy variables.

Reorder Point (s)
$s_1 = (\mu_D \times \mu_{LT}) + (\mu_D \times 3)$
$s_2 = (\mu_D \times \mu_{LT}) + (\mu_D \times 4.5)$
$s_3 = (\mu_D \times \mu_{LT}) + (\mu_D \times 6)$
$s_4 = (\mu_D \times \mu_{LT}) + 3.72\sqrt{(\mu_D + \sigma_L)^2 + (\mu_{LT} + \sigma_D^2)}$
Order-Up-To-Level (S)
$S_1 = (\mu_D \times \mu_{LT}) + 3.72 \times \sigma_D \times \sqrt{\mu_{LT}}$
$S_2 = (\mu_D \times \mu_{LT}) \times 2.5$
Reorder Frequency (R)
$R_1 = 1$
$R_2 = 2$
$R_3 = 3$
$R_4 = 4$
Reorder Quantity (Q)
$Q_1 =$ Exponential smoothing, with $\alpha = 0.1$
$Q_2 =$ Exponential smoothing, with $\alpha = 0.5$
$Q_3 =$ Exponential smoothing, with $\alpha = 0.9$

Each of the alternative values in Table 7.3 will be applied to each of the five inventory policies, where applicable. This results in:

- 8 possible combinations of s and S for the (s, S) policy;
- 8 possible combinations of R and S for the (R, S) policy;
- 32 possible combinations of R, s and S for the (R, s, S) policy;
- 12 possible combinations of s and Q for the (s, Q) policy; and
- 48 possible combinations of R, s and Q for the (R, s, Q) policy.

As mentioned in Section 7.3.1.3, an R value of one week will function in an identical manner to a continuous review policy, since the model follows a weekly time step. Therefore, any combination with R_1 in the (R, s, S) and (R, s, Q) policy can be omitted since it will yield the same results as the (s, S) and (s, Q) policy where the same values of s and S and s and Q are used, respectively. This reduces the number of scenarios to be modelled to 88, all of which are summarised in Appendix G.

It should also be noted that the reorder point s_4, is larger than both order-up-to-levels. Therefore, in scenarios where s_4 is applied to a (s, S) or (R, s, S) policy, the inventory position will always be below the order-up-to-level and an order will be placed to manufacturers at every opportunity.

7.4 Scenario results

The impact that the various proposed inventory management policies have on the performance of Model C will be discussed in this section. As previously mentioned, this will be communicated through the performance measures and metrics that were identified and discussed in Section 7.1. The performance of each policy and its alternatives will be compared to the performance of the base case, where applicable. The full set of results for capreomycin, kanamycin and cycloserine are provided in Appendix H. However, to illustrate how these results should be interpreted, the scenarios that exhibited the best and the worst performance, in the case of capreomycin, will be discussed. This will be done separately for each performance measure.

7.4.1 Stock performance

The following tables provides a summary of the stock performance metrics that measures how well the stock is being used to satisfy demand. The results include the fraction of orders that were backlogged, the volume of the backlog as well as the average and maximum length of time that an order is backlogged. The policies that resulted in the least number of backlogs and where these backlogs were fulfilled in the shortest amount of time, are summarised in Table 7.4. These policies also resulted in the lowest total volume of the backlog. The majority of the policies in the table are (R, S) policies, with 7 of the 8 (R, S) scenarios included in the table. It is interesting to note, that of all of the policies that were modelled, the (R, S) policy is the only one that does not implement a reorder point s. The (R, S) policy attempts to replenish the stockpile to its full capacity, every R periods, while the other policies dictate that an order is only placed when the stockpile is below the reorder point s.

Table 7.4: Scenario results – Capreomycin high stock performance policies.

Policy #	R	s	S	Q	%BLs	μ_{BL_Age}	Max_{BL_Age}	Total Vol.
(s,S) 5		s3	S1		2.63%	2.44	6	1 859 470
(R,S) 1	R1		S1		2.63%	2.44	6	722 871
(R,S) 2	R1		S2		2.11%	5.68	14	651 444
(R,S) 3	R2		S1		2.26%	3.89	11	1 006 581
(R,S) 5	R3		S1		1.58%	2.31	5	159 302
(R,S) 6	R3		S2		5.79%	4.41	13	1 000 613
(R,S) 7	R4		S1		1.58%	2.57	5	252 229
(s,Q) 11		s4		Q2	5.26%	3.14	8	1 023 422
(R,s,Q) 24	R3	s4		Q3	4.74%	4.00	11	876 604
(R,s,Q) 36	R4	s4		Q3	4.70%	3.00	9	1 003 628

The policies that resulted in the most backlogs are summarised in Table 7.5. These policies also have the highest average and maximum waiting time until a backlogged order is fulfilled. All of the policies listed in Table 7.5, are (R, s, Q) policies. The order quantity, in (R, s, Q) policies, is based on an exponential smoothing forecast of previous demand. However, the high variability of the demand could lead to inefficient forecasts, resulting in inadequate levels of stock and more backlogs. The majority of the (R, s, Q) policies resulted in high backlogs, although there are exceptions. The exceptions, two of which were included in Table 7.4, are the (R, s, Q) policies where the reorder point was set to the highest alternative, namely s_4, and a smoothing factor of 0.5 (Q_2) or 0.9 (Q_3) was applied. This is expected since forecasts with higher smoothing factors place more emphasis on the latest data, which would cause the reorder quantities to be a more accurate reflection of recent trends, although more dynamic.

Table 7.5: Scenario results – Capreomycin poor stock performance policies.

Policy #	R	s	S	Q	%BLs	μ_{BL_Age}	Max_{BL_Age}
(R,s,Q) 13	R3	s1		Q1	35.26%	17	58
(R,s,Q) 16	R3	s2		Q1	34.74%	16	58
(R,s,Q) 19	R3	s3		Q1	34.74%	16	58
(R,s,Q) 22	R3	s4		Q1	35.79%	14	54
(R,s,Q) 25	R4	s1		Q1	41.10%	29	75
(R,s,Q) 28	R4	s2		Q1	30.00%	28	71
(R,s,Q) 31	R4	s3		Q1	34.70%	28	71
(R,s,Q) 34	R4	s4		Q1	32.60%	23	73

7.4.2 Order variability performance

The policies with the best order variability performance are summarised in

Table 7.6. In the scenarios listed in the table, the orders were placed to manufacturers on regular intervals and the order sizes varied less than in the base case. It should be noted that several of the policies that exhibited poor stock performance, had the best order variability performance. Again, the policies in

Table 7.6 implement a reorder quantity that is based on an exponential smoothing forecast of previous demand. The standard deviations are primarily affected by the smoothing factor. A lower smoothing factor results in more uniform forecasts, while the opposite is true for higher smoothing factors. In general, the (R, s, Q) and (s, Q) scenarios exhibit lower standard deviations than other policies. The standard deviation is lowest with a reorder quantity of Q_1 which has the lowest smoothing factor (0.1); while the higher standard deviations are associated with Q_3, which has the highest smoothing factor (0.9).

Table 7.6: Scenario results – Capreomycin high order variability performance policies.

Policy #	R	s	S	Q	σ_{os}	σ_{mo}
Base	NA	NA	NA	NA	59 466	132 118
(s,Q) 1		s1		Q1	11 575	46 945
(s,Q) 4		s2		Q1	11 634	47 068
(s,Q) 7		s3		Q1	11 620	47 124
(s,Q) 10		s4		Q1	11 623	45 102
(R,s,Q) 13	R3	s1		Q1	20 178	46 992
(R,s,Q) 16	R3	s2		Q1	20 325	46 751
(R,s,Q) 19	R3	s3		Q1	20 325	46 751
(R,s,Q) 22	R3	s4		Q1	20 325	46 751

The policies that generate the highest order variability are summarised in Table 7.7. The orders in these policies are placed at irregular times and are of inconsistent size. In general, the majority of the (R, s, S) policies resulted in high standard deviations, except for those that implemented the highest reorder point, namely s_4. A study by De Kok and Inderfurth (1997), concluded that (s, S) type policies generally exhibit the worst performance with regards to "nervousness and stability" among a number of policies considered. This is evident in the scenario results, since the policies with the highest order variability are the (s, S) and (R, s, S) policies.

Table 7.7: Scenario results – Capreomycin poor order variability performance policies.

Policy #	R	s	S	Q	σ_{os}	σ_{mo}
Base	NA	NA	NA	NA	59 466	132 118
(R,s,S) 2	R2	s1	S2		277 018	233 650
(R,s,S) 4	R2	s2	S2		275 298	211 417
(R,s,S) 6	R2	s3	S2		214 604	195 895
(R,s,S) 10	R3	s1	S2		271 853	230 097
(R,s,S) 12	R3	s2	S2		273 173	209 015
(R,s,S) 14	R3	s3	S2		263 082	193 342
(R,s,S) 18	R4	s1	S2		274 002	224 721
(R,s,S) 20	R4	s2	S2		274 998	214 604
(R,s,S) 22	R4	s3	S2		268 781	193 069

7.4.3 Cost performance

The scenarios which resulted in the lowest total costs are depicted in Table 7.8. As with the order variability, the policies that generally resulted in lower total costs than the other policies, are those that implement a reorder quantity that is based on an exponential smoothing forecast of previous demand. This is predominantly due to the

lower holding costs, which can be ascribed to the lower stock levels associated with these policies.

Table 7.8: Scenario results – Capreomycin high cost performance policies.

Policy #	R	s	S	Q	C_O	C_P	C_H	C_T
Base	NA	NA	NA	NA	-	43 141 280	18 764 428	61 905 708
(s,Q) 3		s1		Q3	-	39 046 015	8 047 223	47 093 238
(R,s,Q) 13	R3	s1		Q1	-	39 653 475	7 804 489	47 457 964
(R,s,Q) 22	R3	s4		Q1	-	39 936 146	7 675 583	47 611 729
(R,s,Q) 25	R4	s1		Q1	-	39 482 690	7 717 470	47 200 160
(R,s,Q) 26	R4	s1		Q2	-	38 590 165	6 318 457	44 908 622
(R,s,Q) 28	R4	s2		Q1	-	39 482 690	8 020 257	47 502 947
(R,s,Q) 31	R4	s3		Q1	-	39 482 690	8 020 257	47 502 947
(R,s,Q) 34	R4	s4		Q1	-	39 482 690	7 416 403	46 899 093

The policies associated with the highest costs are summarised in Table 7.9. The total cost for these policies is elevated by their high holding costs. This is ascribed to the high inventory levels of these policies, possibly caused by the high order-up-to-level S_1 and/or reorder point s_4.

Table 7.9: Scenario results – Capreomycin poor cost performance policies.

Policy #	R	s	S	Q	C_O	C_P	C_H	C_T
Base	NA	NA	NA	NA	-	43 141 280	18 764 428	61 905 708
(s,S) 7		s4	S1		-	39 632 701	59 832 891	99 465 592
(R,S) 1	R1		S1		-	39 632 701	59 832 891	99 465 592
(R,S) 3	R2		S1		-	39 733 608	52 517 777	92 251 385
(R,S) 5	R3		S1		-	39 337 908	59 290 396	98 628 304
(R,S) 7	R4		S1		-	39 733 612	56 526 390	96 260 002
(R,s,S) 7	R2	s4	S1		-	39 733 608	52 517 777	92 251 385
(R,s,S) 15	R3	s4	S1		-	39 337 908	59 290 396	98 628 304
(R,s,S) 23	R4	s4	S1		-	38 733 612	56 526 390	95 260 002

7.4.4 Summary of scenario results

As made clear by the results, the best and worst alternatives that are concluded from a separate analysis of the performance measures, are often contradicting; policies that generated good results in terms of order variability or cost performance, resulted in poor stock performance. Therefore, it would be infeasible to make any conclusions based on the results of the separate performance measures.

7.5 Analysis of scenario results

This section will discuss the analysis of the results, obtained from Model C, for each of the three formulations. Only the optimal policies, as obtained through the methodology presented in the following section, will be described while general findings and conclusions will be discussed in Section 7.6.

7.5.1 Analysis methodology

As previously mentioned, the goal of the stockpile in Model C is to ensure the availability of stock for countries and reduce the variability of the demand to the manufacturers. Therefore, the primary focus of the analysis will be on the backlogs and the standard deviation of the volume of orders placed per month (order variability). Considering the importance of costs to the supply chain, the total cost will be added as a third objective.

To compare the performance of the scenarios in terms of the backorders, a single backlog metric is required. This metric should provide an indication of:

i. the percentage of the total orders that were backlogged;
ii. the volume of the backlog; and
iii. the average length of time for which orders were backlogged.

Various potential metrics were considered (and tested through application to the scenario modelling results) before selecting the product of the three stock performance metrics, namely the percentage of backlogs, the average age of a backorder and the total volume of backorders. Though this metric does not have a unit that makes intuitive sense, this is considered acceptable as the only purpose of the metric is to provide a relative indication of the performance of each scenario in terms of backlog.

To illustrate the performance of the scenarios, the order variability, backlog metric and total costs will be plotted against one another for each of the scenarios and be grouped according to the type of inventory policy. Determining which scenario performed better, depends on both the backlogs, order variability and costs, making it a multi-objective minimisation decision, since all of these factors should be as low as possible. Multi-objective optimisation involves the optimisation of several objectives simultaneously, where the objectives are often opposing each other. To determine the optimal points, a Pareto optimal set will be generated. A Pareto optimal set comprises of a complete set of Pareto optimal solutions. A Pareto optimal solution is defined as a solution for which the improvement of one objective function will cause another objective value to deteriorate. In other words, a solution is a Pareto optimal if there is no other solution that dominates it. A solution $x1$ is said to dominate another solution $x2$ if both the following are true:

1. The solution $x1$ is no worse than $x2$ in all of the three objectives; and
2. The solution $x1$ is strictly better than $x2$ in at least one objective.

In effect, each Pareto optimal solution reaches a trade-off between the objectives. In this study, the Pareto optimal set of outcomes are the policies for which:

i. the variability of the demand to the suppliers cannot be reduced without decreasing the availability of stock and/or increasing the total costs;
ii. the availability of stock cannot be guaranteed without increasing the variability of the demand to the supplier and/or increasing the total costs; or
iii. the total costs cannot be reduced without increasing the variability of the demand to the supplier and/or decreasing the availability of stock.

Furthermore, for each formulation, a summary will be provided of the scenarios in the Pareto optimal set as well as the impact each of these scenarios have on:

- the percentage of backlogs;
- the average age of a backorder;
- the total volume of backorders;
- the standard deviation of the volume of orders placed per month; and
- the total cost.

7.5.2 Capreomycin

Figure 7.4 provides a 3-dimensional scatter plot of the backlog measurement, order variability and total cost of all 88 scenarios for capreomycin. The figure also illustrates three 2-dimensional scatter plots that compare two of the objectives, namely (i) order variability and backlog performance, (ii) order variability and total costs, and (iii) backlog performance and total costs. The Pareto optimal solutions as well as those that are close to the Pareto frontier are circled in the plots in the figure, while more detailed results for these scenarios are given in Table 7.10.

As depicted in Table 7.10, there are 31 solutions included in the Pareto optimal policies for capreomycin. Two thirds of the policies in the Pareto frontier implement a reorder quantity that is based on an exponential smoothing forecast of previous demand, specifically the (R, s, Q) and (s, Q) policies. In general, these policies, have both a lower order variability and lower total cost than the other policies. Furthermore, the lower order variability is typically associated with the policies that implement a smoothing factor of 0.1 for the exponential smoothing forecast. Although the (s, Q) and (R, s, Q) policies are generally associated with more backlogs, there are a few exceptions; most of which implement the highest reorder point, namely s_4. In contrast, the Pareto set policies with the most backlogs generally implement the lowest reorder point, namely s_1.

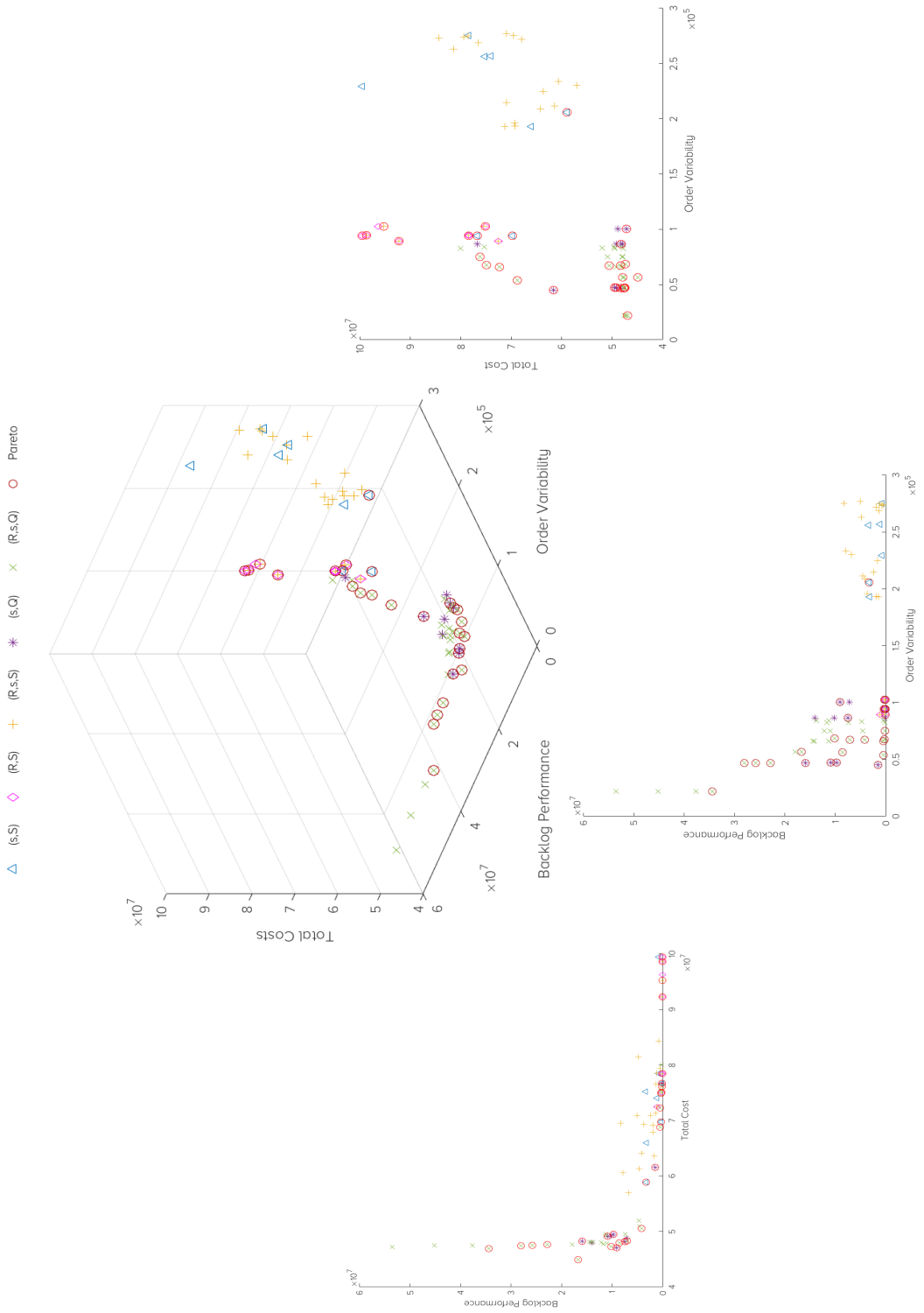

Figure 7.4: Scatter plots of the scenario results for capreomycin.

Table 7.10: Summary of Pareto optimal solutions for capreomycin.

Scenario	Variables				% Backlogs	Average Age	Total Volume	Std Dev (Monthly)	Total Cost
	Reorder	Reorder Point	Order-up-to-level	Order Quantity					
Base					NA	NA	NA	132 118	61 905 708
(s,S) 2		s_1	S_2		17.37%	7	2 728 524	205 729	58 868 469
(s,S) 5		s_3	S_1		2.63%	2	1 859 470	94 309	76 702 211
(s,S) 6		s_3	S_2		2.11%	6	2 541 754	94 309	69 735 512
(R,S) 1	R_1		S_1		2.63%	2	722 871	94 309	99 465 592
(R,S) 2	R_1		S_2		2.11%	6	651 444	94 309	78 428 309
(R,S) 3	R_2		S_1		2.26%	4	1 006 581	89 510	92 251 385
(R,S) 5	R_3		S_1		1.58%	2	159 302	94 524	98 628 304
(R,S) 8	R_4		S_2		6.32%	3	1 249 302	102 599	75 049 318
(R,s,S) 15	R_3	s_4	S_1		1.58%	2	159 302	94 524	98 628 304
(R,s,S) 23	R_4	s_4	S_1		1.58%	3	252 229	102 599	95 260 002
(s,Q) 1		s_1		Q_1	27.37%	14	4 135 590	46 945	48 243 738
(s,Q) 3		s_1		Q_3	35.26%	6	4 105 420	100 498	47 093 238
(s,Q) 4		s_2		Q_1	21.58%	15	3 451 015	47 068	49 130 166
(s,Q) 7		s_3		Q_1	21.58%	15	3 059 089	47 124	49 469 712
(s,Q) 8		s_3		Q_2	25.26%	8	3 929 361	86 469	48 182 180
(s,Q) 10		s_4		Q_1	10.53%	6	2 374 224	45 102	61 565 939
(R,s,Q) 10	R_2	s_4		Q_1	7.37%	4	1 555 461	65 895	72 267 341
(R,s,Q) 11	R_2	s_4		Q_2	7.37%	4	1 555 461	65 895	72 267 341
(R,s,Q) 13	R_3	s_1		Q_1	35.26%	17	4 677 504	46 992	47 457 964
(R,s,Q) 14	R_3	s_1		Q_2	30.53%	8	4 160 316	68 506	47 300 611
(R,s,Q) 16	R_3	s_2		Q_1	34.74%	16	4 637 472	46 751	47 520 342
(R,s,Q) 17	R_3	s_2		Q_2	28.42%	7	3 556 032	67 176	48 283 681
(R,s,Q) 19	R_3	s_3		Q_1	34.74%	16	4 637 472	46 751	47 520 342
(R,s,Q) 20	R_3	s_3		Q_2	19.47%	7	3 078 278	67 176	50 553 123
(R,s,Q) 22	R_3	s_4		Q_1	35.79%	14	4 559 710	46 751	47 611 729
(R,s,Q) 23	R_3	s_4		Q_2	5.79%	4	1 258 965	67 612	74 928 108
(R,s,Q) 26	R_4	s_1		Q_2	41.60%	8	5 026 680	56 552	44 908 622
(R,s,Q) 32	R_4	s_3		Q_2	30.00%	6	4 770 356	56 373	47 927 979
(R,s,Q) 34	R_4	s_4		Q_1	32.60%	23	4 585 716	21 733	46 899 093
(R,s,Q) 35	R_4	s_4		Q_2	7.40%	4	1 603 273	53 757	68 811 742
(R,s,Q) 36	R_4	s_4		Q_3	4.70%	3	1 003 628	75 241	76 138 223

7.5.3 Kanamycin

A 3-dimensional scatter plot of the backlog measurement, order variability and total cost of all 88 scenarios for kanamycin, is depicted in Figure 7.5. The 2-dimensional

scatter plots of the (i) order variability and backlog performance, (ii) order variability and total costs, and (iii) backlog performance and total costs, are also illustrated in the figure. The Pareto optimal solutions as well as those that are close to the Pareto frontier are circled in the figure. The detailed results for these scenarios are provided in Table 7.11.

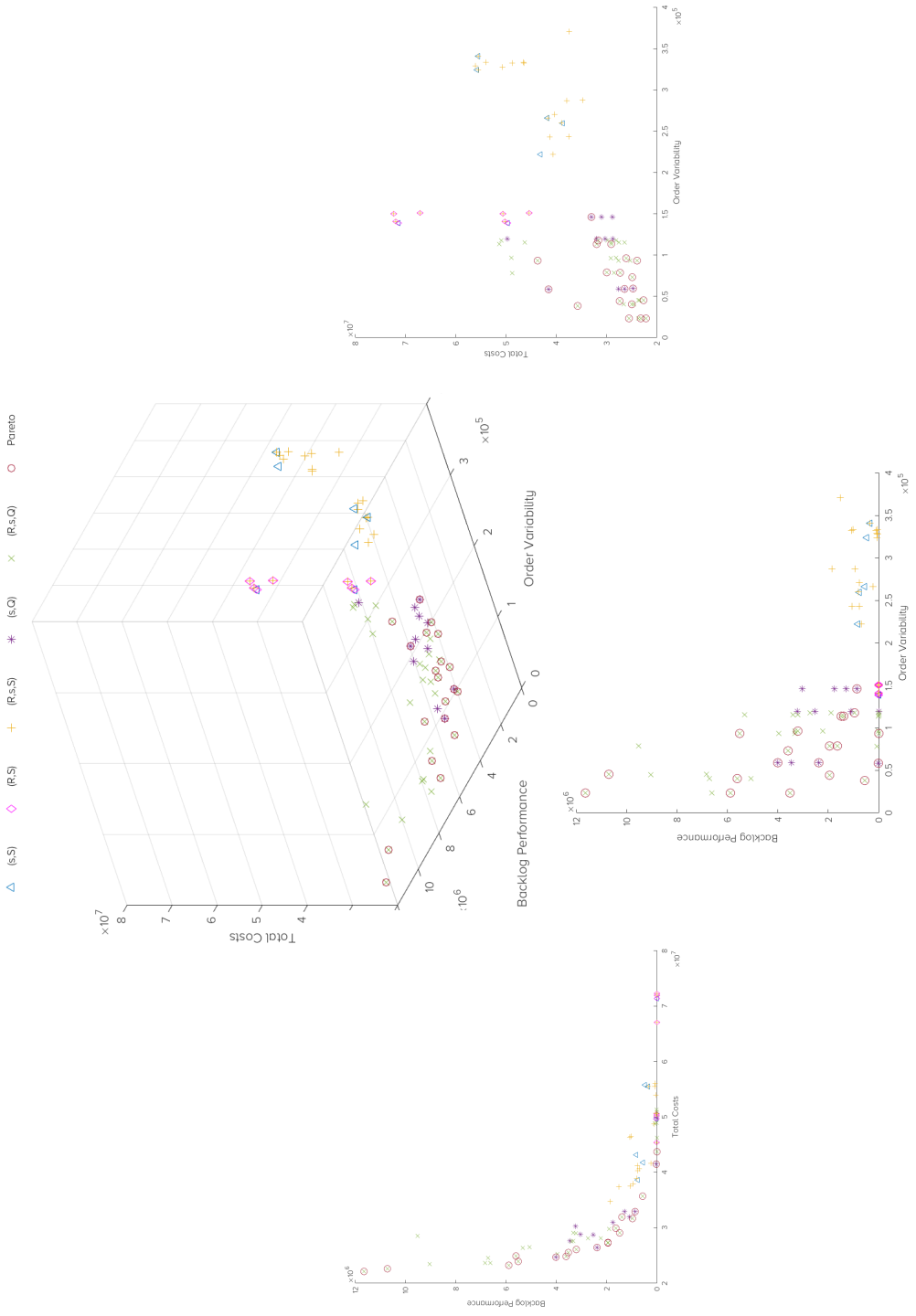

Figure 7.5: Scatter plots of the scenario results for kanamycin.

Table 7.11: Summary of Pareto optimal solutions for kanamycin.

Scenario	Variables: Reorder	Variables: Reorder Point	Variables: Order-up-to-level	Variables: Order Quantity	% Backlogs	Average Age	Total Volume	Std Dev (Monthly)	Total Cost
Base					NA	NA	NA	132 118	28 193 353
(s,Q) 1		s_1		Q_1	9.60%	16	2 683 523	59 321	24 681 673
(s,Q) 4		s_2		Q_1	7.20%	13	2 592 497	59 228	26 434 033
(s,Q) 10		s_4		Q_1	1.60%	3	432 487	58 707	41 509 888
(s,Q) 12		s_4		Q_3	5.60%	9	1 813 642	146 092	32 950 187
(R,s,Q) 2	R_2	s_1		Q_2	11.20%	10	2 859 217	96 437	26 089 148
(R,s,Q) 4	R_2	s_2		Q_1	13.60%	12	3 434 096	40 472	24 940 842
(R,s,Q) 9	R_2	s_3		Q_3	6.40%	7	2 161 586	117 518	31 642 430
(R,s,Q) 10	R_2	s_4		Q_1	4.80%	8	1 450 940	38 393	35 683 918
(R,s,Q) 13	R_3	s_1		Q_1	16.80%	17	3 752 626	45 321	22 603 511
(R,s,Q) 14	R_3	s_1		Q_2	15.20%	11	3 297 102	93 415	23 928 385
(R,s,Q) 22	R_3	s_4		Q_1	7.20%	12	2 253 633	44 240	27 321 994
(R,s,Q) 23	R_3	s_4		Q_2	0.00%	-	-	93 389	43 721 039
(R,s,Q) 25	R_4	s_1		Q_1	16.80%	19	3 649 091	23 194	22 110 732
(R,s,Q) 26	R_4	s_1		Q_2	8.00%	10	2 430 360	78 604	27 315 424
(R,s,Q) 27	R_4	s_1		Q_3	6.40%	10	2 309 863	113 583	29 074 195
(R,s,Q) 28	R_4	s_2		Q_1	14.40%	14	2 922 409	23 194	23 215 047
(R,s,Q) 30	R_4	s_2		Q_3	8.80%	16	2 559 163	73 035	24 836 969
(R,s,Q) 32	R_4	s_3		Q_2	8.80%	8	2 318 406	79 038	29 917 411
(R,s,Q) 33	R_4	s_3		Q_3	8.80%	6	2 635 818	113 583	31 936 723
(R,s,Q) 34	R_4	s_4		Q_1	11.20%	10	3 137 629	23 194	25 521 066

For kanamycin, 20 policies are included in the Pareto optimal set, as depicted in Table 7.11. All of the 20 policies in the Pareto frontier set are either (R, s, Q) or (s, Q). These policies implement a reorder quantity that is based on an exponential smoothing forecast of previous demand. As with capreomycin, these policies have (on average) both a lower order variability and lower total cost when compared with the other policies. As illustrated in the table, the policies that implement a smoothing factor of 0.1, typically results in a lower standard deviation of order variability. Although the (s, Q) and (R, s, Q) policies are generally associated with more backlogs, there are a few exceptions; most of which implement a higher reorder point, such as s_4. In contrast, the majority of Pareto optimal policies in the table with more backlogs implement a lower reorder point, such as s_1 or s_2.

7.5.4 Cycloserine

Figure 7.6 provides a 3-dimensional scatter plot of the backlog measurement, order variability and total cost of all 88 scenarios for cycloserine. Also included in the figure, are the 2-dimensional plots for (i) order variability and backlog performance, (ii) order variability and total costs, and (iii) backlog performance and total costs. The Pareto optimal solutions as well as those that are close to the Pareto frontier are circled in the figure, while more detailed results for these scenarios are given in Table 7.12.

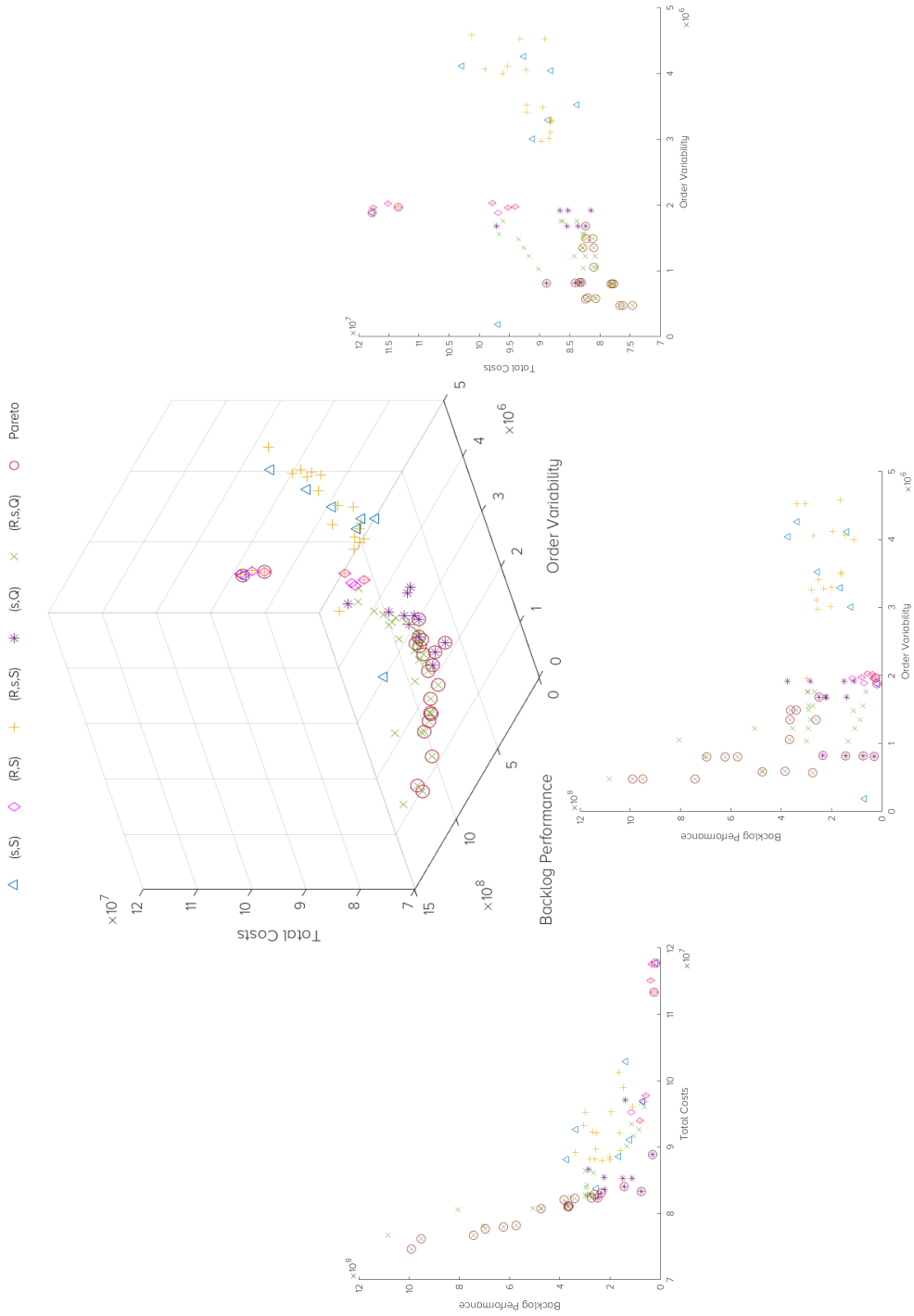

Figure 7.6: Scatter plots of the scenario results for cycloserine.

Table 7.12: Summary of Pareto optimal solutions for cycloserine.

Scenario	Variables: Reorder	Reorder Point	Order-up-to-level	Order Quantity	% Backlogs	Average Age	Total Volume	Std Dev (Monthly)	Total Cost
Base					NA	NA	NA	1 865 129	110 582 702
(R,S) 1	R_1		S_1		8.63%	6	38 540 211	1 881 802	117 726 448
(R,S) 5	R_3		S_1		5.88%	11	36 812 271	1 963 972	113 374 365
(s,Q) 1		s_1		Q_1	20.78%	5	74 677 760	821 523	83 295 165
(s,Q) 4		s_2		Q_1	26.27%	12	74 753 861	823 317	83 070 774
(s,Q) 5		s_2		Q_2	18.82%	15	86 246 305	1 682 445	82 369 294
(s,Q) 7		s_3		Q_1	20.39%	10	73 167 130	818 010	84 070 779
(s,Q) 10		s_4		Q_1	7.45%	6	65 101 767	807 828	88 861 987
(R,s,Q) 1	R_2	s_1		Q_1	24.71%	24	80 040 441	581 001	80 721 402
(R,s,Q) 2	R_2	s_1		Q_2	27.84%	15	87 589 007	1 347 708	81 012 251
(R,s,Q) 4	R_2	s_2		Q_1	22.75%	21	80 234 787	593 517	82 020 833
(R,s,Q) 8	R_2	s_3		Q_2	25.10%	13	80 042 713	1 347 708	82 847 315
(R,s,Q) 10	R_2	s_4		Q_1	18.43%	20	74 513 354	568 449	82 351 128
(R,s,Q) 13	R_3	s_1		Q_1	27.06%	31	82 928 799	802 391	77 670 211
(R,s,Q) 16	R_3	s_2		Q_1	25.10%	31	80 180 710	802 391	77 942 924
(R,s,Q) 22	R_3	s_4		Q_1	24.31%	30	78 593 482	802 391	78 212 188
(R,s,Q) 25	R_4	s_1		Q_1	30.98%	35	87 737 520	476 603	76 186 321
(R,s,Q) 26	R_4	s_1		Q_2	27.45%	16	83 661 572	1 058 420	81 030 528
(R,s,Q) 27	R_4	s_1		Q_3	30.59%	13	91 479 764	1 489 485	81 177 472
(R,s,Q) 31	R_4	s_3		Q_1	24.24%	36	85 136 813	476 603	76 688 962
(R,s,Q) 33	R_4	s_3		Q_3	33.73%	11	91 726 106	1 489 485	82 259 349
(R,s,Q) 34	R_4	s_4		Q_1	34.90%	32	88 781 954	476 603	74 599 586

Table 7.12 summarises the 21 policies included in the Pareto optimal set for cycloserine. Nineteen of the 21 policies in the Pareto frontier are either (R, s, Q) or (s, Q) policies that implements a reorder quantity that is based on an exponential smoothing forecast of previous demand. As with capreomycin and kanamycin, these policies typically results in both a lower order variability and lower total cost when compared with the other policies. As illustrated in the table, a smoothing factor of 0.1, typically results in a lower standard deviation of order variability. Although the (s, Q) and (R, s, Q) policies are generally associated with more backlogs, there are a few exceptions; most of which implement a higher reorder point, such as s_4 or s_3. In contrast, most of the Pareto optimal policies in the table with more backlogs implements a lower reorder point, such as s_1.

7.6 Research findings

This section will provide a discussion of the research findings that were derived from the majority of the 264 scenarios (88 for each formulation) that were implemented and evaluated.

The (s, S) and (R, s, S) policies generally resulted in the highest order variability, with several scenarios where it was higher than the base case. This supports the study by De Kok and Inderfurth (1997), that concluded that (s, S) type policies generally exhibit poor performance with regards to "nervousness and stability". However, the scenarios which resulted in the lowest backlogs were either (s, S) or (R, s, S) policies. Although the (s, Q) and (R, s, Q) policies did result in more backlogs than the other policies (on average), they performed better in terms of cost and variability. There are, however, some exceptions to the (s, Q) and (R, s, Q) policies, where certain combinations of a large reorder point and a smoothing factor of either 0.1 or 0.5 resulted in low order variability, low backlogs and low costs.

The order variability for the (s, Q) and (R, s, Q) policies tend to rise with the smoothing factor. For the majority of these policies, a smoothing factor of 0.1 resulted in the lowest order variability, while a 0.9 smoothing factor caused high variability. As mentioned in Section 7.3.1.4, a lower smoothing factor results in more uniform forecasts, while the opposite is true for higher smoothing factors.

The procurement cost of all scenarios, for each formulation, is less than in the base case. With the holding cost, however, there are several scenarios that resulted in a much higher holding cost, while other resulted in holding cost lower than the base case. This is depicted in Table 7.13, where the procurement cost is fairly similar for all of the scenarios, with small variations, while the holding cost has a much larger range. Therefore, the disparity in the total cost of the different scenarios can be ascribed to the holding costs. A higher holding cost is associated with policies that attempt to keep the stockpile as full as possible, typically resulting in fewer backlogs.

Table 7.13: Comparison of the procurement cost and holding cost range.

	Procurement cost	Holding cost
Capreomycin	\$37.2m - \$41.8m	\$6.3m - \$59.8m
Kanamycin	\$14.1m - \$18.3m	\$7.1m - \$56.5m
Cycloserine	\$63.5m - \$70.8m	\$11.1m - \$46.5m

A typical concern with keeping such a large stockpile, is the potentially high levels of obsolete stock and obsolescence costs. However, as illustrated in the results, obsolescence did not prove to be a problem in the scenarios. For example:

- from the 88 scenarios for capreomycin, there were 16 scenarios that resulted in low levels of obsolete stock with the highest obsolescence cost accounting for 0.9% of the total costs;
- from the 88 scenarios for kanamycin, none resulted in obsolete stock; and
- from the 88 scenarios for cycloserine, there were 21 scenarios that resulted in low levels of obsolete stock with the highest obsolescence cost accounting for 0.7% of the total cost.

Currently, when a country places an order, they have to wait for (i) the order to be processed, (ii) the drugs to be manufactured, and (iii) for the order to be dispatched and delivered. With the larger buffer inventory introduced in Model C, orders are fulfilled directly from the stockpile. Therefore, countries no longer need to wait for the manufacturing of the drugs, subsequently reducing the total lead time that a country has to wait for a delivery. The reduced lead times, if kept relatively stable, would potentially allow countries to plan and forecast more accurately and would potentially either significantly reduce or eliminate the existence for emergency orders. When comparing the performance of the current system with the scenarios in the Pareto frontier, it is clear that a larger stockpile, implemented with the appropriate inventory policies, has the potential to: (i) aid current manufacturers to produce medicines more efficiently and increase market attractiveness to draw in new manufacturers, and (ii) reduce stock-outs at countries by decreasing the current lead time for order delivery.

7.7 Conclusion: Analysis and results

This chapter presented the analysis of the current system (the base case) as well as several alternative stockpile scenarios. The scenarios that were analysed, as well as the results obtained for these, were presented. The general findings that can be concluded from the results were also discussed.

The following chapter will conclude the research by providing an overall summary and by discussing the contributions and limitations of the research. The recommendations to stakeholders will be presented and opportunities for further research will be identified.

Chapter 8:
Conclusions and summary

"In high school, I won a prize for an essay on tuberculosis. When I got through writing the essay, I was sure I had the disease."

- Constance Baker Motley (African-American state senator and Borough President of Manhattan)

The previous chapter presented the analysis results of the base case and the scenarios that were modelled. It also provided the general findings that can be concluded from the results. This chapter will provide an overall summary of the research and discuss some recommendations to stakeholders of the global MDR-TB SLD supply chain. Both the contributions and limitations of the research are provided, followed by suggested opportunities for further research.

8.1 Project summary

The background, problem statement, objectives and scope of the research were defined in Chapter 1. Chapter 2 provided contextual information on TB and MDR-TB. This included information on the causes of the disease, advances in the management of the disease, treatment regimens and risks associated with diabetes and HIV. The chapter concluded with an estimate of the financial commitment required to respond to the epidemic. Chapter 3 consisted of an introduction to supply chains and concepts that are relevant to their management. Chapter 4 introduced several methods for modelling supply chains and the characteristics of system dynamics and discrete event simulation were compared. System dynamics was selected to be applied for the purpose of this study, and an outline on this approach was provided.

In Chapter 5 a description of the supply chain for SLDs for MDR-TB was provided. The challenges and difficulties experienced in the supply chain were summarised together with some recommendations towards improving the supply chain. The notion of implementing a large buffer inventory to improve supply chain performance was also detailed in this chapter. Chapter 6 provided background information and a conceptual model of the segment of the MDR-TB supply chain for SLDs that will be modelled. The modelling process used to simulate this segment of the supply chain was discussed and the scenarios that would bet evaluated were introduced. Analyses of the current system and several alternative stockpile scenarios were presented in Chapter 7. A summary of the results obtained from the scenario modelling and overall conclusions that can be drawn from results were also discussed.

8.2 Recommendations to stakeholders

A key problem in the SLD supply chain is the dynamic and irregular demand patterns, since these makes forecasting and effective planning impossible, consequently reducing the manufacturers' confidence to enter the market and their ability to produce economical batch sizes. This causes higher drug prices and longer, inconsistent lead times. A possible solution to address this problem, is the implementation of a large buffer inventory that could be used to fulfil the erratic demand from countries while consolidating and timing the orders to replenish the stockpile, in an attempt to smooth the demand to manufactures. This research investigated the implementation of such a stockpile and evaluated various scenarios to identify a set of inventory policies that would achieve the goals of the stockpile. From the results, it can be concluded that the (s, Q) and (R, s, Q) inventory policies are present in the Pareto set of solutions for all of the formulations and would seem to be the best policies to implement. There is also an indication that a lower smoothing factor (0.1 or 0.5), combined with a higher reorder point (either $s4$ or $s3$) is has the most positive impact on the supply chain performance. Furthermore, none of the reorder frequencies consistently resulted in better or poorer results. Therefore, it is recommended that the implemented reorder frequency should be based on whichever frequency benefits both the operations of the SRS and the manufacturers.

As mentioned in Chapter 1, Section 1.5, this research forms part of a larger project that incorporates both the upstream and downstream components of the MDR-TB SLD supply chain. In the study of the downstream segment, Coetzee (2015) concluded that placing orders based on an exponential smoothing forecast was not recommended, since it led to high stock-outs. In this research, however, several of these type of policies, namely (s, Q) and (R, s, Q) policies, are present in the Pareto set of solutions. The reason behind the contradictory recommendations is the different objectives associated

with the supply chain segments. For the downstream segment of the supply chain, as in Coetzee's (2015) study, the main objectives are to minimise the total cost and reduce stock-outs. For the upstream segment, however, an added main objective is to reduce the order variability to manufacturers. The addition of this third objective, consequently led to different policies being recommended. This decoupling of the supply chain segments and their associated objectives is illustrated in Figure 8.1.

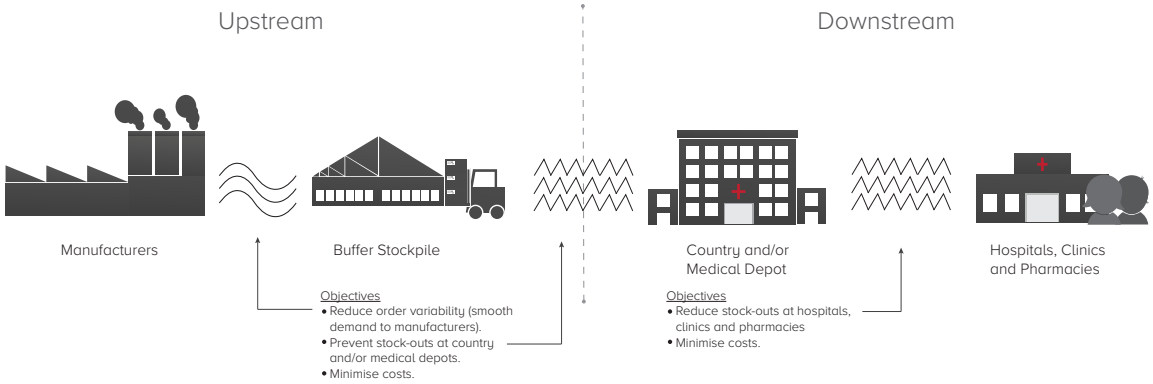

Figure 8.1: Illustration of the different objectives associated with the supply chain segments.

To implement the larger stockpile, it is recommended that a rollout plan is designed that would allow the stockpile to gradually increase in size, while allowing more countries to receive their drugs directly from the stockpile. The plan would have to specify the intended time horizon and how it will grow during this time horizon. Since not all countries will be able to receive drugs directly from the stockpile immediately, further investigation should be done to decide how the stockpile will manage the higher levels of stock during its growth. For example, it should be determined whether the current stock rotation policies can be continued or whether some countries should initially receive their drugs directly from the stockpile with more countries being added as it grows. The required level of stock for the larger buffer stockpile will depend on the policy that is implemented. To provide some indication of how much the current stockpile will potentially have to grow, the size of the stockpile implemented in the base case as well the required size or capacity associated with the policies are summarised in Table 8.1. The level of stock for the policies that implement an order-up-to-level, will never be more than the value of $S1$ or $S2$, as provided in the table. For the (s, Q) and (R, s, Q) policies, there is not a fixed inventory level and it will vary for each policy. Therefore, to illustrate the potential size of the stockpile for these policies, the maximum inventory levels of the policies in the Pareto set were used to generate a range in which the capacity of the stockpile will fall, depending on the exact policy that is implemented.

Table 8.1: Summary of stock levels.

	Current	S1	S2	Range for Q-policies
Capreomycin	221 018	1 211 877	999 690	376 492 - 864 044
Kanamycin	184 984	1 773 273	1 314 240	706 656 - 1 301 290
Cycloserine	3 076 643	14 930 768	11 440 860	6 894 090 - 13 895 700

8.3 Research contributions

This research contributes to the current academic literature in several ways:

- It adds to the system dynamic modelling literature, specifically the modelling of drug supply chains. Although several studies have been done on various supply chains, there is limited literature on the modelling of drug supply chains.
- It provides valuable insights on the SLD supply chain through the quantitative modelling to accurately predict the expected impact of proposed changes to the operation of the supply chain on the availability and delivery of SLDs.
- It adds to the knowledge and understanding of the SLD supply chain by being (one of) the first research studies to provide modelling insights of the supply chain on a global level.
- It adds to the field of donor funded supply chains. As mentioned in Section 5.1, an article was written during the course of this research and was presented at the 2016 SAIIE conference in October. The article mainly served as an exploratory high-level literature study, intended to outline the field of donor funded supply chains and summarise how it differs from commercial supply chains in terms of the main drivers and characteristics.

8.4 Research limitations

The assumptions regarding Model A, Model B and Model C, were discussed in detail in Sections 6.3.3.3, 6.3.5.3, and 6.3.6.3, respectively. This section will summarise all of the known limitations that have been revealed throughout the project. In Section 6.1.2, the limitations associated with the data and the availability of the data were discussed, namely:

- the database does not include procurement data for projects outside of the GLC and GDF, therefore these projects were omitted from the model;
- only the total lead time (between the 'purchase order date' and 'actual delivery date') can be derived from the data, while data about the various separate lead time components are unavailable;
- database entries do not specify the order type making it impossible to confidently distinguish between normal orders, emergency orders and orders fulfilled due to stock rotation;
- no available information or data regarding the stockpile's current replenishment process is available; and
- data regarding the batch sizes, minimum order quantity and lead times of manufacturers are not publically available, making it impossible to accurately model the manufacturers and their processes in detail.

Furthermore, there are some aspects which could not be modelled accurately due to the limitations of systems dynamics. Since system dynamics applies continuous state changes, individual units cannot be tracked and modelled. To overcome this limitation, a discrete function was applied to the stockpile variable to track the age of a unit from when it enters the stockpile; enabling the model to identify when a unit was near a specified age. This feature was used to determine when drugs in the stockpile were eligible for rotation or when the drugs was considered obsolete. However, the model is unable to track the age outside of the stockpile and the age of the units when it reaches the stockpile cannot be determined. The age of the drugs when it reaches the stockpile was assumed to be two months, therefore possibly overcompensating the age of the drugs during most periods and undercompensating during others. This also limited the management of backorders in the model, since the individual units that are added to the backlog cannot be tracked separately, but is instead pooled together. With system dynamics there is no way to track each individual drug through these stages.

From the sensitivity analysis, discussed in Section 6.4.8, it was concluded that the stock on hand is the most sensitive variables, especially when the demand or lead time is increased.

8.5 Opportunity for further work

It is recommended that the following opportunities for further research be explored, since it is believed that each of these proposed studies would contribute to the significant research gap related to the modelling of the SLD supply chain:

i. Evaluate the agility and responsiveness of the different inventory policies. This would prove beneficial as a way to test the impact on the supply chain and its performance if more countries were to order through GDF and the stockpile.
ii. Experiment with different forecasting methods, other than exponential smoothing and evaluate the impact of non-stationary inventory policies on the stockpile.
iii. Attempt to model individual countries, or individual regions, by identifying some relationship or pattern between the prevalence of TB in the country and the orders that the country places. This would allow the inclusion of logistical costs and delivery lead times that vary according to the distance of the delivery. (However, this should only be done if a significant correlation between distance and lead time can be established).
iv. Eventually, an attempt should be made to develop a complete model of the supply chain, incorporating both the upstream and downstream segments, to investigate the possible ripple-effects that decisions in one of the supply chain segments has on the other.

v. With more data, the manufacturers can be modelled as individual entities, where each manufacturer only produces a certain formulation(s). This would enable consideration of each manufacturer's batch size, economic order quantity, etc. in the modelling process. Whilst it is immediately apparent that this would benefit the manufacturer, it is likely that it will also indirectly benefit the entire supply chain. With this in mind, the impact of the order variability on manufacturers can also be evaluated to determine to what extent the demand patterns affect the manufacturers and what effect orders that align more closely to economic order quantities would have on the prices of drugs.
vi. Develop a discrete-event simulation of the models to analyse the impact on individual units and orders.
vii. Evaluate the possibility of having more than one stockpile. For example, having a stockpile in some or each of the WHO regions. With this in mind, local manufacturing in the region of the stockpile could be encouraged, potentially reducing manufacturing and logistical costs.

8.6 Closing summary

The SLD supply chain faces a number of significant challenges highlighting the importance of optimal supply chain management. A large number of MDR-TB cases (as many as 75% according to the World Health Organization (2015) remain undiagnosed. Consequently, there will be an ongoing increase in demand for SLDs. The implementation of new diagnostic technologies is gradually increasing worldwide, with a noteworthy example stemming from South Africa. Since 2011, South Africa implemented GeneXpert MTB/RIF testing technology, which significantly increased the number of MDR-TB diagnoses.

As the number of MDR-TB diagnoses increase worldwide, a substantial burden will be placed on the supply chain as the demand for SLDs increases due to more patients being introduced to MDR-TB treatments. The spread of MDR-TB is worsened by poor adherence to rigorous treatments and the dearth of transmission control (World Health Organization, 2016a). Contrastingly, improved diagnosis and accuracy of surveillance data of MDR-TB will improve forecasts of demand for SLDs. This could potentially relieve some of the main challenges faced in the supply chain, which may positively impact the MDR-TB drug market as it becomes more lucrative to suppliers; thereby increasing competition which in turn improves supplier performance (Keshavjee and Seung, 2008).

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Appendix A Checklist

This appendix provides a checklist that is used to analyse each source throughout the literature review process. This is mainly to strengthen the validity of the study by performing a critical analysis on each source before making assertions and conclusions based thereon. The checklist is provided in Table A.1 and is based on the evaluation method as laid out by Jonathan Paulo in the Madison Research Essentials Toolkit (Paulo, 2014) as well as the Critical Appraisal and Analysis technique from the Cornell University Library (Engle, 2015).

Table A.1: Checklist for literature analysis.

Criteria	Checklist
Credibility of Author	☐ The author seems reputable ☐ The author provides citations ☐ Information of the author's background is available
Accuracy	☐ No grammatical or spelling errors ☐ Information was reviewed before publication ☐ Information seems accurate based on my knowledge ☐ Information can be verified by another source
Relevance	☐ The source covers at least one relevant topic ☐ The content and language is used at an appropriate level ☐ The source has been cited
Currency / Date	☐ The source was written and published at least within the last 10 years ☐ The currency of the source is pertinent to the study
Objectivity / Bias / Reliability	☐ The motive of the source is relevant ☐ The information is objective
Style / Functionality	☐ The source is well-written and organised ☐ The links are working (if a website) ☐ The page is easy to navigate (If a website)

Appendix B Characteristics of Dynamic Complexity

There are various characteristics of systems that can cause dynamic complexity. Table B.1 lists the majority of these characteristics and a short description of each. Many of the characteristics mentioned in the table are discussed in more detail in Section 4.4.2.

Table B.1: Summary of dynamic complexity characteristics.

Characteristic	Description
Dynamic	Changes in systems take place over numerous time scales that sometimes interact. Systems might seem stable and constant, but often when considering the system over a long time period, fluctuations are observed.
Tightly Coupled	Every individual element in a system is connected and interacts with one another and their environment. Therefore, a single action can have a rippling effect.
Governed by Feedback	Due to the tight couplings between elements, decisions cause the system environment to change in some way that triggers other elements to act. This results in a new system state, which influences the next decisions.
Nonlinear	Nonlinearity is often a result of the system's basic physics or due to the interaction of multiple factors in decision-making. Effect is rarely relational to cause – what happens near the current operational point in the system does not necessarily apply in other states of the system.
History-Dependent	Certain choices that are made at one point in time will dismiss the availability of certain options at a later point in time.
Self-Organising	The internal structure of the systems causes its dynamic complexity. Minor complications in the system are often amplified due to feedback loops creating patterns and path dependence.
Adaptive	The decision rules and capabilities of the system elements will adapt and change over time causing some elements to multiply and the extinction of others.
Counterintuitive	In complex systems, the participants often look for causes near the problem area, while in many cases the causes originate from a different event at another time instance. When analysing complex systems, attention is often drawn to the observable consequences of problems instead of the inconspicuous main cause.
Policy Resistant	The human mind is incapable to fully comprehend the complexity of systems, which is why many solutions fail or worsen the problem.
Characterised by Trade-Offs	Feedback loops often contain time delays that cause the short-term and long-term response of the system to differ.

Appendix C The SD Modelling Procedure

This appendix discusses the different steps and substeps in the modelling procedure of System Dynamics, as summarised in Section 4.4.7.

1. Defining the Problem and its Boundaries

The most important part of the modelling process is to clearly define the purpose of the model. Any model represents a system, but for it to be beneficial and valuable, it must capture a specific problem. The purpose should help define the scope and boundaries of the model.

Formulate the Problem Area

The problem area comprises of, among others, a problem statement, which is similar to those provided in Section 1.2. It is also necessary to identify the main stakeholders and their interests. The problem area should clearly communicate the objectives of the model, taking into consideration the different perspectives and goals of the various stakeholders.

Collect data and information

Data and information is important to substantiate and clarify the scope and extent of the identified problem statement and strategic questions. The data and information can be collected from any relevant and reliable sources, such as reports, previous studies, journal articles, interviews, databases etc.

Decide on the time horizon

The time horizon should not only capture the present situation and its future performance, but also include historical events that led to the emergence of the problem and its symptoms. As previously stated, the effects of system changes are often witnessed in the distant future. Therefore, it is important that the time horizon extends far enough into the future that the effects and changes in system behaviour can be identified and analysed.

2. Understanding the Model

After the problem statement and the model boundaries are defined, the system and its environment are illustrated through a CLD. This involves identifying the elements relevant to the system and the strategic questions. Usually the strategic questions will be refined as the understanding of the system and its stakeholders are improved.

Identify key variables and concepts

Once the problem is known, it is best to identify the different variables and concepts of the system, although it is not necessary to assign values to them at this stage. In further

steps of the modelling procedure, these variables and concepts are often adjusted or more are added.

Identify historical and possible future behaviour of variables and concepts

This step involves the identification of patterns that were revealed over time as well as predictions of how it might change and develop in the future. These patterns, represented by graphs and figures, are often referred to as the reference models. The reference models are important to avoid looking at the system from an event-driven view and are referred to throughout the modelling process.

Define links and relationships

The linkages and relationships between different elements are indicated with an arrow. The polarity of the link or relationship should also be stated.

Define feedback loops

The feedback loops and their polarity should be defined as well as any relations where there are information lags or backlogged materials.

Map and Refine the CLD

After creating the CLD it should be refined and simplified to ensure the final format remain as small as possible.

3. Simulating the Model

Once the CLD is completed, the more detailed stock and flow diagram can be built to clearly define the physical structure of the model. This step involves the process of building the stock and flow diagram and simulating the model on the chosen software.

Define variable types

The basic variable types and concepts are described in Table D.1.

Table D.1: Definitions of variable types.

Variable/Concept Name	Description
Stock or State Variables	Accumulations within the system. Determines the decisions that control the flow variables (Campuzano and Mula, 2011; Piewthongngam *et al.*, 2014).
Flow Variables	The elements that determine the variation of stock as quantities are transferred in or out, either immediately or over time (Campuzano and Mula, 2011; Piewthongngam *et al.*, 2014).
Auxiliary Variables	The rest of the elements not included in the abovementioned variables (Campuzano and Mula, 2011).

Construct stock and flow diagram

The stock and flow diagram is usually constructed from the CLD, although in some cases the system is easier visualised by directly constructing the stock and flow diagram.

Characterise the elements

Values are assigned to the variables and concepts that were identified in the first step of the procedure. These values can either be known values or estimates.

Write the equations

Equations are generally used to describe the relationships between elements. The equations can include arithmetic formulae, software functions and rate tables among others.

Stabilise the Stock and Flow Diagram

The first functioning version of the model will often be altered and improved until it runs smoothly. It will still, however, constantly undergo adjustments throughout the modelling process.

Identify the elements that are significant to model improvements and scenarios

When analysing the system not all variables will be evaluated. Instead, only a few significant elements will be monitored throughout the simulation and used as a basis for conclusions.

4. Testing and Validating the Model

Before modelling and analysing different scenarios, it is necessary to ensure that the model performs as expected. This is done through model validation.

Compare the model to reference modes

The first step taken after completing the model is often to compare the system's behaviour with the actual behaviour. The simplest way to do this is to refer back to the reference models. If built correctly, the historical patterns and future predictions in the reference models should more or less match those in the simulation.

Perform validation tests

The aim of model validation is to determine whether the model can be accepted or whether it should be rejected. Some of the most significant validation tests, as summarised by Sterman (2003), are:

i. Boundary Adequacy Tests: Assesses the relevance of the boundary and whether the significant concepts were considered.

ii. Dimensional Consistency Test: Examines the consistency of measurement units.

iii. Behaviour Reproduction Tests: Discovers errors and faults in the structure or parameters and determines whether it will affect the purpose of the model.

iv. Extreme Conditions Test: Assesses whether the model performs realistically regardless of the extremity of the conditions. For example, products cannot be manufactured without materials and inventories cannot be below zero.

v. Sensitivity Analysis: Analyses the system's robustness in terms of changes made to the parameters.

5. Identifying and Implementing Scenarios

After validating the model, scenarios can be designed and modelled to aid in the analysis and improvement of the system.

Identify scenarios to be modelled

The different scenarios to be modelled should be clearly defined as well as the reasoning behind it and the expected outcomes. To enhance the analysis, it is suggested that the expected results be discussed and added to the reference model.

Specify the new decision rules and structures for the scenarios

Each scenario will require the structure and decision rules of the model to be adjusted. It will possibly also demand the adaption of feedback loops, stock and flow structure, time delays and variables. The changes to be made must be clearly defined together with the reasoning behind the changes.

Model the scenarios

Implement the changes and simulate.

Evaluate the system's response to the scenarios

A what if analysis can be done to determine what effects the scenario has on the system. The robustness of the scenario recommendations can be assessed using a sensitivity analysis. Different scenarios can possibly interact with one another. These interactions should be evaluated since it is often not as is expected due to the nonlinearity of complex systems.

Appendix D Historical behaviour

This appendix provides the visual assessments of the available data for kanamycin and cycloserine. The assessment for capreomycin was provided in Section 6.2.2.4.

D.1 Kanamycin

Figure D.1 depicts the weekly purchase order quantity, for kanamycin, as a percentage of the annual order quantity, plotted by week for each of the five years. This provides a visual assessment of any possible trends in the order timing from one year to the next. The figure clearly illustrates the dynamic nature of the data and that there is no trend in the time of year when orders are placed.

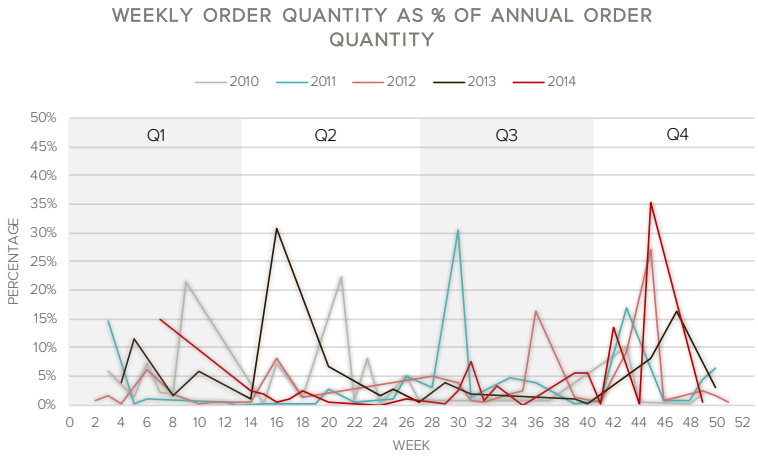

Figure D.1: Visual assessment of trends in order timing for kanamycin.

Figure D.2 illustrates the average weekly order size as well as the average lead time for the orders placed in that week over the last five years. This is to provide a visual assessment of how the lead time and demand fluctuates and whether any correlation possibly exists. The figure clearly demonstrates the inconsistency of both the demand and lead time. It also corresponds with the correlation analysis in Section 6.2.2.3, that there is no correlation between the order size and lead time.

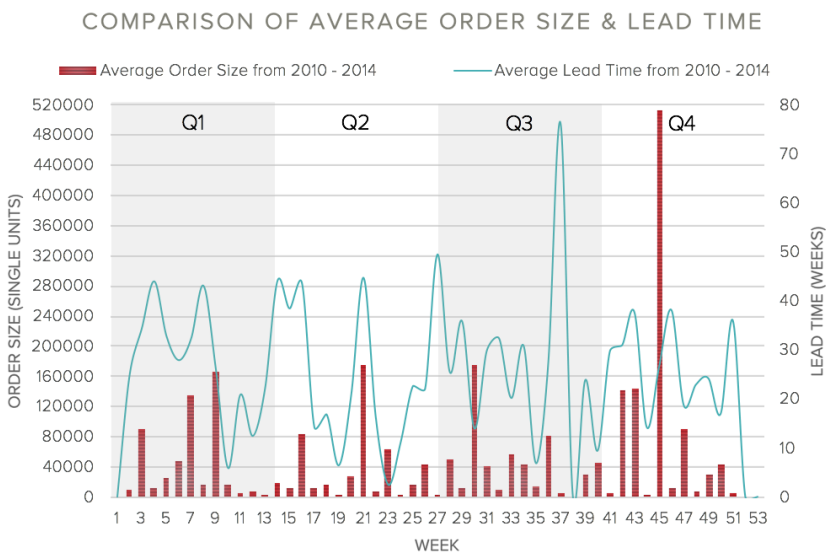

Figure D.2: Visual assessment of the average lead times and order sizes for kanamycin.

Figure D.3 provides a plot of the weekly lead time against the purchase order dates over the five-year period. The lead time is calculated as the difference (in weeks) between the purchase order date and the order delivery date. This is to provide a visual assessment of whether any changes in the lead time is presents over the last five years. A lead time linear regression analysis was performed and no statistically significant relationships were observed, this is consistent with the graphic representation in the figure, which illustrates a relatively stable trend.

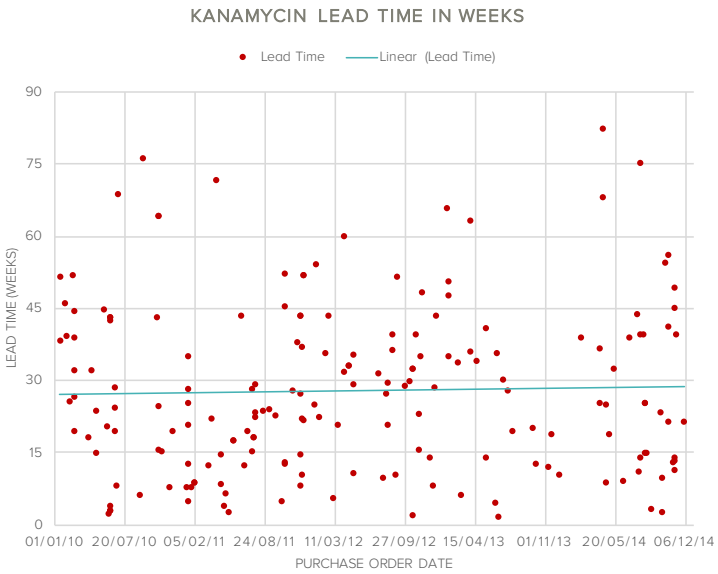

Figure D.3: Visual assessment of changes in lead time for kanamycin.

D.2 Cycloserine

Figure D.4 depicts the weekly purchase order quantity, for cycloserine, as a percentage of the annual order quantity, plotted by week for each of the five years. This provides a

visual assessment of any possible trends in the order timing from one year to the next. The figure clearly illustrates the dynamic nature of the data and that there is no trend in the time of year when orders are placed.

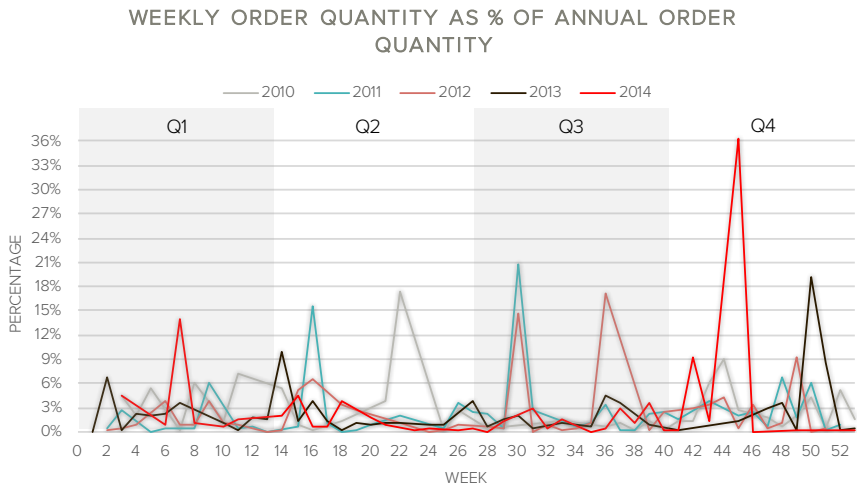

Figure D.4: Visual assessment of trends in order timing for cycloserine.

Figure D.5 illustrates the average weekly order size as well as the average lead time for the orders placed in that week over the last five years. This is to provide a visual assessment of how the lead time and demand fluctuates and whether any correlation possibly exists. The figure clearly demonstrates the inconsistency of both the demand and lead time. It also corresponds with the correlation analysis in Section 6.2.2.3, that there is no correlation between the order size and lead time.

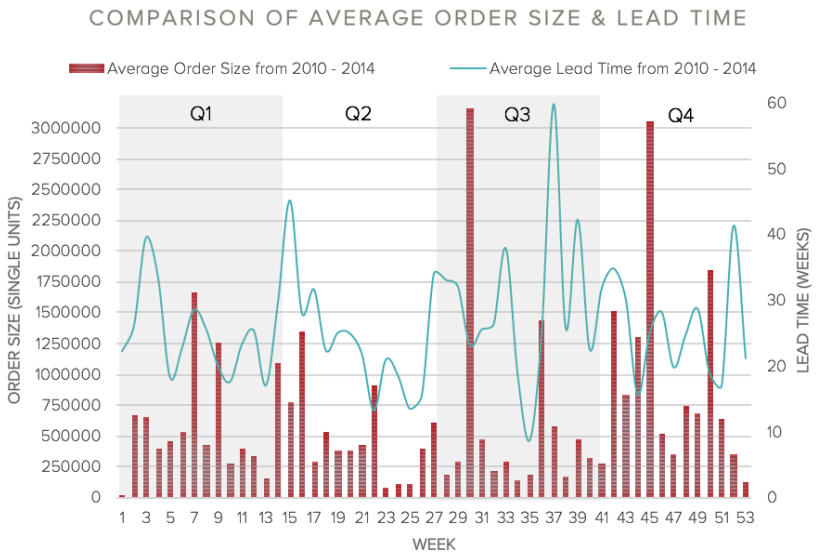

Figure D.5: Visual assessment of the average lead times and order sizes for cycloserine.

Figure D.6 provides a plot of the weekly lead time against the purchase order dates over the five-year period. The lead time is calculated as the difference (in weeks)

between the purchase order date and the order delivery date. This is to provide a visual assessment of whether any changes in the lead time is presents over the last five years.

A lead time linear regression analysis was performed and no statistically significant relationships were observed, although the graphic representation if Figure D.6 illustrates an upward trend.

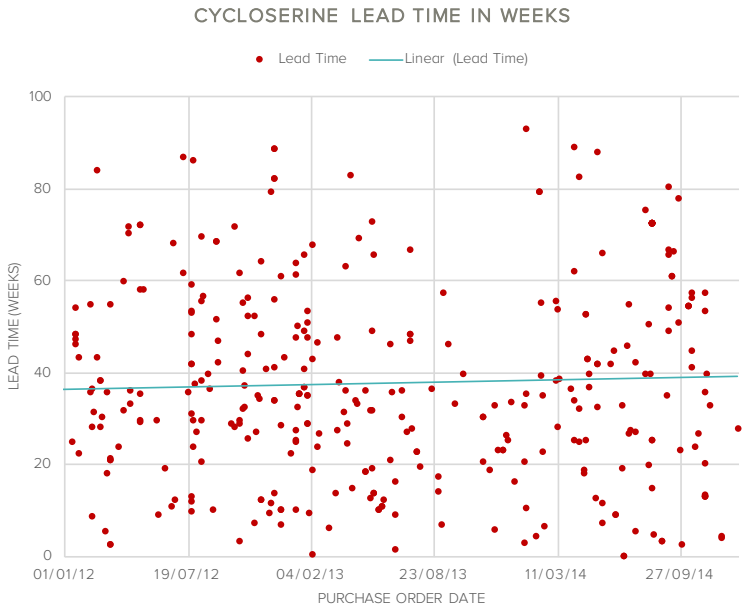

Figure D.6: Visual assessment of changes in lead time for cycloserine.

Appendix E Modelling details

This Appendix provides details of each of the three models. The main purpose of the appendix is to ensure reproducibility of the models by providing all of the equations used for the variables.

E.1 Variable definitions

As mentioned in Section 6.2.1, the key variables and concepts can be derived from the sections discussed in Chapter 5 and the variables to be included in the model are centred around the conceptual model in Figure 6.2. The variables are summarised in Table E.1 and are classified as either: endogenous variables (determined by other variables), exogenous variables (independent of the other variables), or omitted variables. These variables are preliminary and will be modified during the remainder of the Appendix as the modelling process progresses.

Table E.1: Definition of variables.

Variable Name	Description
Endogenous variables:	
Drugs available for emergency orders	The number of drugs ready to be dispatched to countries by the SRS.
Drugs available for GDF/PA	The number of drugs that has been manufactured and is ready to be dispatched to the GDF and their PAs for quality assessment.
Drugs available for SRS	The number of drugs that has been manufactured and is ready to be dispatched to the SRS.
Drugs available for stock rotation	The amount stock, from what the SRS has on hand, that is eligible for stock rotation based on the remaining shelf life.
Drugs received by SRS	The number of drugs that have been received by the SRS from manufacturers.
Emergency order drugs received by countries	The number of drugs that have been received by the countries from the SRS.
Emergency orders from countries	Orders received from countries that are considered an emergency, since treatment interruptions will occur if not received as soon as possible.
GDF/PA orders placed	The number of drugs that the GDF and their PA decides to order from the manufacturers, includes the SRS demand and the orders from countries.
Normal order drugs awaiting dispatch	The number of drugs that have undergone quality assessment by the GDF/PA and is ready to be dispatched to countries.
Normal order drugs received by countries	The number of drugs that have been received by the countries from the GDF/PA.
Normal orders from countries	Orders received from countries.
Normal orders supply line	The orders that have been placed by countries, but not yet fulfilled.
Obsolete stock	Stock that has reached their shelf life and can no longer be used for the treatment of patients.
Production & dispatch to GDF/PA	The production and dispatch of the orders placed by the GDF and their procurement agent.

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SRS demand	The number of drugs that the GDF/PA has to order from manufacturers to satisfy both emergency orders and the drugs required for the SRS.
SRS stock on hand	The stock available at the SRS to be dispatched to countries.
SRS supply line	The amount of stock that has been ordered from manufacturers, but not yet delivered.
Stock shortfall	The amount of stock that the SRS requires to have the desired level of stock on hand.
Exogenous variables:	
Desired level of stock for SRS	The level of inventory that the SRS prefers to have on hand at all times, i.e. the full capacity of the stockpile.
Expiration Value	The shelf life value of the drugs when it is considered obsolete and no longer eligible to be delivered to countries.
Manufacturer lead time	The time it takes for the manufacturer to produce and deliver the drugs.
Obsolescence Cost	The total cost of obsolete drugs; i.e. the per unit cost multiplied by the number of obsolete units.
Per Unit Cost	The (average) cost per unit; i.e. per pill, vial, kit etc.
Rotation Value	The shelf life value of a drug that makes it eligible to be used for stock rotation.
Shelf life	The amount of time that the drugs can be stored, after production, before it becomes obsolete.
Total Cost	The total cost of both unit costs and obsolete costs.
Total Unit Cost	The total cost for an order; i.e. the per unit cost multiplied by the number of units in the order.
Omitted variables:	
API's delivered to manufacturer	The amount of API's delivered to the drug manufacturers.
API's ordered	The amount of API's ordered by the drug manufacturers.
Drugs provided to patients	The drugs provided to the patients by their clinic/doctor/pharmacy.
Logistical Cost	The cost associated with the dispatch and delivery of drugs from one point to another.
Manufacturer Capacity	The maximum number of drugs that the manufacturer can produce due to facility and production line restrictions.
Manufacturer reliability	The ability of manufacturers to consistently deliver orders on time and in full.
Manufacturers' demand of APIs	The amount of API's required by the manufacturers to produce the drugs.
Number of manufacturers	The number of manufacturers/suppliers that are currently manufacturing drugs.
Patient demand	The number of drugs that patients require from their clinic/doctor/pharmacy.
Patient drop-out	The number of patients that has to stop their treatment due to a treatment interruption, such as a stock-out.
SRS Capacity	The maximum amount of inventory that the SRS can store due to space restriction.

E.2 Modelling details of Model A

This section will discuss the modelling details associated with Model A, as defined and discussed in Section 6.3.3. The variables that are included in Model A will be identified and the characteristics and equations for each of these variables will be provided.

E.2.1 Model A: Variable types

All of the variables and concepts identified in Section E.1 were examined to determine a potential model that can be supported by the available historical data. This model will be referred to as Model A. The applicable variables and concepts were identified as either a stock variable (accumulations within the system), flow variable (determines the variation of stock) or auxiliary variable (constants or estimates), refer to Table D.1 in 0 for more detail. A list of the applicable variables, their variable type and their units is given in Table E.2. The table includes several variables, in addition to those initially identified in Section 6.2.1, that were added during the development of the model.

Table E.2: Variable types for Model A.

Variable Name	Units	Variable Type
Country Demand Input	Drugs/Week	Auxiliary
Cumulative Total Unit Cost	Dollar	Stock
Normal Lead Time Lookup	Week	Auxiliary
Normal Order Drugs Awaiting Dispatch	Drugs	Stock
Normal Order Drugs Received By Countries	Drugs/Week	Flow
Normal Orders From Countries	Drugs/Week	Flow
Normal Orders Fulfilled For Countries	Drugs/Week	Flow
Normal Orders Supply Line	Drugs	Stock
Per Unit Cost	Dollar/Drugs	Auxilary
Production	Drugs/Week	Flow
Proportion Of Orders Placed	Dmnl	Auxiliary
Total Costs	Dollar	Auxilary
Total Drugs Received By Countries	Drugs	Stock
Total Unit Cost	Dollar/Week	Flow
Uniform	Dmnl	Auxiliary
Weibull Distribution	Drugs/Week	Auxiliary

E.2.2: Model A: Characteristics and equations of elements

This subsection provides the equations and values that were assigned to the previously identified variables and concepts of Model A.

E.2.2.1 Subscripts

As previously mentioned, two subscripts will be included in the model. The first subscript is named 'Formulations' with three available elements, namely (i) capreomycin, (ii) kanamycin, and (iii) cycloserine. The second subscript is 'Order Number' and has four elements, namely (i) order 1, (ii) order 2, (iii) order 3 and (iv) order 4. Subscripts are enclosed in square brackets [ ] directly following the variable name. Any variable with the subscript range [Formulation, Order Number] will therefore represent the following 12 individual variable ranges: Capreomycin, Order 1; Capreomycin, Order 2; Capreomycin, Order 3; Capreomycin, Order 4; Kanamycin, Order 1; Kanamycin, Order 2; Kanamycin, Order 3; Kanamycin, Order 4; Cycloserine, Order 1; Cycloserine, Order 2; Cycloserine, Order 3; and Cycloserine, Order 4.

A variable can also be followed by a subscript range that specifies which of the 12 variables it represents. For example, the subscript range [Capreomycin, Order Number] will represent all four variables associated with capreomycin (Capreomycin, Order 1; Capreomycin, Order 2; Capreomycin, Order 3; and Capreomycin, Order 4), while the range [Formulation, Order 1] will represent the three variables associated with Order 1 (Capreomycin, Order 1; Kanamycin, Order 1; Cycloserine, Order 1).

E.2.2.2 Demand related variables

The demand section of the model is repeated in Figure E.1 for convenience. As seen in the figure, the variables related to the demand are, (i) Weibull Distribution, (ii) Proportion of Orders Placed, (iii) Uniform, (iv) Country Demand Input, and (v) Normal Orders From Countries.

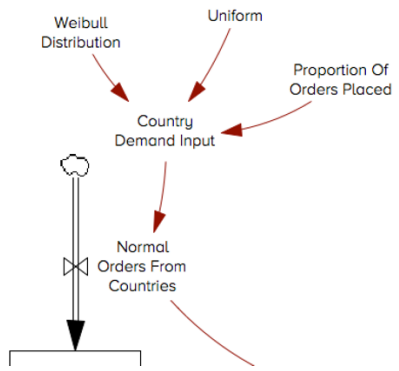

Figure E.1: Demand section of Model A.

- Weibull Distribution

The Weibull Distribution variable generates random values (for the order size) from the chosen Weibull distribution. As previously mentioned, all of the parameter sets in Table 6.2 will be experimented with and used as basis to develop a set of parameters that provide an accurate representation of the data. The equation in Vensim for Weibull Distribution is:

```
RANDOM WEIBULL(m,x,S,h,r,s)
```

where **m** represents the minimum, **x** the maximum, **S** the shape parameter, **h** the location parameter, **r** the scale stretch, and **s** the stream ID. Only values below the minimum and above the maximum will be returned. There are three equations for the Weibull Distribution variable:

```
Weibull Distribution[Capreomycin,Order Number] =
RANDOM WEIBULL(78 , 448000 , 0.6161, 78, 32 500,1)

Weibull Distribution[Kanamycin,Order Number] =
RANDOM WEIBULL(450 , 882000 , 0.4525, 450, 50 000,1)

Weibull Distribution[Cycloserine,Order Number] =
RANDOM WEIBULL(2000 , 9.4491e+06 , 0.4755, 1 500, 420 000,1)
```

- Proportion of Orders Placed

It is important to note the following prerequisites:

- a second order can only be placed if a first order has been placed;
- a third order can only be placed if a second order has been placed; and
- a fourth order can only be placed if a third order has been placed.

Therefore, during the time steps that no (first) order is placed, there cannot be any second, third, or fourth orders. From the available data, the number of orders placed every week can be derived and used to calculate the average probability of a second, third and fourth order being placed on any day of the year can be calculated. Using the multiplication rule these probabilities are used to calculate the probabilities to be used in the model.

These values are provided in Table E.3. For example, if there is 52 weeks in the year, there will be an order placed for capreomycin in 30 (0.574 x 52) of those weeks. Out of that 30 weeks, there will be second order placed in 12 (0.389 x 30) of those weeks, etc. The average probability for 2 orders of capreomycin placed is 0.223, which also gives 12 weeks (0.223 x 52).

Table E.3: Summary of probabilities of more than one order being placed.

	Number of Orders Placed	Probability to use in Model	Average Probability
Capreomycin	1 order	0.574	0.574
	2 orders	0.389	0.223 (0.574 x 0.389)
	3 orders	0.255	0.057 (0.574 x 0.389 x 0.255)
	4 orders	0.263	0.015 (0.574 x 0.389 x 0.255 x 0.263)

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Kanamycin	1 order	0.419	0.419
	2 orders	0.191	0.080 (0.419 x 0.191)
	3 orders	0.287	0.023 (0.419 x 0.191 x 0.287)
	4 orders	0.479	0.011 (0.419 x 0.191 x 0.287 x 0.479)
Cycloserine	1 order	0.721	0.721
	2 orders	0.508	0.366 (0.721 x 0.508)
	3 orders	0.412	0.151 (0.721 x 0.508 x 0.412)
	4 orders	0.298	0.045 (0.721 x 0.508 x 0.412 x 0.298)

Since every order for each formulation will have its own proportion, there will be 12 unique variables. Instead of adding 12 equations to 12 subscript ranges, a comma can be used to separate the values for the four elements (Order1, Order2, Order3, and Order4) of the Order Number subscript. The equations for the variable are:

```
Proportion Of Orders Placed[Capreomycin,Order Number]=
0.574, 0.389, 0.255, 0.263

Proportion Of Orders Placed[Kanamycin,Order Number]=
0.419, 0.191, 0.287, 0.479

Proportion Of Orders Placed[Cycloserine,Order Number]=
0.721, 0.508, 0.412, 0.298
```

- Uniform

This variable is used together with the Proportion of Orders Placed variable as suggested by a Vensim Super Administrator. It will be explained in more detail when discussing the Country Demand Input equations. The equation is similar for all variables:

```
RANDOM 0 1()
```

This will generate a random value between 0 and 1 with equal probability.

- Country Demand Input

The Country Demand Input variable specifies the size of the order. As previously mentioned, the question of whether or not an order is placed, is dependent on (i) the proportions of orders placed, and (ii) the prerequisites mentioned in the proportion of orders placed section. To take these two factors into account, the equation will make use of the following function,

```
IF THEN ELSE( a, b , c ),
```

where **a** is the condition, **b** is the value that will be returned if the condition **a** is met, and **c** is the value that will be returned if the condition **a** is not met.

The equation for the Order1 element of all formulations is:

```
Country Demand Input[Formulations,Order1]= IF THEN ELSE(
Uniform[Formulations,Order1] < Proportion Of Orders
Placed[Formulations,Order1] , Weibull Distribution[Formulations,Order1]
, 0 )
```

Since Order1 has no prerequisite, the only factor taken into consideration is the proportion of orders placed. The condition is whether the random value (between 0 and 1) returned by the Uniform variable is smaller than the Proportion of Orders Placed variable. If this is true, an order is placed that week and the value generated by the Weibull Distribution variable will be returned. If it is not true, however, a value of 0 is returned, indicating that no orders are placed that week.

The equations for the Order2, Order3 and Order4 elements are:

```
Country Demand Input[Formulations,Order2]= IF THEN ELSE( Country Demand
Input[Formulations,Order1] > 0 , IF THEN ELSE(
Uniform[Formulations,Order2] < Proportion Of Orders
Placed[Formulations,Order2] , Weibull Distribution[Formulations,Order2]
, 0 ) , 0 )
```

```
Country Demand Input[Formulations,Order3]= IF THEN ELSE( Country Demand
Input[Formulations,Order2]>0, IF THEN ELSE(
Uniform[Formulations,Order3] < Proportion Of Orders
Placed[Formulations,Order3] , Weibull Distribution[Formulations,Order3]
, 0 ) , 0 )
```

```
Country Demand Input[Formulations,Order4]=IF THEN ELSE( Country Demand
Input[Formulations,Order3]>0, IF THEN ELSE(
Uniform[Formulations,Order4] < Proportion Of Orders
Placed[Formulations,Order4] , Weibull Distribution[Formulations,Order4]
, 0 ) , 0 )
```

As shown in the equation, the first condition tests whether the prerequisite is met. Only if the preceding Order Number element is larger than 0 (i.e. an order was placed) will it continue to consider the Proportion of Orders Placed. The second condition in the equation is the same as the one discussed in the equation for Order1.

- Normal Orders From Countries

The Normal Orders From Countries variable is merely equal to the value generated by Country Demand Input. Its equation is:

```
Normal Orders From Countries[Formulations,Order Number]=
Country Demand Input[Formulations,Order Number]
```

E.2.2.3 Manufacturing related variables

The section of the model related to manufacturing and dispatch of the drugs is repeated in Figure E.2 for convenience. As seen in the figure, the variables related to manufacturing are, (i) Normal Lead Time Lookup, (ii) Production, (iii) Normal Order Drugs Available for Dispatch, and (iv) Normal Orders Fulfilled for Countries.

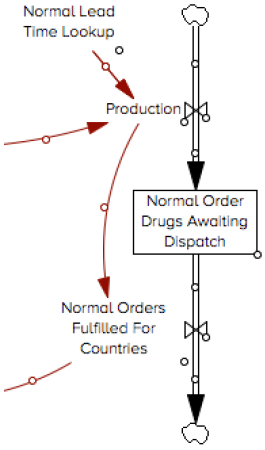

Figure E.2: Manufacturing section of Model A.

- Normal Lead Time Lookup

Since no distributions could be fitter to the normal lead time lookup is merely a lookup value of the average lead time recorded during each time period. The equation is given as:

```
Normal Lead Time Lookup[Formulations, Order Number] = [(0,0)-(10,10)],(1,154),
(2,154),(3,260),(4,267),(5,155),(6,322),(7,322),(8,274),(9,274),(10,180),(11,180),(
12,610),(13,364),(14,95),(15,137),(16,186),(17,224),(18,29),(19,273),(20,142),(21,3
4),(22,74),(23,115),(24,317),(25,61),(26,152),(27,128),(28,14),(29,225),(30,105),(3
1,166),(32,183),(33,313),(34,143),(35,143),(36,285),(37,226),(38,226),(39,285),(40,
194),(41,17),(42,8),(43,16),(44,21),(45,21),(46,21),(47,27),(48,27),(49,30),(50,88)
,(51,171),(52,55),(53,137),(54,32),(55,57),(56,481),(57,481),(58,165),(59,295),(60,
44),(61,44),(62,534),(63,534),(64,194),(65,204),(66,292),(67,193),(68,352),(69,301)
,(70,195),(71,172),(72,109),(73,109),(74,450),(75,450),(76,708),(77,188),(78,118),(
79,126),(80,108),(81,108),(82,146),(83,94),(84,55),(85,143),(86,100),(87,100),(88,8
2),(89,82),(90,75),(91,207),(92,236),(93,234),(94,34),(95,199),(96,285),(97,316),(9
8,271),(99,132),(100,54),(101,35),(102,35),(103,89),(104,146),(105,178),(106,197),(
107,245),(108,55),(109,61),(110,61),(111,61),(112,61),(113,155),(114,263),(115,128)
,(116,370),(117,291),(118,291),(119,152),(120,87),(121,87),(122,155),(123,155),(124
,502),(125,502),(126,363),(127,117),(128,59),(129,102),(130,413),(131,27),(132,419)
,(133,45),(134,45),(135,239),(136,107),(137,65),(138,19),(139,19),(140,123),(141,12
3),(142,123),(143,305),(144,86),(145,251),(146,251),(147,187),(148,200),(149,187),(
150,339),(151,136),(152,348),(153,105),(154,107),(155,312),(156,312),(157,198),(158
,128),(159,127),(160,158),(161,164),(162,367),(163,205),(164,129),(165,165),(166,26
4),(167,371),(168,168),(169,301),(170,205),(171,160),(172,278),(173,360),(174,34),(
175,89),(176,92),(177,225),(178,318),(179,366),(180,21),(181,196),(182,397),(183,85
),(184,85),(185,250),(186,266),(187,57),(188,305),(189,305),(190,305),(191,305),(19
2,305),(193,73),(194,154),(195,154),(196,261),(197,258),(198,232),(199,152),(200,36
3),(201,363),(202,108),(203,174),(204,324),(205,324),(206,379),(207,302),(208,156),
(209,251),(210,216),(211,255),(212,304),(213,304),(214,267),(215,267),(216,267),(21
7,108),(218,39),(219,249),(220,126),(221,183),(222,18),(223,146),(224,223),(225,420
),(226,38),(227,232),(228,232),(229,232),(230,253),(231,94),(232,204),(233,208),(23
4,248),(235,76),(236,204),(237,248),(238,406),(239,134),(240,86),(241,221),(242,264
),(243,69),(244,69),(245,253),(246,166),(247,190),(248,190),(249,145),(250,207),(25
1,145),(252,207),(253,396),(254,278),(255,278),(256,255),(257,255),(258,72),(259,51
3),(260,394),(261,471),(262,505),(263,505),(264,505)
```

• Production

The Production variable takes the value of Normal Orders From Countries and delays it for the amount of time given by Normal Lead Time Lookup before pushing it back into the model. To achieve this, a delay function will be used. From the available delays in Vensim, the Delay Material function is most applicable since it preserves quantities and the delay time can be a variable instead of being a fixed value. The function for delay material is:

```
DELAY MATERIAL( a , b , c , d )
```

where **a** is the input, **b** is the delay time, **c** is the starting value and **d** is the value to be used if no delayed inputs are available. The equation for production is therefore:

```
Production[Formulations,Order Number]=
DELAY MATERIAL(Normal Orders From Countries[Formulations,Order Number],
Normal Lead Time Lookup[Formulations,Order Number](time) , 0 , 0)
```

• Normal Order Drugs Awaiting Dispatch

Normal Order Drugs Awaiting Dispatch is calculated as the integral of the difference between the inflow and the outflow, in this case the production and normal orders fulfilled for countries, respectively. In Vensim, this equation is:

```
Normal Order Drugs Awaiting Dispatch[Formulations,Order Number]=
INTEG(Production[Formulations,Order Number]-Normal Orders Fulfilled For
Countries[Formulations,Order Number],0)
```

As previously mentioned, the model assumes that the manufacturer entity does not keep any stock and that the SLDs are immediately dispatched once the production is completed. Therefore, the value this variable takes represent the drugs that have been received but not yet dispatched and delivered to countries.

• Normal Orders Fulfilled For Countries

Since drugs are immediately dispatched after production, the Normal Orders Fulfilled For Countries variable will take on the same value as the Production variable, as soon as the delay period is over and a value is generated. The equation for the variable is therefore:

```
Normal Orders Fulfilled For Countries[Formulations,Order Number]=
IF THEN ELSE(Production[Formulations,Order Number] > 0 ,
Production[Formulations,Order Number], 0 )
```

E.2.2.4 Country related variables

The section of the model related to the countries is repeated in Figure E.3 for convenience. As seen in the figure, the variables related to the cost are (i) Normal Order

Drugs Received By Countries, (ii) Normal Orders Supply Line, and (iii) Total Drugs Received By Countries.

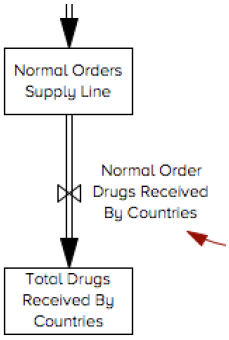

Figure E.3: Country section of Model A.

- Normal Order Drugs Received By Countries

The Normal Order Drugs Received By Countries variable is merely equal to the value generated by Normal Orders Fulfilled For Countries. Its equation is:

```
Normal Order Drugs Received By Countries[Formulations,Order Number]=
Normal Orders Fulfilled For Countries[Formulations,Order Number]
```

- Normal Orders Supply Line

The number of drugs that have been ordered by countries, but not yet received is represented by the Normal Orders Supply Line variable. This variable can be used at the end of the simulation run to identify the number of drugs that have not yet been delivered. The equation for this variable is as follows:

```
Normal Orders Supply Line[Formulations,Order Number]=
INTEG(Normal Orders From Countries[Formulations,Order Number]-
Normal Order Drugs Received By Countries[Formulations,Order Number], 0)
```

- Total Drugs Received By Countries

The Total Drugs Received By Countries variables returns the total number of drugs (for all order numbers) that have been delivered to the countries, for each formulation. This variable is useful to compare with the total demand values from the historical data.

```
Total Drugs Received By Countries[Formulations]=
INTEG(Normal Order Drugs Received By Countries[Formulations,Order
Number!],0)
```

E.2.2.5 Cost related variables

The cost section of the model is repeated in Figure E.4 for convenience. As seen in the figure, the variables related to the cost are, (i) Per Unit Cost, (ii) Total Unit Cost, (iii)

Cumulative Total Unit Cost, and (iv) Total Costs. The Normal Orders From Countries variable is a shadow variable from the main model.

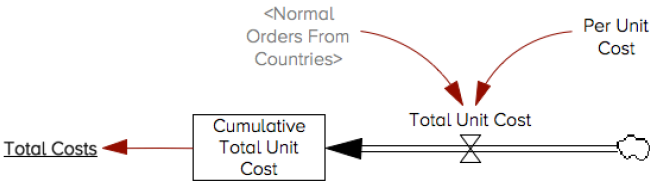

Figure E.4: Cost section of Model A.

- Per Unit Cost

The average unit cost, from 2010 to 2015, for the 3 formulations, as well as the average cost over the six years, is summarised in Table E.4.

Since the per unit cost will be the same for all order numbers, but different for each formulation, the equations for the variable are:

```
Per Unit Cost [Capreomycin,Order Number] = 5.54, 5.54, 5.54, 5.54
Per Unit Cost [Kanamycin,Order Number] = 2.59, 2.59, 2.59, 2.59
Per Unit Cost [Cycloserine,Order Number] = 0.53, 0.53, 0.53, 0.53
```

Table E.4: Summary of costs from 2010 – 2014.

Formulation	Description	Average Unit Cost ($US)					
		2010	2011	2012	2013	2014	Avg
Capreomycin	1g powder for injection	4.00	7.01	6.66	5.53	5.13	5.66
Kanamycin	1g solution for injections (4ml)	2.79	2.61	2.58	2.49	2.50	2.59
Cycloserine	250mg hard capsules	0.67	0.60	0.59	0.49	0.42	0.55

- Total Unit Cost

The total unit cost is calculated separately for each order by multiplying the per unit cost by the number of drugs ordered. The equation in Vensim is:

```
Total Unit Cost[Formulations,Order Number]=
Normal Orders From Countries[Formulations,Order Number] *
Per Unit Cost[Formulations ,Order Number]
```

- Cumulative Total Unit Cost

The cumulative total unit cost is added so that the total costs for each order at any given time step can be viewed. The equation is:

```
Cumulative Total Unit Cost[Formulations,Order Number]=
INTEG (Total Unit Cost[Formulations,Order Number], 0)
```

- Total Costs

The Total Costs variable is intended to include all of the costs; however, since only unit costs are used in this model, it is the only cost included. The equation is:

```
Total Costs[Formulations]=
SUM(Cumulative Total Unit Cost[Formulations,Order Number!])
```

This variable can be used to compare the total costs associated with different policies during the scenario implementation phase.

E.3 Modelling details of Model B

This section provides the modelling details associated with Model B, as defined and discussed in Section 6.3.5. The variables that are included in the model will be identified and their equations and characteristics will be described.

E.3.1 Model B: Variable types

As before, the applicable variables and concepts were identified as either a stock variable (accumulations within the system), flow variable (determines the variation of stock) or auxiliary variable (constants or estimates). The list of the applicable variables, their variable type and their units can be seen in Table E.5. The table includes several variables, in addition to those initially identified in Section E.1, that were added during the development of the model.

Table E.5: Variable types for Model B.

Variable Name	Unit	Variable Type
Country Dispatch Lead Time	Week	Auxiliary
Cumulative Obsolete Stock	Drugs	Stock
Cumulative Purchase Unit Cost	Dollar	Stock
Cumulative Stockpile Replenishment Cost	Dollar	Stock
Cumulative Total Obsolescence Cost	Dollar	Stock
Demand Input	Drugs/Week	Auxiliary
Dispatch Emergency Drugs To Countries	Drugs/Week	Flow
Drugs Available For Emergency Orders	Drugs/Week	Flow
Drugs Available For Stock Rotation	Drugs/Week	Auxiliary
Drugs Dispatched As Stock Rotation	Drugs/Week	Flow
Drugs Received From Manufacturer	Drugs/Week	Flow
Drugs To Be Dispatched For Stock Rotation	Drugs/Week	Auxiliary
Emergency Input	Drugs/Week	Auxiliary
Emergency Order Cost	Dollar/Week	Flow
Emergency Order Drugs Received By Countries	Drugs/Week	Flow
Emergency Orders From Countries	Drugs/Week	Flow
Emergency Orders Supply Line	Drugs	Stock

continued on next page

continued from previous page

Emergency Proportion Of Orders Placed	Dmnl	Auxiliary
Emergency Weibull Distribution	Drugs/Week	Auxiliary
Expiration Value	Week	Auxiliary
Initial Stock On Hand	Drugs	Auxiliary
Normal Order Drugs Awaiting Dispatch	Drugs	Stock
Normal Order Drugs Received By Countries	Drugs/Week	Flow
Normal Order Purchase Cost	Dollar/Week	Flow
Normal Orders From Countries	Drugs/Week	Flow
Normal Orders Supply Line	Drugs	Stock
Obsolete Stock	Drugs/Week	Flow
Order Processing	Drugs/Week	Flow
Order Processing Lead Time	Week	Auxiliary
Orders Placed To Manufacturer	Drugs/Week	Flow
Per Unit Cost	Dollar/Drugs	Auxiliary
Processed Orders	Drugs/Week	Auxiliary
Processing Drugs For Stock Rotation	Drugs/Week	Flow
Production & Dispatch Lead Time	Week	Auxiliary
Production & Dispatch To GDF/PA	Drugs/Week	Flow
Production & Dispatch To SRS	Drugs/Week	Flow
Proportion Of Orders Placed	Dmnl	Auxiliary
QC's & Dispatch To Countries	Drugs/Week	Flow
Rotation Value Start	Week	Auxiliary
Rotation Value Stop	Week	Auxiliary
SRS Demand	Drugs/Week	Auxiliary
SRS Stock On Hand	Drugs	Stock
SRS Supply Line	Drugs	Stock
Stockpile Rotation Cost	Dollar/Week	Flow
TIME STEP	Week	Built-in
Total Costs	Dollar	Auxiliary
Total Emergency Order Drugs Received	Drugs	Stock
Total Normal Order Drugs Received	Drugs	Stock
Total Obsolescence Cost	Dollar/Week	Flow
Uniform	Dmnl	Auxiliary
Weibull Distribution	Drugs/Week	Auxiliary

E.3.2 Model B: Characteristics and equations of elements

This subsection provides the equations and values that were assigned to the previously identified variables and concepts of Model B.

E.3.2.1 Lead times

The main difference in Model B is the implementation of three separate lead times. As discussed in Section 6.3.5.2, the lead times was implemented in the model through triangular distributions. The triangular distribution is based on three values, a minimum, maximum and peak value. Vensim also allows the application of a 'range constraint' of sorts, which limits the output generated by the triangular distribution to fall within the

range. The initial parameters and range values were based on country case studies, averages or estimates obtained from WHO (2008); Giffin and Robinson (2009); Lunte (2012); Nicholson *et al.* (2013); Keravec (2014); Muzafarova (2015). These values were experimented with and adjusted until the total lead time (sum of the three lead times) from the model, represented the lead time in the data.

The equation used for triangular distributions in Vensim is:

```
RANDOM TRIANGULAR( _min_ , _max_ , _start_ , _peak_ , _stop_ , _seed_ )
```

Where `min` and `max` is the range of the output values, and `start`, `peak`, and `stop` is the start, average and stop value of the triangle. The equation for the order processing lead time is:

```
Order Processing Lead Time[Formulations,Order Number]=
RANDOM TRIANGULAR( 2 , 30 , 0 , 4 , 35 , 1 )
```

This is illustrated in Figure E.5. The output values will all fall within the shaded area.

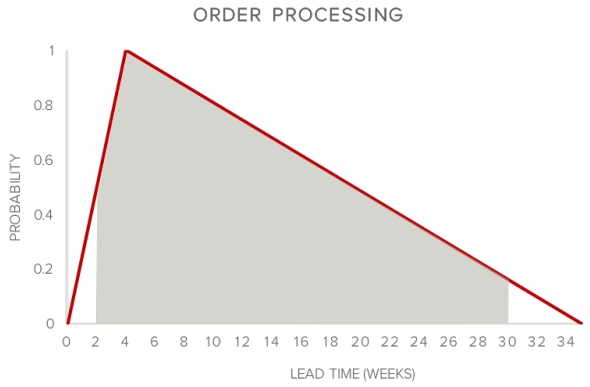

Figure E.5: Illustration of triangular distribution for order processing lead time.

The equation for the production and dispatch lead time is:

```
"Production & Dispatch Lead Time"[Formulations,Order Number]=
RANDOM TRIANGULAR( 5 , 45 , 0 , 6 , 70 , 1 )
```

This is illustrated in Figure E.6. The output values will all fall within the shaded area.

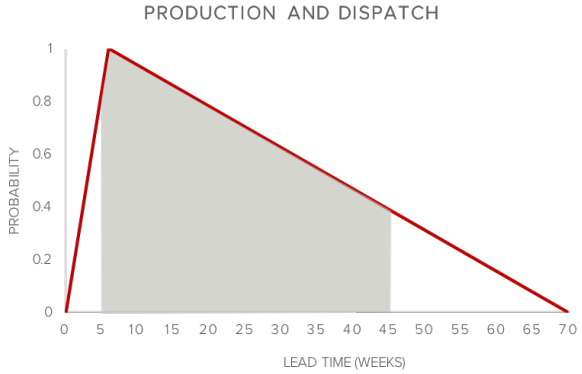

Figure E.6: Illustration of triangular distribution for production and dispatch lead time.

The equation for the country dispatch lead time is:

```
Country Dispatch Lead Time [Formulations,Order Number] =
RANDOM TRIANGULAR( 3 , 15 , 0 , 3 , 35 , 1 )
```

This is illustrated in Figure E.7. The output values will all fall within the shaded area.

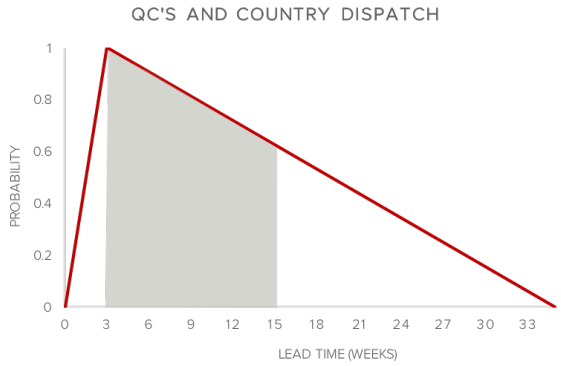

Figure E.7: Illustration of triangular distribution for country dispatch lead time.

E.3.2.2 Normal order related variables

The normal orders section of the model is repeated in Figure E.8 for convenience. As seen in the figure, the variables related to the normal orders are, (i) Weibull Distribution, (ii) Proportion of Orders Placed, (iii) Uniform, (iv) Demand Input, (v) Normal Orders From Countries, (vi) Normal Orders Supply Line, (vii) Normal Order Drugs Received By Countries, (viii) Total Normal Order Drugs Received, (ix) Order Processing, and (x) Processed Orders.

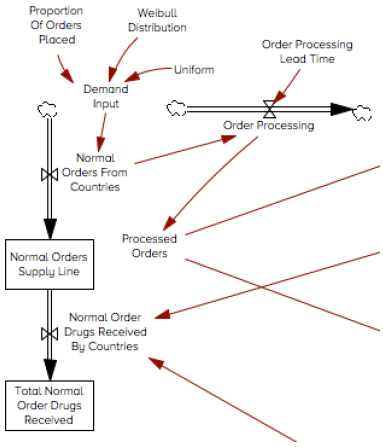

Figure E.8: Normal orders section of Model B.

As with Model A, there can be up to four normal orders placed in any time step. Variables that remained and has the same equations as Model A:

i. Demand Input (Called country demand input in Model A),
ii. Normal Orders From Countries,
iii. Normal Orders Supply Line,
iv. Proportion Of Orders Placed,

v. Total Normal Order Drugs Received (called Total Drugs Received By Countries in Model A),
vi. Uniform, and
vii. Weibull Distribution.

The remaining three variables of the normal orders section are described below.

• Order Processing

Order Processing is a flow variable that was added to represent the ordering process of the normal orders that were placed by countries. A delay function is used to take the value of Normal Orders From Countries and delay it for the amount of time given by Order Processing Lead Time before pushing it back into the model. The equation for this variable is:

```
Order Processing[Formulations,Order Number]=
DELAY MATERIAL (Normal Orders From Countries[Formulations,Order
Number], Order Processing Lead Time[Formulations,Order Number], 0, 0)
```

• Processed Orders

The Processed Orders variable is merely equal to the value generated by Order Processing. Its equation is:

```
Processed Orders[Formulations,Order Number]=
Order Processing[Formulations,Order Number]
```

• Normal Order Drugs Received By Countries

Normal order drugs are fulfilled by the GDF/PA either through stock rotation or by ordering the drugs from manufacturers on behalf of countries. Therefore, the Normal Order Drugs Received By Countries variable equals the sum of both QC's & Dispatch To Countries and Drugs Dispatched As Stock Rotation, as illustrated in the equation:

```
Normal Order Drugs Received By Countries[Formulations,Order Number]=
"QC's & Dispatch To Countries"[Formulations,Order Number] +
Drugs Dispatched As Stock Rotation[Formulations,Order Number]
```

E.3.2.3 Production of normal order drugs

The production of normal order drugs section of the model is repeated in Figure E.9 for convenience. As seen in the figure, the unique variables related to this section are, (i) Production & Dispatch TO GDF/PA, (ii) QC's & Dispatch To Countries, and (iii) Normal Order Drugs Awaiting Dispatch.

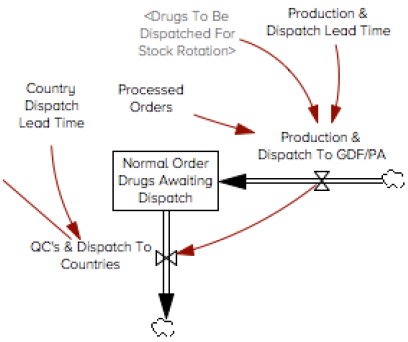

Figure E.9: Production of normal order drugs section of Model B.

- Production & Dispatch To GDF/PA

The Production & Dispatch to GDF/PA variable represents the orders that have been processed and has to be produced by manufacturers and dispatched to the GDF/PA; therefore, it only considers the orders that have completed the order process and that will not be fulfilled through stock rotation. This calculated amount of orders that has to produced are delayed for the amount of time given by Production & Dispatch Lead Time. The equation for the variable is:

```
"Production & Dispatch To GDF/PA"[Formulations,Order Number]=
DELAY MATERIAL(( Processed Orders[Formulations,Order Number] -
Drugs To Be Dispatched For Stock Rotation[Formulations,Order Number]
),"Production & Dispatch Lead Time"[Formulations,Order Number],0, 0)
```

- QC's & Dispatch To Countries

After production, the drugs are dispatched to the GDF/PA for quality checks (QC). This variable takes the value of the Production & Dispatch To GDF/PA variable and delays it for the amount of time given by Country Dispatch Lead Time before pushing it back into the model. The equation is:

```
"QC's & Dispatch To Countries"[Formulations,Order Number]=
DELAY MATERIAL( IF THEN ELSE("Production & Dispatch To
GDF/PA"[Formulations,Order Number] > 0 , "Production & Dispatch To
GDF/PA"[Formulations,Order Number] , 0 ) , Country Dispatch Lead
Time[Formulations,Order Number] , 0 , 0)
```

As illustrated in the equation, an IF THEN ELSE function is used to ensure that the value of the variable is zero if the Production & Dispatch To GDF/PA variable is zero.

- Normal Order Drugs Awaiting Dispatch

The Normal Order Drugs Awaiting Dispatch variable can be seen as a 'buffer' area where drugs that have been produced and dispatched are waiting to be sent to the countries. This variable will mostly have a value of zero, or swiftly return to a value of

zero, since the drugs will immediately go from production to QC and dispatch. The equation is:

```
Normal Order Drugs Awaiting Dispatch[Formulations,Order Number]= INTEG (
"Production & Dispatch To GDF/PA"[Formulations,Order Number]-"QC's &
Dispatch To Countries"[Formulations,Order Number],0)
```

E.3.2.4 Stockpile related variables

This section will describe the four variables specifically related to the stockpile section of Model B. The four variables are (i) Initial Stock On Hand, (ii) SRS Stock On Hand, and (iii) SRS Demand. Although there can be up to four normal orders placed, processed, manufactured and delivered; the stockpile only recognises one order. However, since the subscripts are coded in the model, a value of 0 is assigned to order2, order3 and order4 for the variables related to the stockpile.

- Initial Stock On Hand

The calculations for the initial stock on hand were provided in Section 6.3.5.2. The equations in Vensim are:

```
Initial Stock On Hand[Capreomycin,Order Number] = 221018, 0, 0, 0
Initial Stock On Hand[Kanamycin,Order Number] = 184984, 0, 0, 0
Initial Stock On Hand[Cycloserine,Order Number] = 3.07664e+06, 0, 0, 0
```

- SRS Stock On Hand

The following function was used for the stockpile:

```
QUEUE FIFO (inflow, outflow, profile, initial, age range)
```

This will assume that the stockpile handles drugs on a first-in-first-out basis, to potentially minimise the obsolete stock. Another advantage of the QUEUE function, is that the model now tracks the age of the drugs in the stockpile, which is used to determine when drugs are eligible for rotation and when they become obsolete.

It is assumed initially the stockpile is full and that the drugs still have their full shelf life remaining. The profile variable is a probability distribution function that runs from 0 to age range and has an area of 1. The inflow of the stockpile are drugs delivered from manufacturers based on orders placed by the SRS while the outflow comprises of emergency orders, stock rotation and obsolete stock. This is illustrated in the equation:

```
SRS Stock On Hand[Formulations,Order Number]= QUEUE FIFO( "Production &
Dispatch To SRS"[Formulations,Order Number] , Processing Drugs For
Stock Rotation[Formulations,Order Number] + Obsolete
Stock[Formulations,Order Number] + Drugs Available For Emergency
Orders[Formulations,Order Number]  , Profile , Initial Stock On
Hand[Formulations,Order Number] , 0 )
```

• SRS Demand

Since it is assumed that the SRS currently follows a base stock policy, they will place an order to manufacturers of the exact size of what was removed from the stockpile. The equation for the SRS demand is therefore:

```
SRS Demand[Formulations,Order Number]= Drugs Available For Emergency
Orders[Formulations,Order Number] + Obsolete Stock[Formulations,Order
Number] + Processing Drugs For Stock Rotation [Formulations,Order
Number]
```

E.3.2.5 Stockpile supply line related variables

The stockpile supply line section is illustrated in Figure E.10. The three unique variables associated with this section, are (i) Orders Placed To Manufacturer, (ii) SRS Supply line, (iii) Drugs Received From Manufacturer, and (iv) Production & Dispatch To SRS.

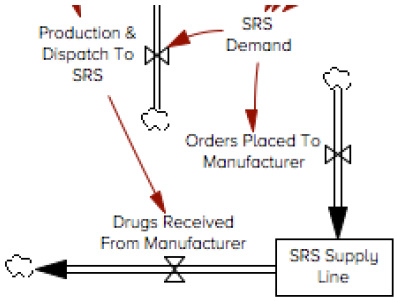

Figure E.10: Stockpile supply line section of Model B.

• Production and dispatch to SRS

The Production & Dispatch To SRS variable takes the value of SRS Demand and delays it for the amount of time given by Production & Dispath Lead Time before pushing it back into the model. The equation is:

```
"Production & Dispatch To SRS"[Formulations,Order Number]= DELAY
MATERIAL (SRS Demand[Formulations,Order Number] , "Production &
Dispatch Lead Time"[Formulations,Order Number] , 0 , 0)
```

• Orders placed to manufacturer

The Orders Placed To Manufacturer variable is merely equal to the value generated by SRS Demand. Its equation is:

```
Orders Placed To Manufacturer[Formulations,Order Number]=
SRS Demand[Formulations,Order Number]
```

• Drugs received from manufacturer

The Drugs Received From Manufacturer variable is merely equal to the value generated by Production & Dispatch To SRS. Its equation is:

```
Drugs Received From Manufacturer[Formulations,Order Number]=
"Production & Dispatch To SRS"[Formulations,Order Number]
```

- SRS supply line

The SRS supply line represents the drugs that have been ordered from manufactures, but not yet delivered. The equation is given as:

```
SRS Supply Line[Formulations,Order Number]= INTEG
(Orders Placed To Manufacturer[Formulations,Order Number]-
Drugs Received From Manufacturer [Formulations,Order Number],0)
```

E.3.2.6 Stock rotation related variables

The stock rotation section of Model B is presented in Figure E.11 for convenience. The related variables that will be discussed are, (i) Rotation Value Start, (ii) Rotation Value Stop, (iii) Drugs Available For Stock Rotation, (iv) Drugs To Be Dispatched For Stock Rotation, and (v) Drugs Dispatched As Stock Rotation.

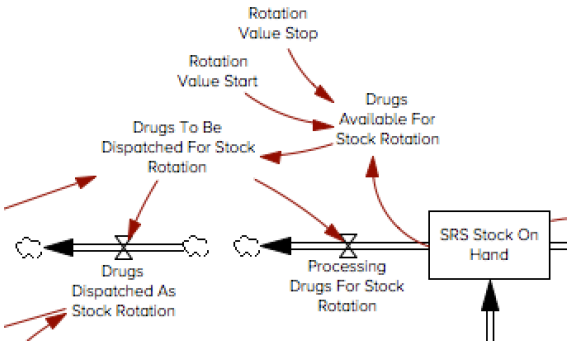

Figure E.11: Stock rotation section of Model B.

- Rotation values

The details of the rotation values was discussed in Section 6.3.5.2. The values were determined based on the shelf life of each formulation, as provided in Table E.6.

Table E.6: Shelf lives of the dormulations.

Formulation	Description	Shelf Life
Capreomycin	1g powder for injection	24 Months
Kanamycin	1g solution for injections (4ml)	36 Months
Cycloserine	250mg hard capsules	24 Months

The rotation value start and rotation value stop are given as:

```
Rotation Value Start[Capreomycin,Order Number]= 16,16,16,16
Rotation Value Start[Kanamycin,Order Number]= 40, 40, 40, 40
Rotation Value Start[Cycloserine,Order Number]= 16,16,16,16

Rotation Value Stop[Capreomycin,Order Number]= 36,36,36,36
Rotation Value Stop[Kanamycin,Order Number]= 84,84,84,84
Rotation Value Stop[Cycloserine,Order Number]= 36,36,36,36
```

- Drugs available for stock rotation

Since all of the orders can be fulfilled through stock rotation, the drugs available for each of the four orders (order1, order2, order3 and order4) are:

```
Drugs Available For Stock Rotation[Formulations,Order Number]=
MAX(0,(QUEUE AGE IN RANGE( SRS Stock On Hand[Formulations,Order1] ,
Rotation Value Start[Formulations,Order1] , Rotation Value
Stop[Formulations,Order1] )/TIME STEP) - Obsolete
Stock[Formulations,Order1])
```

This equation (Queue age in range) ensures that only the drugs that have been in the stockpile between the Rotation Value Start and Rotation Value Stop will be dispatched.

- Drugs to be dispatched for stock rotation

The most orders that can be fulfilled at any time is four (order1, order2, order3 and order4). It is possible that all four of these orders can be fulfilled through means of stock rotation as long as the number of drugs that are eligible for stock rotation is enough for all four of these orders. To implement this in the model, however, it is assumed that order1 will receive preference over order2, which receives preference over order 2, which receives preference over order4. The equation for the drugs to be dispatched for stock rotation for order1 is:

```
Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]= IF THEN
ELSE(Drugs Available For Stock Rotation[Formulations,Order1] > Processed
Orders[Formulations,Order1], Processed Orders[Formulations,Order1] , 0 )
```

As depicted in the equation, all of the drugs required for order1 is dispatched if enough is available, otherwise no drugs are dispatched. For order2, the equation is different. The model first assesses whether drugs were dispatched for order1 from the stockpile. If no drugs for order1 were dispatched through stock rotation, but there are enough drugs available to fulfil order2, the drugs are dispatched for order2; otherwise, zero drugs are dispatched. However, if order1 was fulfilled through stock rotation, the drugs available for stock rotation has to be adjusted by subtracting the number of drugs that was dispatched for order1. This is illustrated in the equation for order2:

```
Drugs To Be Dispatched For Stock Rotation[Formulations,Order2]= IF THEN
ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]>0 ,
IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order2] -
Drugs To Be Dispatched For Stock Rotation [Formulations,Order1] >
Processed Orders[Formulations,Order2],
Processed Orders [Formulations,Order2] , 0 ) ,
IF THEN ELSE( Drugs Available For Stock Rotation[Formulations,Order2] >
Processed Orders [Formulations,Order2] , Processed
Orders[Formulations,Order2] , 0 ) )
```

The same principle is followed for the remaining two equations, however, for order3 the drugs dispatched for order1 and order2 is taken into consideration, while for order4 the

drugs the dispatched for order1, order2 and order3 is taken into consideration. The remaining two equations are:

```
Drugs To Be Dispatched For Stock Rotation[Formulations,Order3]= IF THEN
ELSE( Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] +
Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] > 0 ,
IF THEN ELSE( Drugs Available For Stock Rotation[Formulations,Order3] -
Drugs To Be Dispatched For Stock Rotation [Formulations,Order2] -
Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] >
Processed Orders[Formulations,Order3] ,
Processed Orders[Formulations,Order3] , 0 ) ,
IF THEN ELSE( Drugs Available For Stock Rotation[Formulations,Order3] >
Processed Orders [Formulations,Order3] ,
Processed Orders[Formulations,Order3] , 0 ) )
```

```
Drugs To Be Dispatched For Stock Rotation[Formulations,Order4]= IF THEN
ELSE( Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] +
Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] + Drugs
Available For Stock Rotation [Formulations,Order3] > 0 ,
IF THEN ELSE( Drugs Available For Stock Rotation[Formulations,Order4] -
Drugs To Be Dispatched For Stock Rotation [Formulations,Order3] - Drugs
To Be Dispatched For Stock Rotation[Formulations,Order2] - Drugs To Be
Dispatched For Stock Rotation[Formulations,Order1] > Processed
Orders[Formulations,Order4] , Processed Orders[Formulations,Order4],0 )
, IF THEN ELSE( Drugs Available For Stock Rotation[Formulations,Order4]
> Processed Orders [Formulations,Order4] , Processed
Orders[Formulations,Order4] , 0 ) )
```

- Processing drugs for stock rotation

Although order1, order2, order3 and order4 can be fulfilled through stock rotation from the stockpile, the stockpile only acknowledges order1. To ensure that the stockpile recognises outgoing stock of all four orders, the equation for order1 is given as:

```
Processing Drugs For Stock Rotation[Formulations,Order1]=(
Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]) +
Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] +
Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] +
Drugs To Be Dispatched For Stock Rotation[Formulations,Order4]
```

This ensures that the sum of the drugs that are dispatched for all four orders are removed from the stockpile. The value for order2, order3 and order3 are set to zero:

```
Processing Drugs For Stock Rotation[Formulations,Order2] = 0
```

```
Processing Drugs For Stock Rotation[Formulations,Order3] = 0
```

```
Processing Drugs For Stock Rotation[Formulations,Order4] = 0
```

• Drugs dispatched as stock rotation

This variable takes the output of processing drugs for stock rotation and delays it by the amount of time specified by country dispatch lead time, before returning it to the model. The equation is given as:

```
Drugs Dispatched As Stock Rotation[Formulations,Order Number]= DELAY
MATERIAL(Processing Drugs For Stock Rotation[Formulations,Order Number],
Country Dispatch Lead Time[Formulations,Order Number], 0, 0)
```

E.3.2.7 Obsolete stock related variables

The variables related the obsolete stock are (i) expiration value, (ii) obsolete stock, and (iii) cumulative obsolete stock.

• Expiration value

The expiration value is the age of a drug when it is considered obsolete. These values are less than the shelf life, since it takes into account the average time that it takes a drug to be delivered to a country and that a drug typically needs several months of shelf life left when delivered. The equations are:

```
Expiration Value[Capreomycin,Order Number] = 52, 0, 0, 0
Expiration Value[Kanamycin,Order Number] = 100, 0, 0, 0
Expiration Value[Cycloserine,Order Number] = 52, 0, 0, 0
```

• Obsolete stock

All of the drugs that have been in the stockpile longer than the expiration value, are considered obsolete and removed from the stock. Since the stockpile only keeps one stock for all orders, the value for order2, order3, and order4 is automatically zero. The equations are:

```
Obsolete Stock[Formulations,Order1]= QUEUE AGE IN RANGE( SRS Stock On
Hand[Formulations,Order1] , Expiration Value[Formulations,Order1] ,
:NA: )/TIME STEP
Obsolete Stock[Formulations,Order2]= 0
Obsolete Stock[Formulations,Order3]= 0
Obsolete Stock[Formulations,Order4]= 0
```

• Cumulative obsolete stock

The cumulative obsolete stock, is a stock variable that adds up all of the obsolete stock to provide the total number of units that was 'lost'. The equation is:

```
Cumulative Obsolete Stock[Formulations,Order Number]=
INTEG (Obsolete Stock[Formulations,Order Number],0)
```

E.3.2.8 Emergency order related variables

The emergency order section is illustrated in Figure E.12 for convenience. In generela, this section functions the same as the normal orders section, except that drugs are dispatched from the stockpile instead of being manufactured first. The variables associated with the emergency orders are, (i) Emergency Weibull distribution, (ii) Emergency proportion of orders placed, (iii) Emergency input, (iv) Emergency orders from countries, (v) Drugs available for emergency orders, (vi) Dispatch emergency drugs to countries, (vii) Emergency order drugs received by countries, (viii) Emergency orders supply line, and (ix) Total emergency order drugs received.

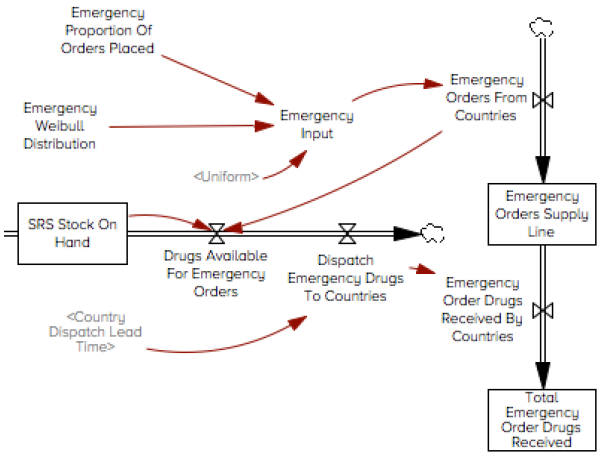

Figure E.12: Emergency order section of Model B.

- Emergency Weibull distribution

The Weibull distributions for emergency orders are assumed to be the same as for normal orders (Weibull Distribution Variable) but the maximum value has been reduced since only small orders are allowed for emergency. It is assumed that the maximum size an emergency order may be is 25% of the stockpile capacity. The equations are:

```
Emergency Weibull Distribution[Capreomycin,Order Number]=
RANDOM WEIBULL( 78 , 55255 , 0.6161 , 78 , 32500 , 0 )

Emergency Weibull Distribution[Kanamycin,Order Number]=
RANDOM WEIBULL( 450 , 46246 ,0.4525 , 450 , 50000 , 1 )

Emergency Weibull Distribution[Cycloserine,Order Number]= RANDOM
WEIBULL( 1500 , 769160 , 0.4755 , 1500 , 420000 , 1 )
```

- Emergency proportion of orders placed

Since it is not stipulated in the data which orders are emergency orders, an assumption on the proportion of orders had to made. From all the SLDs in the data with a total lead time of less than 90 days, roughly 16,9% of the orders from 2010 to 2014 were for cycloserine, while 10,6% was for capreomycin and 11,2% was for kanamycin. This is the values that will be used in the model. The equations are therefore:

```
Emergency Proportion Of Orders Placed[Capreomycin,Order Number]=
0.106, 0, 0, 0

Emergency Proportion Of Orders Placed[Kanamycin,Order Number]=
0.086, 0, 0, 0

Emergency Proportion Of Orders Placed[Cycloserine,Order Number]=
0.168, 0, 0, 0
```

- Emergency input

The emergency input is the same as for normal orders. The equation is given as:

```
Emergency Input[Formulations,Order Number]=
IF THEN ELSE( Uniform[Formulations,Order Number] <
Emergency Proportion Of Orders Placed[Formulations,Order Number] ,
Emergency Weibull Distribution[Formulations,Order Number] , 0 )
```

- Emergency orders from countries

This variable has the same value of the emergency input. The equation therefore is:

```
Emergency Orders From Countries[Formulations,Order Number]=
Emergency Input[Formulations,Order Number]
```

- Drugs available for emergency orders

If the stockpile has enough stock on hand to fulfil an emergency order, it dispatches the number of drugs required by countries. However, if not enough stock is on hand to fulfil the entire order, the stockpile will dispatch all the available drugs. This is illustrated in the equation:

```
Drugs Available For Emergency Orders[Formulations,Order Number]=
MAX(IF THEN ELSE( SRS Stock On Hand[Formulations,Order Number]>=
Emergency Orders From Countries[Formulations,Order Number], Emergency
Orders From Countries[Formulations,Order Number] - Obsolete Stock
[Formulations,Order Number] , SRS Stock On Hand[Formulations,Order
Number] - Obsolete Stock[Formulations,Order Number] ),0)
```

- Dispatch emergency drugs to countries

The dispatch emergency drugs to countries variable, takes the value of drugs available for emergency orders and delays it for the amount of time specified by country dispatch lead time. The equation is:

```
Dispatch Emergency Drugs To Countries[Formulations,Order Number]= DELAY
MATERIAL(Drugs Available For Emergency Orders[Formulations,Order
Number], Country Dispatch Lead Time[Formulations,Order Number], 0, 0)
```

- Emergency order drugs received by countries

The emergency order drugs received by countries are equal to the number of drugs that have been dispatched to countries. The equation is:

```
Emergency Order Drugs Received By Countries[Formulations,Order Number]=
Dispatch Emergency Drugs To Countries[Formulations,Order Number]
```

- Emergency orders supply line

This supply line, represents the emergency orders that have been placed, but not yet fulfilled. The equation is:

```
Emergency Orders Supply Line[Formulations,Order Number]= INTEG (Emergency
Orders From Countries[Formulations,Order Number] - Emergency Order Drugs
Received By Countries[Formulations,Order Number], 0)
```

- Total emergency order drugs received

The total emergency order drugs received is the sum of all the drugs that have been received by countries as part of an emergency order. The equation is:

```
Total Emergency Order Drugs Received[Formulations,Order Number]= INTEG (
Emergency Order Drugs Received By Countries[Formulations,Order Number],
0)
```

E.3.2.9 Cost related variables

The cost section of Model B is repeated in Figure E.13 for convenience. The Per Unit Cost variable is the same as in Model A. The variables that will be discussed in this section include (i) Cumulative Purchase Unit Cost, (ii) Cumulative Stockpile Replenishment Cost, (iii) Emergency Order Cost, (iv) Normal Order Purchase Cost, (v) Stockpile Rotation Cost, (vi) Total Obsolescence Cost, (vii) Cumulative Total Obsolescence Cost, and (viii) Total Costs.

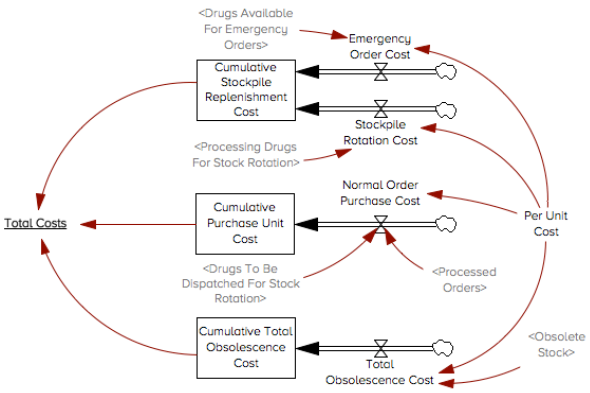

Figure E.13: Cost section of Model B.

- Normal order purchase cost

The normal order purchase cost entails the cost of procuring drugs from manufacturers to send to countries. It is calculated as the product of the per unit cost and the drugs that was manufactured for countries. As depicted in the equation, the drugs that was manufactured for countries is calculated as the difference between the processed orders and the drugs dispatched for stock rotation. The equation is:

```
Normal Order Purchase Cost[Formulations]= (
SUM(Processed Orders[Formulations,Order Number!])-
SUM(Drugs To Be Dispatched For Stock Rotation[Formulations,Order
Number!])) * Per Unit Cost[Formulations]
```

- Cumulative purchase unit cost

The cumulative purchase unit cost is the sum of the normal order purchase cost. It gives the total cost associated with the procurement of drugs for countries from manufacturers over the entire simulation period. The equation is:

```
Cumulative Purchase Unit Cost[Formulations]= INTEG (Normal Order Purchase
Cost[Formulations], 0)
```

- Emergency order cost

The drugs that are dispatched from the stockpile to fulfil emergency orders has to replace in order to keep the stockpile full. The emergency order costs, therefore, represent the total cost of drugs that was dispatched to fulfil the emergency orders. The equation is given as:

```
Emergency Order Cost[Formulations]= SUM(Drugs Available For Emergency
Orders[Formulations,Order Number!])*Per Unit Cost[Formulations]
```

- Stockpile rotation cost

The drugs that are dispatched from the stockpile as part of stock rotation, has to be replaced in order to keep the stockpile full. The stockpile rotation cost, therefore, represent the total cost of drugs that was dispatched at stock rotation. The equation is given as:

```
Stockpile Rotation Cost[Formulations]= SUM(Processing Drugs For Stock
Rotation[Formulations,Order Number!])*Per Unit Cost[Formulations]
```

- Cumulative stockpile replenishment cost

The cumulative stockpile replenishment cost is the sum of the stockpile rotations cost and emergency order cost. It gives the total cost associated with the procurement of drugs from manufacturers to replenish the stockpile, over the entire simulation period. The equation is:

```
Cumulative Stockpile Replenishment Cost[Formulations]= INTEG (Emergency
Order Cost[Formulations]+Stockpile Rotation Cost[Formulations], 0)
```

- Total obsolescence cost

The total obsolescence cost is calculated as the product of the per unit cost and the number of units that has become obsolete. The equation is:

```
Total Obsolescence Cost[Formulations]= Per Unit Cost[Formulations]
* SUM(Obsolete Stock[Formulations,Order Number!])
```

- Cumulative total obsolescence cost

The cumulative total obsolescence cost is the sum of the obsolescence cost. It gives the total cost associated obsolescence. The equation is:

```
Cumulative Total Obsolescence Cost[Formulations]=
INTEG (Total Obsolescence Cost[Formulations], 0)
```

- Total costs

The total costs are simply the sum of all the cumulative costs. The equation is:

```
Total Costs[Formulations]=Cumulative Purchase Unit Cost[Formulations] +
Cumulative Stockpile Replenishment Cost[Formulations] + Cumulative Total
Obsolescence Cost[Formulations]
```

E.4 Modelling details of Model C

This section will discuss the modelling details associated with Model C, as defined and discussed in Section 6.3.6. The variables that are included in the model will be identified and the equations and characteristics for each of these variables will be discussed.

E.4.1 Model C: Variable types

As in the previous sections, the applicable variables and concepts of Model C were identified as either a stock variable (accumulations within the system), flow variable (determines the variation of stock) or auxiliary variable (constants or estimates). The list of the applicable variables, their variable type and their units can be seen in Table E.7. The table includes several variables, in addition to those initially identified in Section E.1, that were added during the development of the model.

Table E.7: Variable types for Model C.

Variable Name	Unit	Variable Type
Backlog Range One	Drugs/Week	Auxiliary
Backlog Range Two	Drugs/Week	Auxiliary
Backlog Reduction	Drugs/Week	Flow
Country Dispatch Lead Time	Week	Auxiliary
Cumulative Obsolete Stock	Drugs	Stock
Cumulative Total Obsolescence Cost	Dollar	Auxiliary
Cumulative Total Unit Cost	Dollar	Auxiliary
Demand Input	Drugs/Week	Auxiliary
Dispatch	Drugs/Week	Flow
Backlog Range One	Drugs/Week	Auxiliary

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Dispatch Drugs To Countries	Drugs/Week	Flow
Drugs Available For Dispatch	Drugs/Week	Auxiliary
Drugs Received From Manufacturer	Drugs/Week	Flow
Drugs To Be Dispatched	Drugs/Week	Auxiliary
Expiration Value	Week	Auxiliary
Incoming	Drugs/Week	Flow
Initial Stock On Hand	Drugs	Auxiliary
Inventory Position	Drugs	Auxiliary
Normal Order Drugs Received By Countries	Drugs/Week	Flow
Normal Orders From Countries	Drugs/Week	Flow
Normal Orders Supply Line	Drugs	Stock
Obsolete Stock	Drugs/Week	Flow
Order Backlogs	Drugs	Stock
Order Processing	Drugs/Week	Flow
Order Processing Lead Time	Week	Auxiliary
Orders Placed To Manufacturer	Drugs/Week	Flow
Per Unit Cost	Dollar/Drugs	Auxiliary
Processed Orders	Drugs/Week	Auxiliary
Production & Dispatch Lead Time	Week	Auxiliary
Production & Dispatch To SRS	Drugs/Week	Flow
Proportion Of Orders Placed	Dmnl	Auxiliary
SRS Demand	Drugs/Week	Auxiliary
SRS Stock On Hand	Drugs	Stock
SRS Supply Line	Drugs	Stock
Total Costs	Dollar	Auxiliary
Total Normal Order Drugs Received	Drugs	Stock
Total Obsolescence Cost	Dollar/Week	Auxiliary
Total Unit Cost	Dollar/Week	Auxiliary
Uniform	Dmnl	Auxiliary
Weibull Distribution	Drugs/Week	Auxiliary

E.4.2 Model C: Characteristics and equations of elements

This subsection provides the equations and values that were assigned to the previously identified variables and concepts of Model C.

E.4.2.1 Lead times

Model C also implements three separate lead times. The equations of the three lead time variables, namely (i) Order Processing Lead Time, (ii) Production & Dispatch Lead Time, and (iii) Country Dispatch Lead Time are equal to those in Model B, as discussed in Section E.3.2.1.

E.4.2.2 Normal order related variables

The normal orders section of the model is repeated in Figure E.14 for convenience. The following variables related to normal orders are identical to those in Model B: (i) Weibull Distribution, (ii) Uniform, (iii) Proportion Of Orders Placed, (iv) Demand Input, (v) Normal Orders From Countries, (vi) Normal Orders Supply Line, (vii) Total Normal Order Drugs Received, (viii) Order Processing, and (ix) Processed Orders. These variables were discussed in Section E.3.2.2.

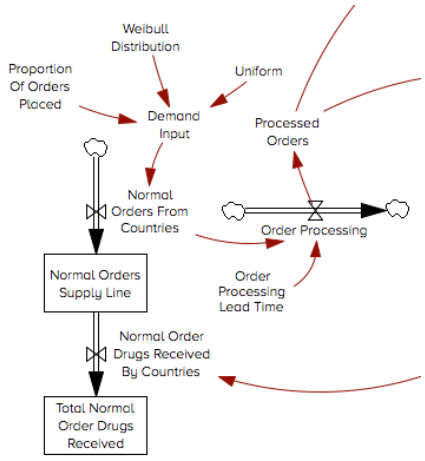

Figure E.14: Normal order section of Model C.

There is only one variable that has a slightly different equation, namely Normal Order Drugs Received By Countries. The new equation is:

```
Normal Order Drugs Received By Countries[Formulations,Order Number]=
Dispatch[Formulations,Order Number]
```

E.4.2.3 Stockpile supply line related variables

The section depicting the stockpile supply line is repeated in Figure E.15 for convenience. The variables that remained the same as in Model B are (i) Orders Placed To Manufacturer, (ii) SRS Supply line, (iii) Drugs Received From Manufacturer, and (iv) Production & Dispatch To SRS. Details on the equations for these variables are provided in Section E.3.2.4.

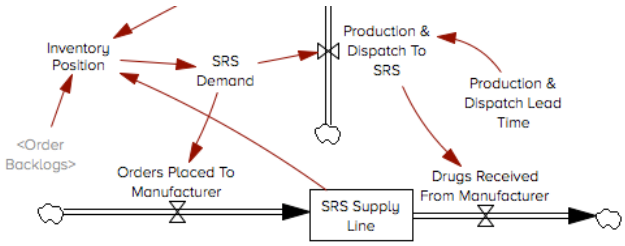

Figure E.15: Stockpile supply line section of Model C.

The equation for the SRS Demand variable will change according to the inventory policy that applies to the scenario being modelled. The inventory position is calculated

with the equation provided in Section 7.3.1. The equations for the inventory position are given as:

```
Inventory Position[Formulations,Order1]=
SRS Stock On Hand[Formulations,Order1] +
SRS Supply Line[Formulations,Order1] -
Order Backlogs[Formulations,Order1] -
Order Backlogs[Formulations,Order2] -
Order Backlogs[Formulations,Order3] -
Order Backlogs[Formulations,Order4]
Inventory Position[Formulations,Order2]= 0
Inventory Position[Formulations,Order3]= 0
Inventory Position[Formulations,Order4]= 0
```

As with Model B, the stockpile only recognises one order, which is why the inventory position of order2, order3 and order4 is always zero.

E.4.2.4 Obsolete stock related variables

All three variables associated with the obsolete stock namely (i) Expiration Values, (ii) Obsolete Stock, and (iii) Cumulative Obsolete Stock are identical to those in Model B, as described in Section E.3.2.7.

E.4.2.5 Cost related variables

The cost section of Model C is repeated in Figure E.16 for convenience. The Per Unit Cost variable is the same as in Model A and Model B. The Total Obsolescence Cost and Cumulative Total Obsolescence Cost variables have the same equation as in Model B and is discussed in Section E.3.2.9.

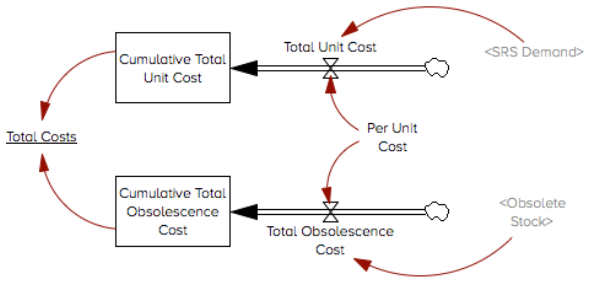

Figure E.16: Cost section of Model C.

The variables to be described are (i) Total Unit Cost, (ii) Cumulative Total Unit Cots, and (iii) Total Costs.

- Total unit cost

The total unit cost represents the cost associated with the procurement of drugs to replenish the stockpile. Other than with the other models, this is the only procurement cost since all of the orders go through the stockpile and is not differentiated in any way. The equation is:

```
Total Unit Cost[Formulations,Order Number]=
SRS Demand[Formulations,Order Number]*Per Unit Cost[Formulations,Order
Number]
```

- Cumulative total unit cost

The cumulative total unit cost is the sum of the total unit cost. It gives the total cost associated with the procurement of drugs from manufacturers over the entire simulation period. The equation is:

```
Cumulative Total Unit Cost[Formulations,Order Number]= INTEG (
Total Unit Cost[Formulations,Order Number],0)
```

- Total costs

The total costs are simply the sum of all the cumulative costs. The equation is:

```
Total Costs[Formulations]=
SUM(Cumulative Total Unit Cost[Formulations,Order Number!]) +
SUM(Cumulative Total Obsolescence Cost[Formulations,Order Number!])
```

E.4.2.6 Stockpile related variables

This section will describe the variables specifically related to the stockpile section of Model C, repeated in Figure E.17 for convenience. The variables are (i) Initial Stock On Hand, (ii) SRS Stock On Hand, (iii) Dispatch Drugs To Countries, (iv) Drugs Available For Dispatch, (v) Drugs To Be Dispatched and (vi) Dispatch.

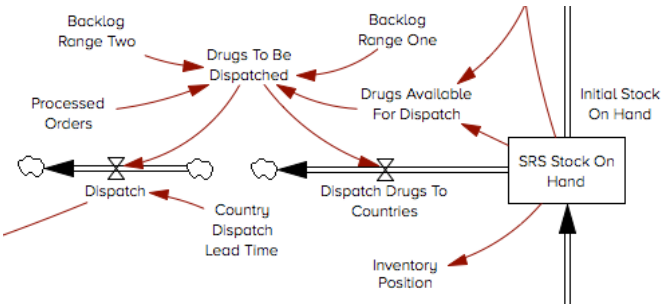

Figure E.17: Stockpile section of Model C.

- Initial stock on hand

The equation for the initial stock on hand will be similar to the one provided in Section E.3.2.4. The values, however, will be dependent on the type of inventory policy applied in the scenario. The values will be equal to the value of the order-up-to-level.

- SRS stock on hand

The same `QUEUE FIFO` equation and assumptions are applied here as in Section E.3.2.4. The only difference is the outflow. The inflow is identical to that of Model B, namely the production and dispatch to the SRS, but for Model C, the outflow is only the obsolete stock and dispatch drugs to countries. The equation is given as:

```
SRS Stock On Hand[Formulations,Order Number]=
```

```
QUEUE FIFO("Production & Dispatch To SRS"[Formulations,Order Number],
Obsolete Stock[Formulations,Order Number] + Dispatch Drugs To
Countries[Formulations,Order Number]  , Profile , Initial Stock On Hand
[Formulations,Order Number] , 0 )
```

- Drugs available for dispatch

As previously mentioned, the stockpile only recognises order1; however, all of the orders (order1, order2, order3 and order4) can be fulfilled from the stockpile. The drugs available for dispatch variable is therefore used to indicate that all of the "order1" drugs in the stockpile is available for all of the order numbers. The equations are given as:

```
Drugs Available For Dispatch[Formulations,Order1]=
MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP -
Obsolete Stock[Formulations,Order1])

Drugs Available For Dispatch[Formulations,Order2]=
MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP -
Obsolete Stock[Formulations,Order1])

Drugs Available For Dispatch[Formulations,Order3]=
MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP -
Obsolete Stock[Formulations,Order1])

Drugs Available For Dispatch[Formulations,Order4]=
MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP -
Obsolete Stock[Formulations,Order1])
```

- Dispatch drugs to countries

The dispatch drugs to countries variable represents the outflow of drugs from the stockpile. Since the stockpile only recognises order1, the drugs that are dispatched for all other orders are also counted towards the order1 subscript of this variable in order to account for their removal from the stockpile. This is made clear in the equations:

```
Dispatch Drugs To Countries[Formulations,Order1]=
Drugs To Be Dispatched[Formulations,Order1] +
Drugs To Be Dispatched[Formulations,Order2] +
Drugs To Be Dispatched[Formulations,Order3] +
Drugs To Be Dispatched[Formulations,Order4]
Dispatch Drugs To Countries[Formulations,Order2]= 0
Dispatch Drugs To Countries[Formulations,Order3]= 0
Dispatch Drugs To Countries[Formulations,Order4]= 0
```

- Dispatch

The dispatch variable is used to delay the drugs that are dispatched to countries by the amount of time specified by country dispatch lead time. The equation is:

```
Dispatch[Formulations,Order Number]= DELAY MATERIAL (
Drugs To Be Dispatched[Formulations,Order Number], Country Dispatch
Lead Time[Formulations,Order Number], 0, 0)
```

- Drugs to be dispatched

This variable follows the same principals discussed in Section E.3.2.4 with some alterations. The drugs to be dispatched equations each has seven IF THEN ELSE statements that prioritises the orders to be dispatched. The priorities that the equations implement is as follows:

1. Firstly, the model evaluates whether enough drugs are available to fulfil both new processed orders, and all of the backorders; if not
2. The model evaluates whether enough drugs are available to fulfil all of the backorders; if not
3. The model evaluates whether enough drugs are available to fulfil the new processed orders as well as the two oldest 'groups' of backlogs if not
4. The model evaluates whether enough drugs are available to fulfil the two oldest groups of backlogs; if not
5. The model evaluates whether enough drugs are available to fulfil the new processed orders as well as the oldest group of backlogs; if not
6. The model evaluates whether enough drugs are available to fulfil the oldest group of backlogs; if not
7. The model evaluates whether enough drugs are available to fulfil the new processed orders; if not
8. No drugs are dispatched.

To ensure that the maximum number of drugs are dispatched, order4 will received priority over order3, order3 will receive priority over order2 and order2 will receive priority over order1. This is due to the chances being less likely that an order4 is backlogged or incoming, while the chances of an order1 being backlogged or incoming is high. The equations are given as:

```
Drugs To Be Dispatched[Formulations,Order1]=
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched [Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1]/TIME
STEP , Processed Orders[Formulations,Order1] +
Order Backlogs[Formulations,Order1]/TIME STEP ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4] > Order
Backlogs[Formulations,Order1]/TIME STEP , Order
Backlogs[Formulations,Order1]/TIME STEP ,

IF THEN ELSE( Backlog Range One[Formulations,Order1] >0 :AND: Backlog
Range Two
[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
```

```
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] +
Processed Orders[Formulations,Order1], Backlog Range
Two[Formulations,Order1] + Backlog Range One[Formulations,Order1] +
Processed Orders[Formulations,Order1],

IF THEN ELSE( Backlog Range One[Formulations,Order1] >0 :AND: Backlog
Range Two
[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] + Backlog Range Two[Formulations,Order1]  ,
Backlog Range Two[Formulations,Order1] + Backlog Range
One[Formulations,Order1] ,

IF THEN ELSE( Processed Orders[Formulations,Order1] > 0 :AND: Backlog
Range One
[Formulations,Order1] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] + Processed Orders[Formulations,Order1] ,
Backlog Range One[Formulations,Order1] + Processed
Orders[Formulations,Order1] ,

IF THEN ELSE( Backlog Range One[Formulations,Order1] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] , Backlog Range One[Formulations,Order1] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4]> Processed
Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0
) ) ) ) ) ) )
```

Drugs To Be Dispatched[Formulations,Order2]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] >
Processed Orders[Formulations,Order2] + Order
Backlogs[Formulations,Order2]/TIME STEP , Processed
Orders[Formulations,Order2] + Order Backlogs[Formulations,Order2]/TIME
STEP ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] >
Order Backlogs[Formulations,Order2]/TIME STEP , Order
Backlogs[Formulations,Order2]/TIME STEP ,
```

```
IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two
[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] +
Processed Orders[Formulations,Order2], Backlog Range
Two[Formulations,Order2] + Backlog Range One[Formulations,Order2] +
Processed Orders[Formulations,Order2],

IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two
[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2]  ,
Backlog Range Two[Formulations,Order2] + Backlog Range
One[Formulations,Order2] ,

IF THEN ELSE( Processed Orders[Formulations,Order2] > 0 :AND: Backlog
Range One [Formulations,Order2] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Processed Orders[Formulations,Order2] ,
Backlog Range One[Formulations,Order2] + Processed
Orders[Formulations,Order2] ,

IF THEN ELSE( Backlog Range One[Formulations,Order2] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] , Backlog Range One[Formulations,Order2] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched [Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2]
, Processed Orders[Formulations,Order2] , 0 )
 ) ) ) ) ) )
```

Drugs To Be Dispatched[Formulations,Order3]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched [Formulations,Order4] > Processed
Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3]/TIME
STEP , Processed Orders[Formulations,Order3] + Order
Backlogs[Formulations,Order3]/TIME STEP ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched [Formulations,Order4] > Order
Backlogs[Formulations,Order3]/TIME STEP , Order
Backlogs[Formulations,Order3]/TIME STEP ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two
[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] +
```

```
Processed Orders[Formulations,Order3], Backlog Range
Two[Formulations,Order3] + Backlog Range One[Formulations,Order3] +
Processed Orders[Formulations,Order3],

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two
[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3]  ,
Backlog Range Two[Formulations,Order3] + Backlog Range
One[Formulations,Order3] ,

IF THEN ELSE( Processed Orders[Formulations,Order3] > 0 :AND: Backlog
Range One[Formulations,Order3] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Processed Orders[Formulations,Order3] ,
Backlog Range One[Formulations,Order3] + Processed
Orders[Formulations,Order3] ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] , Backlog Range One[Formulations,Order3] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] , 0
) ) ) ) ) ) )
```

Drugs To Be Dispatched[Formulations,Order4]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders[Formulations,Order4] + Order
Backlogs[Formulations,Order4]/TIME STEP , Processed
Orders[Formulations,Order4] +Order Backlogs[Formulations,Order4]/TIME
STEP ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] > Order
Backlogs[Formulations,Order4]/TIME STEP , Order
Backlogs[Formulations,Order4]/TIME STEP ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Backlog Range Two[Formulations,Order4] + Processed
Orders[Formulations,Order4], Backlog Range Two[Formulations,Order4] +
Backlog Range One[Formulations,Order4] + Processed
Orders[Formulations,Order4],

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Backlog Range Two[Formulations,Order4]  , Backlog Range
Two[Formulations,Order4] + Backlog Range One[Formulations,Order4] ,

IF THEN ELSE( Processed Orders[Formulations,Order4] > 0 :AND: Backlog
Range One[Formulations,Order4] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4]
```

```
+ Processed Orders[Formulations,Order4] , Backlog Range
One[Formulations,Order4] + Processed Orders[Formulations,Order4] ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order4] > Backlog Range
One[Formulations,Order4] , Backlog Range One[Formulations,Order4] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders[Formulations,Order4] , Processed
Orders[Formulations,Order4] , 0 )
) ) ) ) ) )
```

E.4.2.7 Backlog related variables

The backlog section of Model C is repeated in Figure E.18 for convenience. The variables that will be discussed include: (i) Backlog Range One, (ii) Backlog Range Two, (iii) Order Backlogs, (iv) Incoming, and (v) Backlog Reduction. The concept behind these variables were described in Section 6.3.6.2.

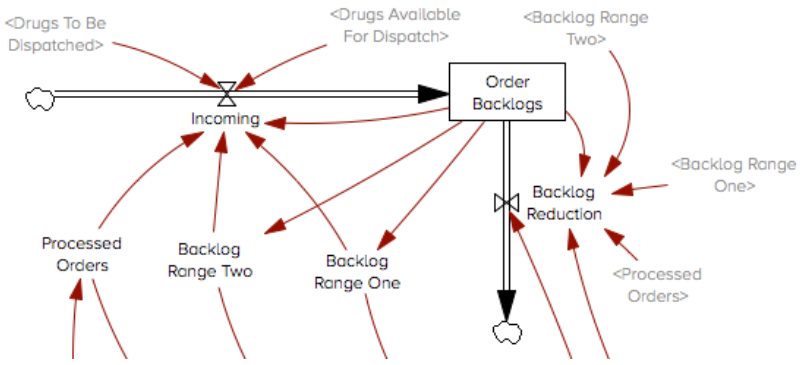

Figure E.18: Backlog section of Model C.

- Order backlogs

The backlogged orders are represented as a queue in order to track the age of the units. The equation is given as:

```
Order Backlogs[Formulations,Order Number]=
QUEUE FIFO(Incoming[Formulations,Order Number],
Backlog Reduction[Formulations,Order Number]  , Profile , 0 , 0 )
```

- Backlog range one

This variable is implemented to track the oldest backlogged units in the queue. The equation returns all of the units in the queue (the order backlogs) that are of equal age or older than the oldest units in the queue. The equation is:

```
Backlog Range One[Formulations,Order Number]=
QUEUE AGE IN RANGE( Order Backlogs[Formulations,Order Number] , QUEUE
AGE OLDEST( Order Backlogs[Formulations,Order Number] ) , :NA: )/TIME
STEP
```

- Backlog range two

This variable is added to track the group of backlogged units that are at least half the age of the oldest backlogged units but not older than the oldest backlogged units. The equation is:

```
Backlog Range Two[Formulations,Order Number]=
QUEUE AGE IN RANGE( Order Backlogs[Formulations,Order Number] , 0.5*
QUEUE AGE OLDEST( Order Backlogs[Formulations,Order Number] ) , QUEUE
AGE OLDEST (Order Backlogs[Formulations,Order Number] ) - 1 )/TIME STEP
```

- Incoming

The incoming variable represents the processed orders that are not fulfilled immediately. The equation is very similar to the drugs to be dispatched variable, in the sense that whenever the newly processed orders are a part of the drugs that are dispatched, then the incoming variable will be equal to zero, and be represented by:

```
MAX(0,Processed Orders[Formulations,Order Number] - Drugs To Be
Dispatched[Formulations,Order Number])
```

If the newly incoming orders are not part of the drugs that are dispatched, the incoming variable will equal `Processed Orders[Formulations,Order Number]`.

The equations are given as:

```
Incoming[Formulations,Order1]=
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order1]
+ Order Backlogs[Formulations,Order1]/TIME STEP , MAX(0,Processed
Orders[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order1]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4] > Order
Backlogs[Formulations,Order1]/TIME STEP , Processed
Orders[Formulations,Order1] ,

IF THEN ELSE( Backlog Range One[Formulations,Order1] >0 :AND: Backlog
Range Two
[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] >
Backlog Range One[Formulations,Order1] + Backlog Range Two
[Formulations,Order1] + Processed Orders[Formulations,Order1],
MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order1]),

IF THEN ELSE( Backlog Range One[Formulations,Order1] >0 :AND: Backlog
Range Two
[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be Dispatched
```

```
[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] >
Backlog Range One[Formulations,Order1] + Backlog Range
Two[Formulations,Order1]  , Processed Orders
[Formulations,Order1] ,

IF THEN ELSE( Processed Orders[Formulations,Order1] > 0 :AND: Backlog
Range One
[Formulations,Order1] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] + Processed Orders[Formulations,Order1] ,
MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order1]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order1] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] , Processed Orders[Formulations,Order1] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4]> Processed Orders[Formulations,Order1]
, MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order1]) , Processed
Orders[Formulations,Order1] )
) ) ) ) ) )
```

Incoming[Formulations,Order2]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2]
+ Order Backlogs[Formulations,Order2]/TIME STEP , MAX(0,Processed
Orders[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order2]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] >
Order Backlogs[Formulations,Order2]/TIME STEP , Processed
Orders[Formulations,Order2] ,

IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] +
Processed Orders[Formulations,Order2], MAX(0,Processed
Orders[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order2]),

IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
```

```
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2]  ,
Processed Orders[Formulations,Order2] ,

IF THEN ELSE( Processed Orders[Formulations,Order2] > 0 :AND: Backlog
Range One[Formulations,Order2] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Processed Orders[Formulations,Order2] ,
MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order2]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order2] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] >
Backlog Range One[Formulations,Order2] , Processed
Orders[Formulations,Order2] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2]
, MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be Dispatched
[Formulations,Order2]) , Processed Orders[Formulations,Order2] )
) ) ) ) ) )
```

Incoming[Formulations,Order3]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3]/TIME
STEP , MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order3]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Order
Backlogs[Formulations,Order3]/TIME STEP , Processed
Orders[Formulations,Order3] ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] +
Processed Orders[Formulations,Order3], MAX(0,Processed
Orders[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order3]),

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3]  ,
Processed Orders[Formulations,Order3] ,

IF THEN ELSE( Processed Orders[Formulations,Order3] > 0 :AND: Backlog
Range One[Formulations,Order3] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range One
[Formulations,Order3] + Processed Orders[Formulations,Order3] ,
```

```
MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order3]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] , Processed Orders[Formulations,Order3],

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order3] , MAX(0,Processed
Orders[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order3]) , Processed
Orders[Formulations,Order3] )
) ) ) ) ) )
```

Incoming[Formulations,Order4]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders[Formulations,Order4] + Order Backlogs
[Formulations,Order4]/TIME STEP , MAX(0,Processed
Orders[Formulations,Order4] - Drugs To Be
Dispatched[Formulations,Order4]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] > Order
Backlogs[Formulations,Order4]/TIME STEP , Processed
Orders[Formulations,Order4] ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Backlog Range Two[Formulations,Order4] + Processed
Orders[Formulations,Order4], MAX(0,Processed
Orders[Formulations,Order4] - Drugs To Be
Dispatched[Formulations,Order4]),

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Backlog Range Two[Formulations,Order4]  , Processed
Orders[Formulations,Order4] ,

IF THEN ELSE( Processed Orders[Formulations,Order4] > 0 :AND: Backlog
Range One
[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Processed Orders[Formulations,Order4] , MAX(0,Processed
Orders[Formulations,Order4] - Drugs To Be
Dispatched[Formulations,Order4]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order4] > Backlog Range
One[Formulations,Order4] , Processed Orders[Formulations,Order4] ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders[Formulations,Order4] , MAX(0,Processed
Orders[Formulations,Order4] - Drugs To Be
Dispatched[Formulations,Order4]) , Processed
Orders[Formulations,Order4] )
) ) ) ) ) )
```

- Backlog reduction

The backlog reduction works in the same way as the incoming variable. The equation is very similar to the drugs to be dispatched variable, in the sense that whenever the newly processed orders are a part of the drugs that are dispatched, then the backlog reduction variable will be equal to zero, and be represented by:

```
MAX(0,Drugs To Be Dispatched[Formulations
,Order1] - Processed Orders[Formulations,Order1])
```

If the newly incoming orders are not part of the drugs that are dispatched, the backlog reduction variable will equal `Drugs To Be Dispatched[Formulations,Order1]`.

The equations are given as:

```
Backlog Reduction[Formulations,Order1]=
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1]/TIME
STEP , MAX(0,Drugs To Be Dispatched[Formulations
,Order1] - Processed Orders[Formulations,Order1]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4] > Order
Backlogs[Formulations,Order1]/TIME STEP , Drugs To Be
Dispatched[Formulations,Order1] ,

IF THEN ELSE( Backlog Range One[Formulations,Order1] >0 :AND: Backlog
Range Two
[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] +
Processed Orders[Formulations,Order1], MAX(0,Drugs To Be
Dispatched[Formulations,Order1] - Processed
Orders[Formulations,Order1]), IF THEN ELSE( Backlog Range
One[Formulations,Order1] >0 :AND: Backlog Range
Two[Formulations,Order1] >0 :AND: Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be Dispatched
[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] >
Backlog Range One[Formulations,Order1] + Backlog Range
Two[Formulations,Order1]  , Drugs To Be Dispatched[Formulations,Order1]
,

IF THEN ELSE( Processed Orders[Formulations,Order1] > 0 :AND: Backlog
Range One
[Formulations,Order1] > 0 :AND:Drugs Available For
Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
```

```
One[Formulations,Order1] + Processed Orders[Formulations,Order1] ,
MAX(0, Drugs To Be Dispatched[Formulations,Order1] - Processed
Orders[Formulations,Order1]) ,
IF THEN ELSE( Backlog Range One[Formulations,Order1] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order1] - Drugs To Be
Dispatched[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3]- Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order1] , Drugs To Be Dispatched[Formulations,Order1]
,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order1] - Drugs
To Be Dispatched
[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]-
Drugs To Be Dispatched[Formulations,Order4]> Processed
Orders[Formulations,Order1] , MAX(0,Drugs To Be
Dispatched[Formulations,Order1] - Processed
Orders[Formulations,Order1]) , Drugs To Be
Dispatched[Formulations,Order1] )
 ) ) ) ) ) )
```

Backlog Reduction[Formulations,Order2]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched [Formulations,Order4] >
Processed Orders[Formulations,Order2] + Order Backlogs
[Formulations,Order2]/TIME STEP , MAX(0,Drugs To Be Dispatched
[Formulations,Order2] - Processed Orders[Formulations,Order2]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched
[Formulations,Order3] - Drugs To Be Dispatched
[Formulations,Order4] > Order Backlogs[Formulations,Order2]/TIME STEP ,
Drugs To Be Dispatched[Formulations,Order2] ,

IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two
[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] +
Processed Orders[Formulations,Order2], MAX(0,Drugs To Be
Dispatched[Formulations,Order2] - Processed
Orders[Formulations,Order2]),

IF THEN ELSE( Backlog Range One[Formulations,Order2] >0 :AND: Backlog
Range Two[Formulations,Order2] >0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] + Backlog Range Two[Formulations,Order2]  ,
Drugs To Be Dispatched[Formulations,Order2] ,

IF THEN ELSE( Processed Orders[Formulations,Order2] > 0 :AND: Backlog
Range One[Formulations,Order2] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be Dispatched
[Formulations,Order4] > Backlog Range One[Formulations,Order2] +
Processed Orders[Formulations,Order2] , MAX(0,Drugs To Be
```

```
Dispatched[Formulations,Order2] - Processed
Orders[Formulations,Order2]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order2] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order2] - Drugs To Be
Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order2] , Drugs To Be Dispatched[Formulations,Order2]
,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order2] - Drugs
To Be Dispatched[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2]
, MAX(0,Drugs To Be Dispatched[Formulations,Order2] - Processed
Orders[Formulations,Order2]) , Drugs To Be
Dispatched[Formulations,Order2] )
) ) ) ) ) )
```

Backlog Reduction[Formulations,Order3]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Processed
Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3]/TIME
STEP , MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed
Orders[Formulations,Order3]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched[Formulations,Order4] > Order
Backlogs[Formulations,Order3]/TIME STEP , Drugs To Be
Dispatched[Formulations,Order3] ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] +
Processed Orders[Formulations,Order3], MAX(0,Drugs To Be
Dispatched[Formulations,Order3] - Processed
Orders[Formulations,Order3]),

IF THEN ELSE( Backlog Range One[Formulations,Order3] >0 :AND: Backlog
Range Two[Formulations,Order3] >0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Backlog Range Two[Formulations,Order3]  ,
Drugs To Be Dispatched[Formulations,Order3] ,

IF THEN ELSE( Processed Orders[Formulations,Order3] > 0 :AND: Backlog
Range One[Formulations,Order3] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] + Processed Orders[Formulations,Order3] ,
MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed
Orders[Formulations,Order3]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order3] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order3] - Drugs To Be
Dispatched[Formulations,Order4] > Backlog Range
One[Formulations,Order3] , Drugs To Be Dispatched[Formulations,Order3],
```

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order3] - Drugs
To Be Dispatched
[Formulations,Order4] > Processed Orders [Formulations,Order3] ,
MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed
Orders[Formulations,Order3]) , Drugs To Be
Dispatched[Formulations,Order3] )
 ) ) ) ) ) )
```

Backlog Reduction[Formulations,Order4]=

```
IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders [Formulations,Order4] + Order
Backlogs[Formulations,Order4]/TIME STEP , MAX(0,Drugs To Be
Dispatched[Formulations,Order4] - Processed
Orders[Formulations,Order4]) ,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] > Order
Backlogs [Formulations,Order4]/TIME STEP , Drugs To Be
Dispatched[Formulations,Order4] ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two
[Formulations,Order4] >0 :AND: Drugs Available For
Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4]
+ Backlog Range Two[Formulations,Order4] + Processed
Orders[Formulations,Order4], MAX(0,Drugs To Be
Dispatched[Formulations,Order4] - Processed
Orders[Formulations,Order4]),

IF THEN ELSE( Backlog Range One[Formulations,Order4] >0 :AND: Backlog
Range Two
[Formulations,Order4] >0 :AND: Drugs Available For Dispatch
[Formulations,Order4] > Backlog Range One[Formulations,Order4] +
Backlog Range Two[Formulations,Order4]  , Drugs To Be
Dispatched[Formulations,Order4] ,

IF THEN ELSE( Processed Orders[Formulations,Order4] > 0 :AND: Backlog
Range One
[Formulations,Order4] > 0 :AND: Drugs Available For
Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4]
+ Processed Orders[Formulations,Order4] , MAX(0,Drugs To Be
Dispatched[Formulations,Order4] - Processed
Orders[Formulations,Order4]) ,

IF THEN ELSE( Backlog Range One[Formulations,Order4] > 0 :AND: Drugs
Available For Dispatch[Formulations,Order4] > Backlog Range
One[Formulations,Order4] , Drugs To Be Dispatched[Formulations,Order4]
,

IF THEN ELSE( Drugs Available For Dispatch[Formulations,Order4] >
Processed Orders[Formulations,Order4] , MAX(0,Drugs To Be
Dispatched[Formulations,Order4] - Processed Orders[Formulations,Order4])
, Drugs To Be Dispatched[Formulations,Order4] ) ) ) ) ) )
```

Appendix F Validation results

This appendix provides results from some of the validation tests, namely the behaviour reproduction test for the demand (order size), and the sensitivity analysis. The full description of these tests are provided in Section 6.4 while this appendix merely provides the results on which the conclusions were based.

F.1 Descriptive statistics of demand

This section provides a comparison of the descriptive statistics for the historical data and the data from the model. The percentage that the model output differs from the historical data are also provided in the tables. Additionally, a graph is also provided to illustrate how well the order sizes of the model represents the historical data. The summary of the results for capreomycin is depicted in Table F.1 and the graph is provided in Figure F.1.

Table F.1: Descriptive statistics of capreomycin order size for model output and historical data.

	Hist. Data	Model Output	% Diff
Mean	33 322.96	32 775.91	-1.64%
Standard Error	4 145.87	3 744.82	-9.67%
Median	12 150.00	11 030.00	-9.22%
Standard Deviation	63 011.70	58 495.90	-7.17%
Range	447 922.00	411 721.61	-8.08%
Minimum	78.00	78.39	0.50%
Maximum	448 000.00	411 800.00	-8.08%
Sum	7 697 603.00	7 997 321.70	3.89%

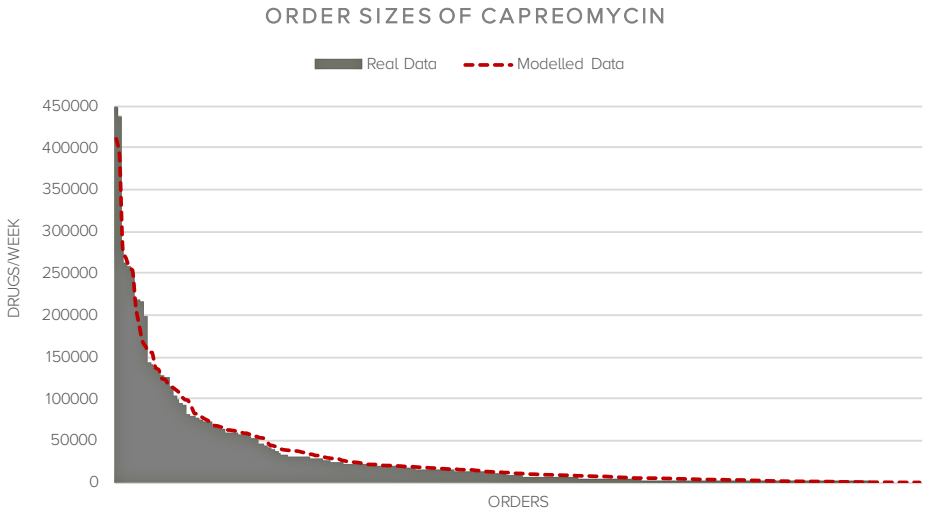

Figure F.1: Capreomycin order size comparison of model output and historical data.

The results for kanamycin are provided in Table F.2 and illustrated in Figure F.2.

Table F.2: Descriptive statistics of kanamycin order size for model output and historical data.

	Hist. Data	Model Output	% Diff
Mean	43 808.31	42 967.96	-1.92%
Standard Error	8 124.35	8 258.60	1.65%
Median	13 900.00	12 170.00	-12.45%
Standard Deviation	96 812.77	100 809.05	4.13%
Range	881 550.00	759 650.00	-13.83%
Minimum	450.00	450.00	0.00%
Maximum	882 000.00	760 100.00	-13.82%
Sum	6 220 780.00	6 402 226.00	2.92%

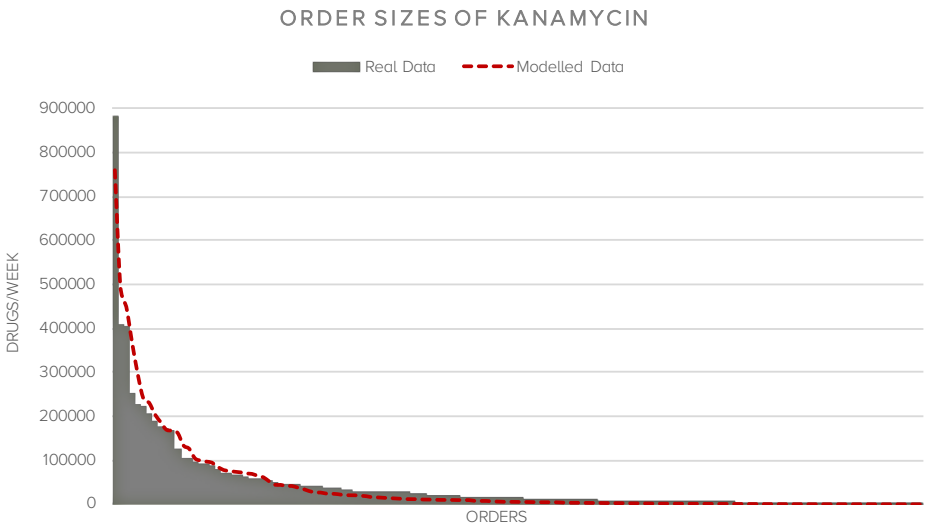

Figure F.2: Kanamycin order size comparison of model output and historical data.

The results for cycloserine are summarised in Table F.3 and Figure F.3.

Table F.3: Descriptive statistics of cycloserine order size for model output and historical data.

	Hist. Data	Model Output	% Diff
Mean	381 362.36	350 169.41	-8.18%
Standard Error	43 072.77	41 728.11	-3.12%
Median	129 600.00	117 790.00	-9.11%
Standard Deviation	803 512.19	783 999.94	-2.43%
Range	9 447 600.00	9 313 500.00	-1.42%
Minimum	1 500.00	1 500.00	0.00%
Maximum	9 449 100.00	9 315 000.00	-1.42%
Sum	132 714 100.00	123 609 803.00	-6.86%

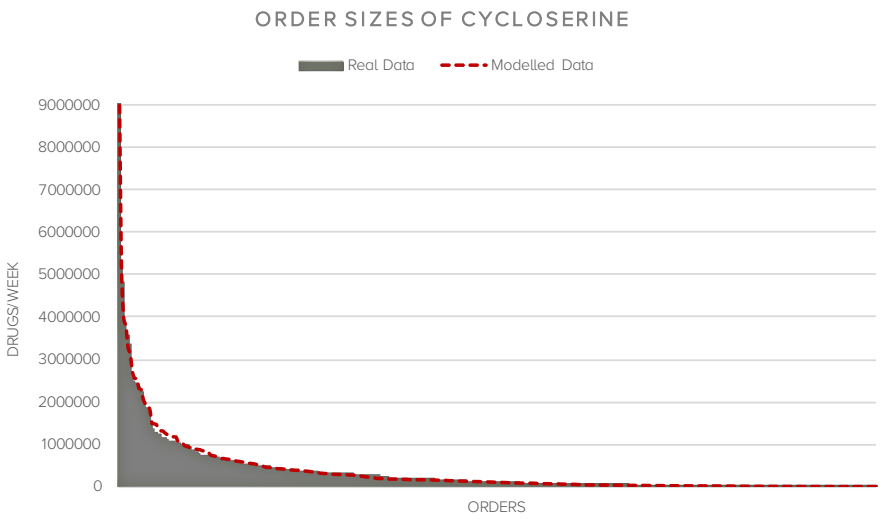

Figure F.3: Cycloserine order size comparison of model output and historical data.

F.2 Sensitivity analysis results

This section provides the results of the sensitivity analysis for Model A, Model B and Model C for all the formulations. The sensitivity analysis is discussed in more detail in Section 6.4.8.

F.2.1 Model A

The sensitivity analysis results of Model A for capreomycin, kanamycin and cycloserine are provided in Tables F.4, Table F.5 and Table F.6, respectively.

Table F.4: Sensitivity analysis results for Model A, capreomycin.

Capreomycin (Model A)	Total drugs received	Drugs awaiting dispatch
Base Case	4 648 000	0
Increase demand	5 112 000	0
Decrease demand	4 183 000	0
Increase lead times	4 431 000	0
Decrease lead times	5 472 601	0

Table F.5: Sensitivity analysis results for Model A, kanamycin.

Kanamycin (Model A)	Total drugs received	Drugs awaiting dispatch
Base Case	3 249 000	0
Increase demand	3 574 000	0
Decrease demand	2 924 000	0
Increase lead times	3 161 000	0
Decrease lead times	3 601 000	0

Table F.6: Sensitivity analysis results for Model A, cycloserine.

Cycloserine (Model A)	Total drugs received	Drugs awaiting dispatch
Base Case	45 430 000	0
Increase demand	49 970 000	0
Decrease demand	40 880 000	0
Increase lead times	41 820 000	0
Decrease lead times	59 040 000	0

F.2.2 Model B

The results for capreomycin were provided in Section 6.4.8. The results for kanamycin and cycloserine are provided in Tables F.7 and Table F.8, respectively.

Table F.7: Sensitivity analysis results for Model B, kanamycin.

Kanamycin (Model B)	Obsolete Stock	Received through Mfg	Received through SRS	Emergency Orders	Stock on hand
Base Case	0	7 757 300	618 782	194 000	106 800
Increase demand	0 (0%)	7 993 000 (3%)	572 100 (-8%)	203 300 (5%)	117 700 (10%)
Decrease demand	0 (0%)	7 636 000 (-2%)	611 200 (-1%)	184 600 (-5%)	116 300 (9%)
Increase lead times	0 (0%)	7 772 000 (0%)	611 400 (-1%)	194 000 (0%)	115 200 (8%)
Decrease lead times	0 (0%)	7 632 000 (-2%)	586 800 (-5%)	194 000 (0%)	114 700 (7%)

Table F.8: Sensitivity analysis results for Model B, cycloserine.

Cycloserine (Model B)	Obsolete Stock	Received through Mfg	Received through SRS	Emergency Orders	Stock on hand
Base Case	0	121 373 000	16 526 400	8 893 000	1 625 000
Increase demand	0 (0%)	126 810 000 (4%)	15 130 000 (-8%)	9 083 000 (2%)	1 756 000 (8%)
Decrease demand	0 (0%)	116 500 000 (-4%)	16 620 000 (1%)	8 504 000 (-4%)	1 484 000 (-9%)
Increase lead times	0 (0%)	117 300 000 (-3%)	15 480 000 (-6%)	8 893000 (0%)	1 537 000 (-5%)
Decrease lead times	0 (0%)	120 700 000 (-1%)	15 921 000 (-4%)	8 295 000 (-7%)	1 752 000 (8%)

F.2.3 Model C

The sensitivity analysis results of Model C for capreomycin, kanamycin and cycloserine are provided in Tables F.9, Table F.10 and Table F.11, respectively.

Table F.9: Sensitivity analysis results for Model C, capreomycin.

Capreomycin (Model C)	Obsolete Stock	Received through Mfg	Received through SRS	Stock on hand	Backlogged units
Base Case	0	6 393 000	6 903 000	270 500	1 678 000
Increase demand	0 (0%)	5 953 000 (3%)	7 190 000 (4%)	289 300 (-5%)	1 648 000 (6%)
Decrease demand	0 (0%)	6 612 000 (-7%)	6 588 000 (-5%)	257 200 (7%)	1 779 000 (-8%)
Increase lead times	0 (0%)	6 393 000 (0%)	6 903 000 (0%)	270 500 (0%)	1 653 000 (-1%)
Decrease lead times	0 (0%)	5 998 000 (-6%)	6 902 000 (0%)	273 000 (1%)	1 688 000 (1%)

Table F.10: Sensitivity analysis results for Model C, kanamycin.

Kanamycin (Model C)	Obsolete Stock	Received through Mfg	Received through SRS	Stock on hand	Backlogged units
Base Case	0	4 773 000	6 093 000	155 400	265 300
Increase demand	0 (0%)	4 428 000 (5%)	6 379 000 (5%)	146 560 (-6%)	261 800 (3%)
Decrease demand	0 (0%)	4 988 000 (-7%)	5 784 000 (-5%)	159 630 (3%)	272 600 (-1%)
Increase lead times	0 (0%)	4 843 000 (1%)	5 903 000 (-3%)	160 500 (3%)	279 100 (5%)
Decrease lead times	0 (0%)	4 927 000 (3%)	6 092 000 (0%)	163 200 (5%)	266 400 (0%)

Table F.11: Sensitivity analysis results for Model C, cycloserine.

Cycloserine (Model C)	Obsolete Stock	Received through Mfg	Received through SRS	Stock on hand	Backlogged units
Base Case	413 100	93 570 000	101 500 000	17 840	68 500 000
Increase demand	391 100 (2%)	95 830 000 (2%)	92 960 000 (4%)	16 960 (-5%)	69 270 000 (1%)
Decrease demand	419 820 (-5%)	89 970 000 (-4%)	105 900 000 (-8%)	18 798 (5%)	63 210 000 (-8%)
Increase lead times	403 450 (-2%)	93 530 000 (0%)	102 200 000 (1%)	17 300 (-3%)	69 640 000 (2%)
Decrease lead times	398 200 (-4%)	93 180 000 (0%)	102 300 000 (1%)	17 000 (5%)	69 060 000 (1%)

Appendix G Summary of inventory policy scenarios

This appendix provides a detailed summary of each scenario that was modelled. The alternative values for the reorder point, order-up-to-level, reorder frequency and reorder quantity are provided in the tables below. Where different values are assigned to each of the three formulations, it is given as:

$$\langle Capreomycin \mid Kanamycin \mid Cycloserine \rangle$$

Table G.1 provides the four alternatives of the reorder point.

Table G.1: Summary of reorder point alternatives.

Reorder Point (s)
$s_1 = (\mu_D \times \mu_{LT}) + (\mu_D \times 3) = \langle 499\,845 \mid 657\,120 \mid 5\,720\,427 \rangle$
$s_2 = (\mu_D \times \mu_{LT}) + (\mu_D \times 4.5) = \langle 549\,830 \mid 722\,832 \mid 6\,292\,469 \rangle$
$s_3 = (\mu_D \times \mu_{LT}) + (\mu_D \times 6) = \langle 599\,814 \mid 788\,544 \mid 6\,864\,510 \rangle$
$s_4 = (\mu_D \times \mu_{LT}) + 3.72\sqrt{(\mu_D + \sigma_L)^2 + (\mu_{LT} + \sigma_D^2)} =$ $\langle 3\,382\,746 \mid 4\,604\,496 \mid 39\,623\,974 \rangle$

The two alternatives of the order-up-to-level is provided in Table G.2.

Table G.2: Summary of order-up-to-level alternatives.

Order-Up-To-Level (S)
$S_1 = (\mu_D \times \mu_{LT}) + 3.72 \times \sigma_D \times \sqrt{\mu_{LT}} = \langle 1\,211\,877 \mid 1\,773\,273 \mid 14\,930\,768 \rangle$
$S_2 = (\mu_D \times \mu_{LT}) \times 2.5 = \langle 999\,690 \mid 1\,314\,240 \mid 11\,440\,860 \rangle$

The four alternative values for the reorder frequency is provided in Table G.3.

Table G.3: Summary of reorder frequency alternatives.

Reorder Frequency (R)
$R_1 = 1$
$R_2 = 2$
$R_3 = 3$
$R_4 = 4$

Table G.4 provides the three alternatives for the reorder quantity.

Table G.4: Summary of the reorder quantity alternatives.

Reorder Quantity (Q)
$Q_1 =$ Exponential smoothing, with $\alpha = 0.1$
$Q_2 =$ Exponential smoothing, with $\alpha = 0.5$
$Q_3 =$ Exponential smoothing, with $\alpha = 0.9$

G.1 (s,S) Policy scenarios

The first set of scenarios will be for the (s, S) policy. There are eight possible combinations of s and S for this policy, as provided in Table G.5.

Table G.5: Summary of (s,S) policy scenarios.

	Policy	s	S	Value of s	Value of S
1	(s,S) 1	s_1	S_1	⟨499 845 | 657 120 | 5 720 427⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
2	(s,S) 2	s_1	S_2	⟨499 845 | 657 120 | 5 720 427⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
3	(s,S) 3	s_2	S_1	⟨549 830 | 722 832 | 6 292 469⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
4	(s,S) 4	s_2	S_2	⟨549 830 | 722 832 | 6 292 469⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
5	(s,S) 5	s_3	S_1	⟨599 814 | 788 544| 6 864 510⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
6	(s,S) 6	s_3	S_2	⟨599 814 | 788 544| 6 864 510⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
7	(s,S) 7	s_4	S_1	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
8	(s,S) 8	s_4	S_2	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨999 690 | 1 314 240 | 11 440 860⟩

G.2 (R,S) Policy scenarios

The second set of scenarios will be for the (R, S) policy. There are again eight possible combinations of R and S for this policy, as provided in Table G.6.

Table G.6: Summary of (R,S) policy scenarios.

	Policy	R	S	Value of R	Value of S
9	(R,S) 1	R_1	S_1	1 week	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
10	(R,S) 2	R_1	S_2	1 week	⟨999 690 | 1 314 240 | 11 440 860⟩
11	(R,S) 3	R_2	S_1	2 weeks	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
12	(R,S) 4	R_2	S_2	2 weeks	⟨999 690 | 1 314 240 | 11 440 860⟩
13	(R,S) 5	R_3	S_1	3 weeks	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
14	(R,S) 6	R_3	S_2	3 weeks	⟨999 690 | 1 314 240 | 11 440 860⟩
15	(R,S) 7	R_4	S_1	4 weeks	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
16	(R,S) 8	R_4	S_2	4 weeks	⟨999 690 | 1 314 240 | 11 440 860⟩

G.3 (R,s,S) Policy scenarios

The third set of scenarios will be for the (R, s, S) policy. There are 24 applicable, possible combinations of R, s and S for this policy, as provided in Table G.7.

Table G.7: Summary of (R,s,S) policy scenarios.

	Policy	R	s	S	Value of R	Value of s	Value of S
17	(R,s,S) 1	R_2	s_1	S_1	2 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
18	(R,s,S) 2	R_2	s_1	S_2	2 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
19	(R,s,S) 3	R_2	s_2	S_1	2 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
20	(R,s,S) 4	R_2	s_2	S_2	2 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
21	(R,s,S) 5	R_2	s_3	S_1	2 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
22	(R,s,S) 6	R_2	s_3	S_2	2 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
23	(R,s,S) 7	R_2	s_4	S_1	2 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
24	(R,s,S) 8	R_2	s_4	S_2	2 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨999 690 | 1 314 240 | 11 440 860⟩

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25	(R,s,S) 9	R_3	s_1	S_1	3 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
26	(R,s,S) 10	R_3	s_1	S_2	3 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
27	(R,s,S) 11	R_3	s_2	S_1	3 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
28	(R,s,S) 12	R_3	s_2	S_2	3 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
29	(R,s,S) 13	R_3	s_3	S_1	3 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
30	(R,s,S) 14	R_3	s_3	S_2	3 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
31	(R,s,S) 15	R_3	s_4	S_1	3 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
32	(R,s,S) 16	R_3	s_4	S_2	3 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
33	(R,s,S) 17	R_4	s_1	S_1	4 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
34	(R,s,S) 18	R_4	s_1	S_2	4 weeks	⟨499 845 | 657 120 | 5 720 427⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
35	(R,s,S) 19	R_4	s_2	S_1	4 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
36	(R,s,S) 20	R_4	s_2	S_2	4 weeks	⟨549 830 | 722 832 | 6 292 469⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
37	(R,s,S) 21	R_4	s_3	S_1	4 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
38	(R,s,S) 22	R_4	s_3	S_2	4 weeks	⟨599 814 | 788 544| 6 864 510⟩	⟨999 690 | 1 314 240 | 11 440 860⟩
39	(R,s,S) 23	R_4	s_4	S_1	4 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨1 211 877 | 1 773 273 | 14 930 768 ⟩
40	(R,s,S) 24	R_4	s_4	S_2	4 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	⟨999 690 | 1 314 240 | 11 440 860⟩

G.4 (s,Q) Policy scenarios

The fourth set of scenarios will be for the (s, Q) policy. There are 12 possible combinations of s and Q for this policy, as provided in Table G.8.

Table G.8: Summary of (s,Q) policy scenarios.

	Policy	s	Q	Value of s	Value of Q
41	(s,Q) 1	s_1	Q_1	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.1$
42	(s,Q) 2	s_1	Q_2	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.5$
43	(s,Q) 3	s_1	Q_3	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.9$
44	(s,Q) 4	s_2	Q_1	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.1$
45	(s,Q) 5	s_2	Q_2	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.5$
46	(s,Q) 6	s_2	Q_3	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.9$
47	(s,Q) 7	s_3	Q_1	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.1$
48	(s,Q) 8	s_3	Q_2	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.5$
49	(s,Q) 9	s_3	Q_3	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.9$
50	(s,Q) 10	s_4	Q_1	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.1$
51	(s,Q) 11	s_4	Q_2	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.5$
52	(s,Q) 12	s_4	Q_3	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.9$

G.5 (R,s,Q) Policy scenarios

The fifth and final set of scenarios will be for the (R, s, Q) policy. There are 36 applicable, possible combinations of R, s and Q for this policy, as provided in Table G.9.

Table G.9: Summary of (R,s,Q) policy scenarios.

	Policy	R	s	Q	Value of R	Value of s	Value of Q
53	(R,s,Q) 1	R_2	s_1	Q_1	2 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.1$
54	(R,s,Q) 2	R_2	s_1	Q_2	2 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.5$
55	(R,s,Q) 3	R_2	s_1	Q_3	2 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.9$
56	(R,s,Q) 4	R_2	s_2	Q_1	2 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.1$

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57	(R,s,Q) 5	R_2	s_2	Q_2	2 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.5$
58	(R,s,Q) 6	R_2	s_2	Q_3	2 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.9$
59	(R,s,Q) 7	R_2	s_3	Q_1	2 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.1$
60	(R,s,Q) 8	R_2	s_3	Q_2	2 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.5$
61	(R,s,Q) 9	R_2	s_3	Q_3	2 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.9$
62	(R,s,Q) 10	R_2	s_4	Q_1	2 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.1$
63	(R,s,Q) 11	R_2	s_4	Q_2	2 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.5$
64	(R,s,Q) 12	R_2	s_4	Q_3	2 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.9$
65	(R,s,Q) 13	R_3	s_1	Q_1	3 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.1$
66	(R,s,Q) 14	R_3	s_1	Q_2	3 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.5$
67	(R,s,Q) 15	R_3	s_1	Q_3	3 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.9$
68	(R,s,Q) 16	R_3	s_2	Q_1	3 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.1$
69	(R,s,Q) 17	R_3	s_2	Q_2	3 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.5$
70	(R,s,Q) 18	R_3	s_2	Q_3	3 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.9$
71	(R,s,Q) 19	R_3	s_3	Q_1	3 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.1$
72	(R,s,Q) 20	R_3	s_3	Q_2	3 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.5$
73	(R,s,Q) 21	R_3	s_3	Q_3	3 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.9$
74	(R,s,Q) 22	R_3	s_4	Q_1	3 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.1$
75	(R,s,Q) 23	R_3	s_4	Q_2	3 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.5$
76	(R,s,Q) 24	R_3	s_4	Q_3	3 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.9$
77	(R,s,Q) 25	R_4	s_1	Q_1	4 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.1$
78	(R,s,Q) 26	R_4	s_1	Q_2	4 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.5$
79	(R,s,Q) 27	R_4	s_1	Q_3	4 weeks	⟨499 845 | 657 120 | 5 720 427⟩	$\alpha = 0.9$
80	(R,s,Q) 28	R_4	s_2	Q_1	4 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.1$
81	(R,s,Q) 29	R_4	s_2	Q_2	4 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.5$
82	(R,s,Q) 30	R_4	s_2	Q_3	4 weeks	⟨549 830 | 722 832 | 6 292 469⟩	$\alpha = 0.9$
83	(R,s,Q) 31	R_4	s_3	Q_1	4 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.1$
84	(R,s,Q) 32	R_4	s_3	Q_2	4 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.5$
85	(R,s,Q) 33	R_4	s_3	Q_3	4 weeks	⟨599 814 | 788 544| 6 864 510⟩	$\alpha = 0.9$
86	(R,s,Q) 34	R_4	s_4	Q_1	4 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.1$
87	(R,s,Q) 35	R_4	s_4	Q_2	4 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.5$
88	(R,s,Q) 36	R_4	s_4	Q_3	4 weeks	⟨3 382 746 | 4 604 496 | 39 623 974⟩	$\alpha = 0.9$

Appendix H Modelling results

This appendix provides the modelling results of the 88 scenarios. The appendix is divided into three sections, with each section presenting the results for one of the formulations. The results are provided according to the performance measures introduced in Section 7.1.

H.1 Modelling results of capreomycin

This section provides the results of capreomycin for each scenario. Table H.1 summarises the stock performance of each scenario.

Table H.1: Capreomycin - Summary of stock performance for the scenarios.

Policy #	R	s	S	Q	%BLs	μ_{BL_Age}	Max_{BL_Age}	Total Vol.
(s,S) 1		s1	S1		21.05%	6.91	26	2 337 366
(s,S) 2		s1	S2		17.37%	7.00	26	2 728 524
(s,S) 3		s2	S1		15.26%	4.10	13	1 809 564
(s,S) 4		s2	S2		19.47%	6.23	26	2 617 810
(s,S) 5		s3	S1		2.63%	2.44	6	1 859 470
(s,S) 6		s3	S2		2.11%	5.68	14	2 541 754
(s,S) 7		s4	S1		24.21%	4.25	16	722 871
(s,S) 8		s4	S2		17.89%	6.49	26	651 444
(R,S) 1	R1		S1		2.63%	2.44	6	722 871
(R,S) 2	R1		S2		2.11%	5.68	14	651 444
(R,S) 3	R2		S1		2.26%	3.89	11	1 006 581
(R,S) 4	R2		S2		12.63%	4.94	14	1 836 098
(R,S) 5	R3		S1		1.58%	2.31	5	159 302
(R,S) 6	R3		S2		5.79%	4.41	13	1 000 613
(R,S) 7	R4		S1		1.58%	2.57	5	252 229
(R,S) 8	R4		S2		6.32%	3.23	5	1 249 302
(R,s,S) 1	R2	s1	S1		23.68%	6.70	33	3 202 857
(R,s,S) 2	R2	s1	S2		24.74%	9.31	37	3 405 537
(R,s,S) 3	R2	s2	S1		31.05%	7.89	38	3 387 857
(R,s,S) 4	R2	s2	S2		28.42%	6.04	26	2 678 197
(R,s,S) 5	R2	s3	S1		20.00%	5.21	21	2 257 905
(R,s,S) 6	R2	s3	S2		21.58%	6.20	26	2 769 410
(R,s,S) 7	R2	s4	S1		5.26%	3.89	11	1 006 581
(R,s,S) 8	R2	s4	S2		12.63%	4.94	14	1 836 098
(R,s,S) 9	R3	s1	S1		21.58%	5.36	19	1 628 983
(R,s,S) 10	R3	s1	S2		33.68%	5.95	24	3 377 107
(R,s,S) 11	R3	s2	S1		12.63%	5.44	20	1 062 326
(R,s,S) 12	R3	s2	S2		30.53%	5.50	19	2 461 004
(R,s,S) 13	R3	s3	S1		23.68%	8.36	27	2 440 469
(R,s,S) 14	R3	s3	S2		18.42%	4.54	17	2 305 822

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(R,s,S) 15	R3	s4	S1	1.58%	2.31	5	159 302
(R,s,S) 16	R3	s4	S2	5.79%	4.41	13	1 000 613
(R,s,S) 17	R4	s1	S1	10.53%	4.79	17	1 006 652
(R,s,S) 18	R4	s1	S2	17.37%	4.05	13	2 339 140
(R,s,S) 19	R4	s2	S1	15.79%	5.11	17	1 519 781
(R,s,S) 20	R4	s2	S2	20.00%	5.21	21	2 257 905
(R,s,S) 21	R4	s3	S1	14.74%	4.54	14	2 001 373
(R,s,S) 22	R4	s3	S2	14.74%	4.53	17	2 072 481
(R,s,S) 23	R4	s4	S1	1.58%	2.57	5	252 229
(R,s,S) 24	R4	s4	S2	6.32%	3.23	9	1 249 302
(s,Q) 1		s1	Q1	27.37%	14.07	57	4 135 590
(s,Q) 2		s1	Q2	30.53%	10.20	43	4 505 241
(s,Q) 3		s1	Q3	35.26%	6.26	30	4 105 420
(s,Q) 4		s2	Q1	21.58%	14.69	53	3 451 015
(s,Q) 5		s2	Q2	24.21%	11.44	45	3 688 516
(s,Q) 6		s2	Q3	30.53%	6.16	21	3 803 274
(s,Q) 7		s3	Q1	21.58%	14.70	57	3 059 089
(s,Q) 8		s3	Q2	25.26%	7.54	27	3 929 361
(s,Q) 9		s3	Q3	30.53%	6.16	21	3 803 274
(s,Q) 10		s4	Q1	10.53%	6.05	16	2 374 224
(s,Q) 11		s4	Q2	5.26%	3.14	8	1 023 422
(s,Q) 12		s4	Q3	30.53%	6.16	21	3 803 274
(R,s,Q) 1	R2	s1	Q1	26.84%	12	39	4 491 017
(R,s,Q) 2	R2	s1	Q2	26.84%	12	39	4 491 017
(R,s,Q) 3	R2	s1	Q3	31.05%	10	27	4 442 105
(R,s,Q) 4	R2	s2	Q1	32.11%	9	27	4 896 806
(R,s,Q) 5	R2	s2	Q2	32.11%	9	27	4 896 806
(R,s,Q) 6	R2	s2	Q3	32.11%	8	24	4 392 562
(R,s,Q) 7	R2	s3	Q1	31.58%	8	24	4 475 554
(R,s,Q) 8	R2	s3	Q2	31.58%	8	24	4 475 554
(R,s,Q) 9	R2	s3	Q3	32.11%	8	24	4 392 562
(R,s,Q) 10	R2	s4	Q1	7.37%	4	11	1 555 461
(R,s,Q) 11	R2	s4	Q2	7.37%	4	11	1 555 461
(R,s,Q) 12	R2	s4	Q3	8.95%	3	9	1 556 844
(R,s,Q) 13	R3	s1	Q1	35.26%	17	58	4 677 504
(R,s,Q) 14	R3	s1	Q2	30.53%	8	23	4 160 316
(R,s,Q) 15	R3	s1	Q3	32.63%	8	33	4 496 983
(R,s,Q) 16	R3	s2	Q1	34.74%	16	58	4 637 472
(R,s,Q) 17	R3	s2	Q2	28.42%	7	21	3 556 032
(R,s,Q) 18	R3	s2	Q3	26.84%	8	22	3 437 803
(R,s,Q) 19	R3	s3	Q1	34.74%	16	58	4 637 472
(R,s,Q) 20	R3	s3	Q2	19.47%	7	21	3 078 278
(R,s,Q) 21	R3	s3	Q3	21.05%	8	22	2 821 514
(R,s,Q) 22	R3	s4	Q1	35.79%	14	54	4 559 710
(R,s,Q) 23	R3	s4	Q2	5.79%	4	11	1 258 965

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(R,s,Q) 24	R3	s4	Q3	4.74%	4	11	876 604
(R,s,Q) 25	R4	s1	Q1	41.1%	29	75	4 491 281
(R,s,Q) 26	R4	s1	Q2	41.6%	8	43	5 026 680
(R,s,Q) 27	R4	s1	Q3	30.5%	9	43	4 425 539
(R,s,Q) 28	R4	s2	Q1	30.0%	28	71	4 484 190
(R,s,Q) 29	R4	s2	Q2	38.4%	9	43	5 190 082
(R,s,Q) 30	R4	s2	Q3	29.0%	9	43	4 210 921
(R,s,Q) 31	R4	s3	Q1	34.7%	28	71	4 650 234
(R,s,Q) 32	R4	s3	Q2	30.0%	6	26	4 770 356
(R,s,Q) 33	R4	s3	Q3	24.2%	5	19	3 791 853
(R,s,Q) 34	R4	s4	Q1	32.6%	23	73	4 585 716
(R,s,Q) 35	R4	s4	Q2	7.4%	4	12	1 603 273
(R,s,Q) 36	R4	s4	Q3	4.7%	3	9	1 003 628

Table H.2 summarised the order variability performance for each of the scenarios.

Table H.2: Capreomycin - Summary of order variability performance for the scenarios.

Policy #	R	s	S	Q	σ_{os}	σ_{mo}
Base	-	-	-	-	59 466	132 118
(s,S) 1		s1	S1		67 247	256 203
(s,S) 2		s1	S2		256 203	205 729
(s,S) 3		s2	S1		36 996	256 617
(s,S) 4		s2	S2		256 617	192 787
(s,S) 5		s3	S1		56 632	94 309
(s,S) 6		s3	S2		94 309	94 309
(s,S) 7		s4	S1		275 368	229 375
(s,S) 8		s4	S2		51 269	275 368
(R,S) 1	R1		S1		56 632	94 309
(R,S) 2	R1		S2		94 309	94 309
(R,S) 3	R2		S1		70 033	89 510
(R,S) 4	R2		S2		89 510	89 510
(R,S) 5	R3		S1		83 498	94 524
(R,S) 6	R3		S2		94 524	94 524
(R,S) 7	R4		S1		101 674	102 599
(R,S) 8	R4		S2		102 599	102 599
(R,s,S) 1	R2	s1	S1		47 785	277 018
(R,s,S) 2	R2	s1	S2		277 018	233 650
(R,s,S) 3	R2	s2	S1		90 469	275 298
(R,s,S) 4	R2	s2	S2		275 298	211 417
(R,s,S) 5	R2	s3	S1		74 703	214 604
(R,s,S) 6	R2	s3	S2		214 604	195 895
(R,s,S) 7	R2	s4	S1		70 033	89 510
(R,s,S) 8	R2	s4	S2		89 510	89 510
(R,s,S) 9	R3	s1	S1		77 932	271 853

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(R,s,S) 10	R3	s1	S2		271 853	230 097
(R,s,S) 11	R3	s2	S1		67 932	273 173
(R,s,S) 12	R3	s2	S2		273 173	209 015
(R,s,S) 13	R3	s3	S1		62 021	263 082
(R,s,S) 14	R3	s3	S2		263 082	193 342
(R,s,S) 15	R3	s4	S1		83 498	94 524
(R,s,S) 16	R3	s4	S2		94 524	94 524
(R,s,S) 17	R4	s1	S1		72 890	274 002
(R,s,S) 18	R4	s1	S2		274 002	224 721
(R,s,S) 19	R4	s2	S1		101 938	274 998
(R,s,S) 20	R4	s2	S2		274 998	214 604
(R,s,S) 21	R4	s3	S1		75 911	268 781
(R,s,S) 22	R4	s3	S2		268 781	193 069
(R,s,S) 23	R4	s4	S1		101 674	102 599
(R,s,S) 24	R4	s4	S2		102 599	102 599
(s,Q) 1		s1		Q1	11 575	46 945
(s,Q) 2		s1		Q2	27 731	86 469
(s,Q) 3		s1		Q3	44 063	100 498
(s,Q) 4		s2		Q1	11 634	47 068
(s,Q) 5		s2		Q2	27 731	86 469
(s,Q) 6		s2		Q3	44 063	100 498
(s,Q) 7		s3		Q1	11 620	47 124
(s,Q) 8		s3		Q2	27 731	86 469
(s,Q) 9		s3		Q3	44 063	100 498
(s,Q) 10		s4		Q1	11 623	45 102
(s,Q) 11		s4		Q2	27 731	86 469
(s,Q) 12		s4		Q3	44 063	100 498
(R,s,Q) 1	R2	s1		Q1	34 776	65 895
(R,s,Q) 2	R2	s1		Q2	34 776	65 895
(R,s,Q) 3	R2	s1		Q3	45 574	84 163
(R,s,Q) 4	R2	s2		Q1	34 776	65 895
(R,s,Q) 5	R2	s2		Q2	34 776	65 895
(R,s,Q) 6	R2	s2		Q3	45 574	84 163
(R,s,Q) 7	R2	s3		Q1	34 776	65 895
(R,s,Q) 8	R2	s3		Q2	34 776	65 895
(R,s,Q) 9	R2	s3		Q3	45 574	84 163
(R,s,Q) 10	R2	s4		Q1	34 776	65 895
(R,s,Q) 11	R2	s4		Q2	34 776	65 895
(R,s,Q) 12	R2	s4		Q3	45 574	84 163
(R,s,Q) 13	R3	s1		Q1	20 178	46 992
(R,s,Q) 14	R3	s1		Q2	43 310	68 506
(R,s,Q) 15	R3	s1		Q3	57 757	82 663
(R,s,Q) 16	R3	s2		Q1	20 325	46 751
(R,s,Q) 17	R3	s2		Q2	43 503	67 176
(R,s,Q) 18	R3	s2		Q3	57 757	82 663

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(R,s,Q) 19	R3	s3	Q1	20 325	46 751
(R,s,Q) 20	R3	s3	Q2	43 503	67 176
(R,s,Q) 21	R3	s3	Q3	57 937	83 277
(R,s,Q) 22	R3	s4	Q1	20 325	46 751
(R,s,Q) 23	R3	s4	Q2	43 234	67 612
(R,s,Q) 24	R3	s4	Q3	57 757	82 663
(R,s,Q) 25	R4	s1	Q1	21 733	21 733
(R,s,Q) 26	R4	s1	Q2	54 316	56 552
(R,s,Q) 27	R4	s1	Q3	75 241	75 241
(R,s,Q) 28	R4	s2	Q1	21 733	21 733
(R,s,Q) 29	R4	s2	Q2	54 316	56 552
(R,s,Q) 30	R4	s2	Q3	75 241	75 241
(R,s,Q) 31	R4	s3	Q1	21 733	21 733
(R,s,Q) 32	R4	s3	Q2	54 109	56 373
(R,s,Q) 33	R4	s3	Q3	75 241	75 241
(R,s,Q) 34	R4	s4	Q1	21 733	21 733
(R,s,Q) 35	R4	s4	Q2	53 757	53 757
(R,s,Q) 36	R4	s4	Q3	75 241	75 241

The results of the cost performance for each scenario is summarised in Table H.3.

Table H.3: Capreomycin - Summary of cost performance for the scenarios.

Policy #	R	s	S	Q	C_O	C_P	C_H	Total Cost
Base	-	-	-	-	-	43 141 280	18 764 428.20	61 905 708
(s,S) 1		s1	S1		470 646	40 477 570	34 233 723.26	75 181 939
(s,S) 2		s1	S2		-	39 521 810	19 346 658.96	58 868 469
(s,S) 3		s2	S1		226 349	41 688 910	32 146 304.65	74 061 564
(s,S) 4		s2	S2		1 138	41 168 910	24 779 935.63	65 949 984
(s,S) 5		s3	S1		534 457	40 143 040	36 024 713.88	76 702 211
(s,S) 6		s3	S2		1 138	40 008 060	29 726 313.63	69 735 512
(s,S) 7		s4	S1		-	39 632 701	59 832 890.83	99 465 592
(s,S) 8		s4	S2		-	39 632 701	38 795 608.27	78 428 309
(R,S) 1	R1		S1		-	39 632 701	59 832 890.83	99 465 592
(R,S) 2	R1		S2		-	39 632 701	38 795 608.27	78 428 309
(R,S) 3	R2		S1		-	39 733 608	52 517 777.36	92 251 385
(R,S) 4	R2		S2		-	39 733 608	32 753 007.83	72 486 616
(R,S) 5	R3		S1		-	39 337 908	59 290 396.45	98 628 304
(R,S) 6	R3		S2		-	39 337 908	39 023 341.20	78 361 249
(R,S) 7	R4		S1		-	39 733 612	56 526 389.93	96 260 002
(R,S) 8	R4		S2		-	39 337 908	35 711 409.53	75 049 318
(R,s,S) 1	R2	s1	S1		693 741	40 732 350	29 510 007.18	70 936 098
(R,s,S) 2	R2	s1	S2		1 138	40 366 300	20 207 468.19	60 574 906
(R,s,S) 3	R2	s2	S1		244 829	40 283 430	29 023 638.43	69 551 897
(R,s,S) 4	R2	s2	S2		1 138	40 291 070	21 037 813.19	61 330 021
(R,s,S) 5	R2	s3	S1		-	40 777 260	30 136 908.78	70 914 169

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(R,s,S) 6	R2	s3	S2	1 138	40 852 050	28 444 321.16	69 297 509
(R,s,S) 7	R2	s4	S1	-	39 733 608	52 517 777.36	92 251 385
(R,s,S) 8	R2	s4	S2	-	39 733 608	32 753 007.83	72 486 616
(R,s,S) 9	R3	s1	S1	-	37 263 130	30 632 477.86	67 895 608
(R,s,S) 10	R3	s1	S2	1 138	39 753 770	17 186 461.94	56 941 370
(R,s,S) 11	R3	s2	S1	56 074	40 087 340	44 121 967.54	84 265 382
(R,s,S) 12	R3	s2	S2	-	40 031 260	24 079 561.22	64 110 821
(R,s,S) 13	R3	s3	S1	697 426	41 054 920	39 645 248.20	81 397 594
(R,s,S) 14	R3	s3	S2	-	40 336 040	28 837 488.81	69 173 529
(R,s,S) 15	R3	s4	S1	-	39 337 908	59 290 396.45	98 628 304
(R,s,S) 16	R3	s4	S2	-	39 337 908	39 023 341.20	78 361 249
(R,s,S) 17	R4	s1	S1	24 604	37 508 970	41 869 749.18	79 403 323
(R,s,S) 18	R4	s1	S2	-	39 121 970	24 511 814.00	63 633 784
(R,s,S) 19	R4	s2	S1	24 604	37 508 970	41 013 577.96	78 547 152
(R,s,S) 20	R4	s2	S2	-	40 777 216	30 136 908.78	70 914 125
(R,s,S) 21	R4	s3	S1	24 604	41 873 380	34 610 303.58	76 508 288
(R,s,S) 22	R4	s3	S2	-	41 388 890	29 887 589.67	71 276 480
(R,s,S) 23	R4	s4	S1	-	38 733 612	56 526 389.93	95 260 002
(R,s,S) 24	R4	s4	S2	-	39 733 612	35 711 409.53	75 445 022
(s,Q) 1		s1	Q1	-	38 619 594	9 624 144.07	48 243 738
(s,Q) 2		s1	Q2	-	39 231 874	8 689 738.65	47 921 613
(s,Q) 3		s1	Q3	-	39 046 015	8 047 223.36	47 093 238
(s,Q) 4		s2	Q1	-	38 673 448	10 456 718.46	49 130 166
(s,Q) 5		s2	Q2	-	39 231 874	9 953 762.24	49 185 636
(s,Q) 6		s2	Q3	-	39 046 015	9 753 940.17	48 799 955
(s,Q) 7		s3	Q1	-	38 562 878	10 906 833.63	49 469 712
(s,Q) 8		s3	Q2	-	39 231 874	8 950 306.36	48 182 180
(s,Q) 9		s3	Q3	-	39 046 015	9 753 940.17	48 799 955
(s,Q) 10		s4	Q1	-	39 746 974	21 818 965.43	61 565 939
(s,Q) 11		s4	Q2	-	39 231 874	37 420 785.09	76 652 659
(s,Q) 12		s4	Q3	-	39 046 015	9 753 940.17	48 799 955
(R,s,Q) 1	R2	s1	Q1	-	39 194 765	8 883 180.32	48 077 945
(R,s,Q) 2	R2	s1	Q2	-	39 194 765	8 883 180.32	48 077 945
(R,s,Q) 3	R2	s1	Q3	-	39 171 271	8 897 468.14	48 068 739
(R,s,Q) 4	R2	s2	Q1	-	39 194 765	8 863 997.01	48 058 762
(R,s,Q) 5	R2	s2	Q2	-	39 194 765	8 863 997.01	48 058 762
(R,s,Q) 6	R2	s2	Q3	-	39 171 271	10 366 956.39	49 538 227
(R,s,Q) 7	R2	s3	Q1	-	39 194 765	9 989 044.00	49 183 809
(R,s,Q) 8	R2	s3	Q2	-	39 194 765	9 989 044.00	49 183 809
(R,s,Q) 9	R2	s3	Q3	-	39 171 271	10 366 956.39	49 538 227
(R,s,Q) 10	R2	s4	Q1	-	39 194 765	33 072 576.44	72 267 341
(R,s,Q) 11	R2	s4	Q2	-	39 194 765	33 072 576.44	72 267 341
(R,s,Q) 12	R2	s4	Q3	-	39 171 271	36 158 736.18	75 330 007
(R,s,Q) 13	R3	s1	Q1	-	39 653 475	7 804 488.84	47 457 964
(R,s,Q) 14	R3	s1	Q2	-	38 778 944	8 521 667.01	47 300 611

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(R,s,Q) 15	R3	s1	Q3	-	38 976 491	8 767 945.81	47 744 437
(R,s,Q) 16	R3	s2	Q1	-	39 936 146	7 584 196.14	47 520 342
(R,s,Q) 17	R3	s2	Q2	-	38 451 944	9 831 736.72	48 283 681
(R,s,Q) 18	R3	s2	Q3	-	38 976 491	10 531 685.93	49 508 177
(R,s,Q) 19	R3	s3	Q1	-	39 936 146	7 584 196.14	47 520 342
(R,s,Q) 20	R3	s3	Q2	-	38 451 944	12 101 178.92	50 553 123
(R,s,Q) 21	R3	s3	Q3	-	38 754 482	13 153 806.64	51 908 289
(R,s,Q) 22	R3	s4	Q1	-	39 936 146	7 675 582.84	47 611 729
(R,s,Q) 23	R3	s4	Q2	-	39 019 205	35 908 903.36	74 928 108
(R,s,Q) 24	R3	s4	Q3	-	38 976 491	41 060 130.52	80 036 622
(R,s,Q) 25	R4	s1	Q1	-	39 482 690	7 717 469.74	47 200 160
(R,s,Q) 26	R4	s1	Q2	-	38 590 165	6 318 457.28	44 908 622
(R,s,Q) 27	R4	s1	Q3	-	39 146 497	8 849 899.28	47 996 396
(R,s,Q) 28	R4	s2	Q1	-	39 482 690	8 020 257.47	47 502 947
(R,s,Q) 29	R4	s2	Q2	-	38 590 165	9 067 182.85	47 657 348
(R,s,Q) 30	R4	s2	Q3	-	38 146 497	9 692 619.78	47 839 117
(R,s,Q) 31	R4	s3	Q1	-	39 482 690	8 020 257.47	47 502 947
(R,s,Q) 32	R4	s3	Q2	-	38 682 034	9 245 944.68	47 927 979
(R,s,Q) 33	R4	s3	Q3	-	39 146 497	11 737 958.70	50 884 456
(R,s,Q) 34	R4	s4	Q1	-	39 482 690	7 416 402.94	46 899 093
(R,s,Q) 35	R4	s4	Q2	-	39 438 920	29 372 821.55	68 811 742
(R,s,Q) 36	R4	s4	Q3	-	39 146 497	36 991 725.98	76 138 223

H.2 Modelling results of kanamycin

This section provides the results of kanamycin for each scenario. Table H.4 summarises the stock performance of each scenario.

Table H.4: Kanamycin - Summary of stock performance for the scenarios.

Policy #	R	s	S	Q	%BLs	μ_{BL_Age}	Max_{BL_Age}	Total Vol.
(s,S) 1		s1	S1		3.20%	10.40	26	1 402 907
(s,S) 2		s1	S2		9.60%	4.81	14	1 182 645
(s,S) 3		s2	S1		2.40%	11.30	26	1 253 054
(s,S) 4		s2	S2		9.60%	7.69	20	1 029 848
(s,S) 5		s3	S1		2.40%	11.30	26	1 253 054
(s,S) 6		s3	S2		17.60%	5.01	23	928 357
(s,S) 7		s4	S1		0.00%	0.00	0	0
(s,S) 8		s4	S2		1.60%	3.14	6	310 891
(R,S) 1	R1		S1		0.00%	0.00	0	0
(R,S) 2	R1		S2		1.60%	3.14	6	310 891
(R,S) 3	R2		S1		0.00%	0.00	0	0
(R,S) 4	R2		S2		1.60%	1.00	1	547 935
(R,S) 5	R3		S1		0.00%	0.00	0	0

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(R,S) 6	R3		S2		1.60%	1.00	1	547 935
(R,S) 7	R4		S1		0.00%	0.00	0	0
(R,S) 8	R4		S2		2.40%	1.52	2	296 909
(R,s,S) 1	R2	s1	S1		0.80%	13.50	26	705 119
(R,s,S) 2	R2	s1	S2		6.40%	2.81	7	1 283 571
(R,s,S) 3	R2	s2	S1		2.40%	11.30	26	1 253 054
(R,s,S) 4	R2	s2	S2		8.80%	5.76	16	1 584 887
(R,s,S) 5	R2	s3	S1		6.40%	6.32	18	1 874 502
(R,s,S) 6	R2	s3	S2		15.20%	4.34	16	1 050 329
(R,s,S) 7	R2	s4	S1		0.00%	0.00	0	0
(R,s,S) 8	R2	s4	S2		1.60%	1.00	1	547 935
(R,s,S) 9	R3	s1	S1		0.80%	7.00	13	705 119
(R,s,S) 10	R3	s1	S2		16.80%	4.65	16	2 366 099
(R,s,S) 11	R3	s2	S1		1.60%	6.57	13	1 032 648
(R,s,S) 12	R3	s2	S2		7.20%	9.55	29	2 202 031
(R,s,S) 13	R3	s3	S1		0.80%	7.00	13	705 119
(R,s,S) 14	R3	s3	S2		10.40%	6.06	16	1 689 513
(R,s,S) 15	R3	s4	S1		0.00%	0.00	0	0
(R,s,S) 16	R3	s4	S2		1.60%	1.00	1	547 935
(R,s,S) 17	R4	s1	S1		7.20%	9.05	22	1 567 366
(R,s,S) 18	R4	s1	S2		12.00%	3.04	8	2 565 723
(R,s,S) 19	R4	s2	S1		7.20%	9.51	22	1 567 366
(R,s,S) 20	R4	s2	S2		6.40%	6.32	18	1 874 502
(R,s,S) 21	R4	s3	S1		0.80%	11.50	22	705 119
(R,s,S) 22	R4	s3	S2		12.80%	3.77	16	1 599 355
(R,s,S) 23	R4	s4	S1		0.00%	0.00	0	0
(R,s,S) 24	R4	s4	S2		2.40%	1.52	3	296 909
(s,Q) 1		s1		Q1	9.60%	15.56	47	2 683 523
(s,Q) 2		s1		Q2	8.00%	11.81	33	2 674 385
(s,Q) 3		s1		Q3	9.60%	11.74	38	2 693 091
(s,Q) 4		s2		Q1	7.20%	12.73	31	2 592 497
(s,Q) 5		s2		Q2	12.00%	9.82	29	2 738 224
(s,Q) 6		s2		Q3	7.20%	11.88	38	2 043 080
(s,Q) 7		s3		Q1	12.00%	9.57	29	3 011 095
(s,Q) 8		s3		Q2	6.40%	8.50	26	2 001 544
(s,Q) 9		s3		Q3	5.60%	12.66	38	1 813 642
(s,Q) 10		s4		Q1	1.60%	2.50	4	432 487
(s,Q) 11		s4		Q2	0.00%	0.00	0	0
(s,Q) 12		s4		Q3	5.60%	8.50	38	1 813 642
(R,s,Q) 1	R2	s1		Q1	13.60%	14	45	3 528 682
(R,s,Q) 2	R2	s1		Q2	11.20%	10	32	2 859 217
(R,s,Q) 3	R2	s1		Q3	11.20%	8	23	3 049 787
(R,s,Q) 4	R2	s2		Q1	13.60%	12	34	3 434 096
(R,s,Q) 5	R2	s2		Q2	8.80%	9	25	2 805 340
(R,s,Q) 6	R2	s2		Q3	9.60%	7	18	2 822 867

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(R,s,Q) 7	R2	s3	Q1	12.80%	12	33	3 299 687
(R,s,Q) 8	R2	s3	Q2	15.20%	7	21	3 125 870
(R,s,Q) 9	R2	s3	Q3	6.40%	7	18	2 161 586
(R,s,Q) 10	R2	s4	Q1	4.80%	8	18	1 450 940
(R,s,Q) 11	R2	s4	Q2	0.80%	0	0	282 634
(R,s,Q) 12	R2	s4	Q3	0.00%	0	0	0
(R,s,Q) 13	R3	s1	Q1	16.80%	17	50	3 752 626
(R,s,Q) 14	R3	s1	Q2	15.20%	11	29	3 297 102
(R,s,Q) 15	R3	s1	Q3	13.60%	12	29	3 264 355
(R,s,Q) 16	R3	s2	Q1	15.20%	16	45	3 717 209
(R,s,Q) 17	R3	s2	Q2	10.40%	13	30	2 927 042
(R,s,Q) 18	R3	s2	Q3	12.00%	10	29	2 834 506
(R,s,Q) 19	R3	s3	Q1	14.40%	15	39	3 164 916
(R,s,Q) 20	R3	s3	Q2	11.20%	11	29	2 692 339
(R,s,Q) 21	R3	s3	Q3	12.80%	9	29	2 792 261
(R,s,Q) 22	R3	s4	Q1	7.20%	12	29	2 253 633
(R,s,Q) 23	R3	s4	Q2	0.00%	0	0	0
(R,s,Q) 24	R3	s4	Q3	0.00%	0	0	0
(R,s,Q) 25	R4	s1	Q1	16.80%	19	48	3 649 091
(R,s,Q) 26	R4	s1	Q2	8.00%	10	33	2 430 360
(R,s,Q) 27	R4	s1	Q3	6.40%	10	33	2 309 863
(R,s,Q) 28	R4	s2	Q1	14.40%	14	45	2 922 409
(R,s,Q) 29	R4	s2	Q2	28.00%	7	18	4 857 500
(R,s,Q) 30	R4	s2	Q3	8.80%	16	32	2 559 163
(R,s,Q) 31	R4	s3	Q1	15.20%	14	51	3 109 141
(R,s,Q) 32	R4	s3	Q2	8.80%	8	22	2 318 406
(R,s,Q) 33	R4	s3	Q3	8.80%	6	18	2 635 818
(R,s,Q) 34	R4	s4	Q1	11.20%	10	28	3 137 629
(R,s,Q) 35	R4	s4	Q2	2.40%	3	5	1 068 831
(R,s,Q) 36	R4	s4	Q3	0.80%	0	0	282 634

Table H.5 summarised the order variability performance for each of the scenarios.

Table H.5: Kanamycin - Summary of order variability performance for the scenarios.

Policy #	R	s	S	Q	σ_{os}	σ_{mo}
Base	-	-	-	-	88 219	173 929
(s,S) 1		s1	S1		44 350	324 257
(s,S) 2		s1	S2		324 257	266 167
(s,S) 3		s2	S1		68 230	340 846
(s,S) 4		s2	S2		340 846	259 872
(s,S) 5		s3	S1		68 230	340 846
(s,S) 6		s3	S2		340 846	222 252
(s,S) 7		s4	S1		97 627	138 601
(s,S) 8		s4	S2		138 601	138 601
(R,S) 1	R1		S1		97 627	138 601

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(R,S) 2	R1		S2		138 601	138 601
(R,S) 3	R2		S1		116 653	140 780
(R,S) 4	R2		S2		140 780	140 780
(R,S) 5	R3		S1		148 003	150 917
(R,S) 6	R3		S2		150 917	150 917
(R,S) 7	R4		S1		152 724	150 005
(R,S) 8	R4		S2		150 005	150 005
(R,s,S) 1	R2	s1	S1		44 363	324 258
(R,s,S) 2	R2	s1	S2		324 258	266 167
(R,s,S) 3	R2	s2	S1		68 230	340 846
(R,s,S) 4	R2	s2	S2		340 846	260 150
(R,s,S) 5	R2	s3	S1		195 768	270 688
(R,s,S) 6	R2	s3	S2		270 688	222 186
(R,s,S) 7	R2	s4	S1		116 653	140 780
(R,s,S) 8	R2	s4	S2		140 780	140 780
(R,s,S) 9	R3	s1	S1		140 040	333 758
(R,s,S) 10	R3	s1	S2		333 758	287 562
(R,s,S) 11	R3	s2	S1		158 160	332 696
(R,s,S) 12	R3	s2	S2		332 696	371 021
(R,s,S) 13	R3	s3	S1		175 076	327 777
(R,s,S) 14	R3	s3	S2		327 777	243 397
(R,s,S) 15	R3	s4	S1		148 003	150 917
(R,s,S) 16	R3	s4	S2		150 917	150 917
(R,s,S) 17	R4	s1	S1		139 989	333 781
(R,s,S) 18	R4	s1	S2		333 781	287 320
(R,s,S) 19	R4	s2	S1		158 160	332 696
(R,s,S) 20	R4	s2	S2		332 696	270 688
(R,s,S) 21	R4	s3	S1		174 231	329 243
(R,s,S) 22	R4	s3	S2		329 243	243 317
(R,s,S) 23	R4	s4	S1		152 724	150 005
(R,s,S) 24	R4	s4	S2		150 005	150 005
(s,Q) 1		s1		Q1	15 876	59 321
(s,Q) 2		s1		Q2	40 690	119 706
(s,Q) 3		s1		Q3	62 615	146 092
(s,Q) 4		s2		Q1	15 890	59 228
(s,Q) 5		s2		Q2	40 690	119 706
(s,Q) 6		s2		Q3	62 615	146 092
(s,Q) 7		s3		Q1	15 890	59 228
(s,Q) 8		s3		Q2	40 690	119 706
(s,Q) 9		s3		Q3	62 615	146 092
(s,Q) 10		s4		Q1	15 869	58 707
(s,Q) 11		s4		Q2	40 690	119 706
(s,Q) 12		s4		Q3	62 615	146 092
(R,s,Q) 1	R2	s1		Q1	19 226	40 434
(R,s,Q) 2	R2	s1		Q2	52 302	96 437

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(R,s,Q) 3	R2	s1	Q3	68 876	117 518
(R,s,Q) 4	R2	s2	Q1	19 241	40 472
(R,s,Q) 5	R2	s2	Q2	51 974	96 464
(R,s,Q) 6	R2	s2	Q3	68 876	117 518
(R,s,Q) 7	R2	s3	Q1	19 319	40 373
(R,s,Q) 8	R2	s3	Q2	52 228	96 361
(R,s,Q) 9	R2	s3	Q3	68 876	117 518
(R,s,Q) 10	R2	s4	Q1	19 509	38 393
(R,s,Q) 11	R2	s4	Q2	51 974	96 464
(R,s,Q) 12	R2	s4	Q3	68 876	117 518
(R,s,Q) 13	R3	s1	Q1	21 477	45 321
(R,s,Q) 14	R3	s1	Q2	65 816	93 415
(R,s,Q) 15	R3	s1	Q3	91 097	115 479
(R,s,Q) 16	R3	s2	Q1	21 526	45 103
(R,s,Q) 17	R3	s2	Q2	65 816	93 415
(R,s,Q) 18	R3	s2	Q3	91 097	115 479
(R,s,Q) 19	R3	s3	Q1	21 477	45 321
(R,s,Q) 20	R3	s3	Q2	65 816	93 415
(R,s,Q) 21	R3	s3	Q3	91 097	115 479
(R,s,Q) 22	R3	s4	Q1	21 701	44 240
(R,s,Q) 23	R3	s4	Q2	65 416	93 389
(R,s,Q) 24	R3	s4	Q3	91 097	115 479
(R,s,Q) 25	R4	s1	Q1	23 194	23 194
(R,s,Q) 26	R4	s1	Q2	78 362	78 604
(R,s,Q) 27	R4	s1	Q3	113 583	113 583
(R,s,Q) 28	R4	s2	Q1	23 194	23 194
(R,s,Q) 29	R4	s2	Q2	78 362	78 604
(R,s,Q) 30	R4	s2	Q3	68 324	73 035
(R,s,Q) 31	R4	s3	Q1	23 194	23 194
(R,s,Q) 32	R4	s3	Q2	78 551	79 038
(R,s,Q) 33	R4	s3	Q3	113 583	113 583
(R,s,Q) 34	R4	s4	Q1	23 194	23 194
(R,s,Q) 35	R4	s4	Q2	78 022	78 022
(R,s,Q) 36	R4	s4	Q3	113 583	113 583

The results of the cost performance for each scenario is summarised in Table H.6.

Table H.6: Kanamycin - Summary of cost performance for the scenarios.

Policy #	R	s	S	Q	C_O	C_P	C_H	Total Cost
Base	-	-	-	-	-	21 006 724	7 186 628.40	28 193 353
(s,S) 1		s1	S1		-	15 739 410	40 010 791.54	55 750 202
(s,S) 2		s1	S2		-	16 412 520	25 367 851.80	41 780 372
(s,S) 3		s2	S1		-	18 256 470	37 228 955.10	55 485 425
(s,S) 4		s2	S2		-	15 781 060	22 885 709.28	38 666 769
(s,S) 5		s3	S1		-	18 256 470	37 228 955.10	55 485 425

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(s,S) 6		s3	S2	-	16 778 270	26 363 121.79	43 141 392
(s,S) 7		s4	S1	-	15 827 879	55 559 061.57	71 386 941
(s,S) 8		s4	S2	-	15 827 879	33 838 250.12	49 666 129
(R,S) 1	R1		S1	-	15 827 879	55 559 061.57	71 386 941
(R,S) 2	R1		S2	-	15 827 879	33 838 250.12	49 666 129
(R,S) 3	R2		S1	-	15 829 627	56 093 109.86	71 922 737
(R,S) 4	R2		S2	-	15 829 627	34 387 814.13	50 217 441
(R,S) 5	R3		S1	-	15 827 875	51 277 975.30	67 105 850
(R,S) 6	R3		S2	-	15 827 875	29 572 691.23	45 400 566
(R,S) 7	R4		S1	-	15 829 627	56 497 171.55	72 326 799
(R,S) 8	R4		S2	-	15 829 627	34 753 711.52	50 583 339
(R,s,S) 1	R2	s1	S1	-	15 739 400	39 740 415.61	55 479 816
(R,s,S) 2	R2	s1	S2	-	16 412 520	25 226 362.53	41 638 883
(R,s,S) 3	R2	s2	S1	-	18 256 470	37 228 955.10	55 485 425
(R,s,S) 4	R2	s2	S2	-	15 781 080	23 165 609.44	38 946 689
(R,s,S) 5	R2	s3	S1	-	16 566 810	23 743 041.20	40 309 851
(R,s,S) 6	R2	s3	S2	-	16 778 280	23 886 048.70	40 664 329
(R,s,S) 7	R2	s4	S1	-	15 829 627	56 093 109.86	71 922 737
(R,s,S) 8	R2	s4	S2	-	15 829 627	34 387 814.13	50 217 441
(R,s,S) 9	R3	s1	S1	-	16 121 800	37 877 883.00	53 999 683
(R,s,S) 10	R3	s1	S2	-	16 412 520	18 322 633.84	34 735 154
(R,s,S) 11	R3	s2	S1	-	16 045 540	32 675 417.01	48 720 957
(R,s,S) 12	R3	s2	S2	-	16 566 790	20 808 526.20	37 375 316
(R,s,S) 13	R3	s3	S1	-	15 779 060	34 913 279.97	50 692 340
(R,s,S) 14	R3	s3	S2	-	15 929 990	21 587 091.53	37 517 082
(R,s,S) 15	R3	s4	S1	-	15 827 875	51 277 975.30	67 105 850
(R,s,S) 16	R3	s4	S2	-	15 827 875	29 572 691.23	45 400 566
(R,s,S) 17	R4	s1	S1	-	16 122 970	30 374 696.70	46 497 667
(R,s,S) 18	R4	s1	S2	-	16 411 370	21 509 051.76	37 920 422
(R,s,S) 19	R4	s2	S1	-	16 045 540	30 362 383.68	46 407 924
(R,s,S) 20	R4	s2	S2	-	16 566 810	23 743 041.20	40 309 851
(R,s,S) 21	R4	s3	S1	-	15 852 240	40 208 254.92	56 060 495
(R,s,S) 22	R4	s3	S2	-	15 929 990	25 319 870.92	41 249 861
(R,s,S) 23	R4	s4	S1	-	15 829 627	56 497 171.55	72 326 799
(R,s,S) 24	R4	s4	S2	-	15 829 627	34 753 711.52	50 583 339
(s,Q) 1		s1	Q1	-	15 752 842	8 928 831.17	24 681 673
(s,Q) 2		s1	Q2	-	15 852 457	12 903 130.12	28 755 587
(s,Q) 3		s1	Q3	-	15 861 991	12 968 923.45	28 830 914
(s,Q) 4		s2	Q1	-	15 763 740	10 670 293.09	26 434 033
(s,Q) 5		s2	Q2	-	15 852 457	14 413 189.50	30 265 647
(s,Q) 6		s2	Q3	-	15 861 991	15 114 064.54	30 976 056
(s,Q) 7		s3	Q1	-	15 763 740	11 835 172.53	27 598 913
(s,Q) 8		s3	Q2	-	15 852 457	16 112 202.58	31 964 660
(s,Q) 9		s3	Q3	-	15 861 991	17 088 195.58	32 950 187
(s,Q) 10		s4	Q1	-	15 890 294	25 619 594.46	41 509 888

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(s,Q) 11		s4	Q2	-	15 852 457	33 897 534.41	49 749 991
(s,Q) 12		s4	Q3	-	15 861 991	17 088 195.58	32 950 187
(R,s,Q) 1	R2	s1	Q1	-	15 522 625	9 038 678.35	24 561 303
(R,s,Q) 2	R2	s1	Q2	-	15 729 830	10 359 318.15	26 089 148
(R,s,Q) 3	R2	s1	Q3	-	15 826 065	12 281 453.11	28 107 518
(R,s,Q) 4	R2	s2	Q1	-	15 519 037	9 421 804.83	24 940 842
(R,s,Q) 5	R2	s2	Q2	-	15 893 193	12 222 718.74	28 115 912
(R,s,Q) 6	R2	s2	Q3	-	15 826 065	13 944 670.64	29 770 736
(R,s,Q) 7	R2	s3	Q1	-	15 491 972	11 040 183.02	26 532 155
(R,s,Q) 8	R2	s3	Q2	-	15 743 597	13 385 232.09	29 128 829
(R,s,Q) 9	R2	s3	Q3	-	15 826 065	15 816 365.22	31 642 430
(R,s,Q) 10	R2	s4	Q1	-	15 724 126	19 959 792.13	35 683 918
(R,s,Q) 11	R2	s4	Q2	-	15 893 193	33 042 697.32	48 935 890
(R,s,Q) 12	R2	s4	Q3	-	15 826 065	35 095 587.80	50 921 653
(R,s,Q) 13	R3	s1	Q1	-	15 230 222	7 373 289.23	22 603 511
(R,s,Q) 14	R3	s1	Q2	-	15 715 627	8 212 758.31	23 928 385
(R,s,Q) 15	R3	s1	Q3	-	15 818 775	10 586 927.65	26 405 703
(R,s,Q) 16	R3	s2	Q1	-	15 341 294	8 086 361.83	23 427 656
(R,s,Q) 17	R3	s2	Q2	-	15 715 627	9 543 430.65	25 259 058
(R,s,Q) 18	R3	s2	Q3	-	15 818 775	11 707 501.57	27 526 277
(R,s,Q) 19	R3	s3	Q1	-	15 230 222	8 450 736.86	23 680 959
(R,s,Q) 20	R3	s3	Q2	-	15 715 627	11 922 360.97	27 637 988
(R,s,Q) 21	R3	s3	Q3	-	15 818 775	13 237 427.60	29 056 203
(R,s,Q) 22	R3	s4	Q1	-	15 430 499	11 891 494.74	27 321 994
(R,s,Q) 23	R3	s4	Q2	-	15 856 881	27 864 157.64	43 721 039
(R,s,Q) 24	R3	s4	Q3	-	15 818 775	30 413 888.75	46 232 664
(R,s,Q) 25	R4	s1	Q1	-	15 027 452	7 083 279.50	22 110 732
(R,s,Q) 26	R4	s1	Q2	-	15 744 060	11 571 364.08	27 315 424
(R,s,Q) 27	R4	s1	Q3	-	15 826 358	13 247 836.79	29 074 195
(R,s,Q) 28	R4	s2	Q1	-	15 027 452	8 187 594.90	23 215 047
(R,s,Q) 29	R4	s2	Q2	-	15 744 060	12 766 363.73	28 510 424
(R,s,Q) 30	R4	s2	Q3	-	14 065 763	10 771 206.40	24 836 969
(R,s,Q) 31	R4	s3	Q1	-	15 027 452	8 603 552.67	23 631 005
(R,s,Q) 32	R4	s3	Q2	-	15 669 900	14 247 511.47	29 917 411
(R,s,Q) 33	R4	s3	Q3	-	15 826 358	16 110 364.94	31 936 723
(R,s,Q) 34	R4	s4	Q1	-	15 027 452	10 493 614.01	25 521 066
(R,s,Q) 35	R4	s4	Q2	-	15 851 004	32 929 537.21	48 780 541
(R,s,Q) 36	R4	s4	Q3	-	15 826 358	35 521 004.66	51 347 363

H.3 Modelling results of cycloserine

This section provides the results of cycloserine for each scenario. Table H.7 summarises the stock performance of each scenario.

Table H.7: Cycloserine - Summary of stock performance for the scenarios.

Policy #	R	s	S	Q	%BLs	μ_{BL_Age}	Max_{BL_Age}	Total Vol.
(s,S) 1		s1	S1		46.67%	8.66	34	83 176 395
(s,S) 2		s1	S2		39.22%	7.34	36	88 612 986
(s,S) 3		s2	S1		47.45%	8.71	34	90 381 221
(s,S) 4		s2	S2		35.29%	5.62	22	82 997 205
(s,S) 5		s3	S1		28.63%	7.21	25	66 417 405
(s,S) 6		s3	S2		30.20%	5.96	31	67 878 296
(s,S) 7		s4	S1		8.63%	5.51	18	38 540 211
(s,S) 8		s4	S2		13.33%	8.83	29	58 292 077
(R,S) 1	R1		S1		8.63%	5.51	18	38 540 211
(R,S) 2	R1		S2		13.33%	8.93	29	58 292 077
(R,S) 3	R2		S1		9.02%	9.11	35	46 676 508
(R,S) 4	R2		S2		9.02%	13.18	47	47 928 818
(R,S) 5	R3		S1		5.88%	11.00	35	36 812 271
(R,S) 6	R3		S2		13.73%	10.09	40	57 817 621
(R,S) 7	R4		S1		10.59%	7.68	31	41 238 486
(R,S) 8	R4		S2		22.35%	6.83	31	76 547 597
(R,s,S) 1	R2	s1	S1		39.61%	9.89	47	77 683 979
(R,s,S) 2	R2	s1	S2		24.45%	9.72	39	68 423 989
(R,s,S) 3	R2	s2	S1		34.51%	10.16	52	77 022 352
(R,s,S) 4	R2	s2	S2		36.47%	8.08	36	78 022 953
(R,s,S) 5	R2	s3	S1		35.69%	9.32	43	83 961 230
(R,s,S) 6	R2	s3	S2		38.04%	8.76	43	76 837 229
(R,s,S) 7	R2	s4	S1		9.02%	9.11	35	46 676 508
(R,s,S) 8	R2	s4	S2		9.02%	13.18	47	47 928 818
(R,s,S) 9	R3	s1	S1		42.75%	9.75	47	80 981 714
(R,s,S) 10	R3	s1	S2		26.27%	9.24	42	65 266 420
(R,s,S) 11	R3	s2	S1		29.80%	5.56	22	66 282 991
(R,s,S) 12	R3	s2	S2		36.08%	6.85	35	80 692 333
(R,s,S) 13	R3	s3	S1		29.80%	5.56	22	66 282 991
(R,s,S) 14	R3	s3	S2		32.55%	8.03	40	77 482 121
(R,s,S) 15	R3	s4	S1		5.88%	11.00	35	36 812 271
(R,s,S) 16	R3	s4	S2		13.73%	10.09	40	57 817 621
(R,s,S) 17	R4	s1	S1		30.59%	8.72	41	61 479 860
(R,s,S) 18	R4	s1	S2		35.29%	8.82	43	80 919 966
(R,s,S) 19	R4	s2	S1		29.41%	7.08	29	70 442 660
(R,s,S) 20	R4	s2	S2		35.69%	9.32	43	83 961 230
(R,s,S) 21	R4	s3	S1		35.29%	7.31	30	75 731 691
(R,s,S) 22	R4	s3	S2		33.73%	9.23	39	83 498 211
(R,s,S) 23	R4	s4	S1		10.59%	7.68	31	41 238 486
(R,s,S) 24	R4	s4	S2		22.35%	6.83	35	76 547 597
(s,Q) 1		s1		Q1	20.00%	19.47	59	74 677 760
(s,Q) 2		s1		Q2	20.78%	4.82	49	78 142 881
(s,Q) 3		s1		Q3	28.63%	9.86	71	91 302 763
(s,Q) 4		s2		Q1	21.96%	18.68	52	74 753 861

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(s,Q) 5		s2	Q2	26.27%	11.95	52	86 246 305
(s,Q) 6		s2	Q3	18.82%	15.36	57	75 823 651
(s,Q) 7		s3	Q1	21.57%	17.41	69	73 167 130
(s,Q) 8		s3	Q2	20.39%	9.58	46	84 310 353
(s,Q) 9		s3	Q3	22.35%	11.81	44	78 940 628
(s,Q) 10		s4	Q1	14.12%	10.01	47	65 101 767
(s,Q) 11		s4	Q2	7.45%	6.08	22	53 111 554
(s,Q) 12		s4	Q3	5.60%	8.50	38	78 940 628
(R,s,Q) 1	R2	s1	Q1	24.71%	24	77	80 040 441
(R,s,Q) 2	R2	s1	Q2	27.84%	15	51	87 589 007
(R,s,Q) 3	R2	s1	Q3	22.35%	18	57	73 721 325
(R,s,Q) 4	R2	s2	Q1	22.75%	21	58	80 234 787
(R,s,Q) 5	R2	s2	Q2	26.27%	14	47	77 206 440
(R,s,Q) 6	R2	s2	Q3	20.00%	18	57	73 951 817
(R,s,Q) 7	R2	s3	Q1	29.02%	19	58	86 130 188
(R,s,Q) 8	R2	s3	Q2	25.10%	13	47	80 042 713
(R,s,Q) 9	R2	s3	Q3	24.71%	15	47	79 450 824
(R,s,Q) 10	R2	s4	Q1	18.43%	20	74	74 513 354
(R,s,Q) 11	R2	s4	Q2	14.51%	10	38	58 473 269
(R,s,Q) 12	R2	s4	Q3	11.37%	10	35	55 008 050
(R,s,Q) 13	R3	s1	Q1	27.06%	31	114	82 928 799
(R,s,Q) 14	R3	s1	Q2	30.59%	19	73	87 155 846
(R,s,Q) 15	R3	s1	Q3	23.53%	16	57	72 976 172
(R,s,Q) 16	R3	s2	Q1	25.10%	31	114	80 180 710
(R,s,Q) 17	R3	s2	Q2	25.10%	18	52	78 611 972
(R,s,Q) 18	R3	s2	Q3	24.31%	16	57	74 734 963
(R,s,Q) 19	R3	s3	Q1	27.84%	31	114	81 535 142
(R,s,Q) 20	R3	s3	Q2	22.35%	17	68	76 633 355
(R,s,Q) 21	R3	s3	Q3	24.31%	16	57	74 734 963
(R,s,Q) 22	R3	s4	Q1	24.31%	30	114	78 593 482
(R,s,Q) 23	R3	s4	Q2	12.16%	15	49	58 238 857
(R,s,Q) 24	R3	s4	Q3	9.41%	15	40	53 210 826
(R,s,Q) 25	R4	s1	Q1	30.98%	35	125	87 737 520
(R,s,Q) 26	R4	s1	Q2	27.45%	16	50	83 661 572
(R,s,Q) 27	R4	s1	Q3	30.59%	13	43	91 479 764
(R,s,Q) 28	R4	s2	Q1	33.73%	36	125	89 229 194
(R,s,Q) 29	R4	s2	Q2	50.20%	14	41	114 612 732
(R,s,Q) 30	R4	s2	Q3	21.96%	16	50	83 053 057
(R,s,Q) 31	R4	s3	Q1	24.24%	36	125	85 136 813
(R,s,Q) 32	R4	s3	Q2	24.31%	15	53	81 983 954
(R,s,Q) 33	R4	s3	Q3	33.73%	11	41	91 726 106
(R,s,Q) 34	R4	s4	Q1	34.90%	32	101	88 781 954
(R,s,Q) 35	R4	s4	Q2	21.18%	9	47	69 736 558
(R,s,Q) 36	R4	s4	Q3	17.65%	9	35	71 205 931

Table H.8 summarised the order variability performance for each of the scenarios.

Table H.8: Cycloserine - Summary of order variability performance for the scenarios.

Policy #	R	s	S	Q	σ_{os}	σ_{mo}
Base	-	-	-	-	976 715	1 865 129
(s,S) 1		s1	S1		2 227 686	4 258 829
(s,S) 2		s1	S2		4 258 829	3 523 724
(s,S) 3		s2	S1		1 128 154	4 040 870
(s,S) 4		s2	S2		4 040 870	3 292 663
(s,S) 5		s3	S1		2 153 086	4 110 091
(s,S) 6		s3	S2		4 110 091	3 002 954
(s,S) 7		s4	S1		1 120 426	1 881 802
(s,S) 8		s4	S2		1 881 802	1 885 686
(R,S) 1	R1		S1		1 120 426	1 881 802
(R,S) 2	R1		S2		1 881 802	1 885 686
(R,S) 3	R2		S1		1 383 606	2 024 841
(R,S) 4	R2		S2		2 024 841	2 032 348
(R,S) 5	R3		S1		1 694 425	1 963 972
(R,S) 6	R3		S2		1 963 972	1 972 002
(R,S) 7	R4		S1		1 951 608	1 957 691
(R,S) 8	R4		S2		1 957 691	1 961 676
(R,s,S) 1	R2	s1	S1		2 585 030	4 529 082
(R,s,S) 2	R2	s1	S2		4 529 082	3 518 645
(R,s,S) 3	R2	s2	S1		1 217 499	4 057 245
(R,s,S) 4	R2	s2	S2		4 057 245	3 275 589
(R,s,S) 5	R2	s3	S1		1 668 797	3 255 103
(R,s,S) 6	R2	s3	S2		3 255 103	2 970 890
(R,s,S) 7	R2	s4	S1		1 389 120	2 029 394
(R,s,S) 8	R2	s4	S2		2 029 394	2 030 348
(R,s,S) 9	R3	s1	S1		2 577 835	4 528 512
(R,s,S) 10	R3	s1	S2		4 528 512	3 488 431
(R,s,S) 11	R3	s2	S1		1 252 360	4 000 222
(R,s,S) 12	R3	s2	S2		4 000 222	3 296 693
(R,s,S) 13	R3	s3	S1		1 252 360	4 000 222
(R,s,S) 14	R3	s3	S2		4 000 222	3 013 954
(R,s,S) 15	R3	s4	S1		1 694 425	1 963 972
(R,s,S) 16	R3	s4	S2		1 963 972	1 972 002
(R,s,S) 17	R4	s1	S1		3 252 206	4 579 653
(R,s,S) 18	R4	s1	S2		4 579 653	3 409 336
(R,s,S) 19	R4	s2	S1		1 282 070	4 060 609
(R,s,S) 20	R4	s2	S2		4 060 609	3 255 103
(R,s,S) 21	R4	s3	S1		2 068 930	4 115 789
(R,s,S) 22	R4	s3	S2		4 115 789	3 104 662
(R,s,S) 23	R4	s4	S1		1 951 608	1 957 691
(R,s,S) 24	R4	s4	S2		1 957 691	1 961 676
(s,Q) 1		s1		Q1	208 094	821 523

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(s,Q) 2		s1	Q2	569 995	1 682 445
(s,Q) 3		s1	Q3	901 720	1 914 757
(s,Q) 4		s2	Q1	208 142	823 317
(s,Q) 5		s2	Q2	569 995	1 682 445
(s,Q) 6		s2	Q3	901 720	1 914 757
(s,Q) 7		s3	Q1	208 703	818 010
(s,Q) 8		s3	Q2	569 995	1 682 445
(s,Q) 9		s3	Q3	901 720	1 914 757
(s,Q) 10		s4	Q1	210 363	807 828
(s,Q) 11		s4	Q2	569 995	1 682 445
(s,Q) 12		s4	Q3	901 720	1 914 757
(R,s,Q) 1	R2	s1	Q1	284 907	581 001
(R,s,Q) 2	R2	s1	Q2	705 988	1 347 708
(R,s,Q) 3	R2	s1	Q3	946 858	1 758 389
(R,s,Q) 4	R2	s2	Q1	281 454	593 517
(R,s,Q) 5	R2	s2	Q2	705 988	1 347 708
(R,s,Q) 6	R2	s2	Q3	946 858	1 758 389
(R,s,Q) 7	R2	s3	Q1	281 454	593 517
(R,s,Q) 8	R2	s3	Q2	705 988	1 347 708
(R,s,Q) 9	R2	s3	Q3	946 858	1 758 389
(R,s,Q) 10	R2	s4	Q1	287 315	568 449
(R,s,Q) 11	R2	s4	Q2	705 988	1 347 708
(R,s,Q) 12	R2	s4	Q3	946 858	1 758 389
(R,s,Q) 13	R3	s1	Q1	370 893	802 391
(R,s,Q) 14	R3	s1	Q2	853 129	1 221 153
(R,s,Q) 15	R3	s1	Q3	1 189 165	1 557 662
(R,s,Q) 16	R3	s2	Q1	370 893	802 391
(R,s,Q) 17	R3	s2	Q2	853 129	1 221 153
(R,s,Q) 18	R3	s2	Q3	1 189 165	1 557 662
(R,s,Q) 19	R3	s3	Q1	370 893	802 391
(R,s,Q) 20	R3	s3	Q2	853 129	1 221 153
(R,s,Q) 21	R3	s3	Q3	1 189 165	1 557 662
(R,s,Q) 22	R3	s4	Q1	370 893	802 391
(R,s,Q) 23	R3	s4	Q2	853 129	1 221 153
(R,s,Q) 24	R3	s4	Q3	1 189 165	1 557 662
(R,s,Q) 25	R4	s1	Q1	476 603	476 603
(R,s,Q) 26	R4	s1	Q2	1 020 224	1 058 420
(R,s,Q) 27	R4	s1	Q3	1 482 178	1 489 485
(R,s,Q) 28	R4	s2	Q1	476 603	476 603
(R,s,Q) 29	R4	s2	Q2	1 014 085	1 052 977
(R,s,Q) 30	R4	s2	Q3	1 490 715	1 497 665
(R,s,Q) 31	R4	s3	Q1	476 603	476 603
(R,s,Q) 32	R4	s3	Q2	1 019 544	1 038 835
(R,s,Q) 33	R4	s3	Q3	1 482 178	1 489 485
(R,s,Q) 34	R4	s4	Q1	476 603	476 603
(R,s,Q) 35	R4	s4	Q2	1 027 680	1 027 680
(R,s,Q) 36	R4	s4	Q3	1 484 202	1 484 202

The results of the cost performance for each scenario is summarised in Table H.9.

Table H.9: Cycloserine - Summary of cost performance for the scenarios.

Policy #	R	s	S	Q	C_O	C_P	C_H	Total Costs
Base	-	-	-	-	-	85 200 421	25 382 280	110 582 702
(s,S) 1		s1	S1		576 229	67 151 870	24 909 804	92 637 903
(s,S) 2		s1	S2		12 215	69 125 360	14 621 438	83 759 013
(s,S) 3		s2	S1		586 663	68 167 390	19 372 124	88 126 177
(s,S) 4		s2	S2		-	69 770 890	18 805 247	88 576 137
(s,S) 5		s3	S1		576 229	68 156 970	34 150 203	102 883 402
(s,S) 6		s3	S2		-	69 126 200	22 003 133	91 129 333
(s,S) 7		s4	S1		576 229	70 642 597	46 507 648	117 726 474
(s,S) 8		s4	S2		-	70 066 368	26 793 576	96 859 944
(R,S) 1	R1		S1		576 212	70 642 581	46 507 655	117 726 448
(R,S) 2	R1		S2		-	70 066 368	26 793 939	96 860 307
(R,S) 3	R2		S1		576 212	70 642 587	43 890 158	115 108 957
(R,S) 4	R2		S2		-	70 066 374	27 748 334	97 814 708
(R,S) 5	R3		S1		576 212	69 615 265	43 182 888	113 374 365
(R,S) 6	R3		S2		-	69 039 052	24 984 597	94 023 649
(R,S) 7	R4		S1		576 212	70 716 665	46 260 643	117 553 520
(R,S) 8	R4		S2		-	70 140 457	25 121 724	95 262 181
(R,s,S) 1	R2	s1	S1		583 589	67 327 740	25 352 394	93 263 723
(R,s,S) 2	R2	s1	S2		12 215	70 152 660	21 997 202	92 162 077
(R,s,S) 3	R2	s2	S1		576 229	68 372 530	23 308 431	92 257 190
(R,s,S) 4	R2	s2	S2		-	70 796 150	17 211 507	88 007 657
(R,s,S) 5	R2	s3	S1		-	70 660 900	17 524 276	88 185 176
(R,s,S) 6	R2	s3	S2		-	70 796 140	18 890 734	89 686 874
(R,s,S) 7	R2	s4	S1		576 229	70 642 603	43 890 148	115 108 980
(R,s,S) 8	R2	s4	S2		-	70 066 374	27 748 334	97 814 708
(R,s,S) 9	R3	s1	S1		583 589	67 372 730	21 226 877	89 183 196
(R,s,S) 10	R3	s1	S2		-	66 133 460	23 339 603	89 473 063
(R,s,S) 11	R3	s2	S1		576 229	67 365 370	28 164 834	96 106 433
(R,s,S) 12	R3	s2	S2		-	69 768 830	18 343 111	88 111 941
(R,s,S) 13	R3	s3	S1		576 229	67 365 370	28 164 834	96 106 433
(R,s,S) 14	R3	s3	S2		-	69 768 830	18 709 381	88 478 211
(R,s,S) 15	R3	s4	S1		576 229	69 615 281	43 182 875	113 374 385
(R,s,S) 16	R3	s4	S2		-	69 039 052	24 984 597	94 023 649
(R,s,S) 17	R4	s1	S1		583 589	67 237 520	33 444 682	101 265 791
(R,s,S) 18	R4	s1	S2		-	70 140 460	22 023 801	92 164 261
(R,s,S) 19	R4	s2	S1		576 229	68 372 510	30 056 022	99 004 761
(R,s,S) 20	R4	s2	S2		-	70 660 900	17 524 276	88 185 176
(R,s,S) 21	R4	s3	S1		586 663	68 382 970	26 337 257	95 306 890
(R,s,S) 22	R4	s3	S2		-	70 660 900	17 583 028	88 243 928
(R,s,S) 23	R4	s4	S1		576 229	70 716 685	46 260 636	117 553 550
(R,s,S) 24	R4	s4	S2		-	70 140 457	25 121 724	95 262 181
(s,Q) 1		s1		Q1	-	68 782 909	14 512 255.73	83 295 165

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(s,Q) 2		s1	Q2	-	69 851 754	13 773 775.90	83 625 530
(s,Q) 3		s1	Q3	-	70 261 800	11 199 358.51	81 461 159
(s,Q) 4		s2	Q1	-	68 788 513	14 282 260.58	83 070 774
(s,Q) 5		s2	Q2	-	69 851 754	12 517 540.11	82 369 294
(s,Q) 6		s2	Q3	-	70 261 800	16 360 479.47	86 622 280
(s,Q) 7		s3	Q1	-	68 864 110	15 206 669.47	84 070 779
(s,Q) 8		s3	Q2	-	69 851 754	15 608 918.44	85 460 672
(s,Q) 9		s3	Q3	-	70 261 800	15 032 101.15	85 293 902
(s,Q) 10		s4	Q1	-	69 115 679	19 746 307.93	88 861 987
(s,Q) 11		s4	Q2	-	69 851 754	27 271 515.89	97 123 270
(s,Q) 12		s4	Q3	-	70 261 800	15 032 101.15	85 293 902
(R,s,Q) 1	R2	s1	Q1	-	67 383 067	13 338 335	80 721 402
(R,s,Q) 2	R2	s1	Q2	-	68 745 104	12 267 147	81 012 251
(R,s,Q) 3	R2	s1	Q3	-	68 892 901	17 542 526	86 435 427
(R,s,Q) 4	R2	s2	Q1	-	67 185 053	14 835 780	82 020 833
(R,s,Q) 5	R2	s2	Q2	-	68 745 104	14 194 913	82 940 017
(R,s,Q) 6	R2	s2	Q3	-	68 892 901	17 246 054	86 138 955
(R,s,Q) 7	R2	s3	Q1	-	67 185 053	13 577 847	80 762 900
(R,s,Q) 8	R2	s3	Q2	-	68 745 104	14 102 211	82 847 315
(R,s,Q) 9	R2	s3	Q3	-	68 892 901	14 993 151	83 886 052
(R,s,Q) 10	R2	s4	Q1	-	67 615 000	14 736 128	82 351 128
(R,s,Q) 11	R2	s4	Q2	-	68 745 104	23 886 528	92 631 632
(R,s,Q) 12	R2	s4	Q3	-	68 892 901	27 175 833	96 068 734
(R,s,Q) 13	R3	s1	Q1	-	65 558 502	12 111 709	77 670 211
(R,s,Q) 14	R3	s1	Q2	-	68 557 835	12 248 235	80 806 070
(R,s,Q) 15	R3	s1	Q3	-	68 575 407	14 296 409	82 871 816
(R,s,Q) 16	R3	s2	Q1	-	65 558 502	12 384 422	77 942 924
(R,s,Q) 17	R3	s2	Q2	-	68 557 835	13 847 342	82 405 177
(R,s,Q) 18	R3	s2	Q3	-	68 575 407	13 964 932	82 540 339
(R,s,Q) 19	R3	s3	Q1	-	65 558 502	12 568 687	78 127 189
(R,s,Q) 20	R3	s3	Q2	-	68 557 835	15 725 923	84 283 758
(R,s,Q) 21	R3	s3	Q3	-	68 575 407	13 964 932	82 540 339
(R,s,Q) 22	R3	s4	Q1	-	65 558 502	12 653 686	78 212 188
(R,s,Q) 23	R3	s4	Q2	-	68 557 835	23 175 679	91 733 514
(R,s,Q) 24	R3	s4	Q3	-	68 575 407	28 187 337	96 762 744
(R,s,Q) 25	R4	s1	Q1	-	63 491 419	12 694 902	76 186 321
(R,s,Q) 26	R4	s1	Q2	-	68 022 237	13 008 291	81 030 528
(R,s,Q) 27	R4	s1	Q3	-	68 428 907	12 748 565	81 177 472
(R,s,Q) 28	R4	s2	Q1	-	63 491 419	13 197 543	76 688 962
(R,s,Q) 29	R4	s2	Q2	-	68 209 401	12 373 200	80 582 601
(R,s,Q) 30	R4	s2	Q3	-	68 086 581	14 782 339	82 868 920
(R,s,Q) 31	R4	s3	Q1	-	63 491 419	13 197 543	76 688 962
(R,s,Q) 32	R4	s3	Q2	-	68 544 248	14 205 865	82 750 113
(R,s,Q) 33	R4	s3	Q3	-	68 428 907	13 830 442	82 259 349
(R,s,Q) 34	R4	s4	Q1	-	63 491 419	11 108 167	74 599 586
(R,s,Q) 35	R4	s4	Q2	-	68 791 426	21 364 636	90 156 062
(R,s,Q) 36	R4	s4	Q3	-	68 590 228	24 891 676	93 481 904

Appendix I SDM documents

This appendix provides the SDM documents for all three models.

I.1 SDM document for Model A

This section provides the HTML output of the SDM document tool, for Model A.

Model Assessment Results

Model Information	Result
Total Number Of Variables	20|126
Total Number Of State Variables	5 (25.0%)|51 (40.5%)
Total Number Of Stocks	4 (20.0%)|39 (31.0%)
Total Number Of Causal Links	20 (11|2|7)|211 (103|24|84)
Total Number of Rate-to-rate Links	0
Time Unit	Week
Initial Time	0
Final Time	264
Reported Time Interval	TIME STEP
Time Step	1
Model Is Fully Formulated	Yes
Model Defined Groups	No

Potential Omissions	Result
Unused Variables	0
Supplementary Variables	4
Supplementary Variables Being Used	0
Complex Variable	4
Complex Stock	4

Variable Types

L: Level (4 / 39)*	SM: Smooth (0 / 0)*	DE: Delay (1 / 12)*†	LI: Level Initial (0)	I: Initial (0 / 0)
C: Constant (5 / 27)	F: Flow (5 / 60)	A: Auxiliary (11 / 101)	Sub: Subscripts (2)	D: Data (0 / 0)
G: Game (0 / 0)	T: Lookup (1 / 1)*††			

* (State Variables/Total Stocks) † Total Stocks Do Not Include Fixed Delay Variables. †† (Lookup Tables).

Views

View: Cost (5) Variables
View: Main Model (12) Variables

Variables

top	(View) Cost (5 Variables)	
Group	Type	*Variable Name And Description*
ModelA	#5 L	Cumulative Total Unit Cost (Dollar) Cumulative Total Unit Cost[Formulations,Order Number] = ∫"Total Unit Cost"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
ModelA	#13 F,A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Country Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Production Total Unit Cost
ModelA	#17 C	Per Unit Cost (Dollar/Drugs) Per Unit Cost[Capreomycin,Order Number] = 1,1,1,1 Per Unit Cost[Kanamycin,Order Number] = 1,1,1,1 Per Unit Cost[Cycloserine,Order Number] = 1,1,1,1 Present In 2 Views: Not in View Cost Used By Total Unit Cost
ModelA	#27 A	Total Costs (Dollar) Total Costs[Formulations] = SUM(Cumulative Total Unit Cost[Formulations,Order Number!]) Present In 1 View: Cost Used By
ModelA	#29 F,A	Total Unit Cost (Dollar/Week) Total Unit Cost[Formulations,Order Number] = Normal Orders From Countries[Formulations,Order Number] * Per Unit Cost[Formulations,Order Number] Present In 1 View: Cost Used By Cumulative Total Unit Cost

top	(View) Main Model (12 Variables)	
Group	Type	*Variable Name And Description*
ModelA	#1 A	Country Demand Input (Drugs/Week) Country Demand Input[Formulations,Order1] = IF THEN ELSE(Uniform[Formulations,Order1] < Proportion Of Orders Placed[Formulations,Order1] , Weibull Distribution[Formulations,Order1] , 0) Country Demand Input[Formulations,Order2] = IF THEN ELSE(Country Demand Input[Formulations,Order1] > 0 , IF THEN ELSE(Uniform[Formulations,Order2] < Proportion Of

		Orders Placed[Formulations,Order2] , Weibull Distribution[Formulations,Order2] , 0) , 0) Country Demand Input[Formulations,Order3] = IF THEN ELSE(Country Demand Input[Formulations,Order2]>0, IF THEN ELSE(Uniform[Formulations,Order3] < Proportion Of Orders Placed[Formulations,Order3] , Weibull Distribution[Formulations,Order3] , 0) , 0) Country Demand Input[Formulations,Order4] = IF THEN ELSE(Country Demand Input[Formulations,Order3]>0, IF THEN ELSE(Uniform[Formulations,Order4] < Proportion Of Orders Placed[Formulations,Order4] , Weibull Distribution[Formulations,Order4] , 0) , 0) Present In 2 Views: Not in View Main Model Used By Normal Orders From Countries
Model A	#10A, D, T	Normal Lead Time Lookup[Formulations,Order Number] (Week) Normal Lead Time Lookup[Formulations,Order Number]([(0,0)-(10,10)],(1,154),(2,154),(3,260),(4,267),(5,155),(6,322),(7,322),(8,274),(9,274),(10,180),(11,180),(12,610),(13,364),(14,95),(15,137),(16,186),(17,224),(18,29),(19,273),(20,142),(21,34),(22,74),(23,115),(24,317),(25,61),(26,152),(27,128),(28,14),(29,225),(30,105),(31,166),(32,183),(33,313),(34,143),(35,143),(36,285),(37,226),(38,226),(39,285),(40,194),(41,17),(42,8),(43,16),(44,21),(45,21),(46,21),(47,27),(48,27),(49,30),(50,88),(51,171),(52,55),(53,137),(54,32),(55,57),(56,481),(57,481),(58,165),(59,295),(60,44),(61,44),(62,534),(63,534),(64,194),(65,204),(66,292),(67,193),(68,352),(69,301),(70,195),(71,172),(72,109),(73,109),(74,450),(75,450),(76,708),(77,188),(78,118),(79,126),(80,108),(81,108),(82,146),(83,94),(84,55),(85,143),(86,100),(87,100),(88,82),(89,82),(90,75),(91,207),(92,236),(93,234),(94,34),(95,199),(96,285),(97,316),(98,271),(99,132),(100,54),(101,35),(102,35),(103,89),(104,146),(105,178),(106,197),(107,245),(108,55),(109,61),(110,61),(111,61),(112,61),(113,155),(114,263),(115,128),(116,370),(117,291),(118,291),(119,152),(120,87),(121,87),(122,155),(123,155),(124,502),(125,502),(126,363),(127,117),(128,59),(129,102),(130,413),(131,27),(132,419),(133,45),(134,45),(135,239),(136,107),(137,65),(138,19),(139,19),(140,123),(141,123),(142,123),(143,305),(144,86),(145,251),(146,251),(147,187),(148,200),(149,187),(150,339),(151,136),(152,348),(153,105),(154,107),(155,312),(156,312),(157,198),(158,128),(159,127),(160,158),(161,164),(162,367),(163,205),(164,129),(165,165),(166,264),(167,371),(168,168),(169,301),(170,205),(171,160),(172,278),(173,360),(174,34),(175,89),(176,92),(177,225),(178,318),(179,366),(180,21),(181,196),(182,397),(183,85),(184,85),(185,250),(186,266),(187,57),(188,305),(189,305),(190,305),(191,305),(192,305),(193,73),(194,154),(195,154),(196,261),(197,258),(198,232),(199,152),(200,363),(201,363),(202,108),(203,174),(204,324),(205,324),(206,379),(207,302),(208,156),(209,251),(210,216),(211,255),(212,304),(213,304),(214,267),(215,267),(216,267),(217,108),(218,39),(219,249),(220,126),(221,183),(222,18),(223,146),(224,223),(225,420),(226,38),(227,232),(228,232),(229,232),(230,253),(231,94),(232,204),(233,208),(234,248),(235,76),(236,204),(237,248),(238,406),(239,134),(240,86),(241,221),(242,264),(243,69),(244,69),(245,253),(246,166),(247,190),(248,190),(249,145),(250,207),(251,145),(252,207),(253,396),(254,278),(255,278),(256,255),(257,255),(258,72),(259,513),(260,394),(261,471),(262,505),(263,505),(264,505))  Present In 1 View: Main Model Used By Production
Mod	#11L	Normal Order Drugs Awaiting Dispatch (Drugs) Normal Order Drugs Awaiting Dispatch[Formulations,Order Number] = ∫"Production"["Formulations","Order Number"]-"Normal Orders Fulfilled For Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View:

el A		Main Model Used By
Model A	#12F, A	Normal Order Drugs Received By Countries (Drugs/Week) Normal Order Drugs Received By Countries[Formulations,Order Number] = Normal Orders Fulfilled For Countries[Formulations,Order Number] Present In 1 View: Main Model Used By Normal Orders Supply Line Total Drugs Received By Countries
Model A	#13F, A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Country Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Production Total Unit Cost
Model A	#14F, A	Normal Orders Fulfilled For Countries (Drugs/Week) Normal Orders Fulfilled For Countries[Formulations,Order Number] = IF THEN ELSE(Production[Formulations,Order Number]>0 , Production[Formulations,Order Number] , 0) Present In 1 View: Main Model Used By Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries
Model A	#15L	Normal Orders Supply Line (Drugs) Normal Orders Supply Line[Formulations,Order Number] = ∫"Normal Orders From Countries"["Formulations","Order Number"]-"Normal Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
Model A	#20DE, F, A	Production (Drugs/Week) Production[Formulations,Order Number] = DELAY MATERIAL (Normal Orders From Countries[Formulations,Order Number] , Normal Lead Time Lookup[Formulations,Order Number](Time) , 0 , 0) Present In 1 View: Main Model Used By Normal Order Drugs Awaiting Dispatch Normal Orders Fulfilled For Countries
Model A	#21C	Proportion Of Orders Placed (Dmnl) Proportion Of Orders Placed[Capreomycin,Order Number] = 0.574, 0.389, 0.255, 0.263 Proportion Of Orders Placed[Kanamycin,Order Number] = 0.45, 0.191, 0.287, 0.479 Proportion Of Orders Placed[Cycloserine,Order Number] = 0.721, 0.508, 0.412, 0.298 Present In 2 Views: Not in View Main Model Used By Country Demand Input
Model A	#28L	Total Drugs Received By Countries (Drugs) Total Drugs Received By Countries[Formulations] = ∫SUM("Normal Order Drugs Received By Countries"["Formulations","Order Number!"]) *dt* + 0.0 Present In 1 View: Main Model Used By

Model A	#30A	Uniform (Dmnl) Uniform[Capreomycin,Order Number] = RANDOM 0 1() Uniform[Kanamycin,Order Number] = (RANDOM 0 1()) Uniform[Cycloserine,Order Number] = (RANDOM 0 1()) Present In 2 Views: Not in View Main Model Used By Country Demand Input
Model A	#33A	Weibull Distribution (Drugs/Week) Weibull Distribution[Capreomycin,Order Number] = RANDOM WEIBULL(0 , 448000 , 0.8161 , 78 , 32500 , 0) Weibull Distribution[Kanamycin,Order Number] = RANDOM WEIBULL(0 , 882000 ,0.6525 , 0 , 52000 , 1) Weibull Distribution[Cycloserine,Order Number] = RANDOM WEIBULL(1500 , 9.4491e+06 , 0.4755 , 1500 , 420000 , 1) Present In 2 Views: Not in View Main Model Used By Country Demand Input

top | (Type) Subscripts (2 Variables)

Group	Type	*Variable Name And Description*
ModelA	#7 Sub	Formulations () Formulations:Capreomycin, Kanamycin, Cycloserine Present In 2 Views: Cost Main Model Used By Country Demand Input Cumulative Total Unit Cost Normal Lead Time Lookup Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries Normal Orders From Countries Normal Orders Fulfilled For Countries Normal Orders Supply Line Per Unit Cost Production Proportion Of Orders Placed Total Costs Total Drugs Received By Countries Total Unit Cost Uniform Weibull Distribution
ModelA	#16 Sub	Order Number () Order Number:Order1, Order2, Order3, Order4 Present In 2 Views: Cost Main Model Used By Country Demand Input Cumulative Total Unit Cost Normal Lead Time Lookup Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries Normal Orders From Countries Normal Orders Fulfilled For Countries Normal Orders Supply Line Per Unit Cost Production Proportion Of Orders Placed

		Total Unit Cost Uniform Weibull Distribution	

top

All Variables (20)

Group	Type	Variable
ModelA	A	Country Demand Input (Drugs/Week)
ModelA	L	Cumulative Total Unit Cost (Dollar)
.Control	C	FINAL TIME (Week)
.Control	C	INITIAL TIME (Week)
ModelA	A,D,T	Normal Lead Time Lookup (Week)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelA	F,A	Normal Orders From Countries (Drugs/Week)
ModelA	F,A	Normal Orders Fulfilled For Countries (Drugs/Week)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	C	Per Unit Cost (Dollar/Drugs)
ModelA	DE,F,A	Production (Drugs/Week)
ModelA	C	Proportion Of Orders Placed (Dmnl)
.Control	A	SAVEPER (Week)
.Control	C	TIME STEP (Week)
ModelA	A	Total Costs (Dollar)
ModelA	L	Total Drugs Received By Countries (Drugs)
ModelA	F,A	Total Unit Cost (Dollar/Week)
ModelA	A	Uniform (Dmnl)
ModelA	A	Weibull Distribution (Drugs/Week)

top

Undocumented Variables (18)

Group	Type	Variable
ModelA	A	Country Demand Input (Drugs/Week)
ModelA	L	Cumulative Total Unit Cost (Dollar)
ModelA	Sub	Formulations ()
ModelA	A,D,T	Normal Lead Time Lookup (Week)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelA	F,A	Normal Orders From Countries (Drugs/Week)
ModelA	F,A	Normal Orders Fulfilled For Countries (Drugs/Week)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	Sub	Order Number ()
ModelA	C	Per Unit Cost (Dollar/Drugs)
ModelA	DE,F,A	Production (Drugs/Week)
ModelA	C	Proportion Of Orders Placed (Dmnl)
ModelA	A	Total Costs (Dollar)
ModelA	L	Total Drugs Received By Countries (Drugs)
ModelA	F,A	Total Unit Cost (Dollar/Week)
ModelA	A	Uniform (Dmnl)
ModelA	A	Weibull Distribution (Drugs/Week)

top

Supplementary Variables (4)

Group	Type	Variable

ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	A	Total Costs (Dollar)
ModelA	L	Total Drugs Received By Countries (Drugs)

top

Stock Variables (4)

Group	Type	Variable
ModelA	L	Cumulative Total Unit Cost (Dollar)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	L	Total Drugs Received By Countries (Drugs)

top

Equations With Embedded Data (5)

Group	Type	Variable
ModelA	L	Cumulative Total Unit Cost (Dollar)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	L	Total Drugs Received By Countries (Drugs)
ModelA	A	Weibull Distribution (Drugs/Week)

top

Nonmonotonic Lookup Functions (1)

Group	Type	Variable
ModelA	A,D,T	Normal Lead Time Lookup (Week)

top

Equations With If Then Else Functions (2)

Group	Type	Variable
ModelA	A	Country Demand Input (Drugs/Week)
ModelA	F,A	Normal Orders Fulfilled For Countries (Drugs/Week)

top

State Variables (5)

Group	Type	Variable
ModelA	L	Cumulative Total Unit Cost (Dollar)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	DE,F,A	Production (Drugs/Week)
ModelA	L	Total Drugs Received By Countries (Drugs)

top

Variables With Dimensionless Units (2)

Group	Type	Variable
ModelA	C	Proportion Of Orders Placed (Dmnl)
ModelA	A	Uniform (Dmnl)

top

Variables without Predefined Min or Max Values (16)

Group	Type	Variable
ModelA	A	Country Demand Input (Drugs/Week)
ModelA	L	Cumulative Total Unit Cost (Dollar)

ModelA	A,D,T	Normal Lead Time Lookup (Week)
ModelA	L	Normal Order Drugs Awaiting Dispatch (Drugs)
ModelA	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelA	F,A	Normal Orders From Countries (Drugs/Week)
ModelA	F,A	Normal Orders Fulfilled For Countries (Drugs/Week)
ModelA	L	Normal Orders Supply Line (Drugs)
ModelA	C	Per Unit Cost (Dollar/Drugs)
ModelA	DE,F,A	Production (Drugs/Week)
ModelA	C	Proportion Of Orders Placed (Dmnl)
ModelA	A	Total Costs (Dollar)
ModelA	L	Total Drugs Received By Countries (Drugs)
ModelA	F,A	Total Unit Cost (Dollar/Week)
ModelA	A	Uniform (Dmnl)
ModelA	A	Weibull Distribution (Drugs/Week)

Units (4/3)

Units	Type	Alternates
$	Basic	[Dollar]
Dmnl	Basic	
Drugs	Basic	
Week	Basic	
$/Drugs	Combined	[Dollar/Drugs]
$/Week	Combined	[Dollar/Week]
Drugs/Week	Combined	

Positive Polarity Causal Links (11)

Cause	Effect	Polarity
Country Demand Input	Normal Orders From Countries	+
Cumulative Total Unit Cost	Total Costs	+
Normal Order Drugs Received By Countries	Total Drugs Received By Countries	+
Normal Orders From Countries	Normal Orders Supply Line	+
Normal Orders From Countries	Total Unit Cost	+
Normal Orders Fulfilled For Countries	Normal Order Drugs Received By Countries	+
Per Unit Cost	Total Unit Cost	+
Production	Normal Order Drugs Awaiting Dispatch	+
TIME STEP	SAVEPER	+
Total Unit Cost	Cumulative Total Unit Cost	+
Weibull Distribution	Country Demand Input	+

top

Negative Polarity Causal Links (2)

Cause	Effect	Polarity
Normal Order Drugs Received By Countries	Normal Orders Supply Line	-
Normal Orders Fulfilled For Countries	Normal Order Drugs Awaiting Dispatch	-

topFunction-based Polarity Causal Links (7)

Cause	Effect	Polarity
Country Demand Input	Country Demand Input	If Then Else Switch
Normal Lead Time Lookup	Production	Function[DELAYMATERIAL,LOOKUP]
Normal Orders From Countries	Production	Function[DELAYMATERIAL,LOOKUP]
Production	Normal Orders Fulfilled For Countries	If Then Else Switch

Proportion Of Orders Placed	Country Demand Input	If Then Else Switch
Time	Production	Function[DELAYMATERIAL,LOOKUP]
Uniform	Country Demand Input	If Then Else Switch

top View-Variable Profile

View	View-Variable Profile
Cost	5 vars (20.8%)
Main Model	12 vars (50%)

top

List Of 2 views and their 16 Variables

	Cost	Main Model	
Total:	5	12	Total:
Normal Orders Fulfilled For Countries (In 1 View)			Normal Orders Fulfilled For Countries (In 1 View)
Proportion Of Orders Placed (In 1 View)			Proportion Of Orders Placed (In 1 View)
Total Drugs Received By Countries (In 1 View)			Total Drugs Received By Countries (In 1 View)
Weibull Distribution (In 1 View)			Weibull Distribution (In 1 View)
Normal Order Drugs Received By Countries (In 1 View)			Normal Order Drugs Received By Countries (In 1 View)
Country Demand Input (In 1 View)			Country Demand Input (In 1 View)
Production (In 1 View)			Production (In 1 View)
Normal Orders From Countries (In 2 Views)			Normal Orders From Countries (In 2 Views)
Normal Lead Time Lookup (In 1 View)			Normal Lead Time Lookup (In 1 View)
Normal Orders Supply Line (In 1 View)			Normal Orders Supply Line (In 1 View)
Uniform (In 1 View)			Uniform (In 1 View)
Normal Order Drugs Awaiting Dispatch (In 1 View)			Normal Order Drugs Awaiting Dispatch (In 1 View)
Total Unit Cost (In 1 View)			Total Unit Cost (In 1 View)
Per Unit Cost (In 1 View)			Per Unit Cost (In 1 View)
Total Costs (In 1 View)			Total Costs (In 1 View)
Cumulative Total Unit Cost (In 1 View)			Cumulative Total Unit Cost (In 1 View)
Total:	5	12	Total:
	Cost	Main Model	

Source File: /Users/deonlingervelder/Desk/All/Masters/6. Dynamic Modelling Main Models/DAILY/ModelA.mdl (Sat Nov 19 12:10:11 SAST 2016)
Report Created On Sat Nov 19 12:41:05 SAST 2016
SDM-Doc Tool Version 1.2.44
Global Security Sciences Division
Argonne National Laboratory

I.2 SDM document for Model B

This section provides the HTML output of the SDM document tool, for Model B.

Model Assessment Results

Model Information	Result
Total Number Of Variables	56|384
Total Number Of State Variables	16 (28.6%)|165 (43.0%)
Total Number Of Stocks	10 (17.9%)|93 (24.2%)
Total Number Of Causal Links	83 (39|8|36)|841 (331|78|432)
Total Number of Rate-to-rate Links	0
Time Unit	Week
Initial Time	0
Final Time	316
Reported Time Interval	TIME STEP
Time Step	1
Model Is Fully Formulated	Yes
Model Defined Groups	No

Potential Omissions	Result
Unused Variables	0
Supplementary Variables	2
Supplementary Variables Being Used	0
Complex Variable	6
Complex Stock	0

Variable Types

L: Level (10 / 93)*	SM: Smooth (0 / 0)*	DE: Delay (6 / 72)*†	LI: Level Initial (0)	I: Initial (0 / 0)
C: Constant (10 / 78)	F: Flow (13 / 120)	A: Auxiliary (36 / 365)	Sub: Subscripts (2)	D: Data (0 / 0)
G: Game (0 / 0)	T: Lookup (1 / 1)*††			

* (State Variables/Total Stocks) † Total Stocks Do Not Include Fixed Delay Variables. †† (Lookup Tables).

Views

View: Cost (16) Variables
View: Main Model (43) Variables

Variables

(View) Cost (16 Variables)

Top	(View) Cost (16 Variables)

Group	Type	*Variable Name And Description*
MODEL B	#14 L	Cumulative Purchase Unit Cost (Dollar) Cumulative Purchase Unit Cost[Formulations] = ∫Normal Order Purchase Cost[Formulations] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
MODEL B	#15 L	Cumulative Stockpile Replenishment Cost (Dollar) Cumulative Stockpile Replenishment Cost[Formulations] = ∫Emergency Order Cost[Formulations]+Stockpile Rotation Cost[Formulations] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
MODEL B	#16 L	Cumulative Total Obsolescence Cost (Dollar) Cumulative Total Obsolescence Cost[Formulations] = ∫Total Obsolescence Cost[Formulations] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
MODEL B	#22 A	Drugs Available For Emergency Orders (Drugs/Week) Drugs Available For Emergency Orders[Formulations,Order Number] = MAX(IF THEN ELSE(SRS Stock On Hand[Formulations,Order Number]>=Emergency Orders From Countries[Formulations,Order Number] , Emergency Orders From Countries[Formulations,Order Number] - Obsolete Stock[Formulations,Order Number] , SRS Stock On Hand[Formulations,Order Number] - Obsolete Stock[Formulations,Order Number]), 0) Present In 2 Views: Cost Main Model Used By Dispatch Emergency Drugs To Countries Emergency Order Cost SRS Demand SRS Stock On Hand
MODEL B	#29 A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week) Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] = IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]>0 ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order2] , Processed Orders[Formulations,Order2] , 0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order2] > Processed Orders[Formulations,Order2] , Processed Orders[Formulations,Order2] , 0)) Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] > 0 ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order3] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] ,0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order3] > Processed Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] , 0)) Drugs To Be Dispatched For Stock

		Rotation[Formulations,Order4] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] + Drugs Available For Stock Rotation[Formulations,Order3] > 0,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order4] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order4] , Processed Orders[Formulations,Order4] , 0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order4] > Processed Orders[Formulations,Order4] , Processed Orders[Formulations,Order4] , 0)) Present In 3 Views: Not in View Cost Main Model Used By Drugs Dispatched As Stock Rotation Normal Order Purchase Cost Processing Drugs For Stock Rotation Production & Dispatch To GDF/PA
MODEL B	#34 F,A	Emergency Order Cost (Dollar/Week) Emergency Order Cost[Formulations] = SUM(Drugs Available For Emergency Orders[Formulations,Order Number!])*Per Unit Cost[Formulations] Present In 1 View: Cost Used By Cumulative Stockpile Replenishment Cost
MODEL B	#56 F,A	Normal Order Purchase Cost (Dollar/Week) Normal Order Purchase Cost[Formulations] = (SUM(Processed Orders[Formulations,Order Number!])-SUM(Drugs To Be Dispatched For Stock Rotation[Formulations,Order Number!])) * Per Unit Cost[Formulations] Present In 1 View: Cost Used By Cumulative Purchase Unit Cost
MODEL B	#57 F,A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Order Processing
MODEL B	#59 C,F	Obsolete Stock (Drugs/Week) Obsolete Stock[Formulations,Order1] = QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Expiration Value[Formulations,Order1] , NAREPLACEMENT)/TIME STEP Obsolete Stock[Formulations,Order2] = 0 Obsolete Stock[Formulations,Order3] = 0 Obsolete Stock[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By Cumulative Obsolete Stock Drugs Available For Emergency Orders Drugs Available For Stock Rotation SRS Demand SRS Stock On Hand

		Total Obsolescence Cost
MODEL B	#77 F,A	Orders Placed To Manufacturer (Drugs/Week) Orders Placed To Manufacturer[Formulations,Order Number] = SRS Demand[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By SRS Supply Line
MODEL B	#78 C	Per Unit Cost (Dollar/Drugs) Per Unit Cost[Capreomycin] = 5.66 Per Unit Cost[Kanamycin] = 2.59 Per Unit Cost[Cycloserine] = 0.55 Present In 2 Views: Not in View Cost Used By Emergency Order Cost Normal Order Purchase Cost Stockpile Rotation Cost Total Obsolescence Cost
MODEL B	#81 A	Processed Orders (Drugs/Week) Processed Orders[Formulations,Order Number] = Order Processing[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Drugs To Be Dispatched For Stock Rotation Normal Order Purchase Cost Production & Dispatch To GDF/PA
MODEL B	#82 C	Processing Drugs For Stock Rotation (Drugs/Week) Processing Drugs For Stock Rotation[Formulations,Order1] = (Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]) + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order4] Processing Drugs For Stock Rotation[Formulations,Order2] = 0 Processing Drugs For Stock Rotation[Formulations,Order3] = 0 Processing Drugs For Stock Rotation[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By SRS Demand SRS Stock On Hand Stockpile Rotation Cost
MODEL B	#115 F,A	Stockpile Rotation Cost (Dollar/Week) Stockpile Rotation Cost[Formulations] = SUM(Processing Drugs For Stock Rotation[Formulations,Order Number!])*Per Unit Cost[Formulations] Present In 1 View: Cost Used By Cumulative Stockpile Replenishment Cost
MODEL B	#119 A	Total Costs (Dollar) Total Costs[Formulations] = Cumulative Purchase Unit Cost[Formulations] + Cumulative Stockpile Replenishment Cost[Formulations] + Cumulative Total Obsolescence Cost[Formulations] Present In 1 View: Cost Used By

MODEL B	#122 F,A	Total Obsolescence Cost (Dollar/Week) Total Obsolescence Cost[Formulations] = Per Unit Cost[Formulations] * SUM(Obsolete Stock[Formulations,Order Number!]) Present In 1 View: Cost Used By Cumulative Total Obsolescence Cost

(View) Main Model (43 Variables)

Top	(View) Main Model (43 Variables)

Group	Type	*Variable Name And Description*
MODEL B	#1 A	Country Dispatch Lead Time (Week) Country Dispatch Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order2] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Present In 2 Views: Not in View Main Model Used By Dispatch Emergency Drugs To Countries Drugs Dispatched As Stock Rotation QC's & Dispatch To Countries
MODEL B	#13 L	Cumulative Obsolete Stock (Drugs) Cumulative Obsolete Stock[Formulations,Order Number] = ∫"Obsolete Stock"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
MODEL B	#17 A	Demand Input (Drugs/Week) Demand Input[Formulations,Order1] = IF THEN ELSE(Uniform[Formulations,Order1] < Proportion Of Orders Placed[Formulations,Order1] , Weibull Distribution[Formulations,Order1] , 0) Demand Input[Formulations,Order2] = IF THEN ELSE(Demand Input[Formulations,Order1] > 0 , IF THEN ELSE(Uniform[Formulations,Order2] < Proportion Of Orders Placed[Formulations,Order2] , Weibull Distribution[Formulations,Order2] , 0) , 0) Demand Input[Formulations,Order3] = IF THEN ELSE(Demand Input[Formulations,Order2]>0, IF THEN ELSE(Uniform[Formulations,Order3] < Proportion Of Orders Placed[Formulations,Order3] , Weibull Distribution[Formulations,Order3] , 0) , 0) Demand Input[Formulations,Order4] = IF THEN ELSE(Demand Input[Formulations,Order3]>0, IF THEN ELSE(Uniform[Formulations,Order4] < Proportion Of Orders Placed[Formulations,Order4] , Weibull Distribution[Formulations,Order4] , 0) , 0) Present In 2 Views: Not in View

		Main Model Used By Normal Orders From Countries
MODEL B	#21 DE,A	Dispatch Emergency Drugs To Countries (Drugs/Week) Dispatch Emergency Drugs To Countries[Formulations,Order Number] = DELAY MATERIAL (Drugs Available For Emergency Orders[Formulations,Order Number], Country Dispatch Lead Time[Formulations,Order Number],0, 0) Present In 1 View: Main Model Used By Emergency Order Drugs Received By Countries
MODEL B	#22 A	Drugs Available For Emergency Orders (Drugs/Week) Drugs Available For Emergency Orders[Formulations,Order Number] = MAX(IF THEN ELSE(SRS Stock On Hand[Formulations,Order Number]>=Emergency Orders From Countries[Formulations,Order Number] , Emergency Orders From Countries[Formulations,Order Number] - Obsolete Stock[Formulations,Order Number] , SRS Stock On Hand[Formulations,Order Number] - Obsolete Stock[Formulations,Order Number]), 0) Present In 2 Views: Cost Main Model Used By Dispatch Emergency Drugs To Countries Emergency Order Cost SRS Demand SRS Stock On Hand
MODEL B	#23 A	Drugs Available For Stock Rotation (Drugs/Week) Drugs Available For Stock Rotation[Formulations,Order1] = MAX(0,(QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Rotation Value Start[Formulations,Order1] , Rotation Value Stop[Formulations,Order1])/TIME STEP) - Obsolete Stock[Formulations,Order1]) Drugs Available For Stock Rotation[Formulations,Order2] = MAX(0,(QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Rotation Value Start[Formulations,Order1] , Rotation Value Stop[Formulations,Order1])/TIME STEP) - Obsolete Stock[Formulations,Order1]) Drugs Available For Stock Rotation[Formulations,Order3] = MAX(0,(QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Rotation Value Start[Formulations,Order1] , Rotation Value Stop[Formulations,Order1])/TIME STEP) - Obsolete Stock[Formulations,Order1]) Drugs Available For Stock Rotation[Formulations,Order4] = MAX(0,(QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Rotation Value Start[Formulations,Order1] , Rotation Value Stop[Formulations,Order1])/TIME STEP) - Obsolete Stock[Formulations,Order1]) Present In 2 Views: Not in View Main Model Used By Drugs To Be Dispatched For Stock Rotation
MODEL B	#27 DE,A	Drugs Dispatched As Stock Rotation (Drugs/Week) Drugs Dispatched As Stock Rotation[Formulations,Order Number] = DELAY MATERIAL (Drugs To Be Dispatched For Stock Rotation[Formulations,Order Number], Country Dispatch Lead Time[Formulations,Order Number], 0, 0) Present In 1 View: Main Model Used By Normal Order Drugs Received By Countries
MODEL B	#28 F,A	Drugs Received From Manufacturer (Drugs/Week) Drugs Received From Manufacturer[Formulations,Order Number] = "Production & Dispatch To SRS"[Formulations,Order Number] Present In 1 View:

		Main Model Used By SRS Supply Line
MODEL B	#29 A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week) Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] = IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]>0 ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order2] , Processed Orders[Formulations,Order2] , 0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order2] > Processed Orders[Formulations,Order2] , Processed Orders[Formulations,Order2] , 0)) Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] > 0 ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order3] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] ,0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order3] > Processed Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] , 0)) Drugs To Be Dispatched For Stock Rotation[Formulations,Order4] = IF THEN ELSE(Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] + Drugs Available For Stock Rotation[Formulations,Order3] > 0,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order4] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order1] > Processed Orders[Formulations,Order4] , Processed Orders[Formulations,Order4] , 0) ,IF THEN ELSE(Drugs Available For Stock Rotation[Formulations,Order4] > Processed Orders[Formulations,Order4] , Processed Orders[Formulations,Order4] , 0)) Present In 3 Views: Not in View Cost Main Model Used By Drugs Dispatched As Stock Rotation Normal Order Purchase Cost Processing Drugs For Stock Rotation Production & Dispatch To GDF/PA
MODEL B	#33 A	Emergency Input (Drugs/Week) Emergency Input[Formulations,Order Number] = IF THEN ELSE(Uniform[Formulations,Order Number] < Emergency Proportion Of Orders Placed[Formulations,Order Number] , Emergency Weibull Distribution[Formulations,Order Number] , 0) Present In 1 View: Main Model Used By Emergency Orders From Countries
MODEL B	#35 F,A	Emergency Order Drugs Received By Countries (Drugs/Week) Emergency Order Drugs Received By Countries[Formulations,Order Number] = Dispatch Emergency Drugs To Countries[Formulations,Order Number] Present In 1 View: Main Model Used By

		Emergency Orders Supply Line Total Emergency Order Drugs Received
MODEL B	#36 F,A	Emergency Orders From Countries (Drugs/Week) Emergency Orders From Countries[Formulations,Order Number] = Emergency Input[Formulations,Order Number] Present In 1 View: Main Model Used By Drugs Available For Emergency Orders Emergency Orders Supply Line
MODEL B	#37 L	Emergency Orders Supply Line (Drugs) Emergency Orders Supply Line[Formulations,Order Number] = ∫"Emergency Orders From Countries"["Formulations","Order Number"]-"Emergency Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
MODEL B	#38 C	Emergency Proportion Of Orders Placed (Dmnl) Emergency Proportion Of Orders Placed[Capreomycin,Order Number] = 0.106, 0, 0, 0 Emergency Proportion Of Orders Placed[Kanamycin,Order Number] = 0.086, 0, 0, 0 Emergency Proportion Of Orders Placed[Cycloserine,Order Number] = 0.168, 0, 0, 0 Present In 2 Views: Not in View Main Model Used By Emergency Input
MODEL B	#41 A	Emergency Weibull Distribution (Drugs/Week) Emergency Weibull Distribution[Capreomycin,Order Number] = RANDOM WEIBULL(78 , 55255 , 0.6161 , 78 , 32500 , 0) Emergency Weibull Distribution[Kanamycin,Order Number] = RANDOM WEIBULL(450 , 46246 ,0.4525 , 450 , 50000 , 1) Emergency Weibull Distribution[Cycloserine,Order Number] = RANDOM WEIBULL(1500 , 769160 , 0.4755 , 1500 , 420000 , 1) Present In 2 Views: Not in View Main Model Used By Emergency Input
MODEL B	#44 C	Expiration Value (Week) Expiration Value[Capreomycin,Order Number] = 56, 0, 0, 0 Expiration Value[Kanamycin,Order Number] = 140, 0, 0, 0 Expiration Value[Cycloserine,Order Number] = 56, 0, 0, 0 Present In 2 Views: Not in View Main Model Used By Obsolete Stock
MODEL B	#49 C	Initial Stock On Hand (Drugs) Initial Stock On Hand[Capreomycin,Order Number] = 221018, 0, 0, 0 Initial Stock On Hand[Kanamycin,Order Number] = 184984, 0, 0, 0 Initial Stock On Hand[Cycloserine,Order Number] = 3.07664e+06, 0, 0, 0 Present In 2 Views: Not in View Main Model Used By SRS Stock On Hand
MODEL B	#54 L	Normal Order Drugs Awaiting Dispatch (Drugs) Normal Order Drugs Awaiting Dispatch[Formulations,Order Number] = ∫"Production & Dispatch To GDF/PA"["Formulations","Order Number"]-"QC's & Dispatch To Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View:

		Main Model Used By
MODEL B	#55 F,A	Normal Order Drugs Received By Countries (Drugs/Week) Normal Order Drugs Received By Countries[Formulations,Order Number] = "QC's & Dispatch To Countries"[Formulations,Order Number] + Drugs Dispatched As Stock Rotation[Formulations,Order Number] Present In 1 View: Main Model Used By Normal Orders Supply Line Total Normal Order Drugs Received
MODEL B	#57 F,A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Order Processing
MODEL B	#58 L	Normal Orders Supply Line (Drugs) Normal Orders Supply Line[Formulations,Order Number] = ∫"Normal Orders From Countries"["Formulations","Order Number"]-"Normal Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
MODEL B	#59 C,F	Obsolete Stock (Drugs/Week) Obsolete Stock[Formulations,Order1] = QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Expiration Value[Formulations,Order1] , NAREPLACEMENT)/TIME STEP Obsolete Stock[Formulations,Order2] = 0 Obsolete Stock[Formulations,Order3] = 0 Obsolete Stock[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By Cumulative Obsolete Stock Drugs Available For Emergency Orders Drugs Available For Stock Rotation SRS Demand SRS Stock On Hand Total Obsolescence Cost
MODEL B	#64 DE,A	Order Processing (Drugs/Week) Order Processing[Formulations,Order Number] = DELAY MATERIAL (Normal Orders From Countries[Formulations,Order Number], Order Processing Lead Time[Formulations,Order Number], 0, 0) Present In 1 View: Main Model Used By Processed Orders
MODEL B	#65 A	Order Processing Lead Time (Week) Order Processing Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order

		Processing Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Present In 2 Views: Not in View Main Model Used By Order Processing
MODEL B	#77 F,A	Orders Placed To Manufacturer (Drugs/Week) Orders Placed To Manufacturer[Formulations,Order Number] = SRS Demand[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By SRS Supply Line
MODEL B	#81 A	Processed Orders (Drugs/Week) Processed Orders[Formulations,Order Number] = Order Processing[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Drugs To Be Dispatched For Stock Rotation Normal Order Purchase Cost Production & Dispatch To GDF/PA
MODEL B	#82 C	Processing Drugs For Stock Rotation (Drugs/Week) Processing Drugs For Stock Rotation[Formulations,Order1] = (Drugs To Be Dispatched For Stock Rotation[Formulations,Order1]) + Drugs To Be Dispatched For Stock Rotation[Formulations,Order2] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order3] + Drugs To Be Dispatched For Stock Rotation[Formulations,Order4] Processing Drugs For Stock Rotation[Formulations,Order2] = 0 Processing Drugs For Stock Rotation[Formulations,Order3] = 0 Processing Drugs For Stock Rotation[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By SRS Demand SRS Stock On Hand Stockpile Rotation Cost
MODEL B	#86 A	Production & Dispatch Lead Time (Week) Production & Dispatch Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1)

		Production & Dispatch Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Present In 2 Views: Not in View Main Model Used By Production & Dispatch To GDF/PA Production & Dispatch To SRS
MODEL B	#98 DE,F,A	Production & Dispatch To GDF/PA (Drugs/Week) Production & Dispatch To GDF/PA[Formulations,Order Number] = DELAY MATERIAL ((Processed Orders[Formulations,Order Number] - Drugs To Be Dispatched For Stock Rotation[Formulations,Order Number]),"Production & Dispatch Lead Time"[Formulations,Order Number],0, 0) Present In 1 View: Main Model Used By Normal Order Drugs Awaiting Dispatch QC's & Dispatch To Countries
MODEL B	#99 DE,A	Production & Dispatch To SRS (Drugs/Week) Production & Dispatch To SRS[Formulations,Order Number] = DELAY MATERIAL (SRS Demand[Formulations,Order Number] , "Production & Dispatch Lead Time"[Formulations,Order Number] , 0 , 0) Present In 1 View: Main Model Used By Drugs Received From Manufacturer SRS Stock On Hand
MODEL B	#100 A,D,T	Profile (Dmnl) Profile([(0,0)-(1,1)],(0,1),(1,1)) Main Model Used By SRS Stock On Hand
MODEL B	#101 C	Proportion Of Orders Placed (Dmnl) Proportion Of Orders Placed[Capreomycin,Order Number] = 0.574, 0.389, 0.255, 0.263 Proportion Of Orders Placed[Kanamycin,Order Number] = 0.45, 0.191, 0.287, 0.479 Proportion Of Orders Placed[Cycloserine,Order Number] = 0.721, 0.508, 0.412, 0.298 Present In 2 Views: Not in View Main Model Used By Demand Input
MODEL B	#104 DE,F,A	QC's & Dispatch To Countries (Drugs/Week) QC's & Dispatch To Countries[Formulations,Order Number] = DELAY MATERIAL (IF THEN ELSE("Production & Dispatch To GDF/PA"[Formulations,Order Number] > 0 , "Production & Dispatch To GDF/PA"[Formulations,Order Number] , 0) , Country Dispatch Lead Time[Formulations,Order Number] , 0 , 0) Present In 1 View: Main Model Used By Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries
MODEL B	#105 C	Rotation Value Start (Week) Rotation Value Start[Capreomycin,Order Number] = 16,16,16,16 Rotation Value

		Start[Kanamycin,Order Number] = 40, 40, 40, 40 Rotation Value Start[Cycloserine,Order Number] = 16,16,16,16 Present In 2 Views: Not in View Main Model Used By Drugs Available For Stock Rotation
MODEL B	#108 C	Rotation Value Stop (Week) Rotation Value Stop[Capreomycin,Order Number] = 36,36,36,36 Rotation Value Stop[Kanamycin,Order Number] = 84,84,84,84 Rotation Value Stop[Cycloserine,Order Number] = 36,36,36,36 Present In 2 Views: Not in View Main Model Used By Drugs Available For Stock Rotation
MODEL B	#112 A	SRS Demand (Drugs/Week) SRS Demand[Formulations,Order Number] = Drugs Available For Emergency Orders[Formulations,Order Number] + Obsolete Stock[Formulations,Order Number] + Processing Drugs For Stock Rotation[Formulations,Order Number] Present In 1 View: Main Model Used By Orders Placed To Manufacturer Production & Dispatch To SRS
MODEL B	#113 A	SRS Stock On Hand (Drugs) SRS Stock On Hand[Formulations,Order Number] = QUEUE FIFO("Production & Dispatch To SRS"[Formulations,Order Number] , Processing Drugs For Stock Rotation[Formulations,Order Number] + Obsolete Stock[Formulations,Order Number] + Drugs Available For Emergency Orders[Formulations,Order Number] , Profile , Initial Stock On Hand[Formulations,Order Number] , 0) Present In 1 View: Main Model Used By Drugs Available For Emergency Orders Drugs Available For Stock Rotation Obsolete Stock
MODEL B	#114 L	SRS Supply Line (Drugs) SRS Supply Line[Formulations,Order Number] = ∫"Orders Placed To Manufacturer"["Formulations","Order Number"]-"Drugs Received From Manufacturer"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By Supply Line Position
MODEL B	#116 A	Supply Line Position (Drugs/Week) Supply Line Position[Formulations,Order Number] = SRS Supply Line[Formulations,Order Number]/TIME STEP Present In 1 View: Main Model Used By
MODEL B	#120 L	Total Emergency Order Drugs Received (Drugs) Total Emergency Order Drugs Received[Formulations,Order Number] = ∫"Emergency Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
MODEL B	#121 L	Total Normal Order Drugs Received (Drugs) Total Normal Order Drugs Received[Formulations,Order Number] = ∫"Normal Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View:

		Main Model Used By
MODEL B	#123 A	Uniform (Dmnl) Uniform[Capreomycin,Order Number] = RANDOM 0 1() Uniform[Kanamycin,Order Number] = (RANDOM 0 1()) Uniform[Cycloserine,Order Number] = RANDOM 0 1() Present In 2 Views: Not in View Main Model Used By Demand Input Emergency Input
MODEL B	#126 A	Weibull Distribution (Drugs/Week) Weibull Distribution[Capreomycin,Order Number] = RANDOM WEIBULL(78 , 448000 , 0.6161 , 78 , 32500 , 0) Weibull Distribution[Kanamycin,Order Number] = RANDOM WEIBULL(450 , 882000 ,0.4525 , 450 , 50000 , 1) Weibull Distribution[Cycloserine,Order Number] = RANDOM WEIBULL(1500 , 9.4491e+06 , 0.4755 , 1500 , 420000 , 1) Present In 2 Views: Not in View Main Model Used By Demand Input

Top | (Type) Subscripts (2 Variables)

Group	Type	*Variable Name And Description*
MODEL B	#48 Sub	Formulations () Formulations:Capreomycin, Kanamycin, Cycloserine Present In 2 Views: Cost Main Model Used By Country Dispatch Lead Time Cumulative Obsolete Stock Cumulative Purchase Unit Cost Cumulative Stockpile Replenishment Cost Cumulative Total Obsolescence Cost Demand Input Dispatch Emergency Drugs To Countries Drugs Available For Emergency Orders Drugs Available For Stock Rotation Drugs Dispatched As Stock Rotation Drugs Received From Manufacturer Drugs To Be Dispatched For Stock Rotation Emergency Input Emergency Order Cost Emergency Order Drugs Received By Countries Emergency Orders From Countries Emergency Orders Supply Line Emergency Proportion Of Orders Placed Emergency Weibull Distribution Expiration Value Initial Stock On Hand Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries Normal Order Purchase Cost Normal Orders From Countries Normal Orders Supply Line Obsolete Stock

		Order Processing Order Processing Lead Time Orders Placed To Manufacturer Per Unit Cost Processed Orders Processing Drugs For Stock Rotation Production & Dispatch Lead Time Production & Dispatch To GDF/PA Production & Dispatch To SRS Proportion Of Orders Placed QC's & Dispatch To Countries Rotation Value Start Rotation Value Stop SRS Demand SRS Stock On Hand SRS Supply Line Stockpile Rotation Cost Supply Line Position Total Costs Total Emergency Order Drugs Received Total Normal Order Drugs Received Total Obsolescence Cost Uniform Weibull Distribution
MODEL B	#63 Sub	Order Number () Order Number:Order1, Order2, Order3, Order4 Present In 2 Views: Cost Main Model Used By Country Dispatch Lead Time Cumulative Obsolete Stock Demand Input Dispatch Emergency Drugs To Countries Drugs Available For Emergency Orders Drugs Dispatched As Stock Rotation Drugs Received From Manufacturer Drugs To Be Dispatched For Stock Rotation Emergency Input Emergency Order Drugs Received By Countries Emergency Orders From Countries Emergency Orders Supply Line Emergency Proportion Of Orders Placed Emergency Weibull Distribution Expiration Value Initial Stock On Hand Normal Order Drugs Awaiting Dispatch Normal Order Drugs Received By Countries Normal Orders From Countries Normal Orders Supply Line Obsolete Stock Order Processing Order Processing Lead Time Orders Placed To Manufacturer Processed Orders Processing Drugs For Stock Rotation Production & Dispatch Lead Time

		Production & Dispatch To GDF/PA Production & Dispatch To SRS Proportion Of Orders Placed QC's & Dispatch To Countries Rotation Value Start Rotation Value Stop SRS Demand SRS Stock On Hand SRS Supply Line Supply Line Position Total Emergency Order Drugs Received Total Normal Order Drugs Received Uniform Weibull Distribution	

All Variables (56)

Group	Type	Variable
MODEL B	A	Country Dispatch Lead Time (Week)
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	A	Demand Input (Drugs/Week)
MODEL B	DE,A	Dispatch Emergency Drugs To Countries (Drugs/Week)
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)
MODEL B	A	Drugs Available For Stock Rotation (Drugs/Week)
MODEL B	DE,A	Drugs Dispatched As Stock Rotation (Drugs/Week)
MODEL B	F,A	Drugs Received From Manufacturer (Drugs/Week)
MODEL B	A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week)
MODEL B	A	Emergency Input (Drugs/Week)
MODEL B	F,A	Emergency Order Cost (Dollar/Week)
MODEL B	F,A	Emergency Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Emergency Orders From Countries (Drugs/Week)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	C	Emergency Proportion Of Orders Placed (Dmnl)
MODEL B	A	Emergency Weibull Distribution (Drugs/Week)
MODEL B	C	Expiration Value (Week)
.Control	C	FINAL TIME (Week)
MODEL B	C	Initial Stock On Hand (Drugs)
.Control	C	INITIAL TIME (Week)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Normal Order Purchase Cost (Dollar/Week)
MODEL B	F,A	Normal Orders From Countries (Drugs/Week)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	F,A	Obsolete Stock (Drugs/Week)
MODEL B	A	Order Processing Lead Time (Week)
MODEL B	DE,A	Order Processing (Drugs/Week)
MODEL B	F,A	Orders Placed To Manufacturer (Drugs/Week)
MODEL B	C	Per Unit Cost (Dollar/Drugs)
MODEL B	A	Processed Orders (Drugs/Week)
MODEL B	A	Processing Drugs For Stock Rotation (Drugs/Week)
MODEL B	A	Production & Dispatch Lead Time (Week)
MODEL B	DE,F,A	Production & Dispatch To GDF/PA (Drugs/Week)

MODEL B	DE,A	Production & Dispatch To SRS (Drugs/Week)
MODEL B	A,D,T	Profile (Dmnl)
MODEL B	C	Proportion Of Orders Placed (Dmnl)
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)
MODEL B	C	Rotation Value Start (Week)
MODEL B	C	Rotation Value Stop (Week)
.Control	A	SAVEPER (Week)
MODEL B	A	SRS Demand (Drugs/Week)
MODEL B	A	SRS Stock On Hand (Drugs)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	F,A	Stockpile Rotation Cost (Dollar/Week)
MODEL B	A	Supply Line Position (Drugs/Week)
.Control	C	TIME STEP (Week)
MODEL B	A	Total Costs (Dollar)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)
MODEL B	F,A	Total Obsolescence Cost (Dollar/Week)
MODEL B	A	Uniform (Dmnl)
MODEL B	A	Weibull Distribution (Drugs/Week)

Undocumented Variables (54)

Group	Type	Variable
MODEL B	A	Country Dispatch Lead Time (Week)
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	A	Demand Input (Drugs/Week)
MODEL B	DE,A	Dispatch Emergency Drugs To Countries (Drugs/Week)
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)
MODEL B	A	Drugs Available For Stock Rotation (Drugs/Week)
MODEL B	DE,A	Drugs Dispatched As Stock Rotation (Drugs/Week)
MODEL B	F,A	Drugs Received From Manufacturer (Drugs/Week)
MODEL B	A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week)
MODEL B	A	Emergency Input (Drugs/Week)
MODEL B	F,A	Emergency Order Cost (Dollar/Week)
MODEL B	F,A	Emergency Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Emergency Orders From Countries (Drugs/Week)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	C	Emergency Proportion Of Orders Placed (Dmnl)
MODEL B	A	Emergency Weibull Distribution (Drugs/Week)
MODEL B	C	Expiration Value (Week)
MODEL B	Sub	Formulations ()
MODEL B	C	Initial Stock On Hand (Drugs)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Normal Order Purchase Cost (Dollar/Week)
MODEL B	F,A	Normal Orders From Countries (Drugs/Week)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	F,A	Obsolete Stock (Drugs/Week)
MODEL B	Sub	Order Number ()
MODEL B	A	Order Processing Lead Time (Week)
MODEL B	DE,A	Order Processing (Drugs/Week)

MODEL B	F,A	Orders Placed To Manufacturer (Drugs/Week)
MODEL B	C	Per Unit Cost (Dollar/Drugs)
MODEL B	A	Processed Orders (Drugs/Week)
MODEL B	A	Processing Drugs For Stock Rotation (Drugs/Week)
MODEL B	A	Production & Dispatch Lead Time (Week)
MODEL B	DE,F,A	Production & Dispatch To GDF/PA (Drugs/Week)
MODEL B	DE,A	Production & Dispatch To SRS (Drugs/Week)
MODEL B	A,D,T	Profile (Dmnl)
MODEL B	C	Proportion Of Orders Placed (Dmnl)
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)
MODEL B	C	Rotation Value Start (Week)
MODEL B	C	Rotation Value Stop (Week)
MODEL B	A	SRS Demand (Drugs/Week)
MODEL B	A	SRS Stock On Hand (Drugs)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	F,A	Stockpile Rotation Cost (Dollar/Week)
MODEL B	A	Supply Line Position (Drugs/Week)
MODEL B	A	Total Costs (Dollar)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)
MODEL B	F,A	Total Obsolescence Cost (Dollar/Week)
MODEL B	A	Uniform (Dmnl)
MODEL B	A	Weibull Distribution (Drugs/Week)

Supplementary Variables (2)

Group	Type	Variable
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)

Unused Variables (6)

Group	Type	Variable
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	A	Supply Line Position (Drugs/Week)
MODEL B	A	Total Costs (Dollar)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)

Stock Variables (10)

Group	Type	Variable
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)

Equations With Embedded Data (15)

Group	Type	Variable
MODEL B	A	Country Dispatch Lead Time (Week)

MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	A	Emergency Weibull Distribution (Drugs/Week)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	A	Order Processing Lead Time (Week)
MODEL B	A	Production & Dispatch Lead Time (Week)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)
MODEL B	A	Weibull Distribution (Drugs/Week)

Equations With If Then Else Functions (5)

Group	Type	Variable
MODEL B	A	Demand Input (Drugs/Week)
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)
MODEL B	A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week)
MODEL B	A	Emergency Input (Drugs/Week)
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)

Equations With Min Or Max Functions (2)

Group	Type	Variable
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)
MODEL B	A	Drugs Available For Stock Rotation (Drugs/Week)

Complex Variable (Richardson's Rule Threshold = 3) (6)

Group	Type	Variable	Complexity
MODEL B	F,A	Obsolete Stock (Drugs/Week)	4
MODEL B	A	Processing Drugs For Stock Rotation (Drugs/Week)	4
MODEL B	A	Drugs Available For Stock Rotation (Drugs/Week)	5
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)	5
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)	6
MODEL B	A	SRS Stock On Hand (Drugs)	6

State Variables (16)

Group	Type	Variable
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	DE,A	Dispatch Emergency Drugs To Countries (Drugs/Week)
MODEL B	DE,A	Drugs Dispatched As Stock Rotation (Drugs/Week)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	DE,A	Order Processing (Drugs/Week)
MODEL B	DE,F,A	Production & Dispatch To GDF/PA (Drugs/Week)
MODEL B	DE,A	Production & Dispatch To SRS (Drugs/Week)
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)

MODEL B	L	Total Normal Order Drugs Received (Drugs)

Variables With Dimensionless Units (4)

Group	Type	Variable
MODEL B	C	Emergency Proportion Of Orders Placed (Dmnl)
MODEL B	A,D,T	Profile (Dmnl)
MODEL B	C	Proportion Of Orders Placed (Dmnl)
MODEL B	A	Uniform (Dmnl)

Variables without Predefined Min or Max Values (52)

Group	Type	Variable
MODEL B	A	Country Dispatch Lead Time (Week)
MODEL B	L	Cumulative Obsolete Stock (Drugs)
MODEL B	L	Cumulative Purchase Unit Cost (Dollar)
MODEL B	L	Cumulative Stockpile Replenishment Cost (Dollar)
MODEL B	L	Cumulative Total Obsolescence Cost (Dollar)
MODEL B	A	Demand Input (Drugs/Week)
MODEL B	DE,A	Dispatch Emergency Drugs To Countries (Drugs/Week)
MODEL B	A	Drugs Available For Emergency Orders (Drugs/Week)
MODEL B	A	Drugs Available For Stock Rotation (Drugs/Week)
MODEL B	DE,A	Drugs Dispatched As Stock Rotation (Drugs/Week)
MODEL B	F,A	Drugs Received From Manufacturer (Drugs/Week)
MODEL B	A	Drugs To Be Dispatched For Stock Rotation (Drugs/Week)
MODEL B	A	Emergency Input (Drugs/Week)
MODEL B	F,A	Emergency Order Cost (Dollar/Week)
MODEL B	F,A	Emergency Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Emergency Orders From Countries (Drugs/Week)
MODEL B	L	Emergency Orders Supply Line (Drugs)
MODEL B	C	Emergency Proportion Of Orders Placed (Dmnl)
MODEL B	A	Emergency Weibull Distribution (Drugs/Week)
MODEL B	C	Expiration Value (Week)
MODEL B	C	Initial Stock On Hand (Drugs)
MODEL B	L	Normal Order Drugs Awaiting Dispatch (Drugs)
MODEL B	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
MODEL B	F,A	Normal Order Purchase Cost (Dollar/Week)
MODEL B	F,A	Normal Orders From Countries (Drugs/Week)
MODEL B	L	Normal Orders Supply Line (Drugs)
MODEL B	F,A	Obsolete Stock (Drugs/Week)
MODEL B	A	Order Processing Lead Time (Week)
MODEL B	DE,A	Order Processing (Drugs/Week)
MODEL B	F,A	Orders Placed To Manufacturer (Drugs/Week)
MODEL B	C	Per Unit Cost (Dollar/Drugs)
MODEL B	A	Processed Orders (Drugs/Week)
MODEL B	A	Processing Drugs For Stock Rotation (Drugs/Week)
MODEL B	A	Production & Dispatch Lead Time (Week)
MODEL B	DE,F,A	Production & Dispatch To GDF/PA (Drugs/Week)
MODEL B	DE,A	Production & Dispatch To SRS (Drugs/Week)
MODEL B	A,D,T	Profile (Dmnl)
MODEL B	C	Proportion Of Orders Placed (Dmnl)
MODEL B	DE,F,A	QC's & Dispatch To Countries (Drugs/Week)
MODEL B	C	Rotation Value Start (Week)
MODEL B	C	Rotation Value Stop (Week)
MODEL B	A	SRS Demand (Drugs/Week)

MODEL B	A	SRS Stock On Hand (Drugs)
MODEL B	L	SRS Supply Line (Drugs)
MODEL B	F,A	Stockpile Rotation Cost (Dollar/Week)
MODEL B	A	Supply Line Position (Drugs/Week)
MODEL B	A	Total Costs (Dollar)
MODEL B	L	Total Emergency Order Drugs Received (Drugs)
MODEL B	L	Total Normal Order Drugs Received (Drugs)
MODEL B	F,A	Total Obsolescence Cost (Dollar/Week)
MODEL B	A	Uniform (Dmnl)
MODEL B	A	Weibull Distribution (Drugs/Week)

Units (4/3)

Units	Type	Alternates
$	Basic	[Dollar]
Dmnl	Basic	
Drugs	Basic	
Week	Basic	
$/Drugs	Combined	[Dollar/Drugs]
$/Week	Combined	[Dollar/Week]
Drugs/Week	Combined	

Positive Polarity Causal Links (39)

Cause	Effect	Polarity
Cumulative Purchase Unit Cost	Total Costs	+
Cumulative Stockpile Replenishment Cost	Total Costs	+
Cumulative Total Obsolescence Cost	Total Costs	+
Demand Input	Normal Orders From Countries	+
Dispatch Emergency Drugs To Countries	Emergency Order Drugs Received By Countries	+
Drugs Available For Emergency Orders	Emergency Order Cost	+
Drugs Available For Emergency Orders	SRS Demand	+
Drugs Dispatched As Stock Rotation	Normal Order Drugs Received By Countries	+
Drugs To Be Dispatched For Stock Rotation	Processing Drugs For Stock Rotation	+
Emergency Input	Emergency Orders From Countries	+
Emergency Order Cost	Cumulative Stockpile Replenishment Cost	+
Emergency Order Drugs Received By Countries	Total Emergency Order Drugs Received	+
Emergency Orders From Countries	Drugs Available For Emergency Orders	+
Emergency Orders From Countries	Emergency Orders Supply Line	+
Emergency Weibull Distribution	Emergency Input	+
Normal Order Drugs Received By Countries	Total Normal Order Drugs Received	+
Normal Order Purchase Cost	Cumulative Purchase Unit Cost	+
Normal Orders From Countries	Normal Orders Supply Line	+
Obsolete Stock	Cumulative Obsolete Stock	+
Obsolete Stock	SRS Demand	+
Obsolete Stock	Total Obsolescence Cost	+
Order Processing	Processed Orders	+
Orders Placed To Manufacturer	SRS Supply Line	+
Per Unit Cost	Emergency Order Cost	+
Per Unit Cost	Stockpile Rotation Cost	+
Per Unit Cost	Total Obsolescence Cost	+
Processed Orders	Normal Order Purchase Cost	+
Processing Drugs For Stock Rotation	SRS Demand	+
Processing Drugs For Stock Rotation	Stockpile Rotation Cost	+

Production & Dispatch To GDF/PA	Normal Order Drugs Awaiting Dispatch	+
Production & Dispatch To SRS	Drugs Received From Manufacturer	+
QC's & Dispatch To Countries	Normal Order Drugs Received By Countries	+
SRS Demand	Orders Placed To Manufacturer	+
SRS Stock On Hand	Drugs Available For Emergency Orders	+
SRS Supply Line	Supply Line Position	+
Stockpile Rotation Cost	Cumulative Stockpile Replenishment Cost	+
TIME STEP	SAVEPER	+
Total Obsolescence Cost	Cumulative Total Obsolescence Cost	+
Weibull Distribution	Demand Input	+

Negative Polarity Causal Links (8)

Cause	Effect	Polarity
Drugs Received From Manufacturer	SRS Supply Line	-
Drugs To Be Dispatched For Stock Rotation	Normal Order Purchase Cost	-
Emergency Order Drugs Received By Countries	Emergency Orders Supply Line	-
Normal Order Drugs Received By Countries	Normal Orders Supply Line	-
Obsolete Stock	Drugs Available For Emergency Orders	-
Per Unit Cost	Normal Order Purchase Cost	-
QC's & Dispatch To Countries	Normal Order Drugs Awaiting Dispatch	-
TIME STEP	Supply Line Position	-

Function-based Polarity Causal Links (36)

Cause	Effect	Polarity
Country Dispatch Lead Time	Dispatch Emergency Drugs To Countries	Function[DELAYMATERIAL]
Country Dispatch Lead Time	Drugs Dispatched As Stock Rotation	Function[DELAYMATERIAL]
Country Dispatch Lead Time	QC's & Dispatch To Countries	Undefined(Load)
Demand Input	Demand Input	If Then Else Switch
Drugs Available For Emergency Orders	Dispatch Emergency Drugs To Countries	Function[DELAYMATERIAL]
Drugs Available For Emergency Orders	SRS Stock On Hand	Function[QUEUEFIFO]
Drugs Available For Stock Rotation	Drugs To Be Dispatched For Stock Rotation	If Then Else Switch
Drugs To Be Dispatched For Stock Rotation	Drugs Dispatched As Stock Rotation	Function[DELAYMATERIAL]
Drugs To Be Dispatched For Stock Rotation	Drugs To Be Dispatched For Stock Rotation	If Then Else Switch
Drugs To Be Dispatched For Stock Rotation	Production & Dispatch To GDF/PA	Function[DELAYMATERIAL]
Emergency Proportion Of Orders Placed	Emergency Input	If Then Else Switch
Expiration Value	Obsolete Stock	Function[QUEUEAGEINRANGE]
Initial Stock On Hand	SRS Stock On Hand	Function[QUEUEFIFO]
NAREPLACEMENT	Obsolete Stock	Function[QUEUEAGEINRANGE]
Normal Orders From Countries	Order Processing	Function[DELAYMATERIAL]
Obsolete Stock	Drugs Available For Stock Rotation	Function[MAX,QUEUEAGEINRANGE]
Obsolete Stock	SRS Stock On Hand	Function[QUEUEFIFO]
Order Processing Lead Time	Order Processing	Function[DELAYMATERIAL]

Processed Orders	Drugs To Be Dispatched For Stock Rotation	If Then Else Switch
Processed Orders	Production & Dispatch To GDF/PA	Function[DELAYMATERIAL]
Processing Drugs For Stock Rotation	SRS Stock On Hand	Function[QUEUEFIFO]
Production & Dispatch Lead Time	Production & Dispatch To GDF/PA	Function[DELAYMATERIAL]
Production & Dispatch Lead Time	Production & Dispatch To SRS	Function[DELAYMATERIAL]
Production & Dispatch To GDF/PA	QC's & Dispatch To Countries	If Then Else Switch
Production & Dispatch To SRS	SRS Stock On Hand	Function[QUEUEFIFO]
Profile	SRS Stock On Hand	Function[QUEUEFIFO]
Proportion Of Orders Placed	Demand Input	If Then Else Switch
Rotation Value Start	Drugs Available For Stock Rotation	Function[MAX,QUEUEAGEINRANGE]
Rotation Value Stop	Drugs Available For Stock Rotation	Function[MAX,QUEUEAGEINRANGE]
SRS Demand	Production & Dispatch To SRS	Function[DELAYMATERIAL]
SRS Stock On Hand	Drugs Available For Stock Rotation	Function[MAX,QUEUEAGEINRANGE]
SRS Stock On Hand	Obsolete Stock	Function[QUEUEAGEINRANGE]
TIME STEP	Drugs Available For Stock Rotation	Function[MAX,QUEUEAGEINRANGE]
TIME STEP	Obsolete Stock	Function[QUEUEAGEINRANGE]
Uniform	Demand Input	If Then Else Switch
Uniform	Emergency Input	If Then Else Switch

View-Variable Profile

View	View-Variable Profile
Cost	16 vars (26.7%)
Main Model	43 vars (71.7%)

List Of 2 views and their 52 Variables

	Cost	Main Model	
Total:	16	43	Total:
Total Normal Order Drugs Received (In 1 View)			Total Normal Order Drugs Received (In 1 View)
Proportion Of Orders Placed (In 1 View)			Proportion Of Orders Placed (In 1 View)
Obsolete Stock (In 2 Views)			Obsolete Stock (In 2 Views)
SRS Stock On Hand (In 1 View)			SRS Stock On Hand (In 1 View)
Emergency Input (In 1 View)			Emergency Input (In 1 View)
Processed Orders (In 2 Views)			Processed Orders (In 2 Views)
Drugs Available For Emergency Orders (In 2 Views)			Drugs Available For Emergency Orders (In 2 Views)
Production & Dispatch To GDF/PA (In 1 View)			Production & Dispatch To GDF/PA (In 1 View)
Normal Orders Supply Line (In 1 View)			Normal Orders Supply Line (In 1 View)
Uniform (In 1 View)			Uniform (In 1 View)

Drugs Available For Stock Rotation (In 1 View)		■	Drugs Available For Stock Rotation (In 1 View)
Emergency Proportion Of Orders Placed (In 1 View)		■	Emergency Proportion Of Orders Placed (In 1 View)
Processing Drugs For Stock Rotation (In 2 Views)	■	■	Processing Drugs For Stock Rotation (In 2 Views)
Profile (In 1 View)		■	Profile (In 1 View)
Order Processing Lead Time (In 1 View)		■	Order Processing Lead Time (In 1 View)
Emergency Orders Supply Line (In 1 View)		■	Emergency Orders Supply Line (In 1 View)
Rotation Value Stop (In 1 View)		■	Rotation Value Stop (In 1 View)
Demand Input (In 1 View)		■	Demand Input (In 1 View)
Normal Order Drugs Received By Countries (In 1 View)		■	Normal Order Drugs Received By Countries (In 1 View)
Emergency Orders From Countries (In 1 View)		■	Emergency Orders From Countries (In 1 View)
Drugs Dispatched As Stock Rotation (In 1 View)		■	Drugs Dispatched As Stock Rotation (In 1 View)
Country Dispatch Lead Time (In 1 View)		■	Country Dispatch Lead Time (In 1 View)
Production & Dispatch To SRS (In 1 View)		■	Production & Dispatch To SRS (In 1 View)
Drugs Received From Manufacturer (In 1 View)		■	Drugs Received From Manufacturer (In 1 View)
Order Processing (In 1 View)		■	Order Processing (In 1 View)
Expiration Value (In 1 View)		■	Expiration Value (In 1 View)
Orders Placed To Manufacturer (In 2 Views)	■	■	Orders Placed To Manufacturer (In 2 Views)
Weibull Distribution (In 1 View)		■	Weibull Distribution (In 1 View)
Drugs To Be Dispatched For Stock Rotation (In 2 Views)	■	■	Drugs To Be Dispatched For Stock Rotation (In 2 Views)
Emergency Weibull Distribution (In 1 View)		■	Emergency Weibull Distribution (In 1 View)
Production & Dispatch Lead Time (In 1 View)		■	Production & Dispatch Lead Time (In 1 View)
SRS Demand (In 1 View)		■	SRS Demand (In 1 View)
Normal Orders From Countries (In 2 Views)	■	■	Normal Orders From Countries (In 2 Views)
Emergency Order Drugs Received By Countries (In 1 View)		■	Emergency Order Drugs Received By Countries (In 1 View)
Rotation Value Start (In 1 View)		■	Rotation Value Start (In 1 View)
Supply Line Position (In 1 View)		■	Supply Line Position (In 1 View)
Cumulative Obsolete Stock (In 1 View)		■	Cumulative Obsolete Stock (In 1 View)
Total Emergency Order Drugs Received (In 1 View)		■	Total Emergency Order Drugs Received (In 1 View)
SRS Supply Line (In 1 View)		■	SRS Supply Line (In 1 View)
QC's & Dispatch To Countries (In 1 View)		■	QC's & Dispatch To Countries (In 1 View)
Dispatch Emergency Drugs To Countries (In 1 View)		■	Dispatch Emergency Drugs To Countries (In 1 View)
Initial Stock On Hand (In 1 View)		■	Initial Stock On Hand (In 1 View)
Normal Order Drugs Awaiting Dispatch (In 1 View)		■	Normal Order Drugs Awaiting Dispatch (In 1 View)
Cumulative Stockpile Replenishment Cost (In 1 View)	■		Cumulative Stockpile Replenishment Cost (In 1 View)
Cumulative Purchase Unit Cost (In 1 View)	■		Cumulative Purchase Unit Cost (In 1 View)
Total Obsolescence Cost (In 1 View)	■		Total Obsolescence Cost (In 1 View)

Stockpile Rotation Cost (In 1 View)			Stockpile Rotation Cost (In 1 View)
Per Unit Cost (In 1 View)			Per Unit Cost (In 1 View)
Emergency Order Cost (In 1 View)			Emergency Order Cost (In 1 View)
Normal Order Purchase Cost (In 1 View)			Normal Order Purchase Cost (In 1 View)
Total Costs (In 1 View)			Total Costs (In 1 View)
Cumulative Total Obsolescence Cost (In 1 View)			Cumulative Total Obsolescence Cost (In 1 View)
Total:	16	43	Total:
	Cost	Main Model	

Source File: /Users/deonlingervelder/Desktop/All/Masters/6. Dynamic Modelling Main Models/DAILY/MODEL B.mdl (Sat Nov 19 12:44:30 SAST 2016)
Report Created On Sat Nov 19 12:44:48 SAST 2016
SDM-Doc Tool Version 1.2.44
Global Security Sciences Division
Argonne National Laboratory

I.3 SDM document for Model C

This section provides the HTML output of the SDM document tool, for Model C.

Model Assessment Results

Model Information	Result
Total Number Of Variables	51|371
Total Number Of Causal Links	80 (28|5|47)|931 (307|60|564)
Total Number of Rate-to-rate Links	0
Variables without Predefined Min or Max Values	47 (92.2%)|367 (98.9%)
Model Is Fully Formulated	Yes
Model Defined Groups	No

Potential Omissions	Result

Variable Types

L: Level (6 / 72)*	SM: Smooth (0 / 0)*	DE: Delay (3 / 36)*†	LI: Level Initial (0)	I: Initial (0 / 0)
C: Constant (10 / 87)	F: Flow (7 / 84)	A: Auxiliary (35 / 389)	Sub: Subscripts (2)	D: Data (0 / 0)
G: Game (0 / 0)	T: Lookup (1 / 1)*††			

* (State Variables/Total Stocks) † Total Stocks Do Not Include Fixed Delay Variables. †† (Lookup Tables).
Views

View: Cost (10) Variables
View: Main Model (41) Variables

Variables

(View) Cost (10 Variables)

Top	(View) Cost (10 Variables)

Group	Type	*Variable Name And Description*
ModelC	#21 L	Cumulative Total Obsolescence Cost (Dollar) Cumulative Total Obsolescence Cost[Formulations,Order Number] = ∫"Total Obsolescence Cost"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
ModelC	#22 L	Cumulative Total Unit Cost (Dollar) Cumulative Total Unit Cost[Formulations,Order Number] = ∫"Total Unit Cost"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Cost Used By Total Costs
ModelC	#61 F,A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Order Processing
ModelC	#63 C,F	Obsolete Stock (Drugs/Week) Obsolete Stock[Formulations,Order1] = QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Expiration Value[Formulations,Order1] , NAREPLACEMENT)/TIME STEP Obsolete Stock[Formulations,Order2] = 0 Obsolete Stock[Formulations,Order3] = 0 Obsolete Stock[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By Cumulative Obsolete Stock Drugs Available For Dispatch SRS Stock On Hand Total Obsolescence Cost
ModelC	#86 C	Per Unit Cost (Dollar/Drugs) Per Unit Cost[Capreomycin,Order Number] = 5.66 Per Unit Cost[Kanamycin,Order Number] = 2.59 Per Unit Cost[Cycloserine,Order Number] = 0.55 Present In 2 Views: Not in View Cost Used By Total Obsolescence Cost Total Unit Cost
ModelC	#116 A	SRS Demand (Drugs/Week) SRS Demand[Formulations,Order Number] = IF THEN ELSE("Reorder?"[Formulations,Order Number]=0 , IF THEN ELSE(Inventory Position[Formulations,Order Number]/ TIME STEP<Reorder Point[Formulations,Order Number] , (MAX(0,"Order-Up-To-

		Level"[Formulations,Order Number] - Inventory Position[Formulations,Order Number]))/TIME STEP, 0) , 0) Present In 2 Views: Cost Main Model Used By Orders Placed To Manufacturer Production & Dispatch To SRS Total Unit Cost
ModelC	#117 A	SRS Stock On Hand (Drugs) SRS Stock On Hand[Formulations,Order Number] = QUEUE FIFO("Production & Dispatch To SRS"[Formulations,Order Number], Obsolete Stock[Formulations,Order Number] + Dispatch Drugs To Countries[Formulations,Order Number] , Profile , Initial Stock On Hand [Formulations,Order Number] , 0) Present In 2 Views: Cost Main Model Used By Drugs Available For Dispatch Inventory Position Obsolete Stock
ModelC	#121 A	Total Costs (Dollar) Total Costs[Formulations] = SUM(Cumulative Total Unit Cost[Formulations,Order Number!]) + SUM(Cumulative Total Obsolescence Cost[Formulations,Order Number!]) Present In 1 View: Cost Used By
ModelC	#123 F,A	Total Obsolescence Cost (Dollar/Week) Total Obsolescence Cost[Formulations,Order Number] = Per Unit Cost[Formulations,Order Number] * Obsolete Stock[Formulations,Order Number] Present In 1 View: Cost Used By Cumulative Total Obsolescence Cost
ModelC	#124 F,A	Total Unit Cost (Dollar/Week) Total Unit Cost[Formulations,Order Number] = SRS Demand[Formulations,Order Number]*Per Unit Cost[Formulations,Order Number] Present In 1 View: Cost Used By Cumulative Total Unit Cost

(View) Main Model (41 Variables)

Top	(View) Main Model (41 Variables)	
Group	Type	*Variable Name And Description*
ModelC	#2 A	Backlog Range One (Drugs/Week) Backlog Range One[Formulations,Order Number] = QUEUE AGE IN RANGE(Order Backlogs[Formulations,Order Number] , QUEUE AGE OLDEST(Order Backlogs[Formulations,Order Number]) , NAREPLACEMENT) Present In 1 View: Main Model Used By Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0)

		Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order])
ModelC	#3 A	Backlog Range Two (Drugs/Week) Backlog Range Two[Formulations,Order Number] = QUEUE AGE IN RANGE(Order Backlogs[Formulations,Order Number] , 0.5* QUEUE AGE OLDEST(Order Backlogs[Formulations,Order Number]) , QUEUE AGE OLDEST (Order Backlogs[Formulations,Order Number]) - 1) Present In 1 View: Main Model Used By Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order])
ModelC	#4 A	Backlog Reduction (Drugs/Week) Backlog Reduction[Formulations,Order1] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1] , MAX(0,Drugs To Be Dispatched[Formulations,Order1] - Processed Orders[Formulations,Order1]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order1] , Drugs To Be Dispatched[Formulations,Order1] ,IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] + Processed Orders[Formulations,Order1], MAX(0,Drugs To Be Dispatched[Formulations,Order1] - Processed Orders[Formulations,Order1]),IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] , Drugs To Be Dispatched[Formulations,Order1] ,IF THEN ELSE(Processed Orders[Formulations,Order1] > 0 :AND: Backlog Range One[Formulations,Order1] > 0 :AND:Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] +Processed Orders[Formulations,Order1] , MAX(0,Drugs To Be Dispatched[Formulations,Order1] - Processed Orders[Formulations,Order1]) ,IF THEN ELSE(Backlog Range One[Formulations,Order1] > 0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] , Drugs To Be Dispatched[Formulations,Order1] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4]> Processed Orders[Formulations,Order1] , MAX(0,Drugs To Be Dispatched[Formulations,Order1]

		- Processed Orders[Formulations,Order1]) , Drugs To Be Dispatched[Formulations,Order1]))))))) Backlog Reduction[Formulations,Order2] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] + Order Backlogs[Formulations,Order2] , MAX(0,Drugs To Be Dispatched[Formulations,Order2] - Processed Orders[Formulations,Order2]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order2] , Drugs To Be Dispatched[Formulations,Order2] ,IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] + Processed Orders[Formulations,Order2], MAX(0,Drugs To Be Dispatched[Formulations,Order2] - Processed Orders[Formulations,Order2]),IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] , Drugs To Be Dispatched[Formulations,Order2] ,IF THEN ELSE(Processed Orders[Formulations,Order2] > 0 :AND: Backlog Range One[Formulations,Order2] > 0 :AND:Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Processed Orders[Formulations,Order2] , MAX(0,Drugs To Be Dispatched[Formulations,Order2] - Processed Orders[Formulations,Order2]) ,IF THEN ELSE(Backlog Range One[Formulations,Order2] > 0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] , Drugs To Be Dispatched[Formulations,Order2] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] , MAX(0,Drugs To Be Dispatched[Formulations,Order2] - Processed Orders[Formulations,Order2]) , Drugs To Be Dispatched[Formulations,Order2]))))))) Backlog Reduction[Formulations,Order3] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3] , MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed Orders[Formulations,Order3]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order3] , Drugs To Be Dispatched[Formulations,Order3] ,IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3]+ Backlog Range Two[Formulations,Order3] + Processed Orders[Formulations,Order3], MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed Orders[Formulations,Order3]),IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3]+ Backlog Range Two[Formulations,Order3] , Drugs To Be Dispatched[Formulations,Order3] ,IF

		THEN ELSE(Processed Orders[Formulations,Order3] > 0 :AND: Backlog Range One[Formulations,Order3] > 0 :AND:Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Processed Orders[Formulations,Order3] , MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed Orders[Formulations,Order3]) ,IF THEN ELSE(Backlog Range One[Formulations,Order3] > 0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] , Drugs To Be Dispatched[Formulations,Order3],IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] , MAX(0,Drugs To Be Dispatched[Formulations,Order3] - Processed Orders[Formulations,Order3]) , Drugs To Be Dispatched[Formulations,Order3]))))))) Backlog Reduction[Formulations,Order4] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] + Order Backlogs[Formulations,Order4] , MAX(0,Drugs To Be Dispatched[Formulations,Order4] - Processed Orders[Formulations,Order4]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Order Backlogs[Formulations,Order4] , Drugs To Be Dispatched[Formulations,Order4] ,IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] + Processed Orders[Formulations,Order4], MAX(0,Drugs To Be Dispatched[Formulations,Order4] - Processed Orders[Formulations,Order4]),IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] , Drugs To Be Dispatched[Formulations,Order4] ,IF THEN ELSE(Processed Orders[Formulations,Order4] > 0 :AND: Backlog Range One[Formulations,Order4] > 0 :AND:Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Processed Orders[Formulations,Order4] , MAX(0,Drugs To Be Dispatched[Formulations,Order4] - Processed Orders[Formulations,Order4]) ,IF THEN ELSE(Backlog Range One[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] , Drugs To Be Dispatched[Formulations,Order4] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] , MAX(0,Drugs To Be Dispatched[Formulations,Order4] - Processed Orders[Formulations,Order4]) , Drugs To Be Dispatched[Formulations,Order4]))))))) Description: MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Present In 2 Views: Not in View Main Model Used By Order Backlogs QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0)	
ModelC	#8 A	Country Dispatch Lead Time (Week) Country Dispatch Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order2] = RANDOM

		TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Country Dispatch Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(3 , 15 , 0 , 3 , 35 , 1) Present In 2 Views: Not in View Main Model Used By Dispatch
ModelC	#20 L	Cumulative Obsolete Stock (Drugs) Cumulative Obsolete Stock[Formulations,Order Number] = ∫"Obsolete Stock"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
ModelC	#23 A	Demand Input (Drugs/Week) Demand Input[Formulations,Order1] = IF THEN ELSE(Uniform[Formulations,Order1] < Proportion Of Orders Placed[Formulations,Order1] , INTEGER(Weibull Distribution[Formulations,Order1]) , 0) Demand Input[Formulations,Order2] = IF THEN ELSE(Demand Input[Formulations,Order1] > 0 , IF THEN ELSE(Uniform[Formulations,Order2] < Proportion Of Orders Placed[Formulations,Order2] , Weibull Distribution[Formulations,Order2] , 0) , 0) Demand Input[Formulations,Order3] = IF THEN ELSE(Demand Input[Formulations,Order2]>0, IF THEN ELSE(Uniform[Formulations,Order3] < Proportion Of Orders Placed[Formulations,Order3] , Weibull Distribution[Formulations,Order3] , 0) , 0) Demand Input[Formulations,Order4] = IF THEN ELSE(Demand Input[Formulations,Order3]>0, IF THEN ELSE(Uniform[Formulations,Order4] < Proportion Of Orders Placed[Formulations,Order4] , Weibull Distribution[Formulations,Order4] , 0) , 0) Present In 2 Views: Not in View Main Model Used By Normal Orders From Countries
ModelC	#27 DE,A	Dispatch (Drugs/Week) Dispatch[Formulations,Order Number] = DELAY MATERIAL (Drugs To Be Dispatched[Formulations,Order Number], Country Dispatch Lead Time[Formulations,Order Number], 0, 0) Present In 1 View: Main Model Used By Normal Order Drugs Received By Countries
ModelC	#28 C	Dispatch Drugs To Countries (Drugs/Week) Dispatch Drugs To Countries[Formulations,Order1] = Drugs To Be Dispatched[Formulations,Order1] + Drugs To Be Dispatched[Formulations,Order2] + Drugs To Be Dispatched[Formulations,Order3] + Drugs To Be Dispatched[Formulations,Order4] Dispatch Drugs To Countries[Formulations,Order2] = 0 Dispatch Drugs To Countries[Formulations,Order3] = 0 Dispatch Drugs To Countries[Formulations,Order4] = 0 Present In 2 Views:

		Not in View Main Model Used By SRS Stock On Hand
ModelC	#32 A	Drugs Available For Dispatch (Drugs/Week) Drugs Available For Dispatch[Formulations,Order1] = MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP - Obsolete Stock[Formulations,Order1]) Drugs Available For Dispatch[Formulations,Order2] = MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP - Obsolete Stock[Formulations,Order1]) Drugs Available For Dispatch[Formulations,Order3] = MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP - Obsolete Stock[Formulations,Order1]) Drugs Available For Dispatch[Formulations,Order4] = MAX(0, SRS Stock On Hand[Formulations,Order1]/TIME STEP - Obsolete Stock[Formulations,Order1]) Present In 2 Views: Not in View Main Model Used By Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order])
ModelC	#36 F,A	Drugs Received From Manufacturer (Drugs/Week) Drugs Received From Manufacturer[Formulations,Order Number] = "Production & Dispatch To SRS"[Formulations,Order Number] Present In 1 View: Main Model Used By SRS Supply Line
ModelC	#37 A	Drugs To Be Dispatched (Drugs/Week) Drugs To Be Dispatched[Formulations,Order1] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1] , Processed Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order1] , Order Backlogs[Formulations,Order1] ,IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] + Processed Orders[Formulations,Order1], Backlog Range Two[Formulations,Order1] + Backlog Range One[Formulations,Order1] + Processed Orders[Formulations,Order1],IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] , Backlog Range Two[Formulations,Order1] + Backlog Range One[Formulations,Order1] ,IF THEN ELSE(Processed Orders[Formulations,Order1] > 0 :AND: Backlog Range

		One[Formulations,Order1] > 0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Processed Orders[Formulations,Order1] , Backlog Range One[Formulations,Order1] + Processed Orders[Formulations,Order1] ,IF THEN ELSE(Backlog Range One[Formulations,Order1] > 0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] , Backlog Range One[Formulations,Order1] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4]> Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0))))))) Drugs To Be Dispatched[Formulations,Order2] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] + Order Backlogs[Formulations,Order2] , Processed Orders[Formulations,Order2] + Order Backlogs[Formulations,Order2] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order2] , Order Backlogs[Formulations,Order2] ,IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] + Processed Orders[Formulations,Order2], Backlog Range Two[Formulations,Order2] + Backlog Range One[Formulations,Order2] + Processed Orders[Formulations,Order2],IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] , Backlog Range Two[Formulations,Order2] + Backlog Range One[Formulations,Order2] ,IF THEN ELSE(Processed Orders[Formulations,Order2] > 0 :AND: Backlog Range One[Formulations,Order2] > 0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Processed Orders[Formulations,Order2] , Backlog Range One[Formulations,Order2] + Processed Orders[Formulations,Order2] ,IF THEN ELSE(Backlog Range One[Formulations,Order2] > 0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] , Backlog Range One[Formulations,Order2] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] , Processed Orders[Formulations,Order2] , 0))))))) Drugs To Be Dispatched[Formulations,Order3] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3] , Processed Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order3] , Order

		Backlogs[Formulations,Order3] ,IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] + Processed Orders[Formulations,Order3], Backlog Range Two[Formulations,Order3] + Backlog Range One[Formulations,Order3] + Processed Orders[Formulations,Order3],IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] , Backlog Range Two[Formulations,Order3] + Backlog Range One[Formulations,Order3] ,IF THEN ELSE(Processed Orders[Formulations,Order3] > 0 :AND: Backlog Range One[Formulations,Order3] > 0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Processed Orders[Formulations,Order3] , Backlog Range One[Formulations,Order3] + Processed Orders[Formulations,Order3] ,IF THEN ELSE(Backlog Range One[Formulations,Order3] > 0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] , Backlog Range One[Formulations,Order3] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] , Processed Orders[Formulations,Order3] , 0))))))) Drugs To Be Dispatched[Formulations,Order4] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] + Order Backlogs[Formulations,Order4] , Processed Orders[Formulations,Order4] + Order Backlogs[Formulations,Order4] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Order Backlogs[Formulations,Order4] , Order Backlogs[Formulations,Order4] ,IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] + Processed Orders[Formulations,Order4], Backlog Range Two[Formulations,Order4] + Backlog Range One[Formulations,Order4] + Processed Orders[Formulations,Order4],IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] , Backlog Range Two[Formulations,Order4] + Backlog Range One[Formulations,Order4] ,IF THEN ELSE(Processed Orders[Formulations,Order4] > 0 :AND: Backlog Range One[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Processed Orders[Formulations,Order4] , Backlog Range One[Formulations,Order4] + Processed Orders[Formulations,Order4] ,IF THEN ELSE(Backlog Range One[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] , Backlog Range One[Formulations,Order4] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] , Processed Orders[Formulations,Order4] , 0))))))) Description: IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Present In 2 Views: Not in View Main Model Used By	

		Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Dispatch Dispatch Drugs To Countries Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order])
ModelC	#41 C	Expiration Value (Week) Expiration Value[Capreomycin,Order Number] = 56, 0, 0, 0 Expiration Value[Kanamycin,Order Number] = 140, 0, 0, 0 Expiration Value[Cycloserine,Order Number] = 56, 0, 0, 0 Present In 2 Views: Not in View Main Model Used By Obsolete Stock
ModelC	#46 A	Incoming (Drugs/Week) Incoming[Formulations,Order1] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order1] + Order Backlogs[Formulations,Order1] , MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order1]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order1] , Processed Orders[Formulations,Order1] ,IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] + Processed Orders[Formulations,Order1], MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order1]),IF THEN ELSE(Backlog Range One[Formulations,Order1] >0 :AND: Backlog Range Two[Formulations,Order1] >0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Backlog Range Two[Formulations,Order1] , Processed Orders[Formulations,Order1] ,IF THEN ELSE(Processed Orders[Formulations,Order1] > 0 :AND: Backlog Range One[Formulations,Order1] > 0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] + Processed Orders[Formulations,Order1] , MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order1]) ,IF THEN ELSE(Backlog Range One[Formulations,Order1] > 0 :AND: Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order1] , Processed Orders[Formulations,Order1] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3]- Drugs To Be Dispatched[Formulations,Order4]> Processed Orders[Formulations,Order1] , MAX(0,Processed Orders[Formulations,Order1] - Drugs To Be Dispatched[Formulations,Order1]) , Processed Orders[Formulations,Order1])))))))

		Incoming[Formulations,Order2] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] + Order Backlogs[Formulations,Order2] , MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order2]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order2] , Processed Orders[Formulations,Order2] ,IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] + Processed Orders[Formulations,Order2], MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order2]),IF THEN ELSE(Backlog Range One[Formulations,Order2] >0 :AND: Backlog Range Two[Formulations,Order2] >0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Backlog Range Two[Formulations,Order2] , Processed Orders[Formulations,Order2] ,IF THEN ELSE(Processed Orders[Formulations,Order2] > 0 :AND: Backlog Range One[Formulations,Order2] > 0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] + Processed Orders[Formulations,Order2] , MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order2]) ,IF THEN ELSE(Backlog Range One[Formulations,Order2] > 0 :AND: Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order2] , Processed Orders[Formulations,Order2] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order2] , MAX(0,Processed Orders[Formulations,Order2] - Drugs To Be Dispatched[Formulations,Order2]) , Processed Orders[Formulations,Order2]))))))) Incoming[Formulations,Order3] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] + Order Backlogs[Formulations,Order3] , MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order3]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Order Backlogs[Formulations,Order3] , Processed Orders[Formulations,Order3] ,IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] + Processed Orders[Formulations,Order3], MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order3]),IF THEN ELSE(Backlog Range One[Formulations,Order3] >0 :AND: Backlog Range Two[Formulations,Order3] >0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Backlog Range Two[Formulations,Order3] , Processed Orders[Formulations,Order3] ,IF THEN ELSE(Processed Orders[Formulations,Order3] > 0 :AND: Backlog Range One[Formulations,Order3] > 0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be	

		Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] + Processed Orders[Formulations,Order3] , MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order3]) ,IF THEN ELSE(Backlog Range One[Formulations,Order3] > 0 :AND: Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Backlog Range One[Formulations,Order3] , Processed Orders[Formulations,Order3],IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order4] > Processed Orders[Formulations,Order3] , MAX(0,Processed Orders[Formulations,Order3] - Drugs To Be Dispatched[Formulations,Order3]) , Processed Orders[Formulations,Order3]))))))) Incoming[Formulations,Order4] = IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] + Order Backlogs[Formulations,Order4] , MAX(0,Processed Orders[Formulations,Order4] - Drugs To Be Dispatched[Formulations,Order4]) ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Order Backlogs[Formulations,Order4] , Processed Orders[Formulations,Order4] ,IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] + Processed Orders[Formulations,Order4], MAX(0,Processed Orders[Formulations,Order4] - Drugs To Be Dispatched[Formulations,Order4]),IF THEN ELSE(Backlog Range One[Formulations,Order4] >0 :AND: Backlog Range Two[Formulations,Order4] >0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Backlog Range Two[Formulations,Order4] , Processed Orders[Formulations,Order4] ,IF THEN ELSE(Processed Orders[Formulations,Order4] > 0 :AND: Backlog Range One[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] + Processed Orders[Formulations,Order4] , MAX(0,Processed Orders[Formulations,Order4] - Drugs To Be Dispatched[Formulations,Order4]) ,IF THEN ELSE(Backlog Range One[Formulations,Order4] > 0 :AND: Drugs Available For Dispatch[Formulations,Order4] > Backlog Range One[Formulations,Order4] , Processed Orders[Formulations,Order4] ,IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order4] > Processed Orders[Formulations,Order4] , MAX(0,Processed Orders[Formulations,Order4] - Drugs To Be Dispatched[Formulations,Order4]) , Processed Orders[Formulations,Order4]))))))) Description: MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order]) Present In 2 Views: Not in View Main Model Used By Order Backlogs QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0)
ModelC	#50 C	Initial Stock On Hand (Drugs) Initial Stock On Hand[Capreomycin,Order Number] = 1.19963e+06, 0, 0, 0 Initial Stock On Hand[Kanamycin,Order Number] = 1.57709e+06, 0, 0, 0 Initial Stock On Hand[Cycloserine,Order Number] = 9.15269e+06, 0, 0, 0 Description: 7997521.05139e+069.15269e+06 Present In 2 Views: Not in View Main Model

		Used By SRS Stock On Hand
ModelC	#54 C	Inventory Position (Drugs) Inventory Position[Formulations,Order1] = SRS Stock On Hand[Formulations,Order1] + SRS Supply Line[Formulations,Order1] -Order Backlogs[Formulations,Order1] - Order Backlogs[Formulations,Order2] - Order Backlogs[Formulations,Order3] - Order Backlogs[Formulations,Order4] Inventory Position[Formulations,Order2] = 0 Inventory Position[Formulations,Order3] = 0 Inventory Position[Formulations,Order4] = 0 Present In 2 Views: Not in View Main Model Used By SRS Demand
ModelC	#60 F,A	Normal Order Drugs Received By Countries (Drugs/Week) Normal Order Drugs Received By Countries[Formulations,Order Number] = Dispatch[Formulations,Order Number] Present In 1 View: Main Model Used By Normal Orders Supply Line Total Normal Order Drugs Received
ModelC	#61 F,A	Normal Orders From Countries (Drugs/Week) Normal Orders From Countries[Formulations,Order Number] = Demand Input[Formulations,Order Number] Present In 2 Views: Cost Main Model Used By Normal Orders Supply Line Order Processing
ModelC	#62 L	Normal Orders Supply Line (Drugs) Normal Orders Supply Line[Formulations,Order Number] = ∫"Normal Orders From Countries"["Formulations","Order Number"]-"Normal Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
ModelC	#63 C,F	Obsolete Stock (Drugs/Week) Obsolete Stock[Formulations,Order1] = QUEUE AGE IN RANGE(SRS Stock On Hand[Formulations,Order1] , Expiration Value[Formulations,Order1] , NAREPLACEMENT)/TIME STEP Obsolete Stock[Formulations,Order2] = 0 Obsolete Stock[Formulations,Order3] = 0 Obsolete Stock[Formulations,Order4] = 0 Present In 3 Views: Not in View Cost Main Model Used By Cumulative Obsolete Stock Drugs Available For Dispatch SRS Stock On Hand Total Obsolescence Cost
ModelC	#67 A	Order Backlogs (Drugs) Order Backlogs[Formulations,Order Number] = QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0) Description: QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(

		Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0) Present In 1 View: Main Model Used By Backlog Range One Backlog Range Two Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order]) Inventory Position
ModelC	#69 DE,A	Order Processing (Drugs/Week) Order Processing[Formulations,Order Number] = DELAY MATERIAL (Normal Orders From Countries[Formulations,Order Number], Order Processing Lead Time[Formulations,Order Number], 0, 0) Present In 1 View: Main Model Used By Processed Orders
ModelC	#70 A	Order Processing Lead Time (Week) Order Processing Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Order Processing Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(2 , 30 , 0 , 4 , 35 , 1) Present In 2 Views: Not in View Main Model Used By Order Processing
ModelC	#82 C	Order-Up-To-Level (Drugs) Order-Up-To-Level[Capreomycin,Order Number] = 1.19963e+06, 0, 0, 0 Order-Up-To-Level[Kanamycin,Order Number] = 1.57709e+06, 0, 0, 0 Order-Up-To-Level[Cycloserine,Order Number] = 9.15269e+06, 0, 0, 0 Description: 7997521.05139e+069.15269e+06 Present In 2 Views: Not in View Main Model Used By SRS Demand
ModelC	#85 F,A	Orders Placed To Manufacturer (Drugs/Week) Orders Placed To Manufacturer[Formulations,Order Number] = SRS Demand[Formulations,Order Number] Present In 1 View: Main Model

		Used By SRS Supply Line
ModelC	#89 A	Processed Orders (Drugs/Week) Processed Orders[Formulations,Order Number] = INTEGER(Order Processing[Formulations,Order Number]) Present In 1 View: Main Model Used By Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order])
ModelC	#90 A	Production & Dispatch Lead Time (Week) Production & Dispatch Lead Time[Capreomycin,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Capreomycin,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Kanamycin,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order1] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order2] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order3] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Production & Dispatch Lead Time[Cycloserine,Order4] = RANDOM TRIANGULAR(5 , 45 , 0 , 6 , 70 , 1) Present In 2 Views: Not in View Main Model Used By Production & Dispatch To SRS
ModelC	#102 DE,A	Production & Dispatch To SRS (Drugs/Week) Production & Dispatch To SRS[Formulations,Order Number] = DELAY MATERIAL (SRS Demand[Formulations,Order Number] , "Production & Dispatch Lead Time"[Formulations,Order Number] , 0 , 0) Present In 1 View: Main Model Used By Drugs Received From Manufacturer SRS Stock On Hand
ModelC	#103 A,D,T	Profile (Dmnl) Profile([(0,0)-(1,1)],(0,1),(1,1)) Main Model Used By Order Backlogs QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0) SRS Stock On Hand

ModelC	#104 C	Proportion Of Orders Placed (Dmnl) Proportion Of Orders Placed[Capreomycin,Order Number] = 0.574, 0.389, 0.255, 0.263 Proportion Of Orders Placed[Kanamycin,Order Number] = 0.45, 0.191, 0.287, 0.479 Proportion Of Orders Placed[Cycloserine,Order Number] = 0.721, 0.508, 0.412, 0.298 Present In 2 Views: Not in View Main Model Used By Demand Input
ModelC	#107 C	Reorder Frequency (Week) Reorder Frequency[Formulations,Order Number] = 1 Present In 1 View: Main Model Used By Reorder?
ModelC	#108 A	Reorder Point (Drugs/Week) Reorder Point[Capreomycin,Order Number] = 399876 + Safety Stock[Capreomycin,Order Number] Reorder Point[Kanamycin,Order Number] = 525696 + Safety Stock[Kanamycin,Order Number] Reorder Point[Cycloserine,Order Number] = 4.57634e+06 + Safety Stock[Cycloserine,Order Number] Present In 2 Views: Not in View Main Model Used By SRS Demand
ModelC	#111 A	Reorder? (Week) Reorder?[Formulations,Order Number] = MODULO(Time , Reorder Frequency[Formulations,Order Number]) Present In 1 View: Main Model Used By SRS Demand
ModelC	#112 C	Safety Stock (Drugs/Week) Safety Stock[Capreomycin,Order Number] = 33323*6 Safety Stock[Kanamycin,Order Number] = 43808*3 Safety Stock[Cycloserine,Order Number] = 381362*3 Present In 2 Views: Not in View Main Model Used By Reorder Point
ModelC	#116 A	SRS Demand (Drugs/Week) SRS Demand[Formulations,Order Number] = IF THEN ELSE("Reorder?"[Formulations,Order Number]=0 , IF THEN ELSE(Inventory Position[Formulations,Order Number]<Reorder Point[Formulations,Order Number] , (MAX(0,"Order-Up-To-Level"[Formulations,Order Number] - Inventory Position[Formulations,Order Number]))/TIME STEP, 0) , 0) Present In 2 Views: Cost Main Model Used By Orders Placed To Manufacturer Production & Dispatch To SRS Total Unit Cost
ModelC	#117 A	SRS Stock On Hand (Drugs) SRS Stock On Hand[Formulations,Order Number] = QUEUE FIFO("Production & Dispatch To SRS"[Formulations,Order Number], Obsolete Stock[Formulations,Order Number] + Dispatch Drugs To Countries[Formulations,Order Number] , Profile , Initial Stock On Hand [Formulations,Order Number] , 0) Present In 2 Views:

		Cost Main Model Used By Drugs Available For Dispatch Inventory Position Obsolete Stock
ModelC	#118 L	SRS Supply Line (Drugs) SRS Supply Line[Formulations,Order Number] = ∫"Orders Placed To Manufacturer"["Formulations","Order Number"]-"Drugs Received From Manufacturer"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By Inventory Position
ModelC	#122 L	Total Normal Order Drugs Received (Drugs) Total Normal Order Drugs Received[Formulations,Order Number] = ∫"Normal Order Drugs Received By Countries"["Formulations","Order Number"] *dt* + 0.0 Present In 1 View: Main Model Used By
ModelC	#125 A	Uniform (Dmnl) Uniform[Capreomycin,Order Number] = RANDOM 0 1() Uniform[Kanamycin,Order Number] = (RANDOM 0 1()) Uniform[Cycloserine,Order Number] = RANDOM 0 1() Present In 2 Views: Not in View Main Model Used By Demand Input
ModelC	#128 A	Weibull Distribution (Drugs/Week) Weibull Distribution[Capreomycin,Order Number] = RANDOM WEIBULL(78 , 448000 , 0.6161 , 78 , 32500 , 0) Weibull Distribution[Kanamycin,Order Number] = RANDOM WEIBULL(450 , 882000 ,0.4525 , 450 , 50000 , 1) Weibull Distribution[Cycloserine,Order Number] = RANDOM WEIBULL(1500 , 9.4491e+06 , 0.4755 , 1500 , 420000 , 1) Present In 2 Views: Not in View Main Model Used By Demand Input
Top	(Type) Subscripts (2 Variables)	
Group	Type	*Variable Name And Description*
ModelC	#45 Sub	Formulations () Formulations:Capreomycin, Kanamycin, Cycloserine Present In 2 Views: Cost Main Model Used By Backlog Range One Backlog Range Two Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Country Dispatch Lead Time Cumulative Obsolete Stock Cumulative Total Obsolescence Cost Cumulative Total Unit Cost Demand Input Dispatch Dispatch Drugs To Countries Drugs Available For Dispatch

		Drugs Received From Manufacturer Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Expiration Value Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order]) Initial Stock On Hand 7997521.05139e+069.15269e+06 Inventory Position Normal Order Drugs Received By Countries Normal Orders From Countries Normal Orders Supply Line Obsolete Stock Order Backlogs QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0) Order Processing Order Processing Lead Time Order-Up-To-Level 7997521.05139e+069.15269e+06 Orders Placed To Manufacturer Per Unit Cost Processed Orders Production & Dispatch Lead Time Production & Dispatch To SRS Proportion Of Orders Placed Reorder Frequency Reorder Point Reorder? SRS Demand SRS Stock On Hand SRS Supply Line Total Costs Total Normal Order Drugs Received Total Obsolescence Cost Total Unit Cost Uniform Weibull Distribution
ModelC	#68 Sub	Order Number () Order Number:Order1, Order2, Order3, Order4 Present In 2 Views: Cost Main Model Used By Backlog Range One Backlog Range Two Backlog Reduction MAX(0,Drugs To Be Dispatched[Formulations,Order] - Processed Orders[Formulations,Order]) Country Dispatch Lead Time Cumulative Obsolete Stock Cumulative Total Obsolescence Cost Cumulative Total Unit Cost Demand Input Dispatch Dispatch Drugs To Countries

		Drugs Received From Manufacturer Drugs To Be Dispatched IF THEN ELSE(Drugs Available For Dispatch[Formulations,Order1] > Processed Orders[Formulations,Order1] , Processed Orders[Formulations,Order1] , 0) Expiration Value Incoming MAX(0,Processed Orders[Formulations,Order] - Drugs To Be Dispatched[Formulations,Order]) Initial Stock On Hand 7997521.05139e+069.15269e+06 Inventory Position Normal Order Drugs Received By Countries Normal Orders From Countries Normal Orders Supply Line Obsolete Stock Order Backlogs QUEUE FIFO(Incoming[Formulations,Order Number], Backlog Reduction[Formulations,Order Number] , Profile , 0 , 0)QUEUE FIFO ATTRIB(_inflow_ , _outflow_ , _attrib_ , _changerate_ , _initprofile_ , _iattribprof_ , _inittotal_ , _initattrib_ , _initage_)QUEUE FIFO ATTRIB(Incoming[Formulations,Order Number] , Backlog Reduction[Formulations,Order Number] , inatt[Formulations,Order Number] , 1 , Profile , Profile , 0 , -1000 , 0) Order Processing Order Processing Lead Time Order-Up-To-Level 7997521.05139e+069.15269e+06 Orders Placed To Manufacturer Per Unit Cost Processed Orders Production & Dispatch Lead Time Production & Dispatch To SRS Proportion Of Orders Placed Reorder Frequency Reorder Point Reorder? SRS Demand SRS Stock On Hand SRS Supply Line Safety Stock Total Normal Order Drugs Received Total Obsolescence Cost Total Unit Cost Uniform Weibull Distribution

All Variables (51)

Group	Type	Variable
ModelC	A	Backlog Range One (Drugs/Week)
ModelC	A	Backlog Range Two (Drugs/Week)
ModelC	A	Backlog Reduction (Drugs/Week)
ModelC	A	Country Dispatch Lead Time (Week)
ModelC	L	Cumulative Obsolete Stock (Drugs)
ModelC	L	Cumulative Total Obsolescence Cost (Dollar)
ModelC	L	Cumulative Total Unit Cost (Dollar)
ModelC	A	Demand Input (Drugs/Week)
ModelC	A	Dispatch Drugs To Countries (Drugs/Week)
ModelC	DE,A	Dispatch (Drugs/Week)
ModelC	A	Drugs Available For Dispatch (Drugs/Week)
ModelC	F,A	Drugs Received From Manufacturer (Drugs/Week)
ModelC	A	Drugs To Be Dispatched (Drugs/Week)

ModelC	C	Expiration Value (Week)
.Control	C	FINAL TIME (Week)
ModelC	A	Incoming (Drugs/Week)
ModelC	C	Initial Stock On Hand (Drugs)
.Control	C	INITIAL TIME (Week)
ModelC	A	Inventory Position (Drugs)
ModelC	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelC	F,A	Normal Orders From Countries (Drugs/Week)
ModelC	L	Normal Orders Supply Line (Drugs)
ModelC	F,A	Obsolete Stock (Drugs/Week)
ModelC	A	Order Backlogs (Drugs)
ModelC	A	Order Processing Lead Time (Week)
ModelC	DE,A	Order Processing (Drugs/Week)
ModelC	C	Order-Up-To-Level (Drugs)
ModelC	F,A	Orders Placed To Manufacturer (Drugs/Week)
ModelC	C	Per Unit Cost (Dollar/Drugs)
ModelC	A	Processed Orders (Drugs/Week)
ModelC	A	Production & Dispatch Lead Time (Week)
ModelC	DE,A	Production & Dispatch To SRS (Drugs/Week)
ModelC	A,D,T	Profile (Dmnl)
ModelC	C	Proportion Of Orders Placed (Dmnl)
ModelC	C	Reorder Frequency (Week)
ModelC	A	Reorder Point (Drugs/Week)
ModelC	A	Reorder? (Week)
ModelC	C	Safety Stock (Drugs/Week)
.Control	A	SAVEPER (Week)
ModelC	A	SRS Demand (Drugs/Week)
ModelC	A	SRS Stock On Hand (Drugs)
ModelC	L	SRS Supply Line (Drugs)
.Control	C	TIME STEP (Week)
ModelC	A	Total Costs (Dollar)
ModelC	L	Total Normal Order Drugs Received (Drugs)
ModelC	F,A	Total Obsolescence Cost (Dollar/Week)
ModelC	F,A	Total Unit Cost (Dollar/Week)
ModelC	A	Uniform (Dmnl)
ModelC	A	Weibull Distribution (Drugs/Week)

Undocumented Variables (42)

Group	Type	Variable
ModelC	A	Backlog Range One (Drugs/Week)
ModelC	A	Backlog Range Two (Drugs/Week)
ModelC	A	Country Dispatch Lead Time (Week)
ModelC	L	Cumulative Obsolete Stock (Drugs)
ModelC	L	Cumulative Total Obsolescence Cost (Dollar)
ModelC	L	Cumulative Total Unit Cost (Dollar)
ModelC	A	Demand Input (Drugs/Week)
ModelC	A	Dispatch Drugs To Countries (Drugs/Week)
ModelC	DE,A	Dispatch (Drugs/Week)
ModelC	A	Drugs Available For Dispatch (Drugs/Week)
ModelC	F,A	Drugs Received From Manufacturer (Drugs/Week)
ModelC	C	Expiration Value (Week)
ModelC	Sub	Formulations ()
ModelC	A	Inventory Position (Drugs)

ModelC	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelC	F,A	Normal Orders From Countries (Drugs/Week)
ModelC	L	Normal Orders Supply Line (Drugs)
ModelC	F,A	Obsolete Stock (Drugs/Week)
ModelC	Sub	Order Number ()
ModelC	A	Order Processing Lead Time (Week)
ModelC	DE,A	Order Processing (Drugs/Week)
ModelC	F,A	Orders Placed To Manufacturer (Drugs/Week)
ModelC	C	Per Unit Cost (Dollar/Drugs)
ModelC	A	Processed Orders (Drugs/Week)
ModelC	A	Production & Dispatch Lead Time (Week)
ModelC	DE,A	Production & Dispatch To SRS (Drugs/Week)
ModelC	A,D,T	Profile (Dmnl)
ModelC	C	Proportion Of Orders Placed (Dmnl)
ModelC	C	Reorder Frequency (Week)
ModelC	A	Reorder Point (Drugs/Week)
ModelC	A	Reorder? (Week)
ModelC	C	Safety Stock (Drugs/Week)
ModelC	A	SRS Demand (Drugs/Week)
ModelC	A	SRS Stock On Hand (Drugs)
ModelC	L	SRS Supply Line (Drugs)
ModelC	A	Total Costs (Dollar)
ModelC	L	Total Normal Order Drugs Received (Drugs)
ModelC	F,A	Total Obsolescence Cost (Dollar/Week)
ModelC	F,A	Total Unit Cost (Dollar/Week)
ModelC	A	Uniform (Dmnl)
ModelC	A	Weibull Distribution (Drugs/Week)

Stock Variables (6)

Group	Type	Variable
ModelC	L	Cumulative Obsolete Stock (Drugs)
ModelC	L	Cumulative Total Obsolescence Cost (Dollar)
ModelC	L	Cumulative Total Unit Cost (Dollar)
ModelC	L	Normal Orders Supply Line (Drugs)
ModelC	L	SRS Supply Line (Drugs)
ModelC	L	Total Normal Order Drugs Received (Drugs)

State Variables (9)

Group	Type	Variable
ModelC	L	Cumulative Obsolete Stock (Drugs)
ModelC	L	Cumulative Total Obsolescence Cost (Dollar)
ModelC	L	Cumulative Total Unit Cost (Dollar)
ModelC	DE,A	Dispatch (Drugs/Week)
ModelC	L	Normal Orders Supply Line (Drugs)
ModelC	DE,A	Order Processing (Drugs/Week)
ModelC	DE,A	Production & Dispatch To SRS (Drugs/Week)
ModelC	L	SRS Supply Line (Drugs)
ModelC	L	Total Normal Order Drugs Received (Drugs)

Variables without Predefined Min or Max Values (47)

Group	Type	Variable
ModelC	A	Backlog Range One (Drugs/Week)
ModelC	A	Backlog Range Two (Drugs/Week)

ModelC	A	Backlog Reduction (Drugs/Week)
ModelC	A	Country Dispatch Lead Time (Week)
ModelC	L	Cumulative Obsolete Stock (Drugs)
ModelC	L	Cumulative Total Obsolescence Cost (Dollar)
ModelC	L	Cumulative Total Unit Cost (Dollar)
ModelC	A	Demand Input (Drugs/Week)
ModelC	A	Dispatch Drugs To Countries (Drugs/Week)
ModelC	DE,A	Dispatch (Drugs/Week)
ModelC	A	Drugs Available For Dispatch (Drugs/Week)
ModelC	F,A	Drugs Received From Manufacturer (Drugs/Week)
ModelC	A	Drugs To Be Dispatched (Drugs/Week)
ModelC	C	Expiration Value (Week)
ModelC	A	Incoming (Drugs/Week)
ModelC	C	Initial Stock On Hand (Drugs)
ModelC	A	Inventory Position (Drugs)
ModelC	F,A	Normal Order Drugs Received By Countries (Drugs/Week)
ModelC	F,A	Normal Orders From Countries (Drugs/Week)
ModelC	L	Normal Orders Supply Line (Drugs)
ModelC	F,A	Obsolete Stock (Drugs/Week)
ModelC	A	Order Backlogs (Drugs)
ModelC	A	Order Processing Lead Time (Week)
ModelC	DE,A	Order Processing (Drugs/Week)
ModelC	C	Order-Up-To-Level (Drugs)
ModelC	F,A	Orders Placed To Manufacturer (Drugs/Week)
ModelC	C	Per Unit Cost (Dollar/Drugs)
ModelC	A	Processed Orders (Drugs/Week)
ModelC	A	Production & Dispatch Lead Time (Week)
ModelC	DE,A	Production & Dispatch To SRS (Drugs/Week)
ModelC	A,D,T	Profile (Dmnl)
ModelC	C	Proportion Of Orders Placed (Dmnl)
ModelC	C	Reorder Frequency (Week)
ModelC	A	Reorder Point (Drugs/Week)
ModelC	A	Reorder? (Week)
ModelC	C	Safety Stock (Drugs/Week)
ModelC	A	SRS Demand (Drugs/Week)
ModelC	A	SRS Stock On Hand (Drugs)
ModelC	L	SRS Supply Line (Drugs)
ModelC	A	Total Costs (Dollar)
ModelC	L	Total Normal Order Drugs Received (Drugs)
ModelC	F,A	Total Obsolescence Cost (Dollar/Week)
ModelC	F,A	Total Unit Cost (Dollar/Week)
ModelC	A	Uniform (Dmnl)
ModelC	A	Weibull Distribution (Drugs/Week)

Positive Polarity Causal Links (28)

Cause	Effect	Polarity
Cumulative Total Obsolescence Cost	Total Costs	+
Cumulative Total Unit Cost	Total Costs	+
Demand Input	Normal Orders From Countries	+
Dispatch	Normal Order Drugs Received By Countries	+
Drugs To Be Dispatched	Backlog Reduction	+
Drugs To Be Dispatched	Dispatch Drugs To Countries	+
Normal Order Drugs Received By Countries	Total Normal Order Drugs Received	+

Normal Orders From Countries	Normal Orders Supply Line	+
Obsolete Stock	Cumulative Obsolete Stock	+
Obsolete Stock	Drugs Available For Dispatch	+
Obsolete Stock	Total Obsolescence Cost	+
Order-Up-To-Level	SRS Demand	+
Orders Placed To Manufacturer	SRS Supply Line	+
Per Unit Cost	Total Obsolescence Cost	+
Per Unit Cost	Total Unit Cost	+
Production & Dispatch To SRS	Drugs Received From Manufacturer	+
Safety Stock	Reorder Point	+
SRS Demand	Orders Placed To Manufacturer	+
SRS Demand	Total Unit Cost	+
SRS Stock On Hand	Drugs Available For Dispatch	+
SRS Stock On Hand	Inventory Position	+
SRS Supply Line	Inventory Position	+
TIME STEP	Drugs Available For Dispatch	+
TIME STEP	SAVEPER	+
TIME STEP	SRS Demand	+
Total Obsolescence Cost	Cumulative Total Obsolescence Cost	+
Total Unit Cost	Cumulative Total Unit Cost	+
Weibull Distribution	Demand Input	+

Negative Polarity Causal Links (5)

Cause	Effect	Polarity
Drugs Received From Manufacturer	SRS Supply Line	-
Drugs To Be Dispatched	Incoming	-
Inventory Position	SRS Demand	-
Normal Order Drugs Received By Countries	Normal Orders Supply Line	-
Order Backlogs	Inventory Position	-

Function-based Polarity Causal Links (47)

Cause	Effect	Polarity
Backlog Range One	Backlog Reduction	If Then Else Switch
Backlog Range One	Drugs To Be Dispatched	If Then Else Switch
Backlog Range One	Incoming	If Then Else Switch
Backlog Range Two	Backlog Reduction	If Then Else Switch
Backlog Range Two	Drugs To Be Dispatched	If Then Else Switch
Backlog Range Two	Incoming	If Then Else Switch
Backlog Reduction	Order Backlogs	Function[QUEUEFIFO]
Country Dispatch Lead Time	Dispatch	Function[DELAYMATERIAL]
Demand Input	Demand Input	If Then Else Switch
Dispatch Drugs To Countries	SRS Stock On Hand	Function[QUEUEFIFO]
Drugs Available For Dispatch	Backlog Reduction	If Then Else Switch
Drugs Available For Dispatch	Drugs To Be Dispatched	If Then Else Switch
Drugs Available For Dispatch	Incoming	If Then Else Switch
Drugs To Be Dispatched	Dispatch	Function[DELAYMATERIAL]

Drugs To Be Dispatched	Drugs To Be Dispatched	If Then Else Switch
Expiration Value	Obsolete Stock	Function[QUEUEAGEINRANGE]
Incoming	Order Backlogs	Function[QUEUEFIFO]
Initial Stock On Hand	SRS Stock On Hand	Function[QUEUEFIFO]
NAREPLACEMENT	Backlog Range One	Function[QUEUEAGEOLDEST,QUEUEAGEINRANGE]
NAREPLACEMENT	Obsolete Stock	Function[QUEUEAGEINRANGE]
Normal Orders From Countries	Order Processing	Function[DELAYMATERIAL]
Obsolete Stock	SRS Stock On Hand	Function[QUEUEFIFO]
Order Backlogs	Backlog Range One	Function[QUEUEAGEOLDEST,QUEUEAGEINRANGE]
Order Backlogs	Backlog Range Two	Function[QUEUEAGEOLDEST,QUEUEAGEINRANGE]
Order Backlogs	Backlog Reduction	If Then Else Switch
Order Backlogs	Drugs To Be Dispatched	If Then Else Switch
Order Backlogs	Incoming	If Then Else Switch
Order Processing	Processed Orders	Function[INTEGER]
Order Processing Lead Time	Order Processing	Function[DELAYMATERIAL]
Processed Orders	Backlog Reduction	If Then Else Switch
Processed Orders	Drugs To Be Dispatched	If Then Else Switch
Processed Orders	Incoming	If Then Else Switch
Production & Dispatch Lead Time	Production & Dispatch To SRS	Function[DELAYMATERIAL]
Production & Dispatch To SRS	SRS Stock On Hand	Function[QUEUEFIFO]
Profile	Order Backlogs	Function[QUEUEFIFO]
Profile	SRS Stock On Hand	Function[QUEUEFIFO]
Proportion Of Orders Placed	Demand Input	If Then Else Switch
Reorder Frequency	Reorder?	Function[MODULO]
Reorder Point	SRS Demand	If Then Else Switch
Reorder?	SRS Demand	If Then Else Switch
SRS Demand	Production & Dispatch To SRS	Function[DELAYMATERIAL]
SRS Stock On Hand	Obsolete Stock	Function[QUEUEAGEINRANGE]
Time	Reorder?	Function[MODULO]
TIME STEP	Obsolete Stock	Function[QUEUEAGEINRANGE]
Uniform	Demand Input	If Then Else Switch

View-Variable Profile

View	View-Variable Profile
Cost	10 vars (18.2%)
Main Model	41 vars (74.5%)

List Of 2 views and their 47 Variables

	Cost	Main Model	
Total:	10	41	Total:
Total Normal Order Drugs Received (In 1 View)			Total Normal Order Drugs Received (In 1 View)
Proportion Of Orders Placed (In 1 View)			Proportion Of Orders Placed (In 1 View)

Obsolete Stock (In 2 Views)			Obsolete Stock (In 2 Views)
SRS Stock On Hand (In 2 Views)			SRS Stock On Hand (In 2 Views)
Order-Up-To-Level (In 1 View)			Order-Up-To-Level (In 1 View)
Processed Orders (In 1 View)			Processed Orders (In 1 View)
Safety Stock (In 1 View)			Safety Stock (In 1 View)
Dispatch (In 1 View)			Dispatch (In 1 View)
Normal Orders Supply Line (In 1 View)			Normal Orders Supply Line (In 1 View)
Uniform (In 1 View)			Uniform (In 1 View)
Backlog Range Two (In 1 View)			Backlog Range Two (In 1 View)
Dispatch Drugs To Countries (In 1 View)			Dispatch Drugs To Countries (In 1 View)
Backlog Reduction (In 1 View)			Backlog Reduction (In 1 View)
Profile (In 1 View)			Profile (In 1 View)
Reorder Point (In 1 View)			Reorder Point (In 1 View)
Reorder? (In 1 View)			Reorder? (In 1 View)
Order Processing Lead Time (In 1 View)			Order Processing Lead Time (In 1 View)
Order Backlogs (In 1 View)			Order Backlogs (In 1 View)
Demand Input (In 1 View)			Demand Input (In 1 View)
Normal Order Drugs Received By Countries (In 1 View)			Normal Order Drugs Received By Countries (In 1 View)
Country Dispatch Lead Time (In 1 View)			Country Dispatch Lead Time (In 1 View)
Production & Dispatch To SRS (In 1 View)			Production & Dispatch To SRS (In 1 View)
Reorder Frequency (In 1 View)			Reorder Frequency (In 1 View)
Drugs Received From Manufacturer (In 1 View)			Drugs Received From Manufacturer (In 1 View)
Order Processing (In 1 View)			Order Processing (In 1 View)
Drugs Available For Dispatch (In 1 View)			Drugs Available For Dispatch (In 1 View)
Expiration Value (In 1 View)			Expiration Value (In 1 View)
Orders Placed To Manufacturer (In 1 View)			Orders Placed To Manufacturer (In 1 View)
Weibull Distribution (In 1 View)			Weibull Distribution (In 1 View)
Incoming (In 1 View)			Incoming (In 1 View)
Production & Dispatch Lead Time (In 1 View)			Production & Dispatch Lead Time (In 1 View)
SRS Demand (In 2 Views)			SRS Demand (In 2 Views)
Normal Orders From Countries (In 2 Views)			Normal Orders From Countries (In 2 Views)
Backlog Range One (In 1 View)			Backlog Range One (In 1 View)
Cumulative Obsolete Stock (In 1 View)			Cumulative Obsolete Stock (In 1 View)
Inventory Position (In 1 View)			Inventory Position (In 1 View)
SRS Supply Line (In 1 View)			SRS Supply Line (In 1 View)
Drugs To Be Dispatched (In 1 View)			Drugs To Be Dispatched (In 1 View)
Initial Stock On Hand (In 1 View)			Initial Stock On Hand (In 1 View)
Total Unit Cost (In 1 View)			Total Unit Cost (In 1 View)
Total Obsolescence Cost (In 1 View)			Total Obsolescence Cost (In 1 View)
Per Unit Cost (In 1 View)			Per Unit Cost (In 1 View)
Total Costs (In 1 View)			Total Costs (In 1 View)
Cumulative Total Unit Cost (In 1 View)			Cumulative Total Unit Cost (In 1 View)
Cumulative Total Obsolescence Cost (In 1 View)			Cumulative Total Obsolescence Cost (In 1 View)
Total:	10	41	Total:
	Cost	Main Model	

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Report Created On Sat Nov 19 12:52:05 SAST 2016
SDM-Doc Tool Version 1.2.44
Global Security Sciences Division
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