Designing the main characteristics and structure of the upstream supply chain of caffeine to Malawi's neonatal care system

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Master of Science Thesis

TU Delft Delft University of Technology

Transport, Infrastructure and Logistics

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March 4, 2026

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Project duration:	September, 2025 – March, 2026	
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MSc Transport, Infrastructure and Logistics · Delft University of Technology

The work in this Master thesis was supported by Erasmus MC. Their cooperation is gratefully acknowledged.

Acknowledgements

This thesis was completed as part of the MSc programme in Transport, Infrastructure and Logistics at TU Delft, and would not have been possible without the guidance and support of several people.

I would like to thank my supervisors. At TU Delft, Arjan van Binsbergen and Saba Hinrichs-Krapels provided sharp feedback, constructive direction, and the freedom to shape the research into a coherent report. From Erasmus Medical Centre, Kelly Storm supported the project with dedicated supervision and helped connect the research to clinical practice within the neonatal department.

I would also like to thank everyone who contributed through interviews, feedback, and practical support along the way. Your input helped make this research enjoyable, educational, and achievable. Lastly, I would like to give a special acknowledgement to caffeine itself, which proved to be an essential companion during the final days of completing this thesis.

N.C. Cornelissen
Delft, March 4, 2026

Summary

Sub-Saharan Africa (SSA) continues to face one of the world's highest neonatal mortality rates, with apnea of prematurity (AOP) being a significant contributor (WHO 2024). Caffeine is internationally recognized as the first-line pharmacological treatment for AOP and has already been included on the World Health Organization's Model List of Essential Medicines (WHO 2023). Despite this global endorsement, caffeine remains absent from Malawi's Essential Medicines List and unregistered by the national regulatory authority. As a result, the medicine is structurally excluded from national procurement systems, leaving neonatal units dependent on alternatives such as aminophylline, which is less favorable than caffeine due to its narrower therapeutic window and the associated need for therapeutic drug monitoring (Nabwera et al. 2021). Even in SSA countries where caffeine is available, procurement prices can be high and supply can remain unreliable, indicating that access is constrained by both affordability and availability rather than clinical effectiveness.

This thesis addresses the upstream supply chain challenge underlying this access gap: how caffeine could be introduced and sustained in Malawi under low volumes, constrained institutional capacity, and high exposure to financial and coordination frictions. The objective is therefore to investigate the main characteristics and supply structure of the upstream supply chain for caffeine, so that it can help to enable access to Malawi's neonatal care system, with affordability assessed through key upstream cost drivers. The main research question therefore is:
How can the main characteristics and structure of the upstream supply chain of caffeine be designed to enable access to Malawi's neonatal care system?

Methodology

The research follows a design-oriented approach structured around three phases: analysis, design, and evaluation. First, Malawi's current pharmaceutical supply chain was mapped using aminophylline as a proxy, highlighting a strong dependence on Asian manufacturers. This was complemented by a comparative review of caffeine supply chains in selected SSA countries where caffeine is already available. The review suggests a relatively concentrated upstream supplier base, while procurement and execution arrangements differ substantially across countries (e.g., the degree of donor involvement, the extent of managed execution, and observed price levels). These comparisons indicate that supply chain structure is likely to affect cost and, ultimately, affordability, making cost considerations central to the analysis.

Next, the thesis identified upstream cost drivers that influence pharmaceutical prices: economies of scale, dedicated versus pooled supply chains, demand uncertainty, chain complexity, financial risk, regulatory burden, and distribution trade-offs. These insights were

translated into design objectives to guide the development of alternative supply chain archetypes. Because demand uncertainty and financial risk cannot realistically be eliminated through supply chain design in this context, they were treated as exogenous conditions that the alternatives must be able to cope with, rather than as objectives. This resulted in five design objectives: scale potential, fragmentation, transactional efficiency, chain complexity, and logistics cost balance.

Building on these inputs, the design space was generated through morphological analysis. The upstream supply chain was decomposed into key functions relevant to the Malawian context, quantification and sourcing, ordering and procurement, and supply and distribution, and feasible options were defined for each function (see Figure 1) (Initiative 2024).

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled procurement
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent/wholesaler	Regional hub consolidation

Figure 1: Initial morphological chart

After applying feasibility constraints, incompatibility rules, and several iterations of categorising configurations by governance level, sourcing mode, and financing approach, the remaining options were clustered and consolidated into four representative design alternatives, summarised in Table 1 and visualized in Figure 2. Because the aim was to explore the full range of plausible upstream design choices, the four alternatives were deliberately constructed to be clearly distinct, each representing a different configuration logic and trade-off profile.

Design alternative	Description
1: Donor pipeline	Donor-funded, single-source procurement via an agent/wholesaler, with direct shipment to Malawi; represents the status quo set-up and serves as the baseline for cost and disruption risk.
2: Managed multi-sourcing	Dual/multi-sourcing under a long-term contract, coordinated by an agent; reduces supplier dependency and disruption risk while keeping governance and execution manageable.
3: Regional pooling & logistics hub	Pooled regional demand and bundled procurement, with a regional hub for consolidation and onward distribution; targets scale advantages but adds coordination and additional control points.
4: Government-core	Financing and payment shift to the Malawian government budget to increase ownership and decision control; procurement remains centralized and relatively simple to keep implementability feasible.

Table 1: Design alternatives.

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(a) Alternative 1: Donor pipeline

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(b) Alternative 2: Managed multi-sourcing

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(c) Alternative 3: Regional logistic hub

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(d) Alternative 4: Government core

Figure 2: Design alternatives for the upstream supply chain configurations

After the design space was generated, configurations were screened against the design constraints and feasibility requirements. In addition, a plausibility check was conducted through a semi-structured validation interview with a representative of the Access to Medicine Foundation. This interview served to confirm the relevance of the identified upstream cost drivers and to validate whether the selected functions and options in the morphological chart were realistic and complete.

Finally, the four archetypes were evaluated using a structured multi-criteria assessment based on performance matrices and direct pairwise comparisons across five criteria derived from the design objectives. Because reliable quantitative input data were insufficient to support a traditional quantitative MCA or cost–benefit analysis, the evaluation relied on an anchored 1–5 scoring scale and scenario-dependent performance judgements rather than detailed data modelling.

To assess robustness, the assessment was conducted for a base case and two stress scenarios reflecting exogenous risk factors that are widely reported as relevant in the Malawian context: financing instability (e.g., foreign-currency shortages and reduced payment reliability) and low data reliability and transparency. These scenarios were selected as minimum-relevant stress conditions that the designs should be able to handle. Across the base case and both scenarios, the set of alternatives and evaluation criteria was kept constant; only the performance scores were adjusted to reflect scenario-specific impacts.

The evaluation started with the performance matrices, as can be seen in Tables 2, 3, 4. For each matrix (base case and both scenarios), every alternative was scored against each criterion. Since stakeholder input to determine relative criterion importance was not available, all five criteria were assigned equal weights as a baseline assumption.

Base case

Base case	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	4	2
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	3	3	4	2

Table 2: Performance matrix for the base case.

Scenario 1: Financing instability

Scenario 1: Financing instability	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	5	1
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	2	3	4	1

Table 3: Performance matrix for Scenario 1: Financing instability.

Scenario 2: Low data reliability & transparency

Scenario 2: Low data reliability & transparency	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	3	2
C4: Chain complexity	3	2	1	4
C5: Logistics cost balance	2	3	3	2

Table 4: Performance matrix for Scenario 2: Low data reliability & transparency.

Secondly, a direct pairwise comparison was carried out to translate the performance-matrix scores into an overall preference ordering, as can be seen in Tables 5, 6 and 7. For each criterion, alternatives were compared two at a time using their scores: the alternative with the higher score was recorded as the preferred option for that criterion (a tie was recorded when scores were equal). Repeating this across all criteria and combining these pairwise results, an overall ranking of the four alternatives was obtained.

Base case

Outcome: $3 \,\&\, 1 > 2 > 4$

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	A1	A2	A1	∼	A1
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	∼	A2	A3	∼
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 5: Direct pairwise comparison outcomes for the base case.

Scenario 1: financing instability

Outcome: $3 > 1 \,\&\, 2 > 4$.

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	1	2	1	2	∼
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	A3	A2	A3	A3
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 6: Direct pairwise comparison outcomes for Scenario 1: Financing instability.

Scenario 2: Low Data Reliability & Transparency

Outcome: $2 > 3 > 1 \,\&\, 4$.

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	A1	A2	A1	A2	A2
A1 vs A3	A3	A1	∼	A1	A3	∼
A1 vs A4	A1	A4	A1	A4	∼	∼
A2 vs A3	A3	A2	A2	A2	∼	A2
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 7: Direct pairwise comparison outcomes for Scenario 2: Low data reliability & transparency

Key findings

The MCA shows that no single configuration dominates across all conditions; rankings shift across scenarios. In the base case, Alternatives 1 and 3 perform best ($3 \,\&\, 1 > 2 > 4$). Under financing instability, Alternative 3 ranks highest ($3 > 1 \,\&\, 2 > 4$). Under low data reliability and transparency, Alternative 2 ranks highest ($2 > 3 > 1 \,\&\, 4$).

Despite this scenario sensitivity, Alternative 3 (regional pooling with a logistics hub) emerges as the preferred overall design performing most consistently across conditions. The results indicate that consolidation of volumes and execution strengthens affordability-related cost drivers and upstream continuity, particularly when financing conditions deteriorate. Under conditions of limited transparency and unreliable reporting, Alternative 2 performs best,

indicating that supply chain designs with fewer coordination interfaces are more resilient when cross-actor communication breaks down.

The study has also shown that in data-scarce settings, a design-oriented approach provides a practical way to develop and compare upstream supply chain configurations while avoiding over-reliance on certain quantitative inputs. However, the absence of detailed numerical inputs means that the assessment relies more on structured expert judgement and assumption-driven scoring, which reduces numerical outcomes and makes sensitivity to assumptions more important.

Limitations

This study is subject to several limitations that should be considered when interpreting the results.

The evaluation is intentionally ordinal. The pairwise comparison and anchored 1–5 scoring enable a structured assessment without suggesting false numerical precision, but results still depend on qualitative judgement in the scoring and the aggregation logic. Criterion weights were set equal as a baseline assumption because stakeholder input to justify differential weights was not available; rankings may therefore shift under alternative stakeholder priorities.

In terms of the design space, only four configurations were taken forward to the MCA. While the morphological analysis generates many feasible combinations, the study necessarily focused on a manageable subset. The findings should therefore be interpreted as directional rather than exhaustive, and other viable (or superior) configurations may exist outside the selected set.

Regarding scope, the analysis focuses primarily on upstream supply chain design (manufacturing origin, procurement, contracting, and distribution up to national receipt). Downstream elements, such as last-mile distribution, facility-level storage, and clinical usage practices, were not analysed in detail, even though they can materially affect effective availability within neonatal care.

Affordability was primarily assessed through upstream cost-driver mechanisms. Non-cost factors that can shape access in practice (e.g., political constraints, organisational culture, and implementation capacity) were not used, which may limit how well the results translate to real-world feasibility.

In terms of robustness testing, only two stress scenarios were assessed (financing instability and low data reliability/transparency). While both are context-relevant, they do not cover less common but plausible disruptions, so relative performance may change under other conditions.

For validation, the study relied on a single semi-structured expert interview as a plausibility check. Although this supported the realism of the functional choices and the relevance of the identified drivers, it does not constitute comprehensive validation; additional stakeholder perspectives and interviews would strengthen confidence in the assumptions, scoring, and rankings.

Finally, the morphological chart was effective for structuring the design space, but its largely text-based representation is less visually expressive than ideal for communicating supply chain designs. More explicit visualisations of actors, flows, and interfaces could improve readability and make differences between configurations easier to compare.

Recommendations for future research

Based on the findings of this study, several directions for future research emerge to strengthen the evidence base and improve the practical relevance of the proposed caffeine supply chain design for Malawi.

First, future work should prioritize the collection of additional empirical data to enable a more quantitative assessment of the proposed alternatives. In particular, more detailed data on cost drivers (e.g., manufacturing and compounding costs, minimum order quantities, transport tariffs and warehousing and inventory holding costs) would allow the current semi-qualitative analysis to be extended into a more robust cost and sensitivity analysis. This would increase both the realism of the case study and the credibility of conclusions about affordability.

A next step could be to strengthen the empirical foundation so that the evaluation can move beyond a semi-qualitative assessment. More detailed data on key cost drivers, such as manufacturing/compounding costs, minimum order quantities, transport tariffs, warehousing fees, and inventory holding costs, would make it possible to perform a more explicit cost analysis and sensitivity testing. This would improve the realism of the case study and make conclusions about affordability more robust.

In addition, future work could broaden the focus beyond cost drivers alone. While affordability is central, other determinants of access also shape what is feasible in practice, such as regulatory constraints, organisational capacity, governance and coordination arrangements, and implementation barriers. Bringing these factors into the design and evaluation would provide a more complete view of what enables (or blocks) access.

Another important direction is to extend the scope downstream. This thesis mainly considers upstream procurement and international supply pathways, but in-country distribution, storage conditions, stock management, and last-mile delivery to neonatal units can strongly affect effective availability. Including the downstream segment would enable an end-to-end assessment, reveal additional bottlenecks, and capture downstream cost components that may materially affect overall affordability.

Finally, future studies would benefit from broader and deeper stakeholder engagement. Additional semi-structured interviews with actors such as manufacturers/suppliers, the PMRA, professional associations, donors, and implementing partners would strengthen the assessment of feasibility and institutional fit. These interviews could also be used to provide stronger validation than was possible in this study, and elicit relative priorities across evaluation criteria (supporting more grounded weighting in the MCA).

Conclusion

This thesis demonstrates how a design-oriented approach can be applied to develop and evaluate alternative upstream supply chain configurations for caffeine to Malawi. The evaluation indicates that regional pooling with bundled logistics and coordinated execution is the most aligned option for addressing key cost drivers and continuity risks in a thin market. Although implementation depends on multiple factors such as governance and coordination capacity, the results provide actionable direction for stakeholders seeking to expand feasible access to caffeine for neonatal care.

Table of Contents

Glossary

List of Acronyms

Acronym	Definition
AMA	African Medicines Agency
AOP	Apnea of Prematurity
API	Active Pharmaceutical Ingredient
BPMN	Business Process Model and Notation
CHAI	Clinton Health Access Initiative
CHAM	Christian Health Association of Malawi
CMS	Central Medical Store
CMST	Central Medical Stores Trust
DDM	Double Diamond Model
EFDA	Ethiopian Food and Drug Authority
EMA	European Medicine Agency
EML	Essential Medicines List
EOI	Expression of Interest
EPSA	Ethiopian Pharmaceuticals Supply Agency
FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practice
GPO	Group Purchasing Organization
HMF	Healthy Market Frameworks
IV	Intravenous
JMS	Joint Medical Stores
KEML	Kenya Essential Medicines List
KEMSA	Kenya Medical Supplies Authority
LMIC	Low- and Middle-Income Country
MAH	Marketing Authorization Holder
MCA	Multi-Criteria Analysis
MEML	Malawi Essential Medicines List
MoH	Ministry of Health
MSTG	Malawi Standard Treatment Guideline

Acronym	Definition
NASEM	National Academies of Sciences, Engineering, and Medicine
NGO	Non-Governmental Organization
NMS	National Medical Stores
PMRA	Pharmacy and Medicines Regulatory Authority
PPB	Pharmacy and Poisons Board
PQ	Prequalification
QC	Quality Control
SSA	Sub-Saharan Africa
UNPF	United Nations Population Fund
UNICEF	United Nations Children's Emergency Fund
USAID	United States Agency for International Development
VSM	Value Stream Mapping
WHO	World Health Organization

Chapter 1

Introduction

1.1 Design context and knowledge gap

1.1.1 Design context

Sub-Saharan Africa (SSA) continues to face the highest neonatal mortality rates worldwide, with an estimated 2.4 million preventable newborn deaths each year (WHO 2024). A substantial share of these deaths is related to complications of prematurity, particularly respiratory disorders such as respiratory distress syndrome and apnea of prematurity (AOP). AOP is a common and potentially life-threatening condition among preterm infants. Methylxanthines are the standard pharmacological treatment, with caffeine, medical-grade caffeine citrate or base, being internationally regarded as the preferred option due to its favorable safety profile, wider therapeutic window, and the absence of requirements for therapeutic drug monitoring (Patel et al. 2017). Caffeine is included on the World Health Organization (WHO) Model List of Essential Medicines and is one of the few neonatal drugs prioritized for global use (WHO 2023). As a result, caffeine has become part of routine neonatal care in many countries.

Despite Sub-Saharan Africa being a major global producer of caffeine-rich commodities, such as coffee beans, most African countries do not have access to the pharmaceutical formulation of caffeine. Access can be defined by the ability of citizens to reach and use pharmaceuticals that are of good quality and affordable, when needed (Frost et al. 2009). This also applies to Malawi, where neonatal mortality remains high and aminophylline continues to be the standard treatment for AOP, despite having more side effects, requiring therapeutic drug monitoring, and being available only intravenously (Nabwera et al. 2021). The absence of caffeine in Malawi is not due to insufficient clinical evidence but stems from institutional barriers and high market prices. Caffeine is currently not included in the Malawi Essential Medicines List (MEML) and remains unregistered by the Pharmacy and Medicines Regulatory Authority (PMRA), which prevents its procurement through the Central Medical Stores Trust (CMST) (Kaalep 2025).

In other African countries where caffeine is available, prices remain highly variable and often unaffordable, reaching levels that severely constrain access (Nabwera et al. 2021). Even if ongoing regulatory efforts succeed in Malawi, the organization of the supply chain, from sourcing and procurement to transport and distribution, will largely determine whether caffeine becomes practically available and affordable. Without an efficient chain and a clear

understanding of where costs arise, access remains uncertain. Consequently, identifying the main cost drivers along the supply chain and understanding how prices develop across different stages are critical for improving accessibility (O. A. Ekhaguere, Ayede, et al. 2020).

1.1.2 Knowledge gap

Caffeine is globally recognized as the first-line treatment for AOP and is included on the WHO Essential Medicines List (WHO 2023). Despite its clinical effectiveness, caffeine remains unavailable within Malawi's public health system. At the same time, empirical studies show that caffeine prices in SSA are substantially higher than in many high-income countries, raising serious concerns about affordability and procurement feasibility (O. A. Ekhaguere, Ayede, et al. 2020; O. A. Ekhaguere, Bolaji, et al. 2024).

Existing research has primarily framed the lack of access as a pricing and affordability issue. O. A. Ekhaguere, Ayede, et al. (2020) identifies the high prices relative to poverty levels as the most significant barrier to caffeine availability in low- and middle-income countries (LMICs), compounded by regulatory complexity and limited clinician awareness. A follow-up study (O. A. Ekhaguere, Bolaji, et al. 2024) demonstrates substantial variation in end-user prices between countries and shows that up to 70% of eligible neonates in Africa do not receive caffeine, often due to cost-driven substitution with aminophylline. Importantly, availability appears linked to local manufacturing capacity, as illustrated by higher uptake in India where domestic production exists. These findings highlight cost as a critical constraint and suggest that supply chain conditions, including sourcing and manufacturing location, may play a decisive role in determining access.

However, while price differences are well documented, the reasons behind those differences, how costs build up across the pharmaceutical value chain, are still not well understood in this context. Aitken (2016) demonstrates that manufacturer costs as a share of end-user prices vary widely across countries, underlining the importance of analyzing how value is added across the supply chain. Understanding where costs arise,from production and international procurement to importation and contracting, is essential for assessing affordability in resource-constrained settings. Yet, for caffeine in Malawi, such a structured upstream cost and supply chain analysis is lacking.

More broadly, pharmaceutical supply chain literature in SSA has documented systemic barriers, including regulatory weaknesses, financing constraints, counterfeit risks, and limited transparency (Alfaouri et al. 2025) While studies emphasize the importance of improving transparency, regulatory capacity, and scalability of supply chain interventions, they tend to analyse sector-wide challenges rather than conducting product-specific supply chain design assessments (Yenet et al. 2023). Moreover, much of the empirical research in African contexts focuses on downstream distribution challenges, such as last-mile delivery inefficiencies, transportation delays, inventory inaccuracies, and cold chain management (Jatau et al. 2015; Palafox et al. 2014; Oli et al. 2017). Similar analyses in Nigeria, Malawi, Uganda, and Ghana identify operational bottlenecks but primarily address distribution performance rather than upstream sourcing and procurement decisions (McCabe et al. 2009).

As a result, a gap remains at the intersection of affordability, upstream supply chain configuration, and caffeine. While prior studies acknowledge that cost is a barrier and that supply chain processes may influence availability, no study has systematically analysed how

characteristics of upstream supply chain designs for caffeine could affect cost structure within Malawi's public health system.

This research addresses that gap by conducting a structured, product-specific upstream supply chain design analysis for caffeine. By integrating this with cost drivers and supply chain configuration choices within a multi-criteria decision framework, this study moves beyond descriptive identification of barriers and instead evaluates feasible design alternatives. In doing so, it contributes to the literature by linking macro-level access challenges to concrete upstream supply chain design decisions, thereby providing evidence to inform practical implementation strategies in resource-constrained settings.

1.2 Research objectives

This thesis aims to strengthen both the academic and practical understanding of how pharmaceutical supply chains operate in low-resource settings, with a specific focus on access to caffeine for neonatal care in Malawi. By integrating supply chain analysis with cost assessment and multi-criteria considerations, the study seeks to generate insights into the structural and economic factors that shape access to caffeine to Malawi.

- **Current supply chain analysis**
  To analyze the current pharmaceutical supply chain for caffeine relevant to Malawi, including key actors, sourcing routes, and structural characteristics observed in Malawi and comparable Sub-Saharan African contexts.
- **Cost analysis**
  To examine the main cost drivers within the caffeine upstream supply chain and to improve understanding of the observed price differences across countries and supply chain configurations.
- **Supply chain design**
  To explore and analyze alternative ways in which the upstream supply chain for caffeine could be organized, focusing on upstream sourcing and international distribution pathways leading to Malawi.
- **Critical analysis**
  To analyze how different supply chain configurations perform across multiple criteria and to identify key trade-offs and constraints relevant to the Malawian context.

By pursuing these research objectives, the thesis provides a structured analytical foundation for understanding supply chain challenges related to essential neonatal medicines and contributes to the broader academic discussion on pharmaceutical supply chains in low-resource settings.

1.3 Scope of thesis

This section defines the key boundaries and terminology used in this thesis.

Upstream supply chain: The term pharmaceutical supply chain is used deliberately, as broader labels such as medical or healthcare supply chain may also include devices, consumables, and service delivery processes. Here, the pharmaceutical supply chain covers the upstream processes required to make caffeine available for procurement by Malawi's Ministry of Health (MoH). This includes sourcing and procurement arrangements, product development and registration-related steps where relevant, manufacturing and packaging, and international transport up to arrival in Malawi. Downstream in-country distribution (from central storage to regional facilities, hospitals, and end users) is excluded; the analysis therefore focuses on the upstream pharmaceutical supply chain.

Geographical perspective: Although Malawi is the target country, several supply chain stages (e.g., manufacturing, packaging, and international procurement) take place outside its borders. The analysis therefore adopts a transnational perspective, examining how international supply networks can support access to caffeine for Malawi.

Definition of regional: Sub-Saharan Africa (SSA) refers to all countries in the SSA-region. A map specifying the countries included is provided in Appendix C. References to the SSA-region in this thesis denote one or more countries within this set.

Definition of medicine: The medicine of interest is medical-grade caffeine, including both caffeine base and caffeine citrate. Unless stated otherwise, the term caffeine is used to refer to these formulations collectively.

Cost: This thesis evaluates cost in terms of the upstream cost drivers that determine the affordability implications of alternative supply chain designs for supplying caffeine to Malawi. The aim is not to produce precise cost estimates, but to understand how supply chain configuration choices affect the composition and dominance of cost components and where cost pressures are likely to occur. These insights are used to compare alternative upstream configurations in the design and evaluation phase. The focus is therefore on costs rather than prices. While downstream factors can also influence final prices and access, they are held constant in this thesis; the analysis is bounded to upstream activities up to the procurement boundary.

1.4 Research and design questions

This study aims to design an available and affordable supply chain for caffeine to enable its introduction to Malawi's neonatal care system. To guide this process, a central design question and four sub-questions are formulated. The first two sub-questions explore the structure and functioning of existing pharmaceutical supply chains, providing contextual insight into the current system and regional benchmarks. The third sub-question addresses the design of alternative supply chain configurations, while the fourth evaluates their financial feasibility and cost implications.

How can the main characteristics and structure of the upstream supply chain of caffeine be designed to enable access to Malawi's neonatal care system?

To answer this, the following sub-questions were explored:

1. What does the current pharmaceutical supply chain to Malawi look like in terms of the manufacturing of medicines, using aminophylline as a proxy to understand the existing system?
2. How is the supply chain of caffeine organized in Sub-Saharan African countries where it is already available, and what are the main cost drivers?
3. What alternative supply chain configurations could enable the availability of caffeine in Malawi, based on the insights from the current Malawian system and regional reference cases?
4. How do the alternative upstream supply chain configurations score on the evaluation criteria under different scenarios?

1.5 Research and design approach

This thesis adopts a mixed-methods approach that combines qualitative system exploration with a structured, semi-quantitative comparative assessment. This approach is appropriate given the limited availability of reliable numerical data on pharmaceutical supply chains in Malawi, while comparing alternative upstream designs still requires a transparent and systematic evaluation framework.

The research follows a sequential logic consisting of three main phases: analysis, design, and evaluation. Figure 1-1 provides an overview of the research framework and the relationship between the sub-questions and methodological steps. Although this Figure is presented as a sequential process, the research was not strictly linear in practice. Several steps involved iteration and feedback loops. For example, insights from the design phase (SQ3) led to refinement of assumptions derived from the analytical phase (SQ1 and SQ2). For clarity of presentation, not all iterations and interrelations are depicted in the figure, providing a structured overview of the main methodological logic.

Analysis phase

The analysis phase addresses Sub-questions 1 and 2 and aims to develop an understanding of how Malawi's current pharmaceutical supply chain is organized and where its main upstream constraints lie, as well as how caffeine is supplied in comparable SSA settings where the product is already available.

For Malawi, the upstream supply chain is mapped using aminophylline as a proxy medicine, since caffeine is not currently part of the national system. Academic and grey literature, together with policy and procedural documents, are reviewed to reconstruct the main planning, procurement, and importation processes, and to identify institutional constraints that shape feasibility. Two interviews from earlier research are also being used as data for the processes.

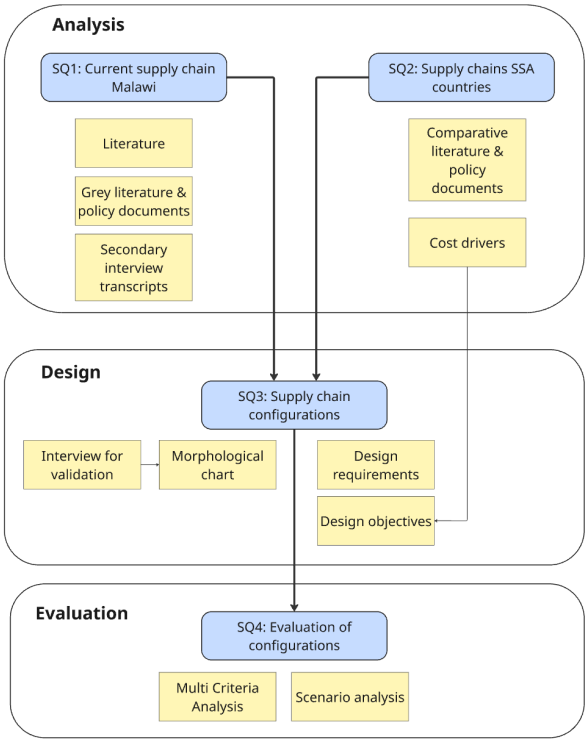

Figure 1-1: Research approach

In parallel, a comparative desk-based review is conducted for selected SSA countries where caffeine is available. This review focuses on extracting the dominant upstream arrangements reported in public sources, such as sourcing routes, procurement set-ups, and the role of external partners, to derive reference practices and structures that inform the design requirements and option set used in the design phase.

Design phase

Building on the findings from the analysis phase, the design phase addresses Sub-question 3 and focuses on developing alternative supply chain configurations for introducing caffeine to Malawi's health system.

Design criteria are derived from the cost drivers observed in both the Malawian and regional SSA analyses. A morphological chart is used to systematically explore feasible options for key supply chain functions and to combine these options into a set of alternative configurations. No new empirical data are collected during this phase; the design activity is based on synthesis of the analysis phase.

Evaluation phase

The evaluation phase addresses Sub-question 4 and provides a structured comparison of the selected upstream supply chain configurations. Prior to the evaluation, a validation step is conducted to assess the design constraints and underlying assumptions of the proposed alternatives. As part of this step, an expert interview is carried out to validate the key assumptions

used in the design of the configurations. The interview aims to assess the operational plausibility of the proposed supply chain structures and to identify whether any refinements to the preferred alternatives are necessary before proceeding with the evaluation.

Because reliable quantitative input data (e.g., costs, lead times, and demand volumes) were insufficient to support a fully quantitative MCA or cost–benefit analysis, the evaluation uses an anchored performance matrix with an ordinal 1–5 scoring scale. Each alternative is scored on the predefined criteria, using the definitions to ensure consistent interpretation across alternatives.

To derive an overall ordering, the performance matrices are combined with a direct pairwise comparison procedure. In addition to a base-case assessment, scenarios are evaluated by adjusting the performance scores where the scenario plausibly affects criterion performance. This set-up allows the analysis to test how the relative attractiveness of the configurations changes across plausible conditions, while maintaining transparency and avoiding spurious precision.

1.6 Thesis structure

The study begins with an introduction in Chapter 1 and presents the design questions, scope and approach. Chapter 2 describes the methodology used to answer the research questions. Chapter 3 contains the background study, in which relevant literature on medical product supply chains, the stakeholders involved, the medicine itself, and existing caffeine supply chains in other Sub-Saharan African countries is reviewed. The insights from this background study form the basis for the supply chain mapping and opportunity analysis for Malawi. Chapter 4 presents the design phase and the resulting supply chain configurations. In Chapter 5, these configurations are validated and evaluated using a multi-criteria analysis. Finally, Chapter 6 concludes the thesis with the main conclusions, a discussion, the limitations, and recommendations for future research.

Chapter 2

Methodology

2.1 Research design and methodological framework

An overview of the research and design methods adopted in this thesis is presented in Figure 2-1. The research begins with a broad exploration of the existing caffeine supply chain, identifying key actors, and contextual factors through a literature review and using preliminary studies. Insights gathered during this stage are then synthesized to clearly define the design scope and key areas for intervention. Building on this understanding, the subsequent design phases focus on generating and refining alternative configurations for supply chains for caffeine.

Given the design-oriented nature of this research, a clear structuring of the research and design process is required to ensure transparency and traceability of design choices. Rather than serving as a prescriptive methodology, the double diamond framework is adopted in this thesis as a structuring device to organize the sequence of analytical and design activities (The Design Council 2005).

The Double Diamond distinguishes four phases—Discover, Define, Develop, and Deliver—and follows a structured process of first exploring up and then narrowing down. In this thesis, the model is not used as a strict path, but as a way to keep the work organised: it separates understanding the problem (mapping, reference cases, barriers, and cost-driver reasoning) from building and testing solutions (design alternatives and evaluation). This is especially helpful in a data-scarce context, because it supports going back and forth when needed, updating assumptions and refining design choices as new insights come in, while still avoiding premature solutioneering and overly precise claims.

In the discover and define phases, the framework supports a broad exploration of the existing caffeine supply chain and its institutional context, followed by a convergence towards a scoped problem definition and a set of design requirements. These phases are primarily analytical in nature and rely on literature review, document analysis, and preliminary empirical insights. The develop and deliver phases subsequently structure the generation,

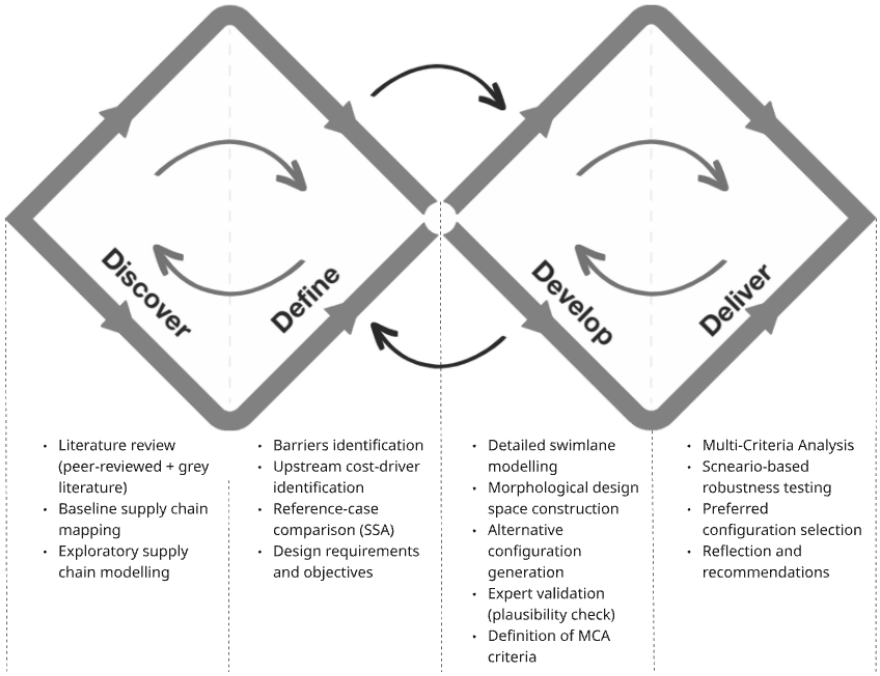

Figure 2-1: Application of DDM framework to design process. Source: The Design Council 2005

refinement, and evaluation of alternative supply chain configurations. Here, the focus shifts from understanding the system to making and justifying design trade-offs.

In this thesis, the four phases of the double diamond correspond to the structure of the research questions. The discover and design phase aligns with SQ1 and SQ2, where the existing Malawian supply chain and comparative SSA arrangements are explored through literature, document analysis, and secondary interview data. The define phase corresponds to the formulation of design requirements and the scoping of intervention space based on identified bottlenecks and cost drivers. The develop phase is operationalized through the construction of a morphological chart and the generation of alternative supply chain configurations (SQ3). Finally, the deliver phase corresponds to SQ4, where the alternatives are comparatively assessed using Multi-Criteria Analysis and scenario analysis to arrive at a preferred configuration.

The added value of the Double Diamond in this research is mainly that it helps to clearly connect the analysis to the design work. It is not meant as a new method on its own, but as a structure that makes the steps in the research easier to follow. This matters in the Malawian context, where access to caffeine is influenced by regulatory gatekeeping, donor financing arrangements, and fragmented responsibilities across actors. By keeping the problem exploration separate from solution development, the framework helps to make assumptions, choices, and trade-offs explicit and easier to justify.

2.2 Literature review approach

The purpose of the structured literature review is not to estimate the price of caffeine in Malawi, but to identify how alternative supply chain configurations are expected to affect two central outcomes of this thesis: availability and cost drivers. The review therefore focuses on factors that determine the direction of cost changes when supply chain structures are redesigned, such as consolidation and economies of scale, as well as the trade-off between transport and inventory. These factors provide the analytical foundation to reason about affordability and access implications of supply chain alternatives, even when precise price data are not available.

2.2.1 Search strategy and sources

A structured search was conducted in PubMed and Scopus to identify peer-reviewed academic literature on pharmaceutical supply chain design in LMIC/SSA contexts, with additional attention to neonatal essential medicines and caffeine citrate. In addition, the TU Delft Repository was used as a complementary academic source (e.g., theses and technical reports). While these materials are not necessarily peer-reviewed, they can provide timely and detailed insights that are relevant for design-oriented research and may not yet appear in journal outlets.

Search terms were derived from the core concepts of the research and grouped into five clusters: problem definition, methodology/design approaches, LMIC/SSA context, Malawi and related neonatal medicines, and cost drivers in supply chains. Table 2-1 provides an overview of the keywords used. Within and across clusters, keywords were combined using Boolean operators (AND/OR). Searches were limited to publications from 2015–2025 to reflect recent developments in global health supply chains and pharmaceutical manufacturing and distribution.

Table 2-1: Keywords used for the structured literature review

Research part	Keywords
Problem definition	"medicine supply chain", "essential medicines", "medicine availability", "neonatal care", "newborn mortality SSA", "AOP", "caffeine citrate"
Methodology	"supply chain design frameworks", "health supply chain modelling", "scenario analysis", "value chain mapping", "process mapping", "multi-criteria analysis"
Background study: LMIC/SSA context	"low- and middle-income countries", "LMIC", "Sub-Saharan Africa", "donor-funded medicines", "global health supply chain", "pharmaceutical supply chain"
Background study: Malawi and related medicines	"Malawi health system", "Malawi medicine supply chain", "Malawi procurement", "caffeine citrate", "aminophylline", "neonatal medicines", "apnoea of prematurity"
Cost factors in supply chains	"cost factors", "pharmaceutical supply chain costs", "economies of scale", "cost-efficiency", "logistics cost structure"

2.2.2 Grey literature

Grey literature was included to capture context-specific and operational information that is often not available in peer-reviewed journals, especially regarding institutional arrangements, governance, procurement practices, and country-specific constraints. Sources included reports and guidelines from international organizations (e.g., WHO, UNICEF, CHAI, Global Fund), national strategies and policies issued by the Malawian Ministry of Health, documents from the Central Medical Stores Trust (CMST), and procurement/regulatory documents from other stakeholders. Grey literature from preliminary studies was also included where it provided operational detail relevant for supply chain design.

Peer-reviewed literature was primarily used to support generalizable cost-driver claims (e.g., consolidation, economies of scale, inventory–transport trade-offs), while grey literature was primarily used to characterize the Malawi-specific institutional set-up and constraints needed to ground the design alternatives.

2.2.3 Selection and quality criteria

The review is design-oriented: the key requirement is that sources provide credible and usable input for reasoning about supply chain configuration choices and their expected direction of impact on availability and cost drivers. The following criteria were applied during title/abstract screening and full-text assessment:

1. **Problem and context fit**
   Sources were included if they were relevant to pharmaceutical (or essential medicines) supply chains in Malawi or comparable Sub-Saharan African/LMIC contexts, or if their insights were explicitly transferable to this setting with stated assumptions or conditions.

2. **Analytical contribution to the thesis (design and/or cost–availability factors)**
   Sources were included if they provided usable input for at least one of the thesis' analytical needs: supply chain design/configuration (e.g., network structure, sourcing/manufacturing choices, procurement and distribution set-ups, pooling vs dedicated capacity), and/or factors affecting cost, affordability, and/or availability to support reasoning about alternative configurations.

3. **Credibility and traceability**
   Peer-reviewed literature was prioritised where available. Grey literature was included when the issuing organisation and purpose were clear and the document provided necessary operational or context-specific information not typically captured in peer-reviewed sources. Key factual claims were cross-checked across multiple sources where feasible.

In addition, all included sources were labelled as peer-reviewed or grey literature and interpreted with different evidentiary weight depending on traceability (presence of method/-data/references) and specificity to supply chain design decisions. This ensured that context-setting documents informed the assumptions and constraints, while the underlying drivers were supported as much as possible by peer-reviewed literature.

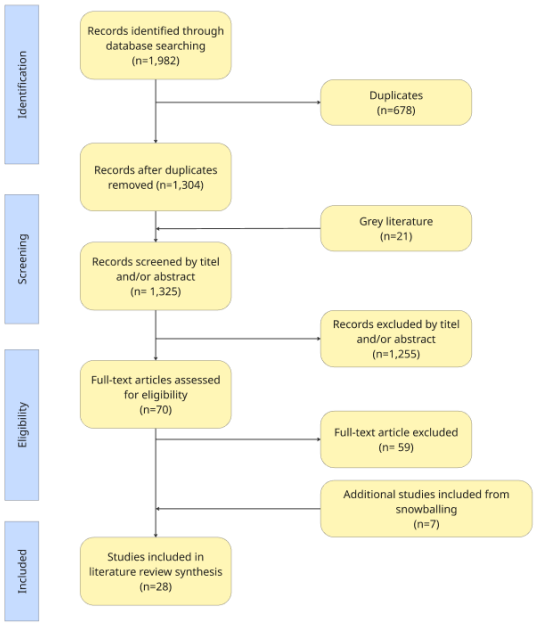

Figure 2-2: Literature research flowchart

2.2.4 Screening, eligibility, and inclusion

Across the databases, the search returned 1,982 records. After removal of duplicates, 1,304 unique academic records remained. Grey literature items were identified separately and added to the screening stage, resulting in 1,325 screened records. The complete selection flow is reported in Figure 2-2.

Title and abstract screening excluded 1,255 records. Exclusions at this stage primarily concerned studies focusing on clinical efficacy without supply chain implications, papers set in high-income settings without clear transferability to LMIC/SSA contexts, and studies that did not address supply chain configuration, governance, sourcing/manufacturing, distribution/procurement, or performance drivers relevant to availability and cost drivers.

The remaining 70 documents were assessed in full text. Full-text exclusions were mainly due to lack of actionable configuration levers (descriptive accounts without design implications), absence of drivers relevant to availability and/or cost/affordability, or insufficient context specification to support transferability to Malawi/SSA settings. In addition, 7 key documents were included through snowballing and cited-by searching, resulting in a final synthesis set of 28 studies.

2.2.5 Interview data and primary sources

This thesis draws on both secondary and primary interview data to inform the analysis and to validate the archetypes.

Secondary interview data

This study draws on two semi-structured interviews previously conducted by Kaalep (2025), a former Msc student whose thesis research formed part of the wider TU Delft–Erasmus

MC research programme aimed at improving access to caffeine in Sub-Saharan Africa. As the previous study was conducted within the same overarching research collaboration as the present thesis, access to the anonymised interview transcripts was granted for secondary analysis. The interviews were held with a representative of an international pharmaceutical supplier and a representative of the UNICEF Supply Division. After reviewing the available interview transcripts from the earlier study, these two were selected for inclusion because they contained substantial, directly relevant insights for this thesis, particularly regarding procurement, quality assurance, and importation processes for medicines in low- and middle-income country contexts. To ensure confidentiality, the interviewees are anonymised and referenced in this thesis as T1 (Transcript 1) and T2 (Transcript 2).

Primary interview for validation

In addition, one semi-structured interview was conducted specifically for this thesis with a research coordinator of the Access to Medicine Foundation. The purpose of this interview was to obtain further insight into upstream supply chain processes and to validate the assumptions and configurations developed in the morphological design phase. This is referenced to as T3 (Transcript 3).

The interview followed the semi-structured protocol presented in Appendix J. Prior to participation, the respondent reviewed and signed the informed consent form included in Appendix K, in accordance with TU Delft ethical and data protection requirements.

ID	Generic Role
T1	International pharmaceutical supplier
T2	UNICEF Supply Division representative
T3	Access to Medicine Foundation research coordinator

Table 2-2: Overview of interview transcripts

Data analysis

All interview data were analysed in ATLAS.ti (version 25) using systematic coding and thematic analysis. A coding scheme was developed iteratively: initial codes were derived from the study's analytical focus on upstream procurement and importation processes, and were refined as additional patterns emerged from the transcripts. The final codebook was organised into the following thematic categories: API sourcing, availability constraints, cost drivers, donor dependency, economies of scale, lead time, manufacturing location, quality, regulatory barriers, and supply chain. Coding was conducted by the author, with iterative cross-checks across transcripts to ensure consistent code application. The resulting themes were synthesised to inform the description of the current system and to support the formulation and validation of the design requirements and configurations.

2.3 Supply chain analysis

To design and evaluate alternative supply chain configurations, it is essential to develop a transparent and systematic understanding of the underlying processes and value flows. Before

selecting appropriate techniques, it is therefore useful to clarify the distinction between several related concepts: supply chains, value chains, value streams, and processes.

2.3.1 Conceptual framing

A supply chain comprises all activities required to produce and deliver a product or service from the initial supplier to the final customer, with a primary focus on efficiency, reliability, and cost (Cooper et al. 1997; Feller et al. 2006). A value chain, in contrast, emphasizes how value is created and captured throughout these activities, shifting attention from operational performance to value generation for the end user (Walters et al. 2004). A value stream further narrows this perspective by identifying only those activities that directly add value, an approach commonly applied in lean management (Hines et al. 1997; Ceylan 2011).

Understanding these conceptual differences is important when analyzing how neonatal medicines move from manufacturers to import into a country. In this research, the objective is not to optimize individual operational steps, but to understand how medicines progress through a sequence of regulated, institutionalized processes involving multiple actors. To make this movement explicit, both in terms of process sequence and actor involvement, the supply chain must be mapped using modeling techniques that balance clarity, comparability, and analytical usefulness.

Two analytical needs follow from this objective. First, the modeling approach must clearly represent the sequence of processes and handovers over time. Second, it must explicitly show which actors are responsible for which activities, including how these responsibilities differ across countries.

The purpose of the modeling step is to make the upstream pharmaceutical supply chain explicit in terms of process steps and decision points, as well as the allocation of responsibilities across actors. The resulting models provide a structured basis to compare how registration, procurement, financing, importation and upstream distribution processes are organized across country cases, and identify recurring cost-relevant aspects embedded in these process structures.

2.3.2 Modelling approaches

Several established modeling approaches can support these goals, including Business Process Model and Notation (BPMN), Value Stream Mapping (VSM), Function Flow Block Diagrams (FFBD) and swimlane diagrams. These approaches are briefly evaluated below.

Business Process Model and Notation

BPMN provides a standardized visual language for modeling complex process logic, including decision points, exceptions, and detailed interactions between actors (Von Rosing et al. 2014). While BPMN offers a high level of expressive power, such detail is not required for the purpose of this research. The aim is to obtain clear and comparable representations of institutional supply chain structures rather than to model detailed operational logic. Applying BPMN would therefore introduce unnecessary complexity without yielding proportional analytical benefits at this stage of the research.

Value Stream Mapping

Value Stream Mapping originates from lean management and focuses on distinguishing value-adding from non-value-adding activities in order to identify process inefficiencies (Rother et al. 2003). Although VSM is well suited for operational improvement within organizations, it is less appropriate for capturing the institutional, regulatory, and governance-related pathways that shape medicine availability across countries. Because this research requires insight into roles, decision rights, and cross-country variation, VSM alone does not sufficiently address the analytical requirements.

Functional Flow Block Diagram

FFBDs are a classic systems engineering tool used to map functional steps and the logical sequence of system operations (Blanchard et al. 2011). FFBDs focus strictly on what a system must do and the required sequence of functions (e.g., Function A must be completed before Function B can start). However, a significant limitation of FFBD is that it is primarily actor-agnostic, meaning it does not explicitly represent who is responsible for each function (Buede et al. 2016). In a multi-actor supply chain, functions often overlap or occur in parallel across different institutional boundaries. As the focus of this study is on institutional responsibility and the handovers between actors, the rigid functional logic of FFBD is less suitable.

Swimlane diagrams

Swimlane diagrams provide a clear and intuitive way to visualize how products, information, or decisions flow across different actors or institutional levels (Damij et al. 2014). Each lane represents an organization or stakeholder, while activities are plotted chronologically. This makes it possible to identify handovers, fragmentation, and coordination challenges, issues frequently cited as barriers to medicine access in SSA (Yadav 2015). The relative simplicity and focus on organizational boundaries make swimlane diagrams particularly advantageous for comparing responsibilities among actors, regulatory authorities, procurement agencies, and medicine providers.

In this thesis, swimlane diagrams are therefore selected as the primary supply chain modeling approach. They provide a transparent, country-specific overview of end-to-end processes while clearly distinguishing actor roles and responsibilities. This enables systematic comparison between different national supply chain arrangements and establishes a coherent foundation for the subsequent design and evaluation of alternative supply chain configurations for Malawi.

2.4 Design method

As outlined in the research design and methodological framework, this thesis follows a DDM as the overarching approach. Within that structure, this section specifies the design methods considered for developing alternative upstream supply chain configurations for the develop phase.

In early-stage supply chain design research, several methodological approaches are commonly used to support the generation and comparison of alternative system configurations.

These include optimisation-based models, simulation approaches, scenario analysis, and morphological analysis (Christopher 2016; Blanchard et al. 2011; Buede et al. 2016). Each method is suited to different design questions and comes with specific assumptions and data requirements.

Optimisation and simulation methods are frequently applied when the objective is to improve or evaluate a predefined system architecture under clearly specified constraints (Blanchard et al. 2011; Buede et al. 2016). Such methods typically require detailed quantitative input data, including demand volumes, lead times, cost parameters, and capacity constraints (Christopher 2016). In the context of this research, these inputs are either unavailable or subject to substantial uncertainty, which is common for health-product supply chains in low-resource settings (Yadav 2015; Alfaouri et al. 2025). Moreover, the primary design challenge addressed in this thesis concerns institutional and organisational configuration choices rather than optimisation of operational parameters (Yadav 2015; Tetteh 2009). For these reasons, optimisation and simulation were not considered the most suitable methods for the design phase.

Scenario analysis was also considered as a design support method. Scenario-based approaches are commonly used to explore how supply chains perform under different external conditions, such as demand fluctuations, funding disruptions, or policy changes (NASEM 2022; Olutuase et al. 2022). While valuable in resilience-focused research, the objective of the present study is not to analyse alternative future environments, but to compare alternative ways in which the upstream pharmaceutical supply chain for caffeine can be organised within a given institutional context (Bigdeli et al. 2013; Yadav 2015). Scenario analysis was therefore not selected as the primary design method for generating alternatives. However, because it is useful for assessing how designs perform under uncertainty, it is applied later in the evaluation phase (Sun et al. 2021; Khalilpoor et al. 2025).

Given these considerations, this thesis adopts morphological analysis as the main design method to develop the alternative configurations. Morphological analysis, originally introduced by Zwicky, supports systematic concept generation by decomposing a system into core functional elements and specifying alternative options per function (Zwicky 1957). By combining these options, multiple coherent system-level configurations can be generated and compared in a transparent manner (Kutz 2017; Ritchey 2018). In design research, morphological charts are a well-established tool for early-stage concept generation and structured exploration of solution spaces (Cross 2008; Pahl et al. 2007; Roozenburg et al. 1995; Delft Design Guide n.d.).

In this study, the morphological chart structures alternative configurations of the upstream caffeine supply chain by making differences explicit in actor involvement, procurement routes, regulatory pathways, and organisational responsibilities. This aligns with health supply chain perspectives that emphasise institutional arrangements, governance, and coordination as key determinants of performance and access (Bigdeli et al. 2013; Yadav 2015; NASEM 2022). Importantly, the chart also aligns with the iterative logic of the DDM: it provides a modular design space that can be revisited and refined as new insights emerge during the design process (Shen et al. 2024). This supports transparent iteration on functional choices and underlying assumptions, and provides a structured basis for qualitative discussion of upstream cost drivers and feasibility considerations (Lee et al. 2021; Ibrahim et al. 2025).

Overall, the combination of DDM and morphological analysis aligns with the exploratory,

design-oriented nature of the study. It enables systematic generation and refinement of alternatives, while avoiding premature quantification or overly restrictive modelling assumptions.

2.5 Validation, evaluation and comparison method

2.5.1 Validation method

Before the evaluation phase, the design alternatives will be validated against the design requirements. These requirements function as hard feasibility constraints and ensure that each alternative is both legally implementable and operationally realistic within the scope of this research. The requirements are derived from the earlier barrier identification based on the context analysis and supply chain mapping.

In addition to this requirements check, a semi-structured expert interview is conducted during the design phase to strengthen contextual validity. The interview is positioned before finalising the design alternatives, so that the selected supply chain functions in the morphological chart and the assumed upstream cost drivers could be validated and, where necessary, refined. This reduced the risk that the alternatives and evaluation criteria would rest on incomplete or incorrect assumptions. The validated functions and cost drivers were subsequently used to finalise the evaluation criteria applied in the next phase.

2.5.2 Evaluation method

To compare the developed supply chain design alternatives, a structured and transparent evaluation approach is required. In supply chain design research, methods such as scenario analysis, sensitivity analysis, cost–effectiveness analysis (CEA), cost–benefit analysis (CBA), and multi-criteria analysis (MCA) are commonly used. In this thesis, the evaluation challenge is twofold: relevant decision criteria include both quantitative and qualitative dimensions (e.g., cost drivers and affordability implications, feasibility, governance complexity, and availability-related performance), and reliable numerical data to populate a traditional performance matrix (e.g., exact costs per activity) are limited. Therefore, multiple evaluation methods were explored to assess their suitability for the research context and data environment.

Cost-Effectiveness Analysis

CEA is commonly used in health systems and supply chain research to compare the costs of an intervention to a measurable effectiveness outcome in a predefined unit. For example, Risko et al. evaluate the cost per health worker infection averted and cost per life saved when scaling up personal protective equipment in low- and middle-income countries (Risko et al. 2020). Similarly, Makkawi et al. apply CEA to compare supply chain performance before and after increased investment in Sudan's National Medical Supplies Fund, linking incremental costs to improvements in availability, coverage, and other performance indicators (Makkawi et al. 2020).

While CEA provides a rigorous framework when a single, measurable effectiveness metric is available, the objective of this thesis is to compare alternative supply chain configurations across multiple dimensions, including cost drivers (and their implications for affordability),

availability-related performance, and institutional feasibility. These dimensions cannot credibly be reduced to one effectiveness metric, and the thesis does not rely on empirically measured outcomes suitable for computing cost-effectiveness ratios. Therefore, CEA is not considered appropriate as the primary validation method.

Cost-Benefit Analysis

CBA monetizes both costs and benefits to estimate net value and is sometimes applied to evaluate specific supply chain investments. For example, Schiffmann et al. conduct a cost–benefit simulation to evaluate the digitalisation of cold supply chains (Schiffmann et al. 2023), and Kim et al. assess the net benefits of an integrated pharmaceutical supply chain information system (Kim et al. 2022). However, applying CBA requires that the most important impacts of the alternatives can be expressed credibly in monetary terms.

In this thesis, several dimensions that differentiate the design alternatives, such as governance complexity, donor dependency, and regulatory pathway feasibility, are difficult to monetize without introducing strong assumptions. Moreover, the aim is not to estimate a single monetary net benefit, but to understand trade-offs across cost drivers, feasibility, and availability-related objectives. For these reasons, CBA is not selected as the primary validation method.

Sensitivity Analysis

Sensitivity analysis is widely applied in quantitative optimization and network design research to test how outcomes change when key parameters (e.g., demand, transportation costs, disruption rates, or capacity limits) are varied. This approach is particularly informative when a model is fully parameterized with reliable numerical inputs and decision variables. For example, Babagoli et al. 2025 perform sensitivity analyses on parameters such as demand, disruption severity, service levels, and import/export-related factors (e.g., customs and tax rates). Similarly, Rajabi et al. 2024 use sensitivity analysis to evaluate how their pharmaceutical network design reacts to demand shocks and changes in resilience levers.

While, conducting a conventional quantitative sensitivity analysis is not feasible due to the lack of reliable numerical data required to vary key parameters in a controlled way (e.g., cost components, lead times, and capacity constraints). The underlying purpose of sensitivity analysis, identifying which drivers the outcomes are most sensitive to, remains relevant. Sensitivity analysis is thus not omitted, but implemented in a qualitative form that is consistent with the data environment of this study.

Multi-Criteria Analysis

MCA is widely used to compare alternatives across multiple (potentially conflicting) criteria, including qualitative considerations. In supply chain design contexts with governance-related trade-offs and limited data, MCA provides a structured way to make trade-offs explicit (Awasthi et al. 2011; Govindan et al. 2016).

In principle, the most reliable evaluation of affordability implications would be a quantified economic assessment (e.g., activity-based costing and/or CBA). However, already during the design phase it became clear that the available data did not allow the development of a credible set of quantitative (ratio-scaled) criteria for such an assessment. Key inputs (especially

upstream cost drivers, price components, and transaction-related costs across interfaces) were too sparse, fragmented, and context-dependent. A full CBA would therefore require extensive, unverifiable assumptions and could create a false sense of precision. For this reason, CBA was excluded early on as the main validation approach.

Given the multi-dimensional nature of the decision problem (affordability-relevant cost drivers, availability-related performance, and institutional feasibility), the initial plan for the validation phase was to apply a traditional MCA. This type of MCA typically requires a performance matrix in which alternatives are scored on a consistent scale per criterion, so that results are comparable beyond a simple ordering (i.e., not only "better/worse", but also reflecting magnitude in a meaningful way across alternatives and criteria).

When operationalising the traditional MCA in the validation phase, it became clear that several criteria were difficult to score consistently and transparently. In particular, even when qualitative and mixed evidence was available, it remained challenging to define a defensible scoring scale that would be comparable across alternatives without introducing subjective quantification. To make this explicit, a pilot evaluation was conducted using a draft traditional MCA structure to test whether consistent scoring across criteria and alternatives was feasible. The pilot confirmed that a traditional (scale-based and potentially weighted) MCA could not be completed in a sufficiently transparent and defensible way within the scope of this study.

Scenario Analysis

Scenario analysis is commonly applied in supply chain design and resilience studies to address uncertainty about the future operating context. Because future conditions cannot be known precisely and may develop along different plausible pathways, key variables (e.g., demand, financing, policy, or disruption exposure) can evolve in different directions and interact in different ways. To capture this type of context or environmental uncertainty, scenario analysis defines a limited number of plausible and internally consistent scenarios and assesses system performance for each scenario separately. In supply chain research, such scenarios often represent external conditions such as demand surges, funding constraints, policy changes, or disruption events.

For example, Babagoli applies scenario analysis to investigate how varying disruption levels and demand scenarios affect the cost, sustainability, and resilience performance of a serum supply chain network (Babagoli et al. 2025). Similarly, Rajabi incorporates multiple demand and disruption scenarios to test the robustness of pharmaceutical supply chain designs under pandemic conditions (Rajabi et al. 2024).

In this thesis, scenario analysis is relevant because it captures exogenous factors that are outside direct design control but may affect the relative attractiveness of supply chain configurations. However, scenario analysis alone does not provide a complete basis for comparing the alternatives, because the primary objective is to evaluate structural trade-offs across multiple criteria rather than performance in isolated future states. Therefore, scenario analysis is not used as a standalone validation method, but is incorporated as a robustness check alongside the selected MCA approach (see below).

2.5.3 Selected approach

Based on the pilot results, the evaluation was adapted to a less data-intensive MCA variant. The criteria used for the MCA are derived from the design objectives formulated in the

design phase. In other words, the objectives are translated into a set of criteria that allow the alternatives to be compared in a consistent and transparent way. This ensures that the evaluation is aligned with the purpose of the design work (i.e., improving access and affordability through upstream configuration choices and their underlying cost-driver factors).

Performance matrices

The evaluation will start with the construction of performance matrices. A performance matrix provides a structured overview in which each design alternative is scored against each criterion using a consistent scale. In this study, an anchored 1–5 scoring scale will be applied, where 1 indicates weak performance and 5 indicates strong performance on a given criterion. This choice reflects the limited availability of reliable quantitative inputs, which makes a fully quantitative MCA or cost–benefit analysis infeasible. In line with MCDA guidance, the anchored scale is used to support transparent, systematic judgement and to make the underlying assumptions in the scoring explicit Belton et al. 2002.

Conceptually, the performance matrix has the criteria on the rows and the design alternatives on the columns; each cell contains the score of an alternative on a criterion. Table 2-3 illustrates the structure.

Table 2-3: Structure of the performance matrix used for scoring the design alternatives (illustrative)

Criterion	Alt 1	Alt 2	Alt 3	Alt 4
C1: ...				
C2: ...				
C3: ...				
C4: ...				
C5: ...				

To assess robustness, the performance matrices will be specified for a base case and for the defined scenarios. Across scenarios, the set of criteria and alternatives will remain constant; only the performance scores will be adjusted to reflect scenario-specific impacts on feasibility and upstream cost drivers.

Direct pairwise comparison

After scoring, a direct pairwise comparison method will be used to synthesise the performance-matrix results into an overall ordering of the alternatives. Pairwise comparison is a well-established way to synthesise multi-criteria preferences and has been applied to assess competitive priorities in supply chain settings where performance information is largely ordinal (Saarijärvi et al. 2012). More data-demanding outranking approaches (e.g., electre/promethee) typically require more detailed preference modelling and parameterisation (including weights and thresholds) than the available evidence could robustly support in this case (Govindan et al. 2016).

In this step, alternatives are compared two at a time. For each criterion, the alternative with the higher score is recorded as preferred for that criterion (ties are recorded when scores are equal). Aggregating these pairwise preferences across all criteria provides a transparent way to derive an overall ranking, showing which alternatives are generally preferred and under which criteria the differences are most pronounced.

Table 2-4 illustrates the logic of the pairwise comparison output: rows represent comparisons between alternatives, columns represent the criteria, and the entries indicate which alternative is preferred for each criterion.

Table 2-4: Structure of the direct pairwise comparison matrix (illustrative)

Comparison	C1	C2	C3	C4	C5
Alt 1 vs Alt 2					
Alt 1 vs Alt 3					
Alt 1 vs Alt 4					
Alt 2 vs Alt 3					
Alt 2 vs Alt 4					
Alt 3 vs Alt 4					

Finally, because stakeholder input to elicit relative criterion importance is not available within the scope of this study, equal weights will be used for both the .

2.6 Use of AI in this thesis

During the writing of this thesis, AI tools are used as writing and research assistants under the supervision of the author. Specifically, OpenAI's ChatGPT (GPT-5.2) was employed to enhance the clarity and structure of the text, support the formulation of the research framework, and summarize relevant academic literature. The tool also assisted in generating LaTeX-compatible formatting and improving overall readability. Similar tools may be used throughout the thesis process for comparable purposes, such as refining academic writing, organizing qualitative insights, and improving analytical clarity. All conceptual development, interpretation of literature, and final research decisions remain the sole responsibility of the author.

Chapter 3

Context and system analysis

This chapter answers sub-question 1 by mapping the current pharmaceutical supply chain to Malawi, using aminophylline as a proxy product. The focus is on describing the structure of the system and the main actors and flows that shape it, from manufacturing and procurement to distribution to Malawi. The mapping is based on desk research complemented by insights from a preliminary study, and it is used to identify key dependencies and bottlenecks in the existing system. In terms of the DDM, the mapping and comparative review in this chapter constitute the Discover phase, as they explore the current system and relevant reference contexts.

The chapter then addresses sub-question 2 by reviewing Sub-Saharan African countries where caffeine is already available. The aim is to characterize how these supply chains are organized, which paths already exist and to see if there are any dominant cost drivers that determine the final price that derive from this. This is where the chapter transitions into the Define phase by synthesizing these findings into a structured set of cost drivers and barriers, which provide the input for the design phase.

3.1 Product

Caffeine citrate is the citrate salt of caffeine. When it is dissolved in water, it separates into its components and the active part is the caffeine base. Because the citrate makes the molecule heavier, the amount on the label is usually expressed as caffeine citrate, while the clinical effect depends on the amount of caffeine base (NASEM 2022). Typical formulations include:

- **Injectable solution**: a sterile water-based solution, supplied in single-use glass vials or ampoules. A common strength is 20 mg/mL caffeine citrate, which corresponds to 10 mg/mL caffeine base (Food and Drug Administration 2020).
- **Oral solution**: pharmacies can prepare a sterile liquid for oral use (for example 10 mg/mL caffeine base), usually packaged in amber, break-resistant bottles for neonatal or paediatric patients.

Manufacturing

Caffeine citrate formulations for neonatal care are typically supplied as a sterile aqueous solution for intravenous and/or oral administration, with pH adjustment and excipients that support solubility and stability (U.S. Food and Drug Administration 2020). Commercial production of such sterile injectable solutions requires controlled manufacturing conditions, including validated aseptic processing or sterilization strategies, in-process controls, and quality testing prior to filling and release (World Health Organization 2011).

Looking at the input materials, the high price of caffeine formulations is unlikely to be driven by scarce or costly raw ingredients. Citric acid is widely produced and described as a commodity chemical, and caffeine itself is produced commercially at industrial scale (Berovič 2007; International Agency for Research on Cancer 1991). This suggests that cost premiums are more plausibly explained by downstream requirements such as sterile manufacturing, quality assurance and quality control, and regulatory compliance (World Health Organization 2011; U.S. Food and Drug Administration 2004).

Caffeine (and its salts) is produced and traded globally, and manufacturing is not inherently country-specific for a single destination market. In this thesis, it is therefore assumed that caffeine could be sourced from multiple potential manufacturers, subject to meeting relevant quality and regulatory requirements (World Integrated Trade Solution (WITS) 2021).

Storage

Caffeine does not require refrigeration and can be stored at controlled room temperature, which supports its use in low-resource settings. Unopened containers have high chemical stability; correctly prepared oral solutions can remain stable for up to one year at room temperature (Khan et al. 1994). However, most formulations do not contain preservatives. As a result, opened containers have a limited in-use shelf life and should be used within one month after opening to maintain microbiological quality (Khan et al. 1994).

For a single injectable caffeine ampoule, vials are typically stored at 15–30 °C (Food and Drug Administration 2020). Because the solution is preservative-free, a vial should be used immediately after opening (Food and Drug Administration 2020). In terms of chemical stability, studies indicate that the injectable solution remains stable at room temperature for at least 24 hours, either undiluted or when mixed with compatible IV fluids.

Conclusion

The product characteristics indicate levers to improve availability and to lower costs. First, caffeine can be stored at controlled room temperature and therefore does not require cold-chain logistics. This reduces distribution complexity and infrastructure needs, which can improve availability in low-resource settings and avoid cold-chain related cost drivers. Second, caffeine is produced from widely available commodity inputs (purified caffeine and citric acid), suggesting that ingredient scarcity is unlikely to drive costs. Therefore, opportunities to lower costs are more likely to be found in downstream supply chain choices (e.g., sterile manufacturing requirements, quality control, and regulatory compliance) rather than in the input materials themselves.

3.2 Pharmaceutical supply chain

Medical product supply chains are complex, global socio-technical systems that connect raw material suppliers, pharmaceutical and device manufacturers, distributors, health systems and, ultimately, patients. They involve numerous actors, production stages and geographies, and are shaped by technologies, information systems, policies and legislation. Structurally, they resemble other supply chains: they are multi-tiered, geographically dispersed and subject to variability in supply and demand. However, they differ in that they must simultaneously pursue commercial viability and public health objectives. In practice, these goals can conflict, for example when cost-containment or profit maximization undermines investment in redundancy or resilience (Shah et al. 2021). Because the consequences of failure include serious patient harm or sometimes even death, medical products and their manufacturing processes are subject to far more stringent regulation and public oversight than most other consumer goods (NASEM 2022).

3.2.1 Supply chain characteristics

Following the framework proposed by the National Academies of Sciences, Engineering, and Medicine (NASEM), medical product supply chains can be understood as a series of linked stages that move products from raw materials to patients (NASEM 2022). Under normal, well-functioning conditions, products flow from suppliers of raw materials and components (e.g. active pharmaceutical ingredients (APIs), excipients, packaging materials) to manufacturing facilities, where they are transformed into finished dosage forms or medical devices. Finished products are then transferred to distributors or wholesalers, who manage storage and onward distribution to health systems, pharmacies and other providers. Finally, clinicians and other care providers dispense or administer these products to patients, who constitute the end users and ultimate source of demand. This structure is often depicted as a simple linear schematic as can be seen in figure 3-1 (NASEM 2022).

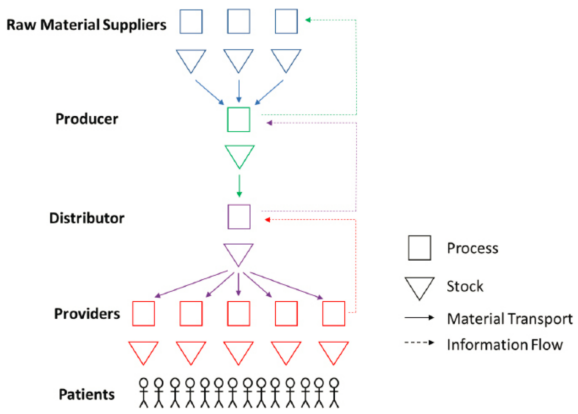

Figure 3-1: Schematic medical product supply chain. Source: NASEM 2022

Although the structure appears linear, several characteristics of medical product supply chains are relevant to this research. Demand for many essential medicines is relatively inelastic: patients and providers require them irrespective of price, which can create imbalances in bargaining power and weaken incentives for firms to invest in resilience. At the same

time, lean and just-in-time practices are widely used by manufacturers and distributors to reduce costs, which limits inventory buffers and increases vulnerability to disruptions (NASEM 2022). As a result, supply chain design in this domain is not only a matter of efficiency, but directly affects public health outcomes.

3.2.2 Malawian pharmaceutical supply chain

To contextualize the supply chain design and ensure a sound fit with the existing system, this study first outlines the organisation of Malawi's health service delivery and essential medicines supply system. Malawi's national supply architecture can be characterised as a centrally coordinated backbone for essential medicines, centred around the CMST, operating alongside several parallel, donor-funded procurement and distribution pipelines (Initiative 2024). Within this system, three core processes can be distinguished: quantification and sourcing, ordering and procurement, and supply and distribution (Initiative 2024).

Quantification and sourcing concerns the estimation of national demand for medicines, expressed both in physical volumes and monetary value. Ordering and procurement then operationalises these estimates into concrete purchasing decisions, such as purchase orders, tenders, and contractual agreements. Finally, the supply and distribution process covers the upstream-to-downstream flow of products, including sourcing, importation, customs clearance, warehousing, and delivery to service delivery points (Initiative 2024).

Appendix B provides additional process detail. Specifically, Figure B-1 summarises Malawi's current workflow for quantification, sourcing, and procurement using a swimlane diagram. The diagram highlights the key actors involved and clarifies the chronological sequence of activities and handovers between them, thereby serving as a reference point for identifying interface constraints and opportunities for the proposed supply chain alternatives.

3.3 Interview-based insights

Prior research has already been conducted on the barriers and enabling conditions for caffeine availability in Malawi. In particular, Kaalep 2025 analyzed the socio-technical barriers to caffeine diffusion in Malawi's health system and conducted several stakeholder interviews to better understand the roles, incentives, and decision-making dynamics of key organizations. This is part of the same larger research about caffeine, as explained in Section 2.2.5.

For the present thesis, two of these interview transcripts are reused as part of the preliminary study. Specifically, interviews with representatives from UNICEF and a procurement agent are leveraged to obtain an initial understanding of the procurement and supply perspective. These two organizations were selected because reliable qualitative data from these interviews was already available and provides a strong starting point for analyzing the supply chain and stakeholder roles from both a donor/procurement perspective (UNICEF) and a supplier/procurement intermediary perspective.

Moreover, during the interviews it became evident that both respondents possess substantial practical expertise in pharmaceutical supply chains. They were able to describe procurement routines and coordination structures, which further strengthened the suitability of these interviews as a foundation for the preliminary analysis. This strengthens the preliminary study, as the insights come from practitioners with direct experience in the institutional and operational functioning of pharmaceutical supply chains.

3.3.1 Role of donors (UNICEF perspective)

In low-resource health systems, access to specialized essential medicines is shaped not only by national procurement agencies but also by donor organizations and global health financiers. These actors influence pharmaceutical markets through funding decisions, procurement modalities, and market-shaping interventions so that medicines become affordable, quality-assured, and reliably supplied.

Within UNICEF-supported medicine procurement, three distinct procurement pathways can be distinguished, which differ fundamentally in terms of initiative, governance, and the role of donors. First, a country-initiated procurement pathway, in which MoHs formally request UNICEF support to procure medicines through established national planning and budgeting processes. Second, a UNICEF-initiated procurement pathway, in which UNICEF Programme Division proactively identifies priority interventions for a country and subsequently mobilizes donor funding and institutional alignment. Third, an emergency procurement pathway, which allows for rapid procurement under exceptional circumstances.

This research focuses explicitly on the first two pathways, as these represent the dominant structures through which access to essential neonatal medicines is pursued under non-emergency conditions. The emergency procurement pathway is not further elaborated through a dedicated swimlane, as caffeine does not constitute an emergency medicine in the strict sense and is unlikely to be procured through humanitarian emergency structures. Instead, its introduction depends on longer-term institutional embedding and donor alignment, making the emergency pathway analytically less relevant for this case. A visual overview of the two pathways is provided in Appendix E (Figures E-1 and E-2). The following subsection elaborates on both pathways in detail.

Procurement pathways

The distinction between the country-initiated and UNICEF-initiated procurement pathways has important implications for the role of donors. In the country-initiated pathway, donor involvement is typically reactive: funding may complement or co-finance national procurement plans once a formal request has been submitted by the Ministry of Health (Transcript T2). By contrast, in the UNICEF-initiated pathway, donors play a much more proactive role. Here, UNICEF Programme Division identifies priority interventions based on global health strategies, epidemiological signals, and system-level gaps, and subsequently engages potential donors to explore funding feasibility. In this pathway, donor alignment is a prerequisite for procurement to proceed, rather than a downstream enabler.

Donor organizations such as UNICEF, the Global Fund, CHAI, and UNFPA operate at the intersection of financing and supply chain management. Their contribution typically extends beyond purchasing alone. Through pooled procurement, long-term agreements with manufacturers, and multi-country demand aggregation, donors stabilize demand and create predictable production environments for products with limited commercial incentives (Transcript T2). For neonatal medicines such as caffeine, where demand is fragmented and volumes are low, such aggregation is often essential to secure sustainable supply (UNICEF Supply Division 2024; UNICEF Supply Division 2023b).

A key operational structure through which this is achieved is UNICEF's Procurement Services platform. Through this platform, governments or partners can access quality-assured

essential medicines without conducting individual tenders (Transcript T2). UNICEF bundles requests across countries, negotiates framework agreements, and ensures manufacturers commit production capacity. These processes are supported by tools such as multi-year forecasting, production planning alignment, and, in exceptional cases, temporary buffer stocks to mitigate supply interruptions (UNICEF Supply Division 2023b). For products like caffeine, UNICEF typically engages multiple pre-qualified manufacturers to reduce supply risk and enhance price competition.

Beyond procurement, donor influence extends upstream to market formation and quality assurance. Through Healthy Market Frameworks (HMFs), organizations such as UNICEF assess market structure, supplier diversity, affordability, and resilience, and deploy targeted levers, such as advance purchase commitments or supported API sourcing, to address identified gaps (UNICEF Supply Division 2023a).

Crucially, both procurement pathways depend on national policy alignment. Before donor-supported procurement can proceed, medicines must be included in national treatment guidelines and essential medicines lists (Transcript T2). In Malawi, this requires inclusion of caffeine in the MSTG and the MEML, after which regulatory approval, financing arrangements, and procurement planning can be pursued (MoH 2023). Once these institutional preconditions are met, donors can support early procurement, reduce financial risk for the government, and facilitate integration into national supply chains.

3.3.2 Role of procurement agent

A procurement agent acts by purchasing and supplying medicines and medical supplies to support public health programs. Its operating model combines a streamlined, routinely stocked catalog of approximately 200-250 items with an extended portfolio (around 2,000-3,000 items) that can be sourced on demand. In sourcing, there is a strong focus on manufacturers in Asia, particularly in India and China, where quality-assured generics can often be obtained at a comparatively lower cost (Transcript T1).

The upstream procurement process for a country working with a procurement agent is summarized in Figure 3-2. In a typical procurement set-up, an implementing organization (e.g., an NGO) receives program funding through a grant structure and subsequently contracts supply partners for the procurement and delivery of health commodities. In this arrangement, the agent coordinates procurement by drawing on its supplier network and selecting a sourcing route depending on whether a product is part of its routinely stocked range. For items held in continuous stock, products can be dispatched directly from the agent's warehouse in Dubai. For non-stock items and/or larger volumes, procurement is typically executed via manufacturer sourcing and subsequent international shipment. Final in-country distribution is generally coordinated with local entities such as CMS organizations and pharmacies, depending on the country context and delivery set-up.

For caffeine, the product is not listed in this agents E-catalog. As a result, supply is expected to follow an on-demand sourcing route via the relevant manufacturer. In such a configuration, shipment may take place directly from the manufacturing and/or distribution point to the destination country rather than via agent's warehouse; however, the exact logistics pathway for caffeine is not publicly confirmed and should therefore be interpreted with caution.

A practical constraint reported by the agent is that transactions are conducted in US Dollar (USD). For countries experiencing foreign currency shortages, such as Malawi during periods

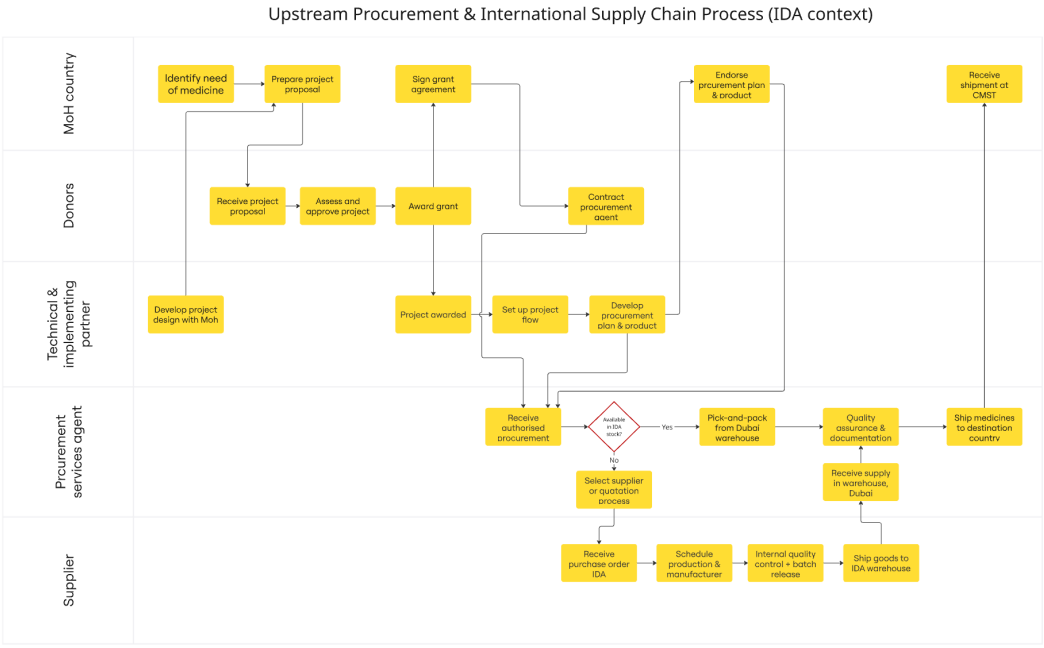

Figure 3-2: Swimlane upstream procurement supply chain with agent

of limited USD availability, this can become a binding barrier to procurement, as importers may be unable to place and settle orders in the required currency.

Regarding in-country presence, the agent operates through a combination of local distributors and local agents in several countries, including Africa. Agents support activities such as sales coordination, logistics arrangements, and communication. Local distributors may hold their own stock of selected agent quality-assured products, which can improve accessibility for smaller facilities with limited ordering capacity. In addition, agent reports collaborations with manufacturing partners located within Africa (e.g., in Nigeria, South Africa, Kenya, Tanzania, Uganda, and Rwanda), which may reduce reliance on intercontinental imports for specific products.

3.3.3 Conclusion

Taken together, the UNICEF and the agent interviews provide additional information for answering sub-question 1 by clarifying how procurement and upstream supply arrangements for low-volume essential medicines typically function in practice, and which institutional interfaces determine feasibility. The UNICEF perspective highlights that access is strongly pathway-dependent: procurement can be country-initiated or partner-initiated, but in both cases it requires prior policy and regulatory alignment (e.g., inclusion in treatment guidelines and essential medicines lists) and benefits from demand aggregation and risk-reduction drivers that improve supplier willingness to serve small markets. The agent perspective complements this by illustrating how procurement agents operationalize sourcing through catalog versus on-demand routes, and by identifying practical constraints that directly affect viability for Malawi, notably USD-based transactions and foreign exchange availability.

3.4 Aminophylline supply chain

To answer sub-question 1, this section uses aminophylline as a proxy medicine to illustrate how the upstream pharmaceutical system functions for a neonatal injectable in Malawi. Aminophylline is clinically relevant in the same therapeutic area as caffeine, is already embedded in Malawi's regulatory and public procurement system, and has a substantially lower unit price. This makes it a useful benchmark to reason about how procurement modality, market maturity, and scale may influence affordability. Based on desk research, the analysis maps aminophylline's registration status, public-sector procurement presence, and an indicative upstream supplier landscape.

3.4.1 Aminophylline pharmaceutical

Aminophylline is made from theophylline combined with ethylene-diamine, which helps it dissolve better in water. This makes aminophylline suitable for giving to newborns through an intravenous (IV) line (Bhatia 2000).

Aminophylline is an effective treatment for AOP, but it has a narrow therapeutic window. This means serum levels often need to be monitored to achieve the desired effect while avoiding toxicity (Henderson-Smart et al. 2010). Despite this drawback, aminophylline remains a clinically relevant and low-cost option, particularly in low-resource settings. Comparative studies indicate that its efficacy can be comparable to caffeine, although caffeine generally offers a wider therapeutic range and fewer adverse effects (T. Kondo et al. 2016).

A key reason aminophylline continues to be used in Malawi and other LMICs is its substantially lower price compared to caffeine. A recent multi-country study across five LMICs (Ethiopia, India, Kenya, Nigeria, and South Africa) found that the average end-customer price for a 25 mg/ml vial of aminophylline ranged from $0.02 in India to $2.00 in Kenya, while caffeine ranged from $2.70 in India to over $24.00 in Nigeria and South Africa (O. A. Ekhaguere, Bolaji, et al. 2024). Based on standard neonatal dosing for a 2 kg premature infant, the cost of managing AOP for seven days using aminophylline was several times lower than for caffeine in both public and private medical institutions. This price gap illustrates why, despite disadvantages in monitoring and convenience, aminophylline remains the predominant treatment for AOP in resource-limited health systems such as Malawi's.

3.4.2 Supply chain

Aminophylline appears in the PMRA product register in multiple dosage forms (e.g., injectable and oral formulations), indicating that aminophylline is formally registered for the Malawian market (PMRA 2025). In the public sector, aminophylline is also included in the CMST catalogue as Aminophylline 25 mg/ml, 10 ml, with a listed unit price of 168.07 MWK (approximately 0.08 EUR/unit, conversion based on December 2025 rates) (CMST 2025). Together, these sources provide evidence of regulatory presence and public-sector procurement eligibility.

However, the register and catalogue do not disclose key upstream characteristics such as the country of origin, the finished pharmaceutical product (FPP) manufacturer, or the marketing authorisation holder/importer responsible for the product supplied to Malawi. As a result, the end-to-end, product-specific supply chain pathway of aminophylline into Malawi cannot be reliably reconstructed using publicly available documentation alone. This constraint motivates the use of reference cases and stakeholder input in subsequent chapters.

Table 3-1: Aminophylline API suppliers. Source: adapted from PharmaCompass 2025

Company	Brand	Type	Country
Aarti Pharmalabs	N/A	API	India
Tenatra Exports	N/A	API	India
Bakul Group	N/A	API	India
Biopeptek Pharmaceuticals	N/A	API	U.S.A.
CSPC New Nova Pharmaceutical	N/A	API	China
CSPC Pharmaceutical Group	N/A	API	China
Fagron Group	N/A	API	Netherlands
Jilin Shulan Synthetic Pharmaceutical Co., Ltd.	N/A	API	China
Roche Diagnostics GmbH	N/A	API	Germany
Shandong Xinhua Pharmaceutical	N/A	API	China
Siegfried AG	N/A	API	Switzerland
Sneha Medicare Pvt Ltd	N/A	API	India
Yashiro Pharmaceutical Co Ltd	N/A	API	Japan

To nevertheless obtain an indicative view of the upstream supplier landscape, Table 3-1 presents a selection of firms listed on PharmaCompass as suppliers/manufacturers of aminophylline API (PharmaCompass 2025). This overview should be interpreted as grey/industry information on supplier presence rather than evidence of which suppliers serve Malawi. Moreover, an API listing does not imply vertical integration into FPP manufacturing, nor does it confirm market access activities (e.g., dossier submission, local registration, or participation in Malawian tenders). With these limitations in mind, the list suggests that the identified API suppliers are geographically concentrated: 9 out of 13 firms in this selection are headquartered in Asia (India, China, or Japan). For Malawi, this indicates potential reliance on international sourcing and import logistics for upstream supply, even if the specific procurement channel cannot be identified from desk sources.

PharmaCompass also reports indicative reference prices for aminophylline API across countries. While such price indications should be interpreted cautiously, they are broadly consistent with the idea that scale and contracting conditions can influence upstream input costs (McCabe et al. 2009). At the same time, reported prices vary with supplier characteristics, specifications (e.g., grade/quality), and contractual and logistical conditions (e.g., shipping terms and routes), indicating that scale effects alone do not explain observed price differences.

Overall, the desk-research evidence primarily supports conclusions about the likely international nature of upstream sourcing rather than the exact procurement route into Malawi. The supplier landscape suggests that aminophylline API is commonly produced by firms headquartered in major generic manufacturing hubs, which is compatible with the low unit price listed in the CMST catalogue. However, the specific manufacturer, importer/MAH, and end-to-end route supplying Malawi cannot be confirmed from the public sources used here.

This proxy analysis contributes to sub-question 1 by showing that Malawi's upstream system can register and procure a neonatal injectable through formal regulatory and public procurement structures (PMRA registration and CMST catalogue inclusion). At the same time, publicly available sources provide limited transparency on manufacturer–importer arrangements and the product-specific pathway into the country, motivating the use of reference cases later in the thesis.

For affordability, aminophylline provides a useful benchmark. Its low public-sector price

is in line with a mature generic market, where scale and competition can reduce unit costs. This suggests that the affordability gap between aminophylline and caffeine is more likely explained by upstream market maturity and procurement configuration than by clinical need alone.

3.5 Price formation and cost drivers

3.5.1 Price formation

Observed procurement prices of essential medicines often differ substantially across countries, even when products are sourced internationally and manufactured by a relatively limited set of suppliers (Mourik et al. 2010). For caffeine in SSA procurement contexts, available price indications suggest comparatively high unit prices. At the same time, caffeine is a widely produced, mature commodity/API that can be supplied at low prices in other markets (O. A. Ekhaguere, Ayede, et al. 2020). This contrast implies that the high prices observed in SSA cannot be attributed to production technology or manufacturing location alone.

Instead, price formation should be understood as the outcome of supply chain characteristics and institutional arrangements. For many medicines, estimated minimum production costs are low relative to observed market prices, suggesting that procurement architecture, market structure, compliance requirements, and demand fragmentation shape procurement outcomes through overhead allocation and risk pricing (Hill et al. 2018). In particular, pooled or donor-supported procurement can stabilize demand signals and reduce transaction costs per unit, whereas fragmented and low-volume purchasing increases coordination burden and induces supplier risk markups. The remainder of this chapter therefore focuses on the upstream cost drivers that can explain observed price levels, and on how these factors affect affordability and availability in low-volume LMIC markets.

3.5.2 Cost drivers

This section brings together upstream cost drivers that commonly appear in pharmaceutical supply chains and that can change with different choices in procurement, sourcing, and financing. The goal is not to have quantitative data, but to clarify which cost components and risks are likely to matter most under different supply chain designs, and where cost pressure is expected to build up.

These cost-driver insights provide the analytical basis for formulating design objectives and for comparing alternative upstream supply chain configurations in later chapters, considering the trade-offs between affordability and availability (Lee et al. 2021; Ibrahim et al. 2025).

Economies of scale

Consolidation and standardization are repeatedly highlighted as key factors to reduce upstream unit costs, because they unlock economies of scale in manufacturing, procurement, and transport (Lee et al. 2021; Aitken 2016). In practice, many upstream activities include fixed or quasi-fixed effort per tender, batch, or shipment (e.g., contracting, batch set-up, QC/testing, documentation, and handling). When demand is pooled, these fixed burdens are spread over more units, which lowers the cost base per ampoule. Consolidation also stabilizes

demand signals, reducing the need for buffers and last-minute expediting, which supports both affordability and supply continuity in low-volume markets (Falcon 2024; Ibrahim et al. 2025). In the case of caffeine, evidence from neonatal drug pricing highlights that the very small NICU patient population translates into a limited market, which makes it harder to spread fixed upstream costs and contributes to disproportionately high unit prices (Zupancic 2021).

Dedicated supply chains

The literature suggests that specialized or dedicated supply chains tend to increase upstream costs, primarily because they limit consolidation and thereby reduce scale advantages while increasing fixed overhead per unit (Ibrahim et al. 2025). When production, handling, or compliance is tailored to a specific channel, volumes cannot easily be combined across markets, so fixed set-up and quality costs are redeemed over smaller batches. In addition, dedicated configurations often require more intensive monitoring and assurance, which raises coordination effort and can translate into higher risk buffers embedded in procurement outcomes (Ibrahim et al. 2025).

Demand uncertainty

In many LMIC settings, demand for medicines is difficult to predict because ordering patterns are irregular and demand signals are weak. Funding constraints, ad-hoc ordering cycles, and limited forecasting capacity often lead to poor demand visibility, which increases the risk of both stockouts and overstocking (Falcon 2024; Lee et al. 2021). Evidence from Nigeria supports this: Sarley et al. report that poor data collection, limited use of data, and low data quality are critical issues affecting supply chain performance (**Citation2017**). In low-volume markets, these effects are more pronounced because variability cannot be absorbed through scale, which can directly undermine availability (Falcon 2024; Ibrahim et al. 2025). Within the defined scope, demand uncertainty is largely exogenous to the upstream supply chain, as it is driven by factors outside direct supply chain control (e.g., irregular procurement cycles driven by funding constraints). However, configuration and contracting choices can reduce how strongly this uncertainty translates into upstream costs, for example by pooling demand to stabilise volumes, improving information sharing, and using more flexible contracting arrangements. Poor demand predictability increases upstream costs through inefficient planning, higher buffer stocks, and reactive replenishment (e.g., short-notice orders and expediting) (Falcon 2024; Lee et al. 2021).

Chain complexity

Each additional echelon typically adds both operational overhead and mark-ups, while each handover introduces extra coordination and control points (Aitken 2016). Interfaces require contracting, information exchange, custody and quality checks, and often additional warehousing and handling. As supply chains become more fragmented, coordination burden and cumulative overhead increase, and the number of potential failure points grows (delays, mismatches, accountability gaps). This tends to push up costs and can reduce supply continuity (Aitken 2016; Lee et al. 2021).

Regulatory burden

Regulatory burden is also largely exogenous to the supply chain within the defined scope, as it is imposed by national and international regulatory regimes (e.g., product registration requirements, country-specific labeling rules, and mandated quality testing/release procedures). However, supply chain and contracting choices can mitigate how strongly these requirements translate into upstream costs. for instance, they can enable compliance consolidation (e.g., shared quality-control and documentation infrastructure), reduce market-specific fragmentation, or apply postponement strategies, such as late-stage packaging and labeling, where feasible. Compliance requirements (registration, labelling, quality testing, and country-specific procedures) increase upstream costs, particularly when requirements differ across countries and thereby limit demand pooling (Lee et al. 2021; Ibrahim et al. 2025). Regulatory heterogeneity fragments demand into smaller compliant batches and increases administrative and quality-related fixed costs per market served. For low-volume medicines, these compliance burdens can become a dominant driver and may discourage suppliers from serving the market, which affects availability (Ibrahim et al. 2025).

Financial risk

In many LMIC settings, upstream supply chain costs are strongly shaped by financing frictions such as delayed payments, pre-financing requirements, and FX volatility (Aitken 2016; Falcon 2024; Ibrahim et al. 2025). While these risks are largely exogenous to the supply chain within the defined scope, configuration and contracting choices can reduce how strongly they translate into costs, for example by shaping payment terms and allocating financial risks across actors. If importers or suppliers have to finance inventory for long periods and hedge currency and payment uncertainty, these costs are typically priced into procurement outcomes. High financial risk therefore raises unit costs and can reduce supplier willingness to participate in small or uncertain tenders, threatening supply continuity (Ibrahim et al. 2025).

Distribution trade-off

Distribution costs are shaped by a classic transport-inventory trade-off (Aitken 2016). More frequent, smaller shipments increase transport and handling cost per unit, while less frequent replenishment increases inventory holding costs and the buffer stock required to protect service levels. Design choices that reduce lead times can lower inventory needs but often require more transport intensity. As a result, affordability and availability objectives are intrinsically linked and need to be balanced through configuration choices (Aitken 2016; Lee et al. 2021).

Conclusion

Taken together, the literature suggests that upstream cost drivers in pharmaceutical supply chains are sensitive to configuration choices, even when absolute cost levels cannot be established with precision (Lee et al. 2021; Aitken 2016). This supports the analytical focus of this thesis on supply chain configurations as a relevant unit of analysis for affordability-related access challenges.

In the remainder of this chapter, these cost-driver principles are used to analyse the SSA reference cases and assess whether the same drivers can be observed in practice. The aim

is to examine how different institutional pathways and procurement structures relate to consolidation, coordination effort, and demand visibility, and to identify where affordability and supply continuity appear to be shaped by these cost drivers or other factors.

3.6 Supply chain of caffeine in Sub-Saharan African countries

Building on the cost-driver principles discussed in the previous section, this section addresses sub-question 2. Therefore, the upstream supply chains in selected SSA countries are examined as reference cases. The cases describe how caffeine supply is organized in practice, focusing on the institutional pathway (regulatory inclusion), procurement modality, and actor roles. In addition, the cases are used to extract configuration features that are plausibly cost-relevant in low-volume settings, such as the extent of demand aggregation and the degree of fragmentation across channels.

The reference cases focus on Ethiopia, Kenya, South Africa, and Uganda. These countries were selected based on three reasons. First, the literature review yielded sufficient and comparable publicly available information on their caffeine introduction pathways, which made them suitable for a reliable cross-country analysis. Second, all four countries have already implemented caffeine for the treatment of AOP, ensuring that the cases reflect operational practice rather than hypothetical plans. Third, the countries represent variation in sourcing and procurement arrangements, which enables comparison across different institutional pathways. In addition, earlier work by O. A. Ekhaguere, Ayede, et al. (2020), which discusses these countries in the context of caffeine access in sub-Saharan Africa, provided a useful starting point and improved the feasibility of collecting consistent information across cases.

Detailed country-specific descriptions (including regulatory pathways, marketing authorization holder (MAH) structures, and donor programs) are provided in Appendix F. Table 3-3 summarizes key upstream characteristics across the reference cases, including manufacturers, suppliers, procurement arrangements, donor involvement, and indicative prices per ampoule where available. The summaries below highlight, for each case, the characteristics that are most informative for understanding how caffeine is brought into and sustained in the public health system, and identifying plausible upstream cost drivers.

Table 3-3: Overview of caffeine supply chains in selected SSA countries

Country	Manufacturer	Mf. country	Supplier	Distributor	Donor	Brand name	Price (€ / amp., 20mg/ml)
Ethiopia	Chiesi	Italy	Chiesi	–	CHAI	Peyona	–
Kenya	Martindale	UK	Ethypharm	KEMSA	CHAI	Cayona	2.65[a]
South Africa	Chiesi	Italy	Safeline Pharma	Safeline Pharma	N/A	Cayona	18.98[b]
Uganda	Martindale	UK	Ethypharm	–	–	Caffeine Citrate	8.64[c]

Note: "–" indicates that the information was not identified in this study. "N/A" indicates that the role is not applicable.
[a] H. B. Kenya 2024
[b] National Department of Health, South Africa 2025
[c] O. A. Ekhaguere, Ayede, et al. 2020

Ethiopia

In Ethiopia, caffeine entered the formal pharmaceutical system through national regulatory authorization based on international regulatory reliance. Public-sector procurement and distribution are centrally organized through the Ethiopian Pharmaceuticals Supply Agency (EPSA), under the strategic oversight of the Ministry of Health. International partners played a critical enabling role during market entry by supporting demand aggregation and tendering. From a cost perspective, this configuration suggests that affordability is supported when early-stage market shaping reduces supplier risk and increases effective order volumes, while the operational pathway remains anchored in a central public procurement structure.

Kenya

Kenya integrated caffeine into the national system through inclusion in the Essential Medicines List and procurement via the Kenya Medical Supplies Authority (KEMSA). Procurement is executed through routine national structure and distributed through established public channels. International partners facilitated market entry by supporting pricing negotiations and supplier engagement. In cost terms, Kenya illustrates a configuration in which donor-supported market shaping complements institutionalized procurement, enabling consolidation benefits while limiting the coordination overhead associated with parallel supply chains.

South Africa

South Africa represents a mature, fully institutionalized market for caffeine. The medicine is locally registered and procured through competitive public tender procedures, supplied via standard public and private distribution channels. There is no donor involvement. This configuration indicates how procurement competition and routine tendering can support predictability for suppliers and reduce reliance on exceptional arrangements. At the same time, the case demonstrates that prices may still be high in settings with different market conditions and specifications, suggesting that cost drivers extend beyond manufacturing and include the broader procurement and market environment.

Uganda

In Uganda, government-financed and donor-financed procurement channels coexist. Registered medicines may be supplied through the National Medical Stores (NMS), while donor-funded commodities are frequently procured through parallel or semi-parallel structure and distributed through alternative channels such as the Joint Medical Stores (JMS). This fragmented procurement architecture implies multiple upstream pathways and limited demand consolidation. From a cost perspective, such fragmentation is expected to increase transaction and coordination burden, reduce predictability for suppliers, and weaken scale advantages, which in turn can contribute to higher unit costs and less stable market participation.

3.7 Comparative insights of SSA countries

This section synthesizes the four SSA reference cases to answer how the upstream supply pathway for caffeine is organized, and which configuration features plausibly act as upstream cost drivers in low-volume markets.

Supply chain organization

Across the reference countries, caffeine is supplied as an imported FPP from a concentrated manufacturer base. The decisive differences, therefore, do not lie in production technology, but in the institutional pathway through which caffeine becomes eligible for procurement and is routinized in the system. Where caffeine is supplied through public channels, regulatory authorization and policy inclusion (e.g., EML and/or guideline alignment) function as enabling conditions: they legitimize demand and allow procurement through formal structure.

Procurement architectures differ across cases. Ethiopia and Kenya represent largely centralized public procurement pathways, in some instances complemented by partner involvement during introduction. South Africa represents a mature, institutionalized pathway through routine tendering without donor intermediation. Uganda reflects a more fragmented architecture in which multiple procurement and distribution routes coexist. These differences determine who aggregates demand, how predictable procurement appears to suppliers, and how many interfaces and handovers are embedded in the pathway.

Main cost drivers

When interpreted through the cost-driver framework developed in Section 3.6, three configuration-sensitive factors recur in the reference cases.

First, consolidation potential and demand signalling appear central. Pathways that aggregate volumes through central procurement and/or partner-supported market shaping are more likely to create a credible and predictable demand signal. In low-volume markets, this plausibly reduces per-unit overhead allocation and supplier risk markups by improving scale and planning stability.

Second, chain complexity and coordination burden differ markedly across pathways. Cases with parallel routes, multiple intermediaries, or repeated handovers embed additional contracting, documentation, handling, and control points. Such fragmentation plausibly increases

transaction effort and cumulative mark-ups and can also reduce continuity due to more failure points.

Third, institutional and compliance effort shapes the administrative load and perceived risk of serving the market. Across cases, procurement is only feasible once regulatory and policy conditions are met; however, the practical burden of documentation, compliance assurance, and contracting still varies by pathway. In low-volume settings, fixed compliance and administrative costs are difficult to spread, which can make these elements dominant cost pressures.

Implications for Malawi

For Malawi, the synthesis narrows the design problem in two ways. First, access is primarily a pathway problem: caffeine must become eligible through a feasible institutional route (registration and policy inclusion or a justified exceptional pathway) before procurement can be routinised. Second, affordability and availability are closely tied to procurement architecture. Designs that strengthen demand aggregation and reduce avoidable coordination burden are expected to reduce upstream cost pressure and support supply continuity, whereas designs that rely on fragmented or exceptional arrangements may remain administratively heavy and less predictable for suppliers.

Accordingly, the alternatives developed in Chapter 4 vary systematically in: how regulatory eligibility is achieved, how demand is aggregated and communicated to suppliers, how procurement and contracting are organised (including partner involvement and risk sharing), and how fragmentation and the number of upstream handovers are minimised while maintaining quality and compliance requirements. These dimensions are subsequently translated into design objectives and MCA criteria.

Conclusion

Overall, the SSA reference cases show that caffeine access is feasible in comparable contexts, but achieved through distinct institutional pathways. The most consequential differences are upstream and organizational: consolidation potential, coordination burden, and compliance-related fixed effort vary by pathway and plausibly shape both affordability and supply continuity in low-volume markets. These insights provide the empirical bridge from the cost-driver framework (Section 3.5.2) to the structured generation of alternative supply chain configurations for Malawi (Chapter 4).

3.8 Synthesis of upstream barriers

The previous sections' analyses examined institutional structures, procurement pathways, and reference cases in comparable SSA contexts. Individually, these analyses provide partial explanations for the absence of routine caffeine supply in Malawi. However, they have not yet been consolidated into a bundled set of findings. This section therefore synthesizes these findings into a set of upstream barriers. The barriers represent structural conditions that are either misaligned or insufficiently institutionalized within the current Malawian context. By articulating these barriers explicitly, this section also provides the analytical foundation for the subsequent design phase (Chapter 4), where design requirements are developed.

3.8.1 Barriers

The analysis of aminophylline, the selected SSA reference cases, and the broader literature provides partial explanations for the absence of caffeine supply in Malawi. Together, these findings indicate that multiple upstream barriers prevent the establishment of a stable and routine procurement pathway. Summarising these barriers helps define the key design requirements for alternative upstream supply chain configurations.

Registration as an entry barrier

Regulatory registration and institutional eligibility function as formal entry gates for routine public-sector procurement. For medicines intended for government supply, inclusion in national treatment guidelines and the Essential Medicines List, alongside a lawful importation and procurement pathway, are prerequisites for institutionalized purchasing and distribution (MoH 2023). Reference cases show that where caffeine supply has been successfully institutionalized, the product is formally registered and embedded within national regulatory and procurement frameworks. In the absence of such a pathway, supply is limited to exceptional or ad-hoc import routes, which are administratively burdensome, difficult to scale, and unsuitable for long-term integration (Transcript T2). The lack of a fully institutionalized entry pathway therefore constitutes a structural upstream barrier.

Financing and payment uncertainty

Financing constraints affect not only affordability but also the practical execution of procurement transactions. International suppliers commonly transact in foreign currency (e.g., USD), while limited access to foreign exchange in Malawi can delay order placement and settlement (Transcript T1). Foreign exchange shortages and payment uncertainty increase perceived counterparty risk for suppliers and may discourage engagement in low-volume markets. Although financing constraints alone do not explain the absence of caffeine supply, they amplify execution risk and reduce the likelihood that stable contractual relationships will emerge. In this sense, financing uncertainty reinforces structural instability in the upstream configuration.

Low-volume market characteristics

Caffeine for AOP serves a relatively small and specialised neonatal population, resulting in structurally low demand volumes (Zupancic 2021). In the Malawian context, expected order quantities are limited and forecasting is uncertain. For manufacturers and suppliers, such conditions weaken incentives to invest in market entry activities, including registration support and supply set-up (Transcript T2). At the same time, public procurement systems are typically optimised for higher-volume, predictable medicines (Transcript T1). The mismatch between caffeine's low-volume profile and standard tender structures reduces institutional compatibility and limits competitive pressure, thereby constraining the spontaneous emergence of routine supply.

Assuring quality

Quality assurance represents an additional upstream concern. In resource-constrained environments, financial pressure and limited regulatory capacity can increase reliance on informal

or weakly regulated procurement channels, raising exposure to substandard and counterfeit medicines (McCabe et al. 2009; Alfaouri et al. 2025). Counterfeit products may enter the legitimate supply chain during logistics activities spanning manufacturing, distribution, and retail (**ManguBanik2021**), underscoring that quality risks can originate upstream and propagate across the chain. Ensuring product quality therefore requires procurement and sourcing arrangements that safeguard regulatory compliance, documentation standards, and traceability, rather than relying solely on downstream inspection.

Implication for the design phase

Taken together, these barriers show that improving access requires more than identifying a supplier. A viable upstream configuration must establish a lawful and institutionalized entry pathway, translate fragmented demand into a credible procurement signal, and allocate supplier and buyer risk through appropriate contracting and financing arrangements. These conclusions are used to derive the design requirements and to structure the functions and options in the morphological chart in Chapter 4.

Collectively, these barriers highlight that the absence of caffeine in Malawi cannot be attributed to a single constraint. Instead, regulatory entry conditions, financing instability, limited market scale, and quality assurance risks interact to create an upstream environment in which routine procurement does not naturally emerge. These consolidated findings form the basis for deriving explicit design requirements for alternative upstream supply chain configurations.

3.9 Takeaways chapter 3

This chapter established the basis for the design phase. The Malawi supply chain mapping, interview transcripts, and the aminophylline proxy case clarify how the upstream chain is organised in practice and which regulatory, procurement, and sourcing processes define the design space for caffeine. At the same time, the aminophylline analysis shows that, based on publicly available information, it is not possible to reliably trace price formation or attribute observed prices to specific upstream cost components or contracting conditions. This lack of transparency reinforces the need for a design-oriented approach: rather than estimating exact costs, the thesis uses supply chain configuration choices to reason about which upstream design principles are likely to increase or decrease cost pressure and improve continuity of supply.

Building on this empirical starting point, the literature-based analysis of price formation and structural cost drivers provides the analytical justification for focusing on supply chain configuration as the central design object. While final prices are influenced by broader market dynamics, upstream configuration choices are expected to have a directional effect on cost pressure through factors such as consolidation potential, fragmentation and handovers, and exposure to financing and payment risk. These considerations are particularly critical in low-volume settings like Malawi, where fixed regulatory and transaction costs are difficult to spread over scale and where foreign-exchange constraints and payment uncertainty can be priced into the supply pathway.

The SSA reference cases show that caffeine access is feasible in contexts comparable to Malawi, but that countries reach this outcome through different pathways. These pathways

matter, because they are linked to differences in observed price levels: how regulatory eligibility is arranged, how procurement is organised (e.g., centralised versus fragmented; routine versus exceptional), and whether intermediaries coordinate introduction can change consolidation potential, transaction effort, and risk exposure, and therefore cost pressure. The cases therefore support the central assumption of this thesis that upstream supply chain structure influences affordability. These insights also guided the definition of the functions included in the morphological chart.

The use of swimlane diagrams to map the current supply chain structures provided a clear overview of the processes involved and the actors responsible for them. The diagrams helped to structure the different steps in the supply chain and made the distribution of responsibilities across actors visible. At the same time, the level of detail included in these diagrams was not strictly necessary for answering the research question. However, as a visualisation tool for understanding complex supply chain structures and actor interactions, swimlane diagrams can be useful and are therefore recommended for future research focusing on process mapping or system visualisation.

Lastly, the upstream barriers synthesised in this chapter help explain why routine caffeine supply has not yet emerged in Malawi. They identify the specific structural frictions that shape affordability and continuity of supply (e.g., fragmentation, weak demand signals, and financing/contracting constraints). These barriers, therefore act as design inputs: they can be used to make the concrete design requirements and evaluation criteria that guide the design and evaluation of the alternative configurations in the next chapters.

Chapter 4

Design

This chapter addresses sub-question 3 by generating alternative upstream supply chain configurations for supplying caffeine to Malawi. Building on the analysis of the current Malawian set-up and the SSA reference cases, the chapter translates the identified barriers and enabling conditions into explicit design requirements and objectives.

Following the Develop phase of the Double Diamond, the chapter proceeds in two steps. First, the design requirements and objectives are derived from the analysis in the previous chapter, mostly the upstream barriers. These requirements define the minimum feasibility conditions that any configuration must satisfy in the Malawian context. Second, the upstream supply chain is decomposed into key functions and corresponding options, which are combined using a morphological chart. After screening infeasible options and incompatible combinations, a small set of distinct design alternatives is selected. The purpose of this chapter is not to choose a preferred design, but to document and justify the final alternatives (and their underlying assumptions) as input for the comparative evaluation in the MCA chapter.

4.1 Requirement analysis

This section specifies the design requirements that guide the construction of the initial morphological chart and the generation of supply chain alternatives. These requirements function as minimum feasibility conditions and are used as screening constraints during the design process: alternatives that violate one or more requirements are excluded from the design space.

The requirements are derived from the contextual analysis presented in Chapter 3, mostly from the upstream barrier synthesis in Section 3.8. While the requirements ensure that all generated designs are feasible in principle, the relative performance of the resulting alternatives is assessed separately in the subsequent multi-criteria analysis.

Design requirements

- **R1 – Legal and regulatory feasibility in Malawi.**
  Constraint: The design shall provide a lawful pathway for product registration (or an applicable exemption pathway), importation, and procurement for use in Malawi, in compliance with relevant regulatory and public procurement frameworks.
  Screening question: Is a formal, legal regulatory and procurement pathway identified for this configuration (including import clearance and procurement legality)?
  Rationale: The configuration must be adoptable by accountable public actors. Although informal import routes may occur in SSA contexts, they cannot serve as a reliable basis for an officially implemented supply chain. Regulatory and procurement feasibility is therefore treated as a hard constraint to ensure institutional legitimacy and compliance.

- **R2 – Minimum quality control and product integrity.**
  Constraint: The design shall safeguard product quality by ensuring that the product is subject to at least one credible QC check and release decision at or before entry into Malawi, and in any case prior to release into the Malawian public supply chain.
  Screening question: Does the configuration include at least one defined QC gate (who performs it, where it occurs, and what constitutes release), such that non-compliant products are prevented from entering the Malawian supply chain?
  Rationale: Background analysis and reference cases indicate that affordability pressure and fragmented procurement can incentivise lowest-cost sourcing, which increases exposure to substandard or falsified products. Since the design is intended for clinical use, a minimum QC/release structure is a non-negotiable condition for inclusion in the design space.

- **R3 – Feasibility under SSA operating constraints.**
  Constraint: The design shall be implementable under SSA operating conditions and shall not depend on major upfront capital investments or the construction of new manufacturing capacity as a prerequisite for implementation. The configuration should also be able to function within the current institutional set-up and capabilities of the Malawian public supply chain, without requiring major governance restructuring as a precondition.
  Screening question: Can the configuration be implemented using existing supply chain actors and assets (or realistic incremental adaptations), without requiring a new factory build, and without shifting core responsibilities to actors that currently lack the mandate and operational capacity to execute them?
  Rationale: SSA pharmaceutical supply chains typically face strong financial and capacity constraints. Configurations that require substantial new infrastructure or new production systems are unlikely to be implementable within the scope of this project and are therefore excluded from the design space.

- **R4 – Continuity and sustainability of the configuration.**
  Constraint: The design shall constitute a configuration that can be maintained over time, rather than a one-off or short-term stopgap. It must rely on repeatable arrangements that can be institutionalized (e.g., through ongoing contracting and routinized operational processes). In practice, configurations based on ad-hoc emergency purchasing without an institutionalized contracting structure are considered non-repeatable.

Screening question: Is the configuration structurally repeatable over multiple cycles, without relying on exceptional one-time actions or temporary measures that cannot be maintained?
Rationale: The purpose of the design exercise is to propose a durable supply chain configuration that supports sustained access. Temporary fixes may address short-term shortages but do not provide a basis for long-term adoption; continuity is therefore treated as a hard constraint.

Design objectives

Building on the cost-driver synthesis in Section 3.5.2 and the upstream barrier analysis in Section 3.8, the objectives translate those into evaluation criteria that are directly linked to the design choices in the morphological chart. The cost drivers financial risk and demand uncertainty are treated as exogenous factors: the supply chain design cannot remove them, but the alternatives should be able to cope with them. Therefore, these are not included as objectives, but are used to construct scenarios, further explained in Chapter 5. The remaining drivers are translated into the objectives below, and each objective is assessed using the functions and options from the morphological chart.

1. **Scale potential**
   This comes mainly from economies of scale and the cost penalty of dedicated, low-volume chains. The objective is to prefer configurations that can create volume and consolidate demand, instead of being stuck in small, separated procurement streams.
   This is measured by: the sourcing mode in the morphological chart (single source procurement vs dual/multi-sourcing vs pooled procurement) and the upstream bundling approach (direct shipment vs via agent/wholesaler vs regional hub consolidation).

2. **Fragmentation**
   This comes from dedicated chains and extra steps. The more steps and extra interfaces you introduce (more gates, more intermediaries), the more overhead and coordination effort is needed, which typically increases upstream costs. The objective is therefore to limit unnecessary fragmentation.
   This is measured by: the upstream bundling approach (direct vs agent/wholesaler vs hub) and the quality control design (single QC gate vs two QC gates vs multi gate).

3. **Transactional efficiency**
   This comes from chain complexity and procurement transaction costs. When procurement is more ad-hoc and when financing/payment is more complex, the administrative burden and coordination effort go up. The objective is to have a configuration that makes procurement and payment more smooth and predictable.
   This is measured by: procurement & contracting (ad-hoc vs routine procurement cycle vs strengthened/long-term framework) and financing & payment (donor funded vs government budget vs pooled donor funded). The sourcing mode (single vs multi vs pooled) is included as it influences how many parties are involved in procurement.

4. **Chain complexity**
   This is about how complex the upstream chain becomes in terms of handovers and control points. More actors and more QC gates typically increase coordination needs

and make implementation harder, which also links back to cost. The objective is to keep the chain manageable.
This is measured by: the quality control design (single vs two vs multi gate) and the upstream bundling approach (direct vs agent/wholesaler vs hub). In addition, the sourcing mode (single vs multi vs pooled) is used as a proxy for the number of parties to coordinate.

5. **Logistics cost balance**
This comes from the distribution trade-off: consolidation and bundling can reduce transport cost per unit, but can also affect lead times and responsiveness. Because this research focuses upstream (up to MoH procurement), the objective is to compare alternatives on how they balance consolidation versus shipment fragmentation in the upstream leg.
This is measured by: the upstream bundling approach (direct shipment vs via agent/wholesaler vs regional hub consolidation). Where relevant, the ordering responsibility (facility ordering vs central ordering vs regional pooling) is used to indicate how much consolidation is structurally enabled.

4.2 Morphological chart

To systematically explore alternative supply chain designs for pharmaceutical caffeine, a morphological chart is used as the main concept generation tool. A morphological chart decomposes a complex design problem into key functions and maps multiple solution options per function in a matrix (Delft Design Guide n.d.). The method is suited for early-stage system design because it enables broad and transparent exploration of the design space, rather than premature convergence on a single solution. By separating functions (what the system must achieve) from options (how this can be realized), it supports systematic comparison of fundamentally different configurations.

Functions represent the essential sub-functions that any feasible end-to-end supply chain must fulfill, while options describe alternative ways to organize or execute each function (Pahl et al. 2007; Roozenburg et al. 1995). Following morphological analysis principles, options within a function are defined as mutually exclusive, while the set of options aims to be collectively exhaustive to cover the relevant design space (Chakrabarti et al. 2011; Cross 2008). A design concept is generated by selecting one option per function, resulting in a coherent supply chain configuration. This makes concept generation systematic and traceable, since each alternative is an explicit combination of predefined design choices.

4.2.1 Initial design morphological chart

The morphological chart presented in figure 4-1 defines the initial design for the caffeine supply chain to Malawi. The individual options listed per function do not constitute solutions by themselves. Instead, they represent building blocks from which a number of supply chain configurations (design alternatives) can be composed. In Appendix G, the functions and their options are described.

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 4-1: Morphological chart of alternative design options for the caffeine supply chain

4.3 Design alternatives

The morphological chart includes six functions with three options each, resulting in $3^6 = 729$ theoretical configurations. Evaluating all combinations is not feasible within the scope of this thesis, and several options are maybe either incompatible or do not satisfy the design requirements. Therefore, the option set is first screened using the constraints (R1–R4).

Next, the design space is further reduced by excluding combinations that are structurally incompatible or highly implausible. This step ensures that the morphological chart generates implementable supply chain configurations rather than theoretical mixes of options.

After applying these screening steps, 192 feasible configurations remain. To reduce this set to a manageable number of distinct alternatives, the remaining configurations are clustered based on their dominant governance, sourcing, and financing logic. The detailed procedure and decision rules are described in Appendix H.

Based on this process, four representative design alternatives are selected and discussed below.

Alternative 1: Donor pipeline

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 4-2: Alternative 1: Donor pipeline

This design alternative represents a donor-driven upstream supply chain configuration that closely resembles the current set-up commonly observed in Sub-Saharan African settings. The supply chain is organized around central ordering, single-source procurement, and direct shipment, with an intermediary (agent/wholesaler) coordinating purchasing and upstream logistics on behalf of the donor and the receiving country. In this configuration, procurement and financing are primarily donor-funded and often executed on an ad-hoc basis rather than through a routine, government-budgeted procurement cycle.

A key design choice is the use of a single quality control gate at the manufacturing stage, which reduces process steps and can shorten lead times compared to multi-gate verification. However, this also shifts dependence toward the manufacturer's quality systems and the governance capacity of the donor/intermediary. Overall, this alternative functions as a baseline configuration: it simplifies coordination and can leverage scale through centralized purchasing, but it also concentrates supply risk in one supplier and includes intermediary-related transaction costs, both of which may influence upstream cost drivers and, indirectly, affordability and availability outcomes.

Alternative 2: Managed multi-sourcing

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 4-3: Alternative 2: Managed multi-sourcing

This design alternative extends the baseline donor pipeline by adding redundancy and additional control points, while maintaining a centrally coordinated ordering structure. Demand is still consolidated through central ordering, but procurement shifts from single-sourcing to dual- or multi-sourcing. This increases supply reliability by reducing dependency on one manufacturer and creates more flexibility to respond to disruptions, although it can increase coordination effort due to managing multiple suppliers and contracts.

Procurement is organized through a strengthened long-term contracting framework, which provides greater stability and planning certainty compared to short-term, ad-hoc arrangements. Financing remains donor-funded, but quality assurance is reinforced by introducing two quality control gates: one at the manufacturing stage and a second verification point in Malawi. This second gate is intended to reduce the risk of substandard or non-compliant products entering the downstream system, at the expense of additional process steps, coordination, and potential lead time and cost implications.

As in the baseline, an agent/wholesaler coordinates purchasing and upstream logistics between donor(s), manufacturers, and the receiving country. This intermediary role may be performed by a donor-linked organization or a separate specialized party. Overall, this configuration aims to improve availability and risk resilience through sourcing diversification and enhanced quality control, while accepting higher complexity and potentially higher upstream transaction and compliance-related cost drivers.

Alternative 3: Regional logistic hub

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 4-4: Alternative 3: Regional logistic hub

This design alternative represents a more integrated, regional supply chain configuration in which multiple countries participate in a shared procurement and distribution set-up. Rather than country-level central ordering, demand information is pooled across participating countries and consolidated for quantification. This enables pooled sourcing, potentially improving negotiating power and creating scale benefits, but it also increases governance and coordination complexity because multiple national stakeholders and processes must be aligned.

The physical flow is organized through a regional hub model: one country functions as a hub where products are received, consolidated, and subsequently distributed to other countries in Sub-Saharan Africa. Given the higher interdependence between countries in this configuration, procurement is supported by a strengthened long-term contracting framework to provide planning stability and reduce the risk of interruptions caused by fragmented or short-term agreements. Financing is assumed to remain donor-funded, as a central funding structure can facilitate coordination, contracting, and risk-sharing across countries.

Quality control is organized through multiple verification points to account for additional handovers and cross-country variation in regulatory requirements. Importantly, this alternative aligns with broader policy momentum toward regulatory cooperation and harmonization in Africa (e.g., the African Medicines Agency), which can progressively reduce regulatory fragmentation and administrative burden for cross-border procurement and distribution. In this alternative, QC gates are applied at manufacturing, at the regional hub, and in-country prior to final distribution. This multi-gate approach is intended to reduce the probability of quality failures propagating through the regional network, but it may introduce additional

lead time and compliance-related cost drivers. Overall, this alternative aims to improve availability and affordability drivers through regional scale and consolidation, while trading off against increased organizational complexity and more extensive quality control requirements.

Alternative 4: Government core

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 4-5: Alternative 4: Government core

This design alternative represents a government-core upstream configuration in which coordination and decision-making authority are internalized by the Malawian government rather than delegated to external intermediaries. Central ordering is retained, and procurement is organized through a routine government-led procurement cycle financed from the government budget. To keep the configuration feasible within a context of constrained institutional capacity, the upstream design is intentionally kept low-interface: sourcing remains single-source to limit contracting and supplier-management burden, and direct shipment is used to minimize handovers and reduce dependency on additional upstream actors.

Quality assurance is organized through a single quality control gate at the manufacturing stage, limiting additional in-country coordination and lead-time risk. The main trade-off is execution feasibility: this design places responsibility for procurement execution and payment reliability fully with the government. Given recurring capacity and budget (and FX) constraints, the configuration may be difficult to sustain in practice, even though the upstream structure itself is simple.

4.4 Takeaway chapter 4

The main takeaway from this chapter is that the morphological chart was an effective and systematic method for structuring the upstream caffeine supply chain to Malawi and generating a coherent set of design alternatives. By decomposing the supply chain into key functions and corresponding solution options, the method enabled a transparent exploration of the design space and supported the development of multiple, clearly differentiated alternatives that comply with the predefined design requirements. This structured approach reduced the risk

of prematurely converging on a single dominant pathway and ensured that all alternatives were grounded in the same feasibility constraints.

This chapter forms the Develop stage of the DDM: it translates the earlier problem framing, barriers, and design requirements into a set of concrete upstream configuration alternatives. Using a morphological chart was an effective and systematic way to structure the upstream caffeine supply chain to Malawi and to generate a coherent set of design options. By decomposing the supply chain into key functions and corresponding solution options, the method enabled transparent exploration of the design space and supported the development of multiple, clearly differentiated alternatives that comply with the predefined requirements. This helped avoid premature convergence on a single pathway and ensured that all alternatives were grounded in the same feasibility constraints.

At the same time, the morphological chart mainly supported structuring the design space, rather than providing the kind of intuitive supply chain visualisation one might expect at first. It helped to make the key characteristics and structural differences between alternatives explicit, but it did not automatically make actors, flows, and interfaces“visible in a supply chain sense. In hindsight, this could have been strengthened by complementing the chart with more visual representations of the selected alternatives (e.g., actor–flow maps or simple process diagrams), so that the structural logic becomes clearer at a glance.

Chapter 5

Validation and evaluation

This chapter addresses sub-question 4 by validating and evaluating the alternative supply chain configurations developed in Chapter 4. The purpose of this evaluation is to systematically compare their relative performance and trade-offs.

This chapter initiates the Deliver phase of the Double Diamond model, translating the set of developed alternatives into an evidence-based selection and recommendations. The validation focuses on the plausibility and feasibility of the archetypes made in the previous chapter. The evaluation focuses on the extent to which the different configurations are able to address key challenges associated with upstream pharmaceutical supply chains in a low-resource setting, with particular attention to cost-related feasibility and other structural constraints relevant to the Malawian context. The outcomes of this chapter form the analytical basis for selecting a preferred configuration and for formulating the conclusions and recommendations presented in the final chapter.

5.1 Validation

This section provides a plausibility and feasibility check of the developed design alternatives. The purpose is to ensure that the proposed configurations are coherent and grounded in the operational realities of the Malawian context. Validation is therefore approached in two ways: first, by screening the alternatives against the hard design requirements (R1–R4); and second, by using a semi-structured expert interview.

5.1.1 Validation of design alternatives against requirements

Before proceeding to the MCA, the four design alternatives are screened against the design requirements in Section 4.1. The requirements function as hard feasibility conditions: they ensure that each alternative is legally implementable and operationally coherent. This screening is performed by the researcher, based on the defined constraints and supporting sources, and is not intended to indicate which alternative performs best. All four alternatives satisfy the requirements.

5.1.2 Plausibility check via semi-structured expert interview

To support the design process, a semi-structured expert interview was conducted with a representative from the Access to Medicine Foundation. The interview was used as a plausibility check for the underlying design logic (cost drivers and function choices in the morphological chart) and to assess whether the selected evaluation criteria capture decision-relevant concerns in low-volume LMIC pharmaceutical supply chains.

The interview took place before the final selection and wording of the four design alternatives. Therefore, it is not used to validate or score the final alternatives in the MCA. Instead, it is used to refine assumptions and terminology and to strengthen the link between the cost-driver analysis and the evaluation framework.

Findings

Three insights were particularly relevant for this thesis. First, the expert emphasized that cross-country price differences are rarely explained by manufacturing location alone; instead, they mainly reflect scale effects and institutional set-up. Small and uncertain volumes limit economies of scale and increase perceived supplier risk, which can translate into higher overhead allocation and risk buffers in procurement outcomes.

Second, fragmented pathways with multiple intermediaries were highlighted as a recurring source of cost pressure. Additional interfaces tend to increase coordination effort and transaction burden and can lead to cumulative mark-ups along the chain, while also creating more potential failure points that undermine supply continuity.

Third, the expert noted that regional manufacturing and cross-border supply remain limited in many SSA contexts, largely due to insufficient scale and persistent regulatory fragmentation across countries. Taken together, these insights reinforce the rationale for treating upstream supply chain configuration as the design object in this thesis and support the focus on demand aggregation, risk allocation, and reducing avoidable fragmentation in the design space and evaluation framework.

5.2 Evaluation with Multi-Criteria Analysis

The purpose of the MCA is to make explicit the trade-offs inherent in different design choices. By evaluating each configuration against a consistent set of criteria, the MCA increases transparency regarding how alternative supply chain designs perform relative to one another. It also highlights which configurations are more or less aligned with the study's objectives of enabling access to caffeine in Malawi.

5.2.1 Criteria

The evaluation criteria applied in the MCA are derived directly from the design objectives defined in Chapter 4. This section explains how the criteria are operationalized and applied consistently across the four design alternatives. Where design choices introduce additional actors, interfaces, or control steps that may improve robustness or quality assurance, the intended performance benefit is reflected in the relevant performance-related criterion, while the associated coordination and overhead implications are captured under the complexity- and fragmentation-related criteria.

The alternatives are assessed by populating a performance matrix in which each alternative receives a score per criterion on an anchored 1–5 scale. A coarse ordinal scale is used because reliable quantitative input data are not available for this context, and more fine-grained scoring would therefore introduce spurious precision. The scale allows intermediate values (2 and 4) when differences are minor but defensible. For clarity of presentation, however, Table I-2 reports the anchor descriptions for the main reference points (1 = low, 3 = moderate, 5 = high), which are used to guide consistent scoring across criteria and scenarios.

5.2.2 Scenarios

Two factors identified in the cost-driver analysis in Section 3.5.2, financial risk and demand uncertainty, are treated as scenario variables rather than MCA criteria. The reason is that both factors are largely exogenous: they are not directly determined by the supply chain configuration itself, yet they can materially affect how a configuration performs in practice. Therefore, the factors are translated into two plausible external scenarios. These scenarios are used to test the robustness of the design alternatives, i.e., whether they are sensitive to different scenarios or not.

The scenarios reflect conditions that can realistically occur in Malawi. Financing instability is relevant due to constrained public budgets and recurring foreign-exchange and payment frictions (Initiative 2024). In addition, demand reporting can deteriorate due to power cuts, connectivity issues, and weak data governance, leading to less credible quantification and more reactive ordering (Yenet et al. 2023). The two scenarios are applied in the MCA to assess how alternative configurations perform when these external conditions occur.

Scenario 1: Financing instability

This scenario captures a plausible macro-financing instability situation in Malawi (and comparable SSA settings) in which upstream pharmaceutical supply is constrained by foreign-currency reserve shortages and reduced payment reliability. In such a context, access to hard currency for import-related payments becomes more difficult, while disbursements and invoice settlements are delayed or less predictable. These frictions increase working-capital requirements and financial exposure for upstream actors (manufacturers, intermediaries, and logistics providers). As a result, supplier willingness to serve the market may decline, lead times become less predictable, and buyers may be forced into costly mitigation measures such as expedited shipments, smaller and more frequent orders, or higher buffer stocks.

Recent events in Malawi's aid and FX environment make this scenario particularly plausible. A 2025 suspension and reduction of US-funded aid programs is estimated to cause an approximately $177 million decline in foreign exchange inflows to Malawi, equivalent to a material shock to the country's ability to finance imports (Cockx et al. 2025). Given Malawi's structural reliance on official development assistance, particularly for the health sector, such volatility can quickly translate into upstream procurement risk, especially for imported medicines that require USD-denominated payments.

In the MCA, this scenario is implemented by adjusting the performance scores of the alternatives on criteria directly affected by FX constraints and payment reliability, most notably transactional efficiency (reflecting contracting continuity and settlement reliability) and logistics cost balance (reflecting higher likelihood of expediting, fragmented shipments, and inventory instability).

Scenario 2: Low data reliability & transparency

This scenario represents a situation in which the information flows required for upstream coordination deteriorate, leading to weaker visibility and higher coordination effort across the supply chain. In the Malawian public health supply chain context, such breakdowns are a known challenge: the national supply chain transformation plan highlights persistent issues including low data quality, late data submission and incomplete data collection for quantification, and consistently poor quality and timeliness of reports for decision-making. (MoH Malawi 2023) Similar patterns are reported across pharmaceutical supply chains in developing-country settings, where weak infrastructure (e.g., unreliable power supply and inadequate storage conditions) and broader implementation constraints undermine the reliability of operational information and the feasibility of information-intensive solutions (Ameen et al. 2014; Ashok et al. 2017; Olutuase et al. 2022). These constraints matter particularly upstream, where procurement planning and supplier coordination depend on credible consumption data, stock status, and timely documentation (Sarley et al. 2017).

In addition, data exchange remains partly manual and fragmented across systems, with limited interoperability between key platforms (e.g., OpenLMIS and CMST's ERP/Navision), which contributes to inconsistencies in standards and formats and increases reconciliation workload (MoH Malawi 2023).

In the MCA, this scenario is used to test how robust each configuration is when data quality, reporting performance, and system interoperability break down. Configurations that rely strongly on multi-actor or multi-country alignment and pooled quantification are expected to experience a larger decline in execution performance due to higher reconciliation and coordination effort under degraded information flows. The impact is therefore reflected primarily in transactional efficiency and logistics cost balance, and, where relevant, in chain complexity when interpreted as coordination manageability under weak information transparency. Structural design characteristics such as scale potential and fragmentation remain unchanged, but their operational consequences become more pronounced under this scenario.

5.3 Performance matrix

In this MCA, no differential weights are applied meaning that all criteria are assigned equal importance. Differential weighting would require a defensible representation of stakeholder preferences (i.e., relative criterion importance), which could not be reliably established or validated within the scope of this study. Therefore, to preserve transparency and comparability across scenarios, the weighting scheme is kept constant. The performance scores are scenario-dependent, meaning that each archetype is scored, based on the performance of an alternative under a specific scenario. Thus, the scenarios capture how each configuration performs under different conditions, while the criteria and their equal weighting remain fixed. Below, the results of the performance matrix can be found.

Base case

Base case	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	4	2
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	3	3	4	2

Table 5-1: Performance matrix for the base case.

Scenario 1: Financing instability

Scenario 1: Financing instability	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	5	1
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	2	3	4	1

Table 5-2: Performance matrix for Scenario 1: Financing instability.

Scenario 2: Low data reliability & transparency

Scenario 2: Low data reliability & transparency	Alt 1	Alt 2	Alt 3	Alt 4
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	3	2
C4: Chain complexity	3	2	1	4
C5: Logistics cost balance	2	3	3	2

Table 5-3: Performance matrix for Scenario 2: Low data reliability & transparency.

5.4 Direct pairwise comparison method

When a pairwise comparison, as explained in Section 2.5, did not produce a clear winner, a predefined tie-breaking rule was applied. In scenario-based assessments, ties were resolved by comparing the alternatives on the criteria that are directly impacted by the scenario conditions (i.e., the criteria whose performance scores are adjusted under that scenario). If the tied alternatives also remained indistinguishable on these scenario-affected criteria, or if no scenario-specific criteria applied (as in the base case), the comparison was recorded as a draw and denoted by $\sim$.

5.4.1 Results direct pairwise comparison

A performance matrix is used to give a score to each of the criteria for each alternative. After that, the direct pairwise comparison method is used to compare the alternatives with each other. As discussed in Section 2.5 a fully quantitative and weighted MCA or a CBA was not feasible due to limited reliable numerical input data. Therefore, the results are presented

using an anchored qualitative performance matrix and direct pairwise comparisons. This is done for the base case and two scenarios. The matrices and results can be found below.

Base case

Outcome: $3 \,\&\, 1 > 2 > 4$

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	A1	A2	A1	∼	A1
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	∼	A2	A3	∼
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 5-4: Direct pairwise comparison outcomes for the base case.

In the base case, the alternatives are assessed under business-as-usual conditions, i.e., without introducing additional stressors such as financial frictions or reporting disruptions. The purpose of this baseline comparison is to understand how each configuration performs purely based on its structural design choices and their expected effects on the upstream cost-drivers captured by the criteria.

Under these conditions, Alternatives 1 and 3 rank highest, both for different underlying reasons. Alternative 1 performs strongly because it combines a relatively simple upstream structure with limited coordination requirements. Its low fragmentation and low interface burden reduce exposure to coordination overhead and implementation frictions, resulting in a consistently solid performance profile without pronounced weaknesses. In contrast, Alternative 3 ranks highest due to its pooling and consolidation logic, which maximizes scale potential and supports a favourable logistics cost balance through bundling. These scale advantages are achieved at the expense of higher fragmentation and coordination burden, but in the baseline evaluation, the consolidation benefits compensate for these disadvantages, leading to an overall top ranking together with Alternative 1.

Alternative 2 ranks below the top two because its managed multi-sourcing and strengthened contracting improve robustness and execution discipline, but also introduce additional transactional and coordination requirements compared to the simpler donor pipeline. In the baseline setting, where no specific stressors are assumed, these added requirements are not fully offset by corresponding scale gains, which limits its comparative performance. Finally, Alternative 4 ranks lowest because it places procurement execution and payment reliability primarily within government budget processes. Even without an explicit financing instability shock, this increases exposure to administrative and execution frictions relative to donor-supported configurations, reducing its baseline attractiveness despite its structurally low-interface design.

Scenario 1: financing instability

Outcome: $3 > 1 \,\&\, 2 > 4$.

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	1	2	1	2	∼
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	A3	A2	A3	A3
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 5-5: Direct pairwise comparison outcomes for Scenario 1: Financing instability.

Under macro-financing instability, Alternative 3 ranks highest because it combines pooled demand with a strengthened contracting set-up and donor-funded financing. This configuration is therefore least exposed to country-specific liquidity and FX constraints: joint ordering and consolidation can buffer temporary payment frictions in individual countries and reduce the risk that procurement comes to a standstill. In addition, the larger pooled volume improves bargaining leverage and supports more stable supplier engagement when upstream actors face higher working-capital requirements.

Alternatives 1 and 2 form a shared second tier. Both remain donor-funded and are therefore assumed to face fewer payment-execution disruptions than government-budget procurement under this scenario. Alternative 2 improves resilience through dual/multi-sourcing and strengthened contracting, which supports continuity when supplier participation becomes more sensitive to financial risk. However, these robustness gains come with additional coordination and interface requirements. Alternative 1 is structurally simpler and performs relatively well on fragmentation and coordination burden, but it offers less sourcing redundancy and weaker contractual continuity than Alternative 2. In the pairwise assessment, these opposing strengths balance out, resulting in no clear dominance between the two alternatives.

Alternative 4 performs worst in this scenario because it relies on government budget execution for financing and payment. Under financing instability, delayed disbursements and reduced payment predictability are most likely to affect this configuration first, increasing the risk of contracting frictions, supplier non-participation, and lead-time instability compared to donor-funded arrangements.

Scenario 2: Low Data Reliability & Transparency

Outcome: $2 > 3 > 1 \,\&\, 4$.

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	∼	A1	A2	A1	A2	A2
A1 vs A3	A3	A1	∼	A1	A3	∼
A1 vs A4	A1	A4	A1	A4	∼	∼
A2 vs A3	A3	A2	A2	A2	∼	A2
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 5-6: Direct pairwise comparison outcomes for Scenario 2: Low data reliability & transparency

This scenario captures a breakdown in the information flows needed for quantification and ordering. When consumption and inventory reporting is incomplete or delayed, forecasts become less reliable and more manual reconciliation is required. As a result, procurement becomes more reactive and the risk of delays and corrective shipments increases.

Alternative 2 ranks highest because it is the most managed configuration: strengthened contracting and routine, managed execution help to keep the process running even when data quality deteriorates. In other words, it relies less on smooth information exchange between many parties and more on a controlled execution structure.

Alternative 3 ranks second. Its pooling and hub consolidation still deliver strong scale potential, but under Low data reliability & transparency, it becomes harder to coordinate pooled quantification across countries, which increases reconciliation effort and reduces coordination performance. Alternatives 1 and 4 end up at the same level for different reasons. Alternative 1 is relatively simple and can still rely on intermediary support, but it lacks the additional robustness of Alternative 2 and is more prone to reactive ordering effects. Alternative 4 has the simplest upstream structure, yet it shifts the burden of fixing reporting issues to government execution and remains limited in consolidation options, so it does not clearly outperform Alternative 1 overall.

5.5 Takeaway chapter 5

The main takeaway from the validation step is that it relied on only one expert interview. This provides a useful plausibility check, but it is too limited to be considered strong validation. A broader set of interviews with key stakeholders would strengthen confidence in the assumptions used and in the resulting assessment.

Regarding the evaluation, the results show that design performance is clearly scenario-sensitive. Rankings change when operating conditions change, meaning that the best-performing configuration in the base case does not necessarily remain best under context-relevant stress. The scenario-based performance matrices therefore add an important robustness layer, because they reveal how conclusions shift when financing reliability or information quality deteriorates.

A final takeaway is that the scoring-based approach remains partly judgement-based. Using an anchored 1–5 scale supports structured comparison, but the results still depend on how scores are assigned and on the chosen scale and aggregation assumptions. The findings should therefore be interpreted as directional rather than definitive, and alternative scoring choices (e.g., a different scale or different weightings) could lead to different rankings.

Chapter 6

Conclusion and discussion

To conclude this study, this section synthesizes the answers to all research questions. Furthermore, the limitations of the research are discussed and recommendations for future research are provided.

6.1 Answers to research questions

SQ1: What does the current pharmaceutical supply chain to Malawi look like in terms of the manufacturing of medicines, using aminophylline as a proxy to understand the existing system?

The analysis of the Malawian pharmaceutical supply chain, combined with the interview findings, clarified how the upstream segment of the chain is structured and which regulatory, procurement and sourcing processes shape the design space for caffeine. Three core processes were identified within the upstream supply chain: quantification and sourcing, ordering and procurement, and supply and distribution. Together, these processes provide the structural basis for understanding the current configuration and identifying potential intervention points.

The interviews further complemented the desk-based analysis by providing additional insight into the procurement structure. From the UNICEF perspective, access to medicines appears strongly path dependent, with existing procurement channels and institutional arrangements influencing sourcing decisions. The agent perspective highlights additional operational constraints, particularly those related to foreign currency availability and exchange rate volatility, which affect procurement feasibility and pricing.

Using aminophylline as a proxy illustrates the limitations of publicly available data in tracing the formation of medicine prices. Based on the available information, it is not possible to reliably attribute observed prices to specific upstream cost components such as manufacturing, procurement, or logistics. The analysis nevertheless indicates that aminophylline is generally substantially cheaper than caffeine in many contexts. However, the desk-based evidence does not support a clear single-cause explanation for this difference.

This lack of transparency reinforces the relevance of a design-oriented perspective. Rather than focusing solely on price differences as outcomes, the analysis highlights the importance of examining the underlying structural factors and system configurations that influence cost development within the supply chain.

SQ2: How is the supply chain of caffeine organized in Sub-Saharan African countries where it is already available, and what are the main cost drivers influencing its final price?

The analysis of four Sub-Saharan African countries, Uganda, Kenya, Ethiopia, and South Africa, provides insight into how caffeine is supplied in contexts where it is already available. The cases show that access to caffeine is achieved through different organizational pathways, suggesting that there is no single model that Malawi should replicate. Differences across the countries are primarily related to procurement arrangements, the presence or absence of intermediaries coordinating procurement activities, and the role of donor involvement in financing.

The cases further suggest that procurement structure and the presence of external procurement facilitation may influence outcomes. In Kenya and Uganda, CHAI plays an active role in procurement facilitation and price negotiations. The Kenyan case in particular aligns with the process that coordinated purchasing and negotiation support can contribute to lower unit prices. South Africa represents a contrasting configuration, where procurement occurs without donor intermediation and observed prices are higher. Although causal attribution cannot be established based solely on desk-based evidence, the pattern is consistent with the idea that negotiation leverage and contracting capacity are relevant factors influencing both price levels and supply continuity.

Across the countries, only two manufacturers were identified as supplying caffeine to these countries, with production located in Italy and the United Kingdom. This limited supplier base contrasts with the situation for aminophylline, where a broader and more competitive manufacturing landscape was observed. Price levels also differ considerably across the analysed countries, suggesting that the specific supply chain configuration and procurement pathway can influence the final price paid. Together, these observations support the central assumption of this thesis that upstream supply chain structure plays an important role in shaping affordability.

Building on this analysis, several cost drivers were identified through the literature review and interviews. These include economies of scale, dedicated supply chain set-ups, demand uncertainty, supply chain complexity, regulatory burden, and financial risk. These factors influence how procurement, manufacturing, and distribution are organised, and therefore affect overall cost structures. As a result, they form an important basis for defining the design objectives and evaluation criteria used in the multi-criteria analysis (MCA).

SQ3: What alternative supply chain configurations could enable the availability of caffeine in Malawi, based on the insights from the current Malawian system and regional reference cases?

Using a design-oriented approach, a morphological chart was developed to explore alternative configurations of the upstream supply chain. The chart structured the design space by translating the three core upstream processes identified in SQ1, quantification and sourcing, ordering and procurement, and supply and distribution, into functional categories. For

each function, multiple implementation options were identified based on insights from the Malawian system and the regional reference cases analysed in SQ2. In this way, the morphological chart served as a systematic tool to explore how different combinations of supply chain arrangements could address the identified cost drivers and structural constraints.

The cost drivers identified in SQ2 were subsequently translated into design objectives that guided the development and assessment of potential configurations. Two of these drivers were considered exogenous to the supply chain design and were therefore not included as design objectives. Instead, they were incorporated later in the analysis through scenario conditions.Through an iterative process of combining options, applying feasibility constraints, and removing internally inconsistent combinations, a set of design alternatives was developed. During this process, the intention was to generate alternatives that differ meaningfully in their structural characteristics rather than producing minor variations of a single configuration. Given the exploratory nature of the design exercise and the absence of a predefined supply chain structure for caffeine in Malawi, the focus was placed on generating contrasting configurations that make the influence of key cost drivers more visible.

This process resulted in four distinct design alternatives. These configurations represent: (1) a donor-based baseline pipeline aligned with commonly observed procurement arrangements in SSA, (2) a managed configuration that increases robustness through multi-sourcing and strengthened contracting arrangements, (3) a regional pooling configuration with a shared logistics hub aimed at exploiting economies of scale and shared capacity across countries, and (4) a government-core configuration that increases national ownership through routine procurement and direct shipment.

Together, these alternatives represent different trade-offs between coordination complexity, scale advantages, financial risk exposure, and supply reliability. Rather than representing fixed solutions, they function as structured scenarios that allow the implications of different supply chain configurations to be systematically compared. As such, they form the basis for the subsequent multi-criteria evaluation aimed at identifying which configuration, or combination of configurations, is most suitable for improving caffeine availability in Malawi under varying contextual constraints.

SQ4: How do the alternative upstream supply chain configurations score on the evaluation criteria under different scenarios?

To evaluate the design alternatives, a performance matrix was constructed. The evaluation criteria were derived from the design objectives identified in SQ3, resulting in five criteria: scale potential, fragmentation, transactional efficiency, chain complexity, and logistics cost balance. Two factors, financing instability and low data reliability and transparency, were classified as exogenous conditions and therefore incorporated as scenario parameters rather than evaluation criteria. As a result, three performance matrices were developed: a base case and two scenario-specific matrices reflecting these contextual conditions.

Within each matrix, the four design alternatives were assessed against the five criteria using a qualitative scoring scale ranging from 1 to 5. The weights of the criteria were kept constant across all matrices, as no specific stakeholder group was represented whose preferences could justify differentiated weighting. The scoring therefore reflects an analytical comparison of structural characteristics rather than a stakeholder-driven prioritisation.

In addition to the performance matrix, a direct pairwise comparison method was applied

to compare the alternatives. This method evaluates alternatives by systematically comparing their performance against each other across the same criteria and weights used in the matrices. The pairwise comparison was conducted for the base case and both scenarios. This approach provides an additional layer of robustness to the analysis by examining how alternatives perform relative to each other rather than only in absolute scoring terms.

The results indicate that the relative ranking of alternatives is scenario-dependent. When contextual conditions change, different constraints become dominant, and therefore no single configuration performs best across all criteria in every scenario.

Alternative 3, a regional hub, performs strongly across the scenarios because it is built around demand pooling and consolidation processes. By bundling demand across countries and relying on strengthened contracting arrangements, it maximizes scale potential and increases the likelihood of maintaining upstream supply continuity under stress conditions. However, this configuration also introduces higher coordination requirements and fragmentation across actors, making it more complex to organize and implement.

The scenario analysis further clarifies these trade-offs. Under conditions of financing instability, configurations that are less exposed to country-specific foreign exchange and payment constraints perform more robustly. This favors pooled and donor-supported arrangements, while configurations relying primarily on national government procurement and budgeting (Alternative 4) become more vulnerable. Under conditions of low data reliability and transparency, the ranking shifts towards configurations that can maintain execution discipline despite weaker information flows. In this scenario, Alternative 2 performs best because managed procurement execution and strengthened contracting reduce dependence on coordinated multi-actor data systems.

Main research question: How can the main characteristics and structure of the upstream supply chain of caffeine be designed to enable access to Malawi's neonatal care system?

To enable access to caffeine in Malawi's neonatal care system, the upstream supply chain must be designed to function under conditions of low and uncertain demand while ensuring continuity of supply and supporting affordability. The analysis shows that this requires a structure that mitigates key upstream cost drivers and operational risks. Three structural characteristics are particularly important: creating scale where possible (for example through pooled demand), establishing clear responsibilities across procurement, contracting, and execution, and reducing operational and financial frictions such as fragmented ordering processes, weak information flows, and exposure to payment or foreign exchange constraints.

Based on the design exploration and evaluation, Alternative 3, regional pooling combined with a logistics hub, best reflects these required characteristics. By aggregating demand across countries and consolidating execution through a shared hub structure, this configuration increases supplier attractiveness and improves coordination within the upstream supply chain. These structures support both supply continuity and reduced upstream cost pressure in a thin supplier market. However, the feasibility of this configuration depends on the presence of sufficient regional coordination capacity, governance arrangements, and stable operational routines.

At the same time, the evaluation shows that different configurations may be more suitable under specific contextual constraints. Alternative 1 provides a low-complexity starting

configuration when rapid introduction is required and coordination capacity is limited. Alternative 2 offers increased robustness under conditions of limited data reliability or coordination challenges by maintaining a more manageable procurement structure. Over time, transitioning towards a pooled regional configuration such as Alternative 3 offers the most promising pathway towards a more institutionalised and sustainable upstream supply chain for routine caffeine availability, provided that the necessary coordination structures can be developed.

6.2 Discussion, limitations and future research recommendations

6.2.1 Discussion

An unexpected outcome of the comparative analysis is that, despite the common reliance on Asian manufacturing for medicines supplied to SSA, the caffeine traced in the reference cases is supplied via European manufacturers. This highlights that caffeine sourcing in practice may follow a different pattern than anticipated based on broader pharmaceutical supply chains.

A second observation is the persistent lack of transparency on caffeine-specific cost drivers. Even after stakeholder interviews and desk-based research, the underlying cost structure remains difficult to disentangle. Cost-related information appears commercially sensitive and is rarely documented in public sources, which limits the ability to attribute observed price levels to specific factors beyond plausible upstream explanations such as scale effects, contracting conditions, and risk pricing.

To map the supply chain processes, swimlane diagrams were used to visualise the current supply chain structures. These diagrams provided a clear overview of the different process steps and the actors responsible for them, which helped to structure the analysis of the existing system. In addition, the diagrams made it easier to identify bottlenecks and steps where coordination between actors caused delays or additional complexity. At the same time, the level of detail captured in the swimlane diagrams was not strictly necessary for answering the main research question. For the purpose of this study, a more simplified representation of the supply chain structure would likely have been sufficient. Nevertheless, for research that focuses more explicitly on process optimisation or detailed supply chain design, swimlane diagrams can be a valuable method. As a visualisation tool for understanding process flows, actor interactions, and potential bottlenecks in complex supply chains, their use is therefore recommended for similar types of studies.

Another reflection concerns the choice for the Double Diamond Model (DDM). This model was used because the study's core objective is design-oriented: to develop and compare alternative supply chain configurations that could improve access and affordability. In that sense, the emphasis on "design" is justified, because the main output is not a single estimate or optimisation result, but a set of well-argued configuration alternatives and their expected implications for structural cost drivers. At the same time, reliable quantitative data on caffeine-specific costs is limited and fragmented. DDM therefore helped to explore multiple realistic options first and then narrow them down in a structured and transparent way, supported by iterative refinement and evaluation.

In practice, DDM was useful because it enabled iteration between problem understanding and solution development. Early desk research and stakeholder input helped to sharpen the affordability focus and identify the most relevant upstream cost drivers. This iterative logic

also made it possible to adjust the designs even after development had started. For example, a validation interview was conducted relatively late in the process, but its insights could still be incorporated into the evaluation stage (MCA/robustness checks), strengthening the final comparison of alternatives.

However, the morphological chart may not have been the most effective way to communicate the supply chain designs. While it was useful for structuring the design space and generating alternative configurations, it led to descriptions that remained quite abstract. Supply chains are often easier to understand through visual representations that show actors, flows, and interfaces. In hindsight, presenting the alternatives as supply chain maps would maybe have improved clarity and made differences between configurations more intuitive.

Looking back, this study deliberately focused only on the upstream part of the supply chain, mainly due to time constraints. While the upstream scope was still relevant, the design space turned out to be more constrained than initially expected. In other words, there were meaningful differences between upstream configurations, but not as many distinct levers as anticipated. By contrast, the downstream segment likely offers a wider range of practical design choices and stakeholder interactions that directly shape whether caffeine actually reaches patients. In hindsight, extending the scope downstream could therefore have generated richer and more actionable design insights, especially around implementation and last-mile feasibility.

Finally, an important finding is that the design alternatives are clearly scenario-sensitive. The rankings shift once operating conditions change, meaning that there is no single configuration that consistently dominates the others in every setting. This underlines why robustness testing matters: under financing instability, configurations that reduce exposure to payment reliability and FX frictions perform best, which favours the regional pooling and hub option. Under low data reliability and transparency, the ranking shifts toward configurations that remain manageable when information flows weaken; in that setting, managed multi-sourcing performs best because it relies less on cross-actor alignment and shared reporting routines.

6.2.2 Limitations

This study is subject to several limitations that should be considered when interpreting the results.

First, the evaluation is intentionally ordinal. The pairwise comparison approach supports a structured comparison without suggesting numerical precision, but the results still depend on qualitative judgement in the scoring and on the aggregation rules used. In addition, all criteria were weighted equally. This was a deliberate baseline choice because no stakeholder input was available to justify differential weights and the scenario analysis already introduced a major source of variation. As a result, the rankings should be interpreted as directional and may shift if stakeholders would assign different priorities to the criteria.

As already being mentioned, the scope of the study focuses primarily on upstream supply chain design (manufacturing origin, procurement, contracting, and inbound distribution up to national receipt). Downstream elements such as last-mile distribution, facility-level storage conditions, and clinical usage practices were not analyzed in detail. These downstream factors could materially affect effective availability within neonatal care and would be interesting to incorporate in future work.

Next, the validation step relied on a single semi-structured expert interview as a plausibility check. While this provided useful feedback on the realism of the functional design choices and the relevance of the identified drivers, it does not constitute comprehensive validation. A larger set of interviews with key stakeholders would strengthen confidence in the assumptions, scoring, and resulting rankings.

Also, the analysis deliberately focuses on upstream cost drivers as the primary basis for design and evaluation. As a result, broader non-cost factors, such as political dynamics, organisational culture, and implementation capacity, are not modelled, even though they may materially influence feasibility and real-world performance. This limits the extent to which the findings can be interpreted as a complete representation of all determinants of access.

Another limitation of this study is the narrow scope of the scenario analysis. Only two scenarios were used: financing instability and low data reliability. While these are relevant and commonly observed in similar contexts, do not cover less frequent but still plausible operating conditions. As a result, the robustness assessment of the design alternatives remains incomplete: the relative performance of configurations may change under other scenarios that were not tested. Testing the alternatives against a broader set of scenarios would provide a more comprehensive understanding of their robustness and the trade-offs between cost drivers, feasibility, and continuity of supply.

Finally, the morphological analysis was effective for structuring the design space, but the resulting chart is text-based and therefore less visually expressive than ideal in a design-oriented thesis. A more visual representation of the alternatives and their interfaces could improve readability and make the differences between configurations easier to compare.

6.2.3 Future Research Recommendations

Building on the findings of this thesis, three directions for future research are recommended.

First, future work should strengthen the empirical basis for evaluating caffeine supply chain configurations by collecting more parameterized upstream data. Relevant inputs could include procurement volumes, lead times and their variability, minimum order quantities and quality control timelines. With such data, the conceptual alternatives proposed in this thesis could be evaluated using more quantitative approaches (e.g., sensitivity analysis or CBA), reducing reliance on purely ordinal judgements and enabling more explicit assessment of trade-offs.

Second, the scope should be extended downstream within Malawi to capture end-to-end availability in neonatal care. Incorporating in-country warehousing, distribution, storage requirements, last-mile delivery, and facility-level inventory practices would allow testing whether upstream improvements translate into effective availability at hospital level. A practical next step could be a small-scale pilot or implementation study in a limited number of facilities, combined with process monitoring to identify operational bottlenecks and refine the design iteratively.

Third, future research should broaden and deepen external validation through targeted stakeholder engagement and regional benchmarking. Additional interviews with key actors involved in procurement facilitation and supplier engagement (e.g., procurement intermediaries, donors, and suppliers) could be used to validate scenario assumptions, clarify decision rules used in practice, and elicit criterion prioritization to support a more defensible weighting

approach. In parallel, expanding the set of Sub-Saharan African reference cases and comparing procurement routes, contracting arrangements, and supplier access structures would help identify additional feasible design options and improve the generalization of the recommendations for Malawi and similar settings.

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Appendix A

Scientific article

Designing the main characteristics and structure of the upstream supply chain of caffeine to Malawi's neonatal care system

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Abstract

Caffeine is the internationally recommended first-line treatment for apnoea of prematurity (AOP), yet it remains unavailable in Malawi due to affordability constraints and upstream supply limitations. While prior work has documented high end-user prices and limited uptake of caffeine in sub-Saharan Africa, there is still no structured, product-specific analysis that explains how upstream supply chain design choices and cost build-up factors shape affordability and availability in Malawi's public health system. This study examines how the main characteristics and structure of upstream supply chain for caffeine can be designed to enable access to Malawi's neonatal care system by identifying and assessing upstream cost drivers that influence both price and availability. Malawi's current upstream supply chain is first mapped using aminophylline as a proxy, complemented by desk research on four sub-Saharan African countries where caffeine is available. Drawing on the literature and the desk study, seven upstream cost drivers are identified and used to structure a supply chain design analysis. A morphological chart is then applied to generate alternative configurations, guided by design requirements, and an iterative process results in four deliberately distinct supply chain alternatives: a donor-focused design, a managed multi-sourcing design, a regional logistics hub design, and a government-focused design. Given limited quantitative data, the alternatives are evaluated using a multi-criteria decision analysis in which the cost drivers serve as evaluation criteria, while two exogenous drivers, financial risk and demand uncertainty, are used as scenarios to test robustness under plausible conditions. Using a performance matrix and a direct pairwise comparison approach, the results indicate that the alternatives are scenario-dependent; however, the regional logistics hub design performs most consistently across scenarios and is therefore identified as the most robust upstream supply chain design to improve access to caffeine to Malawi's neonatal care system.

Keywords: Caffeine citrate, apnea of prematurity, pharmaceutical upstream supply chain design, Malawi, multi-criteria analysis

1. Introduction

Sub-Saharan Africa (SSA) continues to face among the highest neonatal mortality rates worldwide, with an estimated 2.4 million preventable newborn deaths each year [1]. A substantial share of these deaths is associated with complications of prematurity, particularly respiratory conditions such as respiratory distress syndrome and apnoea of prematurity (AOP) [2]. AOP is a common and potentially life-threatening condition in preterm infants for which methylxanthines are the standard pharmacological treatment [3, 4]. In this context, caffeine is widely recommended as the first-line therapy due to its favourable safety profile and ease of administration compared with theophylline or aminophylline [4, 5].

Despite its clinical relevance and inclusion on the WHO Essential Medicines List, access to caffeine remains limited and uneven across SSA [6, 7, 8, 9]. Empirical studies show that prices for caffeine in SSA are substantially higher than in many high-income settings, raising concerns about affordability and procurement feasibility [10]. As a result, many health systems substitute caffeine with aminophylline despite having more side effects, requiring therapeutic drug monitoring, and being available only intravenously ([8]).

Existing research has primarily framed the lack of access as a pricing and affordability issue. While these studies document price levels, treatment gaps, and contextual barriers, they provide limited insight into how these prices emerge along the pharmaceutical value chain. Research on pharmaceutical supply chains in SSA has largely focused on sector-wide system challenges or downstream distribution issues such as last-mile delivery inefficiencies and inventory management [11, 12, 13, 14]. But, little attention has been given to upstream supply chain design decisions of caffeine in combination with cost drivers, to look at cost build-up and supply reliability.

Therefore, there is still a gap in understanding how affordability and upstream supply chain configuration shape access to caffeine. While prior studies acknowledge that cost is a barrier and that supply chain processes may influence availability, no study has systematically analysed how characteristics of upstream supply chain designs for caffeine could affect cost structure within Malawi's public health system.

This research addresses that gap by conducting a structured, product-specific upstream supply chain design analysis for caffeine. By linking supply chain configuration choices with key cost drivers within a multi-criteria decision framework, this study moves beyond the descriptive identification of barriers and instead evaluates feasible design alternatives. In doing so, it contributes to the literature by connecting macro-level ac-

cess challenges with concrete upstream supply chain design decisions, thereby providing insights to inform implementation strategies in resource-constrained settings. The central research question is therefore: *How can the main characteristics and structure of the upstream supply chain of caffeine be designed to enable access to Malawi's neonatal care system?*

2. Methodology

This study adopts a design-oriented research approach structured around analysis, design, and evaluation. The central aim is to develop and compare feasible upstream supply chain configurations that can enable access to caffeine to Malawi under institutional constraints, considering cost drivers that influence affordability. The methodological logic is therefore to characterize the current upstream procurement context and constraints, derive design requirements and an actionable design space, and assess the relative robustness of design alternatives under relevant scenarios.

2.1. Research and design approach

First, Malawi's upstream procurement and sourcing context is analysed using aminophylline as a proxy for current pharmaceutical supply chain practices. Additionally, desk research is conducted on four SSA countries where caffeine is already available to identify relevant structural features and price constraints, and to derive design requirements grounded in comparable settings. Third, seven upstream cost drivers are synthesised from the literature and desk research and used to guide the development of supply chain alternatives. A morphological analysis is then applied to generate feasible upstream configurations by decomposing the supply chain into core functions and combining feasible options into coherent design alternatives. Finally, given limited reliable quantitative data, the alternatives are evaluated using a multi-criteria analysis based on performance matrices and direct pairwise comparisons, complemented by scenario-based stress testing in which two exogenous drivers (financial risk and demand uncertainty) are made as plausible operating scenarios.

2.2. Data and system analysis

Data collection relied on desk research and qualitative insights. Because caffeine is not embedded in Malawi's routine public procurement system, the upstream system architecture for pharmaceuticals was mapped using aminophylline as a proxy medicine procured and distributed through existing structures. This proxy mapping was used to identify the dominant upstream supply chain processes and operational dependencies (e.g., quantification cycles, contracting and ordering routines, and upstream logistics arrangements).

To ground the design problem in comparable contexts and to identify feasible upstream configuration patterns, a desk-based comparative review was conducted of selected SSA settings where caffeine is already available. The review mapped how caffeine currently reaches these countries by identifying the upstream supply chain structures, procurement arrangements, and actors involved. Insights from the SSA evidence base were then used to inform which configuration levers are realistic for Malawi. In parallel, the literature review was used to identify the dominant upstream cost drivers shaping affordability and to interpret how these cost factors manifest across the observed SSA supply chain set-ups.

2.3. Design space

Based on the system analysis and stakeholder constraints, the design space was constructed using morphological analysis, a structured method to generate system configurations by decomposing a complex problem into essential functions and listing feasible options for each function [15, 16]. The decomposition focuses on upstream functions relevant to caffeine access and provides the basis for generating internally consistent configurations.

Prior to evaluation, the proposed designs were subjected to a validation step. Each alternative was assessed against the predefined design requirements to ensure legal implementability and operational feasibility within the Malawian context. In addition, a plausibility check was conducted through a semi-structured expert interview with a representative of the Access to Medicine Foundation. This interview served to validate the underlying functional design choices and to assess whether the proposed configurations were realistic from a pharmaceutical market and access perspective.

For the evaluation, the study adopts a scenario-based robustness perspective to test how alternative designs might perform under plausible adverse conditions, given the limited availability of reliable quantitative cost and performance data. Two scenarios are defined to represent exogenous risks that materially affect upstream execution. These scenarios are derived from two drivers, financial risk and demand uncertainty, that are largely outside the control of supply chain design and are therefore not treated as evaluation criteria, but instead used as contextual stressors. The first scenario, financing instability, captures foreign currency reserve shortages and reduced payment reliability [17]. The second scenario, low data reliability and transparency, captures deterioration in reporting performance, limited end-to-end visibility, and an increased need for manual data verification and correction across systems, as documented in Malawi's health supply chain transformation agenda [18]. These scenarios are used to structure the evaluation and to interpret the robustness of the proposed upstream supply chain configurations.

3. Background study

3.1. Malawian health system

Malawi's public medicines supply architecture is centred on the Central Medical Stores Trust (CMST), which operates as the backbone for essential medicines procurement, warehousing, and distribution ([19]). In parallel, several donor-funded vertical programmes maintain separate pipelines with their own governance and logistics arrangements, meaning that

medicines may flow through either the CMST pull-based system or programme-specific push-based distribution channels [19, 20]. For an upstream caffeine design, this implies that access is not only a question of sourcing, but of choosing an institutional pathway that can be integrated into an existing procurement and distribution logic while limiting financial uncertainty and implementation complexity.

The upstream process structure comprises three recurring functions: quantification and sourcing, ordering and procurement, and supply and distribution [19]. While routine ordering occurs frequently through the national LMIS, the decisions that determine whether a medicine enters contracted procurement are concentrated in infrequent, calendar-driven cycles. National quantification is typically consolidated annually and translated into budgeting and contracting, which limits responsiveness for low-volume medicines and increases exposure to forecasting error [19]. Malawi is also structurally import-dependent: local manufacturing accounts for less than 2% of CMST procurement, leaving the public supply chain reliant on international suppliers and exposed to long lead times and foreign-exchange constraints [18]. Combined with funding and procurement-capacity limitations, these characteristics increase vulnerability to stock-outs [19].

3.2. Aminophylline supply chain

Aminophylline was used as a proxy medicine to analyse what the Malawian supply chain looks like. The medicine is registered in Malawi and appears in the CMST catalogue, indicating that it has cleared the key institutional gates required for public procurement eligibility [21, 22]. In procurement terms, aminophylline illustrates that when regulatory entry and catalogue inclusion are achieved, a medicine can be embedded in the existing CMST replenishment architecture rather than relying on exceptional import routes.

However, the aminophylline case also had a practical limitation of desk-based research: publicly available sources confirm registration and catalogue presence, but do not reliably disclose the full end-to-end pathway (e.g., finished-product manufacturer, marketing authorization holder/importer, or the specific contracted channel supplying Malawi) [21, 22]. To still form an indicative upstream picture, supplier landscape information was used to infer likely sourcing characteristics, suggesting concentration of upstream supply in international markets and reinforcing the importance of import logistics and contracting conditions for neonatal injectables [23]. As a benchmark, aminophylline shows that access constraints are not resolved by registration and catalogue listing alone. Desk-based sources confirm institutional eligibility, yet provide insufficient transparency to explain the underlying cost structure, which is likely driven by upstream supply and contracting conditions [7].

3.3. Reference cases

To ensure that the Malawi design space reflects supply chain pathways that are feasible in comparable settings, caffeine supply chains in four selected SSA countries (Uganda, Kenya, South Africa, and Ethiopia) were reviewed as reference cases. These countries were selected because caffeine is already in use and sufficient publicly available information could be identified on prices and supply structures; for many other countries such information was not available and they were therefore excluded from the review. Across the four cases, caffeine is supplied as an imported finished pharmaceutical product, meaning that differences in access are primarily shaped by institutional pathways, procurement arrangements, and financing structures rather than production technology. Together, the cases illustrate three recurring configuration patterns that are directly relevant for Malawi: institutionalised public procurement following regulatory approval and essential-medicine inclusion, donor-supported market, and fragmented coexistence of government and donor procurement channels.

Ethiopia and Kenya illustrate configurations where central public procurement structures are maintained, while external partners support market entry by reducing supplier risk and strengthening demand aggregation and price negotiation capacity [24, 25]. South Africa represents a mature, institutionalized market with competitive tendering and no donor involvement, demonstrating that routine procurement can exist but does not automatically imply low prices, highlighting the role of broader market and specification conditions [26]. Uganda illustrates a more fragmented architecture with coexisting government and donor channels, which could affect consolidation benefits and increase coordination burden, a pattern expected to affect both affordability and supply continuity [27].

Taken together, the SSA reference cases provide a good representation of how upstream supply chains can be structured. They show both variation and recurring patterns in how upstream supply can be organised, often involving a largely similar set of actors, but configured differently, along key dimensions: demand aggregation versus fragmentation, governance and contracting arrangements, and the organization of upstream logistics and implementation capabilities. These insights inform the formulation of the design requirements and the development of Malawi-specific design alternatives.

3.4. Cost drivers

Observed procurement prices of essential medicines often differ substantially across countries, even when products are sourced internationally and manufactured by a relatively limited set of suppliers ([28]). For caffeine in SSA procurement contexts, available price indications suggest comparatively high unit prices. At the same time, caffeine is a widely produced, mature commodity/API that can be supplied at low prices in other markets ([7]). This contrast implies that the high prices observed in SSA cannot be attributed to production technology or manufacturing location alone.

Instead, price formation should be understood as the outcome of supply chain characteristics and institutional arrangements. For many medicines, estimated minimum production costs are low relative to observed market prices, suggesting that procurement architecture, market structure, compliance requirements, and demand fragmentation shape procurement outcomes through overhead allocation and risk pricing ([29]). In particular, pooled or donor-supported procurement can stabilize

demand signals and reduce transaction costs per unit, whereas fragmented and low-volume purchasing increases coordination burden and induces supplier risk markups. Accordingly, the analysis focuses on upstream cost drivers and uncertainties that can account for observed price levels, and on how they translate into affordability and availability outcomes in low-volume LMIC markets.

Therefore, the upstream cost drivers that recur in pharmaceutical supply chains are synthesized. They provide the analytical basis for formulating the design objectives. The drivers are presented in Table 1.

Cost driver	Relevance for upstream configuration
Economies of scale	Consolidation and pooling reduce unit costs by spreading fixed overhead and improving purchasing leverage.
Dedicated supply chains	Country-specific or customized execution reduces consolidation opportunities and increases overhead allocation.
Demand uncertainty	Low and volatile demand increases buffers, expediting and risk pricing, especially when forecasts are unreliable.
Chain complexity	More actors, handovers and interfaces increase transaction costs and coordination effort.
Regulatory burden	Documentation, quality control and country-specific requirements add time and cost, particularly when duplicated across small volumes.
Financial risk	FX constraints and weak payment reliability increase working-capital needs and induce supplier risk mark-ups.
Distribution trade-off	Higher responsiveness and stockout protection often come at the expense of higher logistics and inventory costs.

Table 1: Identified upstream cost-drivers

3.5. Barriers

The analysis of aminophylline, the selected SSA reference cases, and the broader literature provides partial explanations for the absence of caffeine supply in Malawi. Together, these findings indicate that multiple upstream barriers prevent the establishment of a stable and routine procurement pathway. Summarising these barriers helps define the key design requirements for alternative upstream supply chain configurations.

Registration as an entry barrier. Regulatory registration and institutional eligibility function as formal entry gates for routine public-sector procurement. For medicines intended for government supply, inclusion in national treatment guidelines and the Essential Medicines List, alongside a lawful importation and procurement pathway, are prerequisites for institutionalized purchasing and distribution ([30]). Reference cases show that where caffeine supply has been successfully institutionalized, the product is formally registered and embedded within national regulatory and procurement frameworks. In the absence of such a pathway, supply is limited to exceptional or ad-hoc import routes, which are administratively burdensome, difficult to scale, and unsuitable for long-term integration (Transcript T2). The lack of a fully institutionalized entry pathway therefore constitutes a structural upstream barrier.

Financing and payment uncertainty. Financing constraints affect not only affordability but also the practical execution of procurement transactions. International suppliers commonly transact in foreign currency (e.g., USD), while limited access to foreign exchange in Malawi can delay order placement and settlement (Transcript T1). Foreign exchange shortages and payment uncertainty increase perceived counterparty risk for suppliers and may discourage engagement in low-volume markets. Although financing constraints alone do not explain the absence of caffeine supply, they amplify execution risk and reduce the likelihood that stable contractual relationships will emerge. In this sense, financing uncertainty reinforces structural instability in the upstream configuration.

Low-volume market characteristics. Caffeine for AOP serves a relatively small and specialised neonatal population, resulting in structurally low demand volumes ([31]). In the Malawian context, expected order quantities are limited and forecasting is uncertain. For manufacturers and suppliers, such conditions weaken incentives to invest in market entry activities, including registration support and supply set-up (Transcript T2). At the same time, public procurement systems are typically optimised for higher-volume, predictable medicines (Transcript T1). The mismatch between caffeine's low-volume profile and standard tender structures reduces institutional compatibility and limits competitive pressure, thereby constraining the spontaneous emergence of routine supply.

Assuring quality. Quality assurance represents an additional upstream concern. In resource-constrained environments, financial pressure and limited regulatory capacity can increase reliance on informal or weakly regulated procurement channels, raising exposure to substandard and counterfeit medicines ([20, 11]). Counterfeit products may enter the legitimate supply chain during logistics activities spanning manufacturing, distribution, and retail, underscoring that quality risks can originate upstream and propagate across the chain. Ensuring product quality therefore requires procurement and sourcing arrangements that safeguard regulatory compliance, documentation standards, and traceability, rather than relying solely on downstream inspection.

Collectively, these barriers highlight that the absence of caffeine in Malawi cannot be attributed to a single constraint. Instead, regulatory entry conditions, financing instability, limited market scale, and quality assurance risks interact to create an upstream environment in which routine procurement does not naturally emerge. These consolidated findings form the basis for deriving explicit design requirements for alternative upstream supply chain configurations.

4. Designing alternatives

Using the insights of the analysis above, four design requirements were derived from the identified barriers and Malawi's upstream system characteristics. Each alternative must: provide a lawful pathway for importation, procurement, and use in Malawi by aligning with relevant institutional and regulatory entry conditions; safeguard product quality by including at least one credible quality-control structure; be implementable using

existing supply chain actors and infrastructure, without requiring new domestic manufacturing capacity; and be maintainable over time by supporting routine replenishment rather than one-off or emergency procurement.

In addition, design objectives were formulated to capture the upstream cost-driver mechanisms expected to shape affordability and supply availability across alternatives. They are derived from the cost drivers and are later translated into MCA criteria to systematically compare the alternatives.

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

Figure 1: Morphological chart of upstream design options for the caffeine supply chain.

The design space was made using morphological analysis. Figure 1 shows the morphological chart, which decomposes the upstream supply chain into three core functions (derived from the Malawian supply chain structure): quantification and sourcing, ordering and procurement, and supply and distribution, and lists feasible options for each function. After an iterative process, using multiple steps by combining compatible options across these functions and excluding infeasible or internally inconsistent combinations, the broad set of possible configurations was reduced and consolidated into four representative design alternatives, presented in Table 2 and visualized in Figure 2. The selected alternatives were deliberately designed to differ in how demand is aggregated, how sourcing and contracting are structured and governed, and how upstream logistics are organised.

Design alternative	Description
Alt 1: Donor pipeline	Donor-funded, single-source procurement via an agent/wholesaler, with direct shipment to Malawi; represents the status quo set-up and serves as the baseline for cost and disruption risk.
Alt 2: Managed multi-sourcing	Dual/multi-sourcing under a long-term contract, coordinated by an agent; reduces supplier dependency and disruption risk while keeping governance and execution manageable.
Alt 3: Regional pooling & logistics hub	Pooled regional demand and bundled procurement, with a regional hub for consolidation and onward distribution; targets scale advantages but adds coordination and additional control points.
Alt 4: Government-core	Financing and payment shift to the Malawian government budget to increase ownership and decision control; procurement remains centralized and relatively simple to keep implementability feasible.

Table 2: Design alternatives.

5. Validation and evaluation

Before evaluation, the proposed designs are validated against the design requirements. These requirements act as hard feasibility constraints, ensuring that each alternative is legally implementable and operationally feasible in the context of this research. To further support this step, a plausibility check was conducted through a semi-structured expert interview with a representative from the Access to Medicine Foundation. The interview was used to assess whether the functional choices embedded in the designs are realistic and to validate the relevance of the identified cost drivers.

After that, the evaluation compares the four upstream design alternatives using a structured MCA based on performance matrices and direct pairwise comparisons. To assess robustness under context-relevant uncertainty, the evaluation is repeated under two stress scenarios derived from exogenous risk factors that are particularly salient in low-volume LMIC procurement environments: financing instability and low data reliability and transparency. For each setting (base case and both scenarios), a scenario-specific performance matrix is constructed. Therefore each alternative is scored on a 1–5 anchored scale for the five criteria defined earlier. Criterion weights are kept equal (i.e., all weights set to one) to avoid imposing a preference structure that cannot be empirically validated and to ensure that differences in ranking are driven by changes in scenario performance rather than changes in stated preferences. The scores are compiled in a performance matrix, as can be seen in tables 3, 4, 5 below.

Base case

Base case	**Alt 1**	**Alt 2**	**Alt 3**	**Alt 4**
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	4	2
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	3	3	4	2

Table 3: Performance matrix for the base case.

Scenario 1: Financing instability

Scenario 1: Financing instability	**Alt 1**	**Alt 2**	**Alt 3**	**Alt 4**
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	5	1
C4: Chain complexity	4	3	1	5
C5: Logistics cost balance	2	3	4	1

Table 4: Performance matrix for Scenario 1: Financing instability.

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(a) Alternative 1: Donor pipeline

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(b) Alternative 2: Managed multi-sourcing

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(c) Alternative 3: Regional logistic hub

Function				
Quantification & sourcing	**Quantification responsibility**	Facility ordering	Central ordering	Regional pooling
	Sourcing mode	Single source procurement	Dual/multi-sourcing	Pooled sourcing
Ordering & procurement	**Procurement & contracting**	Ad-hoc procurement	Routine procurement cycle	Strengthened / long-term contract
	Financing & payment	Donor funded	Government budget	Pooled donor funded
Supply & distribution	**Quality control**	Single QC gate at manufacturing	Two QC gates (manufacturing + in country)	Multi gate (manufacturing + hub + in country)
	Upstream bundling approach	Direct shipment	Via agent / wholesaler	Regional hub consolidation

(d) Alternative 4: Government core

Figure 2: Design alternatives for the upstream supply chain configurations.

Scenario 2: Low data reliability & transparency

Scenario 2: Low data reliability & transparency	**Alt 1**	**Alt 2**	**Alt 3**	**Alt 4**
C1: Scale potential	3	3	5	2
C2: Fragmentation	4	3	1	5
C3: Transactional efficiency	3	4	3	2
C4: Chain complexity	3	2	1	4
C5: Logistics cost balance	2	3	3	2

Table 5: Performance matrix for Scenario 2: Low data reliability & transparency.

After these scores, the alternatives are compared pairwise across the full criterion set. For each pair, the alternative with the stronger overall performance profile is selected as the best-scoring alternative in comparison, and the overall ranking is derived from the number of pairwise wins. This is presented in Tables 6, 7, 8 .

Base case

Outcome: 3 & 1 > 2 > 4

	C1	**C2**	**C3**	**C4**	**C5**	**Best Alt. in comparison**
A1 vs A2	~	A1	A2	A1	~	A1
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	~	A2	A3	~
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 6: Direct pairwise comparison outcomes for the base case.

Scenario 1: financing instability

Outcome: 3 > 1 & 2 > 4.

	C1	**C2**	**C3**	**C4**	**C5**	**Best Alt. in comparison**
A1 vs A2	~	1	2	1	2	~
A1 vs A3	A3	A1	A3	A1	A3	A3
A1 vs A4	A1	A4	A1	A4	A1	A1
A2 vs A3	A3	A2	A3	A2	A3	A3
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 7: Direct pairwise comparison outcomes for Scenario 1: Financing instability.

Scenario 2: Low Data Reliability & Transparency
Outcome: 2 > 3 > 1 & 4.

	C1	C2	C3	C4	C5	Best Alt. in comparison
A1 vs A2	~	A1	A2	A1	A2	A2
A1 vs A3	A3	A1	~	A1	A3	~
A1 vs A4	A1	A4	A1	A4	~	~
A2 vs A3	A3	A2	A2	A2	~	A2
A2 vs A4	A2	A4	A2	A4	A2	A2
A3 vs A4	A3	A4	A3	A4	A3	A3

Table 8: Direct pairwise comparison outcomes for Scenario 2: Low data reliability & transparency

6. Answer to main research question

This study addresses the main research question: *How can the main characteristics and structure of the upstream supply chain of caffeine be designed to enable access to Malawi's neonatal care system?*

To enable access to caffeine to Malawi's neonatal care system, the upstream supply chain needs to function under conditions of low and uncertain demand while ensuring continuity of supply and supporting affordability. This requires a structure that mitigates key upstream cost drivers by creating scale where possible (e.g., through pooled demand), establishing clear responsibilities across procurement and contracting, and reducing operational and financial frictions such as fragmented ordering processes, weak information flows, and exposure to payment or foreign exchange constraints.

Based on the design exploration and evaluation, a regional pooling configuration with a shared logistics hub (Alternative 3) best reflects these requirements. By aggregating demand across countries and consolidating execution through a hub structure, this configuration increases supplier attractiveness and supports both supply continuity and lower upstream cost pressure in a thin supplier market. However, its feasibility depends on sufficient regional coordination capacity and stable governance arrangements.

At the same time, the analysis indicates that different configurations may be appropriate under specific constraints. A donor-supported baseline configuration (Alternative 1) can facilitate rapid introduction when coordination capacity is limited, while a managed multi-sourcing configuration (Alternative 2) offers greater robustness under conditions of limited data reliability or coordination challenges. Over time, transitioning towards a pooled regional configuration such as Alternative 3 provides the most promising pathway for establishing a more sustainable upstream supply chain for caffeine availability in Malawi.

7. Discussion

This study examines how the characteristics and structure of the upstream supply chain for caffeine can be designed to enable access in Malawi, with a particular focus on identifying and analysing the key cost drivers that influence affordability and availability.

A central contribution is making the upstream cost drivers behind affordability more explicit. Affordability is shaped not only by manufacturing cost, but by upstream factors that are sensitive to configuration choices, including scale leverage, fragmentation, transaction burden, chain complexity, compliance overhead, and exposure to payment risk. This clarifies why examining supply chains is important even when final prices are difficult to observe or predict.

One notable finding of the comparative analysis is that, despite the common reliance on Asian manufacturing for medicines supplied to SSA, the caffeine identified in the reference cases is sourced through European manufacturers. This suggests that the supply structure for caffeine may differ from broader pharmaceutical supply chains and may be shaped by a relatively limited supplier base.

A second observation concerns the limited transparency surrounding caffeine-specific cost drivers. Even after stakeholder interviews and desk-based research, the underlying cost structure remains difficult to disentangle. Cost-related information is often commercially sensitive and rarely documented in public sources, which makes it challenging to attribute observed price differences to specific factors beyond plausible upstream factors such as scale effects, contracting conditions, and financial risk.

The study also highlights the value of a design-oriented approach for exploring supply chain configurations in contexts where quantitative data is limited. The Double Diamond Model supported an iterative process that allowed problem understanding and solution development to inform each other. This made it possible to explore multiple realistic upstream configurations and subsequently narrow them down through structured evaluation.

At the same time, the results show that the performance of the design alternatives is strongly scenario-dependent. No single configuration performs best across all conditions. Under financing instability, configurations that reduce exposure to foreign exchange and payment risks perform more robustly, favouring pooled procurement structures. Under conditions of low data reliability and transparency, configurations with simpler coordination requirements perform better.

Overall, these findings underline that improving access to caffeine is not only a matter of price reduction, but also of how upstream supply chains are organised. Structural choices regarding sourcing, procurement coordination, and contracting arrangements play an important role in shaping both affordability and supply reliability.

8. Limitations

This study is subject to several limitations that should be considered when interpreting the results.

Methodologically, the evaluation is intentionally ordinal. The pairwise comparison and anchored 1–5 scoring enable a structured assessment without suggesting false numerical precision, but results still depend on qualitative judgement in the

scoring and the aggregation logic. Criterion weights were set equal as a baseline assumption because stakeholder input to justify differential weights was not available; rankings may therefore shift under alternative stakeholder priorities.

In terms of the design space, only four configurations were taken forward to the MCA. While the morphological analysis generates many feasible combinations, the study necessarily focused on a manageable subset. The findings should therefore be interpreted as directional rather than exhaustive, and other viable (or superior) configurations may exist outside the selected set.

Regarding scope, the analysis focuses primarily on upstream supply chain design (manufacturing origin, procurement, contracting, and distribution up to national receipt). Downstream elements, such as last-mile distribution, facility-level storage, and clinical usage practices, were not analysed in detail, even though they can materially affect effective availability within neonatal care.

Affordability was primarily assessed through upstream cost-driver factors. Non-cost factors that can shape access in practice (e.g., political constraints, organisational culture, and implementation capacity) were not used, which may limit how well the results translate to real-world feasibility.

In terms of robustness testing, only two stress scenarios were assessed (financing instability and low data reliability/transparency). While both are context-relevant, they do not cover less common but plausible disruptions, so relative performance may change under other conditions.

For validation, the study relied on a single semi-structured expert interview as a plausibility check. Although this supported the realism of the functional choices and the relevance of the identified drivers, it does not constitute comprehensive validation; additional stakeholder perspectives and interviews would strengthen confidence in the assumptions, scoring, and rankings.

Finally, the morphological chart was effective for structuring the design space, but its largely text-based representation is less visually expressive than ideal for communicating supply chain designs. More explicit visualisations of actors, flows, and interfaces could improve readability and make differences between configurations easier to compare.

9. Conclusion

This thesis demonstrates how a design-oriented approach can be applied to develop and evaluate alternative upstream supply chain configurations for caffeine to Malawi. The evaluation indicates that regional pooling with bundled logistics and coordinated execution is the most aligned option for addressing key cost drivers and continuity risks in a thin market. Although implementation depends on multiple factors such as governance and coordination capacity, the results provide actionable direction for stakeholders seeking to expand feasible access to caffeine for neonatal care.

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Appendix B

Background information

B.1 Current quantification, sourcing and procurement process

Figure B-1 summarizes Malawi's current quantification, sourcing, and procurement workflow in a swimlane diagram, specifying the key actors and the chronological processes between them. While routine ordering activities occur monthly through OpenLMIS and are validated at the district level, upstream decisions determining whether new or expanded medicine volumes can actually enter the system are largely organized in infrequent, calendar-driven cycles.

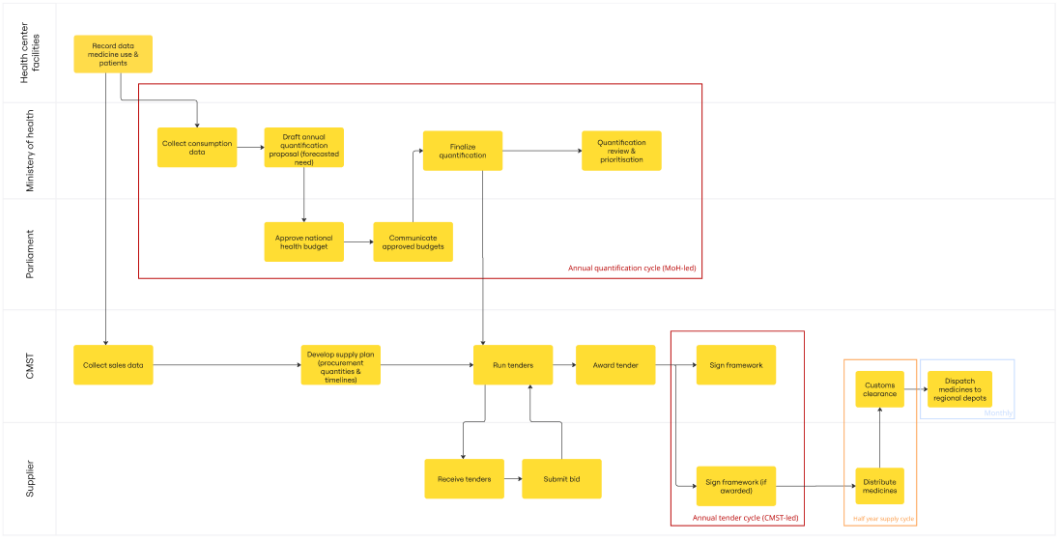

Figure B-1: Swimlane diagram quantification, sourcing and procurement process Malawi

The two red blocks in the diagram capture activities that are only executed annually. The first annual cycle concerns the consolidation, review, and finalization of quantification inputs. In Malawi, national forecasting is translated into an annual quantification proposal that is

reviewed in a national workshop (typically in November) and used to inform budget allocations. Although mid-year reviews may update estimates, the main "decision moment" for adopting, validating, and formally translating needs into a nationally endorsed quantification remains highly concentrated in time. This reduces the system's ability to react to new clinical priorities, changes in consumption patterns, or data quality issues that emerge after the annual exercise. In practice, this creates long waiting times between identifying a gap (e.g., the need for a new medicine) and being able to formally integrate it into the national plan that triggers procurement action.

The second annual cycle (also shown in red) relates to tender outcomes and supplier awarding. This is not merely an administrative repetition: it acts as a hard procurement gate. Even if demand signals and clinical priorities are clear, supplier contracting and onboarding are effectively pushed to the next award window. This is particularly consequential because procurement is already described as lengthy, often taking months from the submission of orders to contract signing due to administrative approvals, supplier delays, and foreign exchange constraints. An annual tender rhythm therefore, compounds existing lead-time drivers rather than absorbing them, making time-to-market for new medicines dependent on the procurement calendar instead of health system urgency.

Finally, the orange block shows that deliveries and distribution follow a six-monthly schedule under normal conditions. With supplier deliveries occurring semi-annually and contractual lead times of roughly 12 weeks (often extending to 16 weeks), the replenishment loop is structurally slow. This reduces flexibility to correct forecast errors, respond to sudden demand peaks, or mitigate emerging stock imbalances across facilities. As a result, the system needs larger buffers to remain resilient, buffers that are difficult to maintain under constrained budgets and warehouse capacity, thereby increasing the likelihood that patients and hospitals experience delays in access when forecasts or delivery timelines deviate from plan. The blue block depicts the downstream dispatch process from CMST to regional depots and onwards to health facilities, which takes place on a monthly basis. While this more frequent dispatch rhythm can redistribute available stock within the country, it does not resolve shortages that originate upstream. When central inventories are used or supplements are delayed, monthly dispatch becomes a rationing exercise rather than a mechanism to ensure continuity of supply. Consequently, low-stock situations at facility level can persist despite regular dispatch cycles, because the binding constraint is the infrequent (six-monthly) replenishment schedule and the limited ability to inject additional volumes into the system between cycles.

Appendix C

Scope: SSA region

Figure C-1: Sub-Saharan African region countries. Source: Encyclopaedia Britannica 2026

Appendix D

Literature search approach list of papers

Table D-1: Papers analysed for literature review

No.	Document title	Description / Relevance	Source	Type	Topic
1	A landscape evaluation of caffeine citrate availability and use in newborn care across five low- and middle-income countries	Cross-country evidence on caffeine citrate availability and use in neonatal care across five LMICs.	O. A. Ekhaguere, Bolaji, et al. 2024	Sci.	LMIC/SSA context
2	Estimated costs of production and potential prices for the WHO Essential Medicines List	Provides an analysis of estimated production costs of WHO essential medicines and implications for pricing and affordability.	Hill et al. 2018	Sci.	Problem
3	Pharmaceutical Supply Chain Management Challenges in Developing Countries: A Systematic Literature Review	Systematic review of pharmaceutical supply chain challenges in low- and middle-income countries.	Alfaouri et al. 2025	Sci.	Problem
4	Health supply chain system in Uganda: current issues, structure, performance, and implications for systems strengthening	Case study of health/pharmaceutical supply chain performance in an African LMIC, highlighting structural and operational bottlenecks.	Lugada et al. 2022	Sci.	LMIC/SSA context
5	CHORD Health Supply Chain Review	Reviews supply chain models including key actors, flows and governance arrangements relevant to access to medicines.	Initiative 2024	Grey	Malawi and medicine
6	Building resilience into the Nation's Medical Product Supply Chains	Conceptual and policy framework for resilient medical product supply chains, with recommendations on awareness, mitigation, preparedness and response.	NASEM 2022	Grey	Methods
7	Barriers in the Supply Chain Management of Essential Medicines in the Public Health Care System in Malawi	Identifies barriers related to warehousing, distribution, information bottlenecks and governance affecting access to medicines in Malawi.	Kaupa et al. 2021	Sci.	Malawi and medicine
8	Is caffeine available and affordable in low- and middle-income countries? A survey in sub-Saharan Africa	Examines availability and affordability of caffeine across LMICs, highlighting price and access challenges.	O. A. Ekhaguere, Ayede, et al. 2020	Sci.	LMIC/SSA context

Continued on next page

No.	Document title	Description / Relevance	Source	Type	Topic
9	UNICEF Supply Division: Medicines and Nutrition Procurement Overview	Describes donor-led procurement structure for essential medicines in low- and middle-income countries, including sourcing, quality assurance and logistics.	UNICEF Supply Division 2024	Grey	LMIC/SSA context
10	Health Product Supply Chains in Developing Countries: Diagnosis of Root Causes of Underperformance and Agenda for Reform	Diagnoses root causes of supply chain underperformance in LMICs, highlighting governance, financing, accountability and coordination failures.	Yadav 2015	Sci.	Problem
11	Private Sector Pharmaceutical Supply and Distribution Chains in Ghana, Mali and Malawi	Provides a comparative analysis of private pharmaceutical supply and distribution chains in Ghana, Mali and Malawi, mapping actors, flows, incentives and structural bottlenecks.	McCabe et al. 2009	Grey	Malawi and medicine
12	Towards the design of Secure Supply Chains	Set of supply chain concepts are identified and compiled in a supply chain design framework.	Ludema 2009	Sci	Methods
13	Understanding the Pharmaceutical Value Chain	Provides a structured overview of the pharmaceutical value chain and typical cost build-up across actors (manufacturing, distribution, mark-ups).	Aitken 2016	Grey	Cost drivers
14	Hidden costs across the pharmaceutical supply chain	Discusses hidden and indirect cost drivers across pharmaceutical supply chains, supporting the identification of structural cost drivers relevant for configuration choices.	Falcon 2024	Grey	Cost drivers
15	Understanding pharmaceutical supply chain costs and price formation in low- and middle-income countries	Peer-reviewed analysis of supply chain cost components and price formation factors in LMIC contexts, directly informing the distinction between price drivers and cost drivers and their relevance for affordability.	Lee et al. 2021	Sci.	Cost drivers
16	Risk, uncertainty, and cost escalation in pharmaceutical supply chains	Peer-reviewed article on how risk and uncertainty propagate through pharmaceutical supply chains and contribute to cost escalation.	Ibrahim et al. 2025	Sci.	Cost drivers
17	A systematic review of policies regulating or removing mark-ups in the pharmaceutical supply and distribution chain	Systematic review on how mark-up regulation/removal in the pharma distribution chain affects medicine prices and expenditures.	Joosse et al. 2023	Sci.	Cost drivers
18	Addressing the supplier selection problem by using the analytical hierarchy process	Applies AHP (pairwise comparisons) to structure supplier selection in a pharmaceutical company using multiple qualitative criteria. Provides a pharma procurement example of MCDA under limited quantitative data.	Manik 2023	Sci.	Methods

Continued on next page

No.	Document title	Description / Relevance	Source	Type	Topic
19	Applying the Combination of AHP and WPM Methods to Prioritize Pharmaceutical Distribution Channel Selection	Uses AHP (pairwise comparisons) to derive weights and WPM to rank pharmaceutical distribution channel options based on expert judgement.	Khoat et al. 2025	Sci.	Methods
20	Using the pairwise comparison method to assess competitive priorities within a supply chain	Demonstrates direct pairwise comparison to prioritize competitive priorities across supply chain members. Serves as a methodological precedent for judgement-based ranking when hard data are scarce.	Saarijärvi et al. 2012	Sci.	Methods
21	Multi-Criteria Decision Analysis-Based framework for supply chain management evaluation with multi-dimensional sensitivity analysis: A green logistics perspective	Presents an MCDA framework to evaluate supply chain alternatives and test ranking robustness via multi-dimensional sensitivity analysis. Useful as a reference for robustness checks under uncertainty.	Więckowski et al. 2025	Sci.	Methods
22	The supply and distribution of essential medicines in Malawi	Country evidence report describing procurement, supply, and distribution bottlenecks behind chronic essential-medicine stock-outs in Malawi.	Wild et al. 2013	Grey	Malawi and medicine
23	The Logistics Handbook: A Practical Guide for the Supply Chain Management of Health Commodities	Practical handbook summarizing core logistics functions for health commodities (procurement, inventory, distribution, LMIS).	USAID DELIVER PROJECT 2011	Grey	Methods
24	A simulation-based analysis for effective distribution of COVID-19 vaccines: A case study in Norway	Simulation-based scenario analysis comparing alternative vaccine distribution configurations under uncertainty and operational constraints.	Sun et al. 2021	Sci.	Methods
25	Resilient COVID-19 vaccine supply chain: An optimization and simulation approach for multi-objective management	Demonstrates scenario-based stress testing of supply chain designs to assess robustness under adverse conditions.	Khalilpoor et al. 2025	Sci.	Methods
26	Challenges to the Availability and Affordability of Essential Medicines in Africa: A Systematic Review	Systematic review identifying key barriers to essential medicine availability and affordability across African settings.	Yenet et al. 2023	Sci.	LMIC/SSA context

Appendix E

Pharmaceutical supply chain structures and flows

E.1 UNICEF

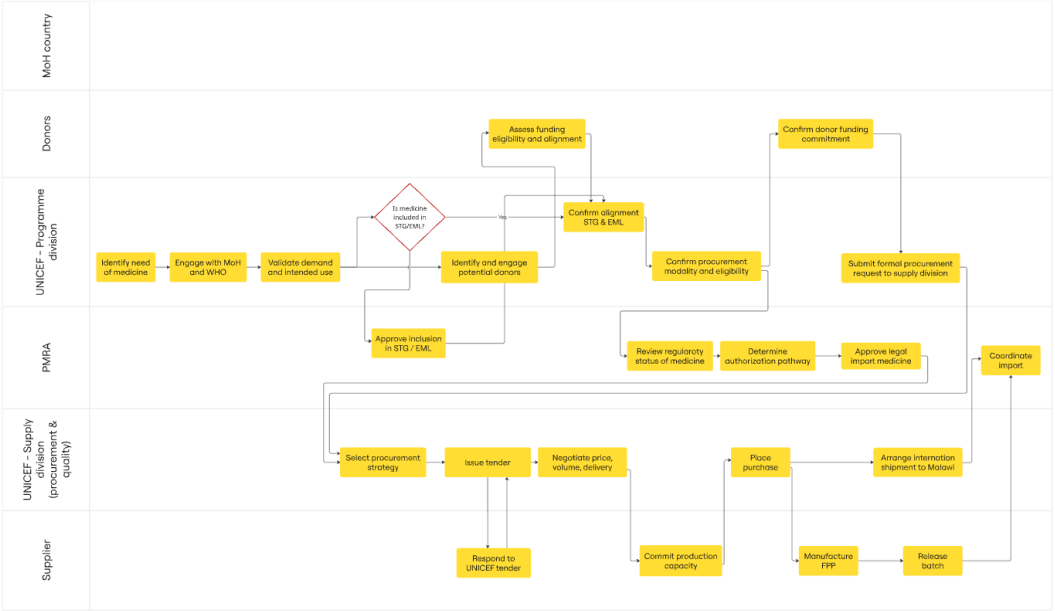

Figure E-1: Swimlane UNICEF initiated

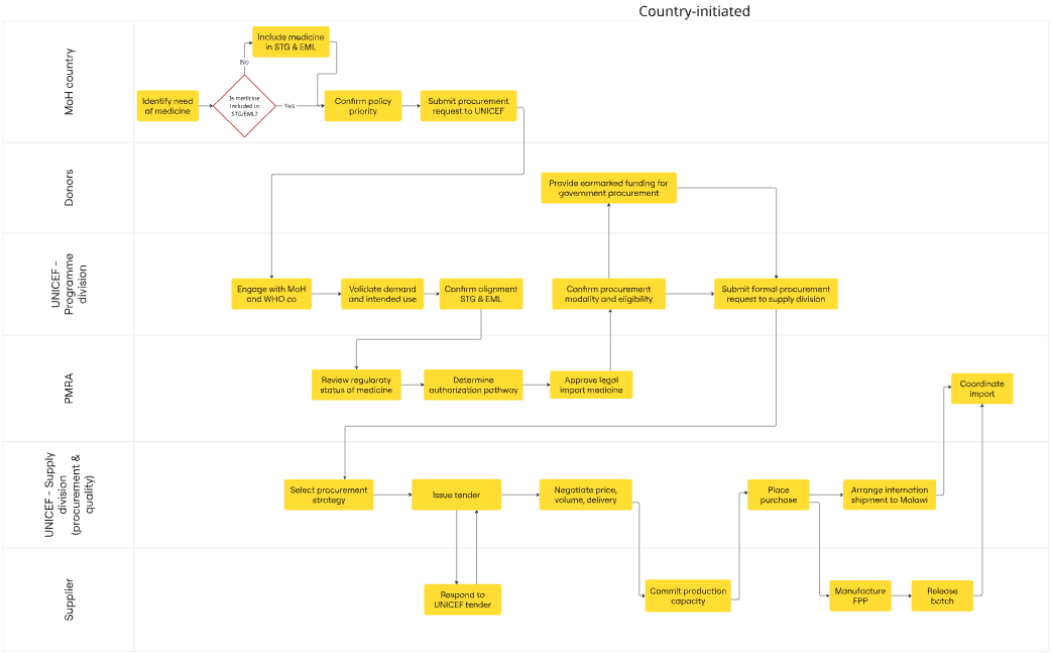

Figure E-2: Swimlane UNICEF country initiated

E.2 Uganda

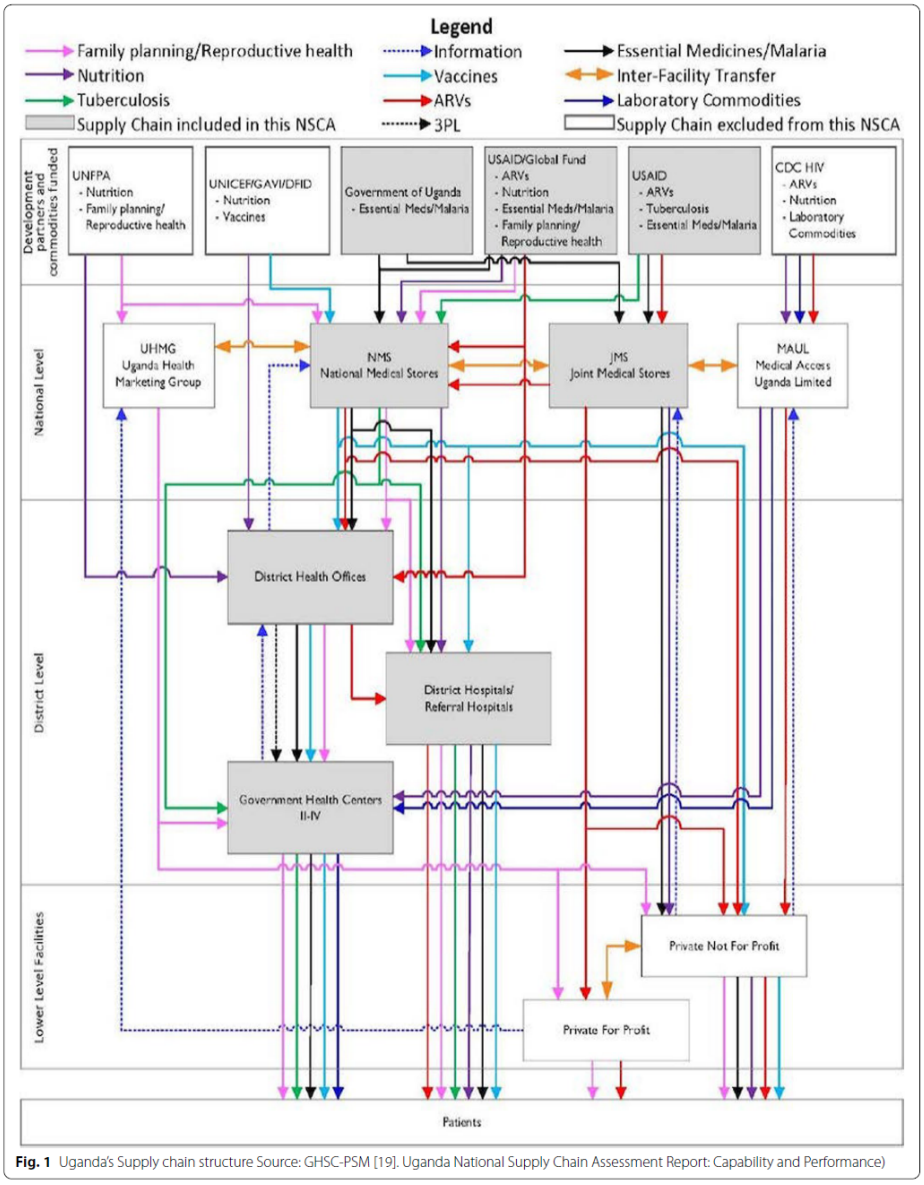

Fig. 1 Uganda's Supply chain structure Source: GHSC-PSM [19]. Uganda National Supply Chain Assessment Report: Capability and Performance)

Figure E-3: Overview of Uganda's health supply chain system. Source: Lugada et al. 2022

E.3 Malawi

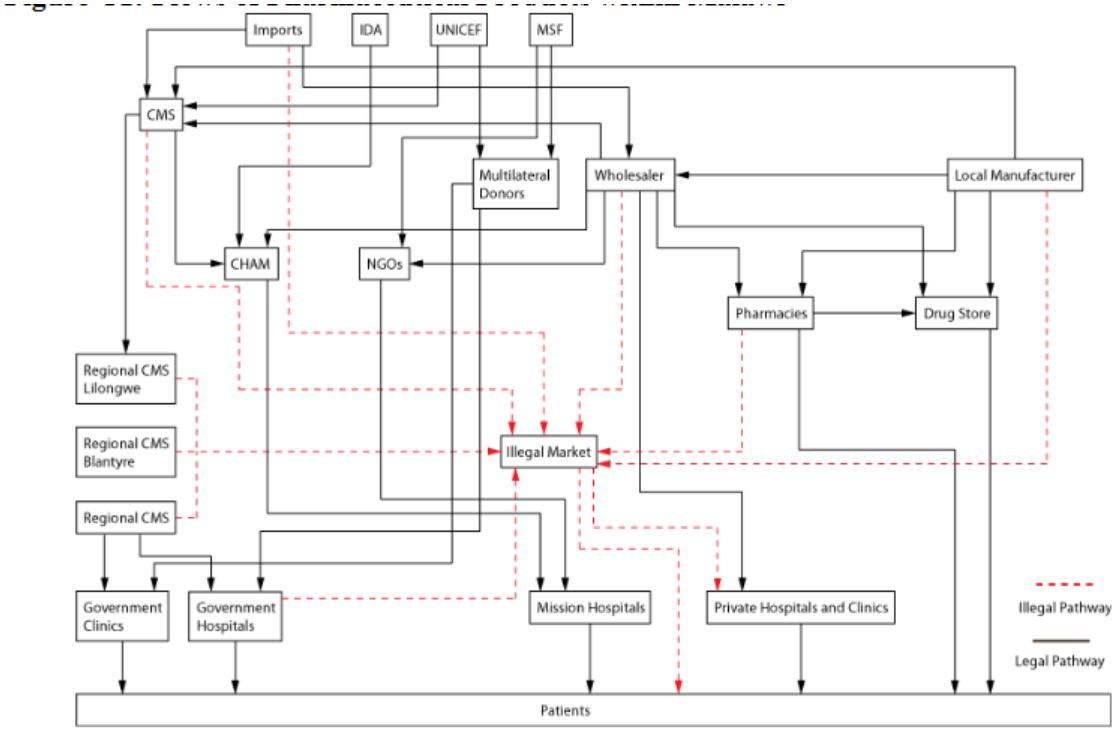

Figure E-4: Flows of pharmaceutical products in Malawi. Source: McCabe et al. 2009

Appendix F

SSA reference case descriptions

F.1 Ethiopia

Regulatory and policy status

In Ethiopia, caffeine has recently become formally authorized for use. Since early 2025, Chiesi has received official marketing authorization for its proprietary caffeine product, marketed as Peyona, through the Ethiopian Food and Drug Administration (EFDA) (Chiesi Farmaceutici S.p.A. 2024). According to the World Health Organization's SRA–CRP product list, Peyona is authorized in Ethiopia on the basis of European Medicines Agency (EMA) approval, making it eligible for accelerated national registration through WHO's Collaborative Registration Procedure.

Product and manufacturing

Chiesi acts as the marketing authorization holder (MAH) and is responsible for placing the finished pharmaceutical product on the Ethiopian market, as well as for maintaining regulatory compliance and product quality throughout the lifecycle.

Procurement pathway

In Ethiopia, procurement and distribution of medicines for public health facilities are centrally organised through the Ethiopian Pharmaceuticals Supply Agency (EPSA), which acts as the national procurement and distribution body. EPSA operates under the strategic oversight of the Ethiopian MoH, which sets national health policy and priorities. Regulatory approval of medicines is provided by the EFDA, which licenses pharmaceutical products for use within the national system.

International partners support this procurement architecture at system level. The USAID Global Health Supply Chain Program–Procurement and Supply Management (GHSC-PSM) works with EPSA to strengthen logistics, forecasting, and supply chain performance for priority health programmes. Based on the available information, Ethiopia's pharmaceutical procurement system reflects a predominantly country-initiated procurement pathway. However, the specific procurement modality through which caffeine is sourced cannot be conclusively determined from the available sources.

Role of donors and international partners

CHAI has played a significant role in shaping demand generation and procurement pathways for neonatal caffeine in Ethiopia. Working in collaboration with the MoH, EFDA, and professional associations, CHAI supported improved accessibility of caffeine. This coordinated approach contributed to a reported 70% price reduction for government purchasers and enabled Ethiopia's first national tenders for caffeine (CHAI 2023).

Distribution and market integration

Within Ethiopia's regulated pharmaceutical supply chain, EFDA identifies several key actors involved in product handling and compliance, including the original manufacturer, importer, distributor, retailer, or designated agent (EFDA 2024). These actors collectively form the supply chain supporting the introduction and distribution of Peyona. Further details on scale of distribution or public versus private sector integration are not specified.

F.2 Kenya

Regulatory and policy status

In Kenya, regulatory oversight of pharmaceutical products is provided by the Pharmacy and Poisons Board (PPB), which is responsible for the registration, licensing, and quality assurance of medicines for use within the country. Caffeine for neonatal use is included in the Kenya Essential Medicines List (KEML) 2023, indicating formal policy recognition of the medicine within the national health system and eligibility for public-sector procurement and use.

Product and manufacturing

Caffeine supplied to Kenya is marketed under the name Cayona. The product is manufactured by Ethypharm through its subsidiary Martindale Pharma, which produces the injectable caffeine formulation used in Kenyan hospitals (Pharma 2024; Kenya 2024). In addition, records from the Kenya Industrial Property Institute indicate that Chiesi Farmaceutici S.p.A. also holds intellectual property protection for caffeine-related products in Kenya (KIPI 2023).

Procurement pathway

Caffeine for the public health sector is procured through the Kenya Medical Supplies Authority (KEMSA), which is responsible for quantification, storage, allocation, and distribution of essential medicines to county and national hospitals. Ethypharm's formulation is incorporated into the national strategy for neonatal care and procured for use in Kenyan referral facilities (Star 2023).

Role of donors and international partners

Access to caffeine in Kenya has been supported through coordinated efforts between CHAI, the Ministry of Health, and pharmaceutical manufacturers. CHAI negotiated with Ethypharm to improve affordability and availability, resulting in a substantial price reduction from approximately 1,500 KSh to 400 KSh per ampoule (approximately EUR 2.65) (H. B. Kenya 2023). CHAI thus played a facilitating role in market shaping and pricing negotiations.

Distribution and market integration

Distribution of caffeine within the public sector occurs through KEMSA, which supplies national and county-level hospitals. Further details on private-sector distribution or nationwide scale are not specified.

F.3 South Africa

Regulatory and policy status

In South Africa, caffeine for the treatment of apnea of prematurity (AOP) is available through a locally registered formulation. The product is marketed under the name Cayona and has been registered since 2015. The marketing authorization holder (MAH) is Safeline Pharmaceuticals, which holds responsibility for regulatory compliance and market authorization within the South African regulatory framework (Safeline Pharmaceuticals (Pty) Ltd 2015). As a result, caffeine is fully embedded within South Africa's national regulatory and policy environment and does not rely on donor-supported structures.

Product and manufacturing

Cayona is supplied as an intravenous and oral caffeine formulation in 1 mL clear, colourless Type I glass ampoules, packaged in boxes of ten. While Safeline Pharmaceuticals functions as the MAH and national supplier, the active pharmaceutical ingredient and finished formulation are manufactured by Chiesi Farmaceutici (Safeline Pharmaceuticals (Pty) Ltd n.d.). This arrangement reflects a common model in regulated pharmaceutical markets, where an international manufacturer supplies the product while a local company manages regulatory approval and domestic distribution.

Procurement pathway

Caffeine is procured through South Africa's public-sector tender system for small-volume parenteral medicines. For the tender period from 1 May 2024 to 30 April 2027, a total of 336,715 units of caffeine were awarded at a contract price of ZAR 377.26 per unit (approximately EUR 18.98 as of November 2025) (National Department of Health, South Africa 2025). This tender-based procurement reflects a standard, country-initiated procurement pathway, in which national authorities define demand, issue tenders, and contract suppliers directly without reliance on external procurement agents.

Role of donors and international partners

Unlike many low-resource settings, donor organizations play no significant role in the procurement or market shaping of caffeine in South Africa. Procurement decisions, pricing, and supplier selection are governed by national tender procedures rather than donor-funded. This absence of donor involvement distinguishes South Africa from other Sub-Saharan African contexts and highlights the extent to which caffeine has been institutionalized within the domestic health system.

Distribution and market integration

Safeline Pharmaceuticals supplies caffeine to both the public and private healthcare sectors. According to the Pharmaceuticals in South Africa market report, the company markets 14 generic products and 2 originator products, supplying a total of 16 products to the private sector and 5 products to the public sector (Helen Suzman Foundation 2018). Distribution to public-sector hospitals occurs through established national logistics channels associated with the public tender system, while private-sector distribution follows conventional commercial pharmaceutical supply routes.

Overall, South Africa represents a mature and fully institutionalized market for neonatal caffeine. The product is locally registered, procured through national tenders, and distributed through standard public and private sector supply chains. As such, South Africa provides a useful contrast to donor-driven or UNICEF-initiated procurement pathways observed in other Sub-Saharan African countries, illustrating how sustained regulatory approval and domestic procurement capacity can enable routine access to caffeine.

F.4 Uganda

Regulatory and policy status

In Uganda, caffeine for neonatal use is registered under the generic name caffeine. According to the National Drug Authority (NDA) drug register, caffeine 10 mg/mL solution is licensed to Macarthys Laboratories Ltd, with Martindale Pharma listed as the manufacturing site, indicating that the product is imported from the United Kingdom (National Drug Authority (Uganda) 2025).

Product and manufacturing

The registered caffeine product is manufactured by Martindale Pharma, with Macarthys Laboratories Ltd acting as the licensed entity responsible for the product in Uganda. No further information on formulation variants or packaging is specified.

Procurement pathway

The Ugandan health supply chain comprises multiple upstream procurement and distribution routes up to national level, as illustrated in Figure E-3 (Appendix E). Government-financed medicines are channelled through the National Medical Stores (NMS). In parallel, donor-financed commodities follow semi-parallel structure: jointly managed donor channels (e.g., USAID/Global Fund) supply both NMS and the Joint Medical Stores (JMS), whereas USAID-only programmes supply exclusively through JMS. As a result, essential medicines financed by development partners, such as UNICEF, the Global Fund, GAVI, and USAID, are typically procured outside the regular government procurement system, either directly by these agencies or via contracted procurement agents, and subsequently channelled through parallel or semi-parallel supply chains (Lugada et al. 2022).

Role of donors and international partners

Essential medicines and health commodities financed by development partners, including UNICEF, the Global Fund, GAVI, and USAID, are not procured through the regular government procurement system. Instead, these agencies or their contracted procurement agents purchase products directly on behalf of the country and channel them through parallel or semi-parallel supply chains (Lugada et al. 2022).

Distribution and market integration

Distribution occurs through both NMS and JMS, depending on the financing source. Further details on the extent to which caffeine is routinely distributed, or its level of integration into public-sector neonatal care, are not specified.

Appendix G

Morphological chart: functions and options

This appendix explains the functions and options used in the final morphological chart (Figure X). The chart is used to generate feasible upstream supply chain configurations for pharmaceutical caffeine up to the point of procurement by the Malawian Ministry of Health. Each function represents a key design decision that affects cost drivers (e.g., scale vs fragmentation, transaction costs, and chain complexity) and/or feasibility within the Malawian and SSA context. For each function, three mutually exclusive options are defined as arrangements observed in comparable settings or derived from the background analysis.

F1. Sourcing mode

Defines how many suppliers are contracted and whether sourcing is organised individually or through a pooled structure.

- **Single source procurement**
  One manufacturer is contracted for supply. This is simple to manage but creates dependency on a single supplier.
- **Dual/multi-sourcing**
  Two or more manufacturers are contracted. This improves continuity but increases contracting and coordination effort.
- **Pooled sourcing**
  Demand is bundled across buyers (e.g., multiple countries/programmes) and sourced through one pooled structure. This aims to increase scale and reduce fragmentation in procurement.

F2. Quantification responsibility

Defines at which level demand is aggregated and translated into procurement volumes.

- **Facility ordering**
  Facilities generate orders directly. This provides local responsiveness but leads to highly fragmented demand signals and higher transaction burden.
- **Central ordering**
  Demand is consolidated centrally (national level), and procurement volumes are determined through a central ordering function. This reduces fragmentation and aligns with current policy direction.
- **Regional pooling**
  Quantification is consolidated across countries/participants. This enables scale, but requires multi-party coordination and governance alignment.

F3. Procurement & contracting

Defines how procurement is organised over time and how contracts are structured.

- **Ad-hoc procurement**
  Procurement is executed case-by-case without an institutionalised cycle. This is flexible but typically not suitable for long-term continuity.
- **Routine procurement cycle**
  Procurement follows a regular cycle (planned tendering/ordering). This increases predictability and reduces emergency-driven transaction costs.
- **Strengthened/long-term contract**
  Multi-year contracting is used to stabilise supply and planning, at the cost of higher upfront contracting effort.

F4. Financing & payment

Defines the dominant funding source and payment responsibility upstream.

- **Donor funded**
  Procurement is financed by a donor. This reduces fiscal burden on government but may reduce national control and long-term continuity.
- **Government budget**
  Procurement is financed through the Malawian public budget. This increases ownership but is sensitive to fiscal constraints and payment capacity.
- **Pooled donor funded**
  Multiple donors fund through a pooled structure. This reduces dependency on a single donor, but requires additional coordination and governance.

F5. Quality control design

Defines where the minimum QC/release gates are placed in the upstream chain (at or before entry into Malawi).

- **Single QC gate**
  One defined QC/release gate (e.g., manufacturer release evidence/documented QC). Lowest complexity, but less redundancy.
- **Two QC gates**
  Two defined gates (e.g., upstream release plus an additional gate at import clearance/entry). Higher assurance with moderate added burden.
- **Multi gate QC (manufacturing + hub + in-country)**
  QC gates at manufacturing, at a regional hub, and at/after entry into Malawi. Highest assurance, but also highest complexity and coordination.

F6. Upstream bundling approach

Defines how physical flows are organised upstream and whether shipments are consolidated.

- **Direct shipment**
  Shipment flows directly from the manufacturer to Malawi. This reduces handovers but limits consolidation opportunities.
- **Via agent/wholesaler**
  An intermediary bundles procurement/logistics and manages delivery. This can reduce government burden but adds an extra actor and potential cost layer.
- **Regional hub consolidation**
  Products are consolidated and stored in a regional hub before distribution. This enables scale and pooling, but adds an extra node and handling requirements.

Appendix H

Design configuration steps

The morphological chart includes six functions with three options each, resulting in $3^6 = 729$ theoretical configurations. Evaluating all combinations is not feasible within this thesis scope, and some options are incompatible or do not satisfy the requirements. Therefore, the option set is first screened using the hard constraints (R1–R4). Based on R4 (continuity and long-term adoption), ad-hoc procurement is excluded, as it represents a temporary rather than an institutionalized structure. In addition, R3 requires feasibility within the current Malawian context. Facility-level ordering is largely manual and IT infrastructure is limited, while policy direction emphasizes centralized ordering. Hence, facility ordering is excluded. The remaining options are considered feasible and are used to construct the final design alternatives.

Next, the design space is further reduced by excluding combinations that are structurally incompatible or highly implausible. This is indicated with the $\not\&$ sign. This step is important because the purpose of the morphological chart is to generate implementable supply chain configurations, rather than theoretical mixes of options.

The following combination rules are applied:

- **Multi gate QC $\not\&$ Direct shipment.** A multi-gate setup explicitly includes a QC gate at a regional hub. With direct shipment, there is no hub in the flow, so the hub QC gate cannot exist.
- **Regional pooling $\not\&$ Single source procurement / Dual/multi-sourcing.** Regional pooling implies pooled, supra-national governance of quantification and sourcing. Combining this with non-pooled sourcing modes mixes governance levels. Therefore, regional pooling is only considered in combination with pooled sourcing.
- **Pooled donor funded $\not\&$ Government budget (and vice versa) as primary financing method.** These financing modes rely on different decision rights and accountability structures. Mixing them as the dominant financing structure is likely to create misalignments regarding who controls funds, who commits volumes, and who bears payment responsibility. Therefore, they are treated as mutually exclusive as the primary financing mode in a configuration.

Following the screening, 192 structurally feasible configurations remained. Evaluating all 192 alternatives individually would neither be analytically meaningful nor practically manageable. A structured clustering and consolidation process was therefore applied to reduce the solution space.

Step 1: Clustering by dominant configuration method

To reduce the 192 feasible configurations, each configuration was first coded along three design dimensions that define the overall governance and operating method of the upstream chain:

1. **Demand governance / quantification level** (central ordering, regional pooling),
2. **Sourcing mode** (single source procurement, dual/multi-sourcing, pooled sourcing),
3. **Primary financing method** (donor funded, government budget, pooled donor funded).

A configuration was assigned to a cluster based on its triple of values on these three dimensions (i.e., configurations with the same [governance level, sourcing mode, financing method] were grouped together).

Applying this coding to the 192 feasible configurations resulted in eight clusters. Based on the governance–sourcing–financing coding, the following archetypes were identified:

- Central–Single–Donor
- Central–Single–Government
- Central–Multi–Donor
- Central–Multi–Government
- Central–Pooled–Pooled donor
- Central–Pooled–Donor
- Regional–Pooled–Donor
- Regional–Pooled–Pooled donor

Each cluster represents a distinct high-level governance and sourcing method. Variations within clusters relate only to secondary parameters (e.g., QC gates, bundling approach, contracting strength).

Step 2: Elimination of near-duplicate variants

Within each cluster, the remaining configurations were inspected for near-duplicates: i.e., alternatives that shared the same dominant governance–sourcing–financing method (Step 1) and differed only in secondary implementation parameters. The aim of this step was to avoid over-representing minor operational variations in the final design set, and to ensure that the selected designs reflect structurally distinct upstream configurations rather than small parameter tweaks.

Consolidation procedure
For each cluster, near-duplicate configurations were consolidated by selecting one representative variant that captured the cluster's dominant methods while remaining implementable in the Malawian context. Where several operational variants were plausible, the representative variant was chosen to reflect a typical or baseline implementation (i.e., the option requiring the least additional institutional change beyond the dominant method). Alternative variants were not discarded conceptually; rather, they were treated as parameter adjustments within the same archetype and were therefore not carried forward as separate design alternatives.

Outcome of Step 2
This consolidation reduced the initial eight clusters into a smaller set of broader strategic categories. These categories reflect different upstream models, whereas remaining differences within categories were treated as performance-relevant parameters to be discussed later (e.g., in the evaluation criteria), rather than as separate supply chain designs.

Step 3: Selection of representative design alternatives

From each consolidated strategic category, one configuration was selected as a representative design alternative. The aim was to keep the alternatives clearly different from each other while still ensuring that each configuration remained internally coherent and relevant from a policy perspective. In this way, the subsequent scenario analysis and multi-criteria evaluation compare fundamentally different upstream supply chain structures, rather than small operational variations within the same type of configuration.

Because Malawi currently does not have an established caffeine supply chain, exploring a set of structurally different design archetypes was found more informative at this stage than analysing alternatives that only differ in minor adjustments, such as additional quality control steps or small contracting changes.

This process resulted in four representative upstream design configurations, discussed and explained further in Section 4.3

Appendix I

Pairwise comparison matrix scale

I.1 Definition of scales

Criterion	Score = 1 (low)	Score = 3 (moderate)	Score = 5 (high)
Scale potential	Low scale leverage: volumes remain country-specific and dispersed; no structural aggregation structure (no bundling/pooling); limited ability to meet MOQ/lot-size constraints or strengthen negotiation position.	Moderate scale leverage: some aggregation is feasible (e.g., within-country bundling or limited pooling through an intermediary), improving ordering discipline and reducing unit overhead, but volumes remain constrained and scale benefits are partial.	High scale leverage: structural aggregation is built in (centralised purchasing and/or multi-country pooling), enabling bundled volumes and stronger economies of scale through improved supplier attractiveness and negotiation leverage.
Fragmentation (scoring: 5 = least fragmented)	Highly fragmented structure with many organisational interfaces and handovers; multiple parallel routes/channels; responsibilities spread across several actors, creating many coordination and possible failure points.	Partly consolidated structure with some standardisation, but still several interfaces and handovers; more than one channel or coordination pathway remains.	Largely consolidated structure with few interfaces and handovers; one dominant route/channel with clearly allocated roles and limited coordination/failure points.
Transactional efficiency	High transaction burden: many approvals, contracts, and administrative steps per procurement cycle; extensive reconciliation and coordination effort required; delays likely and lead times hard to manage within current capacity.	Moderate transaction burden: procurement is executable through routine processes, but requires noticeable coordination and contract management; some reconciliation effort and moderate lead-time predictability.	Low transaction burden: execution is streamlined with clear accountability; limited approvals and administrative steps; contracting and ordering are predictable, resulting in high lead-time reliability.

Chain complexity (scoring: 5 = lowest overhead)	High coordination overhead: multiple governance layers and decision centres must align (e.g., multi-country and/or multi-funder coordination); many interdependencies across actors; high sensitivity to misalignment in roles, timelines, and information flows.	Moderate coordination overhead: several actors and interfaces require coordination, but decision rights and escalation paths are largely defined; alignment is needed but remains manageable within existing governance capacity.	Low coordination overhead: limited number of governance layers and interdependencies; clear decision rights and accountability with minimal cross-actor alignment requirements; the configuration can operate with limited coordination effort.
Logistics cost balance	No consolidation is used and shipments are organised through multiple separate routes. The design implies many physical handovers and small, fragmented movements. As a result, transport utilisation is weak and handling effort is high, making the overall transport–inventory balance unfavourable.	Some consolidation is used, but not as the dominant logistics set-up. The design reduces the number of separate shipment flows compared to score 1, yet still involves additional handovers or parallel movements. Transport utilisation improves, but handling effort and buffering needs remain non-negligible.	A clear consolidation logic is built into the design (e.g., a defined hub or structurally bundled upstream flow). The number of shipment flows and physical handovers is minimised. This supports high transport utilisation and lower handling effort, resulting in a favourable transport–inventory balance.

Table I-2: Definitions for the performance scoring scale used to populate the performance matrices.

Appendix J

Interview protocol

The interview protocol is designed as a semi-structured guide that supports a consistent yet flexible interview approach. It ensures that all topics relevant to the design of a caffeine supply chain for Malawi are addressed, while allowing room for follow-up questions and in-depth exploration of respondents' expertise. This structure facilitates a natural conversational flow and enables the interviewer to probe underlying mechanisms, decision rationales, and system-level constraints where relevant.
At the start of the interview, the participant is informed about the study objectives, data handling procedures, and their rights as participants. Written informed consent is obtained, and explicit permission is requested to audio-record the interview to ensure accurate transcription. Participants are also informed about privacy and consent using the following statement: "To protect your privacy and confirm your voluntary participation in this research, I would like to ask you to sign the informed consent form. Is it acceptable to record the conversation from this point onward for transcription purposes?"

1. Could you briefly describe your role and how it relates to pharmaceutical markets and/or supply chain design?

2. In your work, do you mainly focus on active pharmaceutical ingredients (APIs) or finished pharmaceutical products?

3. What are the main differences between the access or supply strategies you typically see used in practice?

4. When an organisation aims to introduce a medicine in a new country, what does the typical end-to-end process look like (from selecting the product to making it available through procurement and distribution)?

5. How is it usually decided which medicines receive priority attention (e.g., driven by country demand, donor priorities, company engagement, or internal analyses)?

6. When considering regional manufacturing in Sub-Saharan Africa, is the more common model importing the API and producing the finished product locally, or producing the full product end-to-end locally?

7. In your view, what are the main reasons local manufacturing of finished pharmaceutical products is still limited in Sub-Saharan Africa?

8. If a finished-product manufacturer exists in an African country, what typically prevents them from supplying or exporting that product to neighbouring countries?

9. Large price differences for the same medicine are observed across countries, what factors most often explain these differences?

10. In your experience, what are the main upstream cost drivers for low-volume essential medicines (e.g., economies of scale, production complexity, compliance requirements, procurement structure)?

11. What factors most strongly influence availability in low- and middle-income settings, and how does affordability interact with these factors?

Appendix K

Informed consent form

Informed consent

MSc Thesis - TU Delft

Study title: Designing the supply chain of caffeine for Malawi's neonatal care system
Researcher: Naomi Cornelissen (TU Delft, Faculty of Civil Engineering and Geosciences)

Dear participant,

You are being invited to participate in a research study as part of an MSc thesis project within a broader TU Delft initiative aimed at improving the availability of caffeine in Malawi. The study focuses on mapping the upstream supply chain of medical-grade caffeine citrate, including how the product is manufactured, registered, procured, and supplied before it reaches Malawi. The study does not involve medical research, clinical outcomes, or patient data.

What participation involves
If you agree to participate, you will take part in a semi-structured interview lasting approximately 45–60 minutes. The interview will address your experience or expertise related to the upstream production, procurement, regulation, import, or distribution of caffeine citrate (or comparable essential medicines). Participation is entirely voluntary. You may decline to answer any question and you may stop the interview at any time without giving a reason.

Data collection, storage, and use
The interview may be audio-recorded and/or video-recorded for accuracy, depending on the format of the conversation. Recordings will be transcribed and stored securely within TU Delft's institutional data environment. All data will be handled according to GDPR requirements. Personal identifiers will be removed during analysis, and anonymised summaries or aggregated insights may be used in the MSc thesis, possible academic publications, or teaching materials. Full transcripts, video footage, or identifiable information will not be published. All personal data will be deleted at the end of the overarching research project.

Withdrawal
If you wish to withdraw your participation and have your data removed from the dataset, please notify the researcher before **10 February 2026**. After this date, anonymised data

may already be incorporated into the analysis and may no longer be traceable or removable.

Consent statement
By participating, you confirm that you understand the purpose of the study, what your participation involves, and how your data will be collected, stored, and used.

Please indicate your consent by ticking the box below:

☐ **I agree that my responses, views, or other input can be quoted anonymously in research outputs.**

Signatures

Name of participant: _____

Signature: _____

Date: _____

Study contact details for further information
Naomi Cornelissen: nccornelissen@tudelft.nl
Supervisor (TU Delft): Dr. Arjan van Binsbergen: a.j.vanbinsbergen@tudelft.nl