Risk Management for Antidotes and Emergency Preparedness

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Abstract

Antidote preparedness is a major challenge for both acute individual emergencies and mass casualties. Identification and management of risks is a crucial aspect in the development of risk management strategies to ensure no disruptions in the antidote supply chain. The aims of this study were to review the management of antidote preparedness in Malta and to develop local guidelines on emergency preparedness based on risk management principles.

This study was divided into three phases. Phase one assessed local antidote availability and identified risks in emergency preparedness. Risk identification was performed through the performance of (i) vertical audits of eight chosen antidotes at Mater Dei Hospital (MDH), Gozo General Hospital (GGH), and at the Central Procurement and Suppliers Unit (CPSU), (ii) onsite observations at the Emergency Department at MDH, Pharmacy Department at GGH and at CPSU, and (iii) discussions with healthcare professionals in the field. Phase two involved the validation of the identified risks and risk assessment by an expert focus group, in relation to acute cases and mass health threats. Risk matrices were developed to aid in the prioritisation of validated risks. Phase three included the development of guidelines for enhanced local emergency preparedness.

Twelve risk themes emerged from the thematic analysis of data collected from the vertical audits, onsite observations, and meetings with healthcare professionals in the field of antidotes. An additional risk was identified through the focus group discussions. All thirteen risk themes were validated by the nine-membered expert focus group. Thirteen risk matrices were developed highlighting the increased severity of identified risks in the

event of a mass casualty as compared to an individual acute case. Three risk themes were prioritised by the expert focus group as being of major risks in local emergency preparedness: (1) Problematic sourcing, (2) Inadequate stocking of antidotes, and (3) Lack of a national strategy plan. Guidelines were developed, using flow charts, to address the top three risk themes for the optimisation of local emergency preparedness.

Findings from this study indicate inadequate local preparedness for both individual acute poisoning and mass casualty events. This study highlights the need for national healthcare system optimisation to ensure antidote availability and accessibility in a timely manner. Risks associated with availability can be mitigated through the establishment of international cooperation agreements at European and global levels. Risks in antidote and emergency preparedness call for a better coordinated national strategy in the management of emergency preparedness.

Keywords

Antidote availability, emergency preparedness, risk assessment, risk management, risk themes, supply chain

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

A & E	Accident and Emergency Department
CBRN	Chemical, Biological, Radiological and Nuclear material
CPSU	Central Procurement and Supplies Unit
Dynamic AI®	Dynamic Artificial Intelligence
DO	Direct Order
DPA	Directorate of Pharmaceutical Affairs
EC	European Commission
e-PPS	Electronic Public Procurement System
ERU	Emergency Response Unit
GFL	Government Formulary List
GGH	Gozo General Hospital
HyDi	Hybrid Discovery
IPCS	International Programme on Chemical Safety
JPA	Joint Procurement Agreement
MAH	Marketing Authorisation Holder
MDH	Mater Dei Hospital
MOU	Memorandum of Understanding
NPIS	National Poisons Information Service
RCEM	Royal College of Emergency Medicine
SCRM	Supply Chain Risk Management
SOP	Standard Operating Procedure
UMP	Unlicensed Medicinal Product
WHO	World Health Organisation

Chapter 1

Introduction

1.1 Background

Globally, antidote preparedness for acute poisoning has been identified as a major challenge given the unpredictability of case scenarios requiring the use of antidotes (Al-Taweel *et al.*, 2020; Alsugoor, 2022). The healthcare system must be able to ensure antidote availability and effective management for both individual poison cases and for mass causalities, whilst weighing in the financial burden (Murphy *et al.*, 2019). Antidotes are critical medicines in the care of poisoned patients, especially in cases where intensive supportive care is not enough to stabilize the patient. In such cases, antidotes may have a life-saving potential provided that the appropriate antidote is available and administered in the right way, at the right time, to the right patient, using the right dose (Dart *et al.*, 2018; Chacko and Peter, 2019; Aruwa *et al.*, 2020; Al-Jelaify and AlHomidah, 2021; Kaiser and Dart, 2022; Kifle *et al.*, 2022; Antoniello *et al.*, 2023).

The World Health Organisation (WHO) emphasises how risk-based approaches towards emergency preparedness allow for the optimisation of both resource utilisation as well as aid in the prioritisation of actions to be ready to respond to potential emergencies.[1]

Globally the healthcare sector faces various disruptions due to diverse catastrophes including operational crisis, financial crisis, humanitarian crisis, and wars, among others (Senna *et al.*, 2022; Hoang and Bui, 2023; Troger and Burns, 2023). Furthermore, the healthcare sector is also hindered by legislative and regulatory obstructions, making supply chain management even more complex (Bochenek *et al.*, 2017).

[1] World Health Organisation. Strategic Toolkit for Assessing Risks. A comprehensive toolkit for all-hazards health emergency risk assessments. Geneva (CH):WHO;2021 [cited 2024 May 26]. Licence: CC BY-NC-SA 3.0 IGO. Available from URL: https://www.who.int/publications-detail-redirect/9789240036086

The pharmaceutical supply chain starts from the production of a medication or a medical device at the manufacturers' end, till the dispensing of the item at the patient's end. This type of supply chain must be driven with the objective of saving lives and providing efficient healthcare services (Dixit *et al.*, 2019; Lawrence *et al.*, 2020; Senna *et al.*, 2023). Despite the criticality of healthcare supply chains, this sector has been commonly overlooked and taken for granted until the occurrence of several disasters over the past twenty-five years (Azadegan *et al.*, 2020; Handfield *et al.*, 2020). Healthcare services are critical to human life and hence, it is a necessity to build up a resilient supply chain which can ensure continuation of services in cases of unforeseen emergencies especially with regards to natural or man-made disasters (Hundal *et al.*, 2021; Zamiela *et al.*, 2022).

1.2 Healthcare Supply Chain Risks

Supply chain risks can be categorised into two distinct categories; operational risks and disruption risks (Ho *et al.*, 2015; Salamai *et al.*, 2019; Xu *et al.*, 2020). Operational risks refer to those type of risks which may hinder good co-ordination of supply throughout the supply chain. Some examples include uncertain demand, variable lead time and shortage of employees (Duong *et al.*, 2023). Disruption risks are normally associated with risks which may result in greater losses due to a higher impact, for example, risks related to natural disasters, political instability, or equipment malfunction. These risks tend to occur less frequently but have the potential to implicate drastic losses when they do occur (Jabbarzadeh *et al.*, 2018; Truong Quang and Hara, 2018; Dolgui *et al.*, 2019; Leite *et al.*, 2020; Xu *et al.*, 2020; Chowdhury *et al.*, 2021; El Baz and Ruel, 2021; Senna *et al.*, 2022).

With globalisation and information technology advancements, supply chains are applying more sophisticated operational strategies involving lean manufacturing and global sourcing with the aim to establish a competitive advantage. Whilst this global integration has benefitted pharmaceutical businesses in terms of expansion and possible better service, the complex operational strategies together with the rapidly changing asymmetric environment, contribute to a much higher level of vulnerability in the healthcare system (Wagner and Neshat; 2010; Wiengarten *et al.*, 2016; Munir *et al.*, 2020; Aboutorab *et al.*, 2021; Collier and Sarkis, 2021; Gurtu and Johny, 2021; Ibrahim *et al.*, 2021; Chapman *et al.*, 2022; Creazza *et al.*, 2022; Pato *et al.*, 2022; Hoang and Bui, 2023). Unexpected disruptions in any of the building blocks of the enlarging supply chains, may have a ripple effect on the entire system (Ivanov and Dolgui, 2021; Münch and Hartmann, 2022). This has been highlighted through the Covid-19 pandemic whereby the over-reliance on lower cost supply and minimal stocks strategy, has resulted in high vulnerabilities leading to health repercussions (Handfield *et al.*, 2020; Pato *et al.*, 2022). Disruptions occurred in terms of supply, demand, and logistics infrastructure (Ivanov and Dolgui, 2021; Ivanov *et al.*, 2022). Adaptive management in response to system dynamics allows the growth of resilience within the supply chain (Azadegan *et al.*, 2020; Ibrahim *et al.*, 2021; Browning *et al.*, 2023).

1.3 Supply Chain Risk Management

Supply Chain Risk Management (SCRM) is an aspect of studies directed at developing strategies for the identification, analysis, treatment and monitoring of risks in a supply chain (Gurtu and Johny, 2021). According to Fan and Stevenson (2018), this requires a holistic approach with both internal implementation of tools, techniques, and strategies

as well as external coordination and collaboration with supply chain members. An effective risk management strategy implementation is dependent upon the availability of resources and capabilities since it is an information intensive process (Munir *et al.*, 2020). Given that supply chains are composed of different sectors, each with its own characteristics, risk management studies tend to focus on specific areas resulting in a narrow but deep understanding of SCRM. A more consolidated approach to risk management involving supply chain integration practice must be undertaken to integrate the whole supply chain. The collaboration between external and internal building blocks of the supply chain allows for the collection of accurate, timely and reliable data which amplifies the supply chain reactive capabilities (Fan *et al.*, 2017; Shou *et al.*, 2018; Munir *et al.*, 2020; Namdar *et al.*, 2021; Yang *et al.*, 2021).

The four main steps in SCRM are: (i) risk identification, (ii) risk analysis, (iii) risk treatment and (iv) risk monitoring (Shi, 2004; Ho *et al.*, 2015; Fan and Stevenson, 2018; Bolcato *et al.*, 2019; Hardjomidjojo *et al.*, 2022; Senna *et al.*, 2022; Pham *et al.*, 2023).

1.3.1 Risk Identification

An efficient risk management mechanism initiates through the identification and understanding of supply chain risks. The accuracy of risk identification is a critical determinant in the resulting mitigation strategies since if risk events are not identified, they cannot be assessed and managed (Aboutorab *et al.*, 2021; Ganesh *et al.*, 2022). Through a systemic review performed in 2018 by Fan and Stevenson, it was determined that several approaches are proposed in literature for risk identification. According to Aboutorab *et al.*, (2021) three requirements should be met by any risk identification

technique for it to be applicable in the modern world. The first is the ability to consider external risk drivers and resulting risk events. The second requirement is the ability to acknowledge known past events and identify new uncertain events. The third requirement involves the ability to process high volume of information from both internal and external sources. This can be performed through artificial intelligence or data analytics. Aboutorab *et al.,* (2021) classified existing risk identification strategies into three: (i) reactive, (ii) predictive and (iii) proactive. Reactive techniques are aimed at identifying risk events following their occurrence through data analysis investigating the cause leading to the event. The effectiveness of reactive techniques is reflected on the agility of the supply chain (Wieland and Wallenburg, 2012; Ivanov and Dolgui, 2021). Predictive techniques attempt to pre-emptively identify occurrence of future risk events. Proactive strategies aim to avoid occurrence of risk before occurrence and have a positive implication on robustness of the supply chain (Wieland and Wallenburg, 2012).

1.3.2 Risk Analysis

Identified risks are assessed to evaluate the potential of the risk occurring and to estimate its level of impact if it were to occur. The integration of the presence and severity of hazards is denoted as the process of risk estimation (El Baz and Ruel, 2021). This process involves an exercise of familiarisation with risk antecedents and possible triggers resulting in risk occurrence (Jaberidoost *et al.*, 2015; El Baz and Ruel, 2021). Identification of supply chain risk antecedents is followed by the evaluation of probability of the risks occurring, analysis of impact, classification, and prioritisation of risks. Most of the risk analysis procedures proposed in literature are phase specific (El Baz and Ruel, 2021; Münch and Hartmann, 2022). The aim of performing a risk analysis is to prioritise

identified risks in preparation for mitigation of supply chain risks (Van der Fels-Klerx *et al.*, 2018; El Baz and Ruel, 2021).

1.3.3 Risk Treatment and Monitoring

Risk mitigation addresses supply chain risks through the incorporation of measures to prevent risks prior to disruption or to minimise their effect following a disruptive event. The development of contingency plans aids to enhance preparedness in case of a disruption event (Moore *et al.*, 2015; Azadegan *et al*., 2020). The efficacy of risk treatment and monitoring strategies determine the healthcare supply chain's level of resilience and robustness (El Baz and Ruel, 2021).

1.4 Risk Management in Emergency Preparedness

An adequately set up risk management system in healthcare facilities and supply chain has a fundamental impact on emergency preparedness especially in case of a mass toxicological event (Hoke *et al.*, 2020). Timely availability and administration of antidotes is a major determinant in antidote efficacy in decreasing morbidity and mortality in poisoned cases as well as, in reducing length of hospitalisation and duration of therapy (Schwartz *et al.*, 2019; Al-Taweel *et al.*, 2022; de Dios Azorín Abraham *et al.*, 2023; Eljaoudi *et al.*, 2023; Lao, 2023). Emergency cases such as nerve agent intoxication, cyanide poisoning, anaphylaxis, and seizures, require immediate drug administration (Aguilar-Salmerón *et al.*, 2016; Vijayaraghavan, 2020). The WHO declares that

immediate use antidotes must always be available at the hospital site, to ensure uncompromised patient care.[2]

1.5 International Situation of Antidote and Emergency Preparedness

Availability of antidotes varies across different countries and borders, depending on factors such as national recommendations, geospatial implications, technical demands, financial constraints, administrative issues, and regulatory demands (Aruwa *et al.*, 2020; Eljaoudi *et al.*, 2023).

Despite recognition of the importance of antidotes in healthcare systems, insufficient stocking of these medications has remained a global concern for over 35 years (Dart *et al.*, 2018; Abu Esba *et al.*, 2023). Inadequacy in antidote stocking has been documented by multiple countries spread across different continents. These countries include both developed and developing countries namely, the United States (Dart *et al.*, 2009; Gasco *et al.*, 2013; Dart *et al.*, 2018; Pandya *et al.*, 2023), Canada (Bailey *et al.*, 2003), the United Kingdom (Mitchell *et al.*, 2013; Bailey *et al.*, 2016; Harnett *et al.*, 2021), Norway (Lao *et al.*, 2022), Spain (Broto-Sumalla *et al.*, 2018), Qatar (Salem *et al.*, 2017), Pakistan (Arslan *et al.*, 2016), Lebanon (Mansour *et al.*, 2016), Morocco (Eljaoudi *et al.*, 2023), Saudi Arabia (Abu Esba *et al.*, 2022), Kuwait (Al- Taweel *et al.*, 2019; Al- Taweel *et al.*, 2022), South Africa (Wium and Hoffman, 2009), New Zealand (Fountain *et al.*, 2015),

[2] Web Annex A. World Health Organization Model List of Essential Medicines – 23rd list, 2023. Geneva(CH): World Health Organisation; 2023 Apr. [cited 2024 May 26]Report No.: WHO/MHP/HPS/EML/2023.02. Licence: CC BY-NC-SA 3.0 IGO.

Korea (Sohn *et al.*, 2014), and China (Liu *et al.*, 2016). Scholars in this field have identified various possible reasons for the unavailability of antidotes (Table 1.1).

Lack of guidelines and financial restrictions are the most frequently cited reasons for inadequacy in antidote stocking (Bailey *et al.*, 2003; Alhaddad, 2016; Liu *et al.*, 2016; Broto-Sumalla *et al.*, 2018; Murphy *et al.*, 2019; Lao *et al.*, 2022). The necessity of poison control guidelines was recognised at a joint meeting held at the WHO headquarters, Geneva, between the World Federation, the International Programme on Chemical Safety (IPCS), and the European Commission (EC), in October 1985. In 1997, the IPCS published a list of antidotes considered useful in the treatment of poisoning and classified them according to the urgency of availability (Pronczuk de Garbino *et al.*, 1997). Since then, consensus guidelines for antidote stocking were established by countries across different borders including the United States (Dart *et al.*, 2009; Dart *et al.*, 2018), the United Kingdom (Harnett *et al.*, 2021), Kuwait (Al-Taweel *et al.*, 2022), Sweden[3], and Norway[4]. These guidelines have been generated to assist hospitals in the improvement of patient care and to reduce the financial burden.

[3] Antidotregistret[Internet]. Sweden: The Swedish Poison Information Centre; c2023 [cited 2024 May 26]. Available from: http://giftinformation.se/Antidot/Information?utgangspunktId=0

[4] Antidoter – anbefalt lagerhold I norske sykehus [Internet]. Norway: The Poisons Information Centre; c2022 [cited 2024 May 26]. Available from: https://www.helsebiblioteket.no/forgiftninger/antidoter-og-eliminasjon/antidoter-anbefalt-lagerhold-i-norske-sykehus

Table 1.1 Description of possible reasons for antidote unavailability

Reason for unavailability of antidotes	Reference(s)
Lack of guidelines	Bailey *et al.*, 2003; Murphy *et al.*, 2019
High costs of antidotes and short shelf life	Alhaddad, 2016; Liu *et al.*, 2016; Broto-Sumalla *et al.*, 2018; Suchonwanich and Wananukul, 2018, Murphy *et al.*, 2019; Gosselin, 2019; Lao *et al.*, 2022
Drug shortages	Murphy *et al.*, 2019; Lao *et al.*, 2022; Troger and Burns, 2023
Small hospital size and infrequent use	Bailey *et al.*, 2003; Dart *et al.*, 2009; Alhaddad, 2016; Liu *et al.*, 2016; Al-Taweel *et al.*, 2019; Murphy *et al.*, 2019
Reliance on antidote-sharing agreements	Liu *et al.*, 2016; Dart *et al.*, 2018
Small markets for antidotes resulting in lack of incentives for manufacturers to invest in the development of new antidotes or continuation of supply of available antidotes	Suchonwanich and Wananukul, 2018
Limited hospital and pharmacy resources allocated to antidote preparedness	Dart *et al.*, 2009
Changes in types of antidotes available	Dart *et al.*, 2009
Unlicensed antidotes and unavailability of certain antidotes on specific markets	Broto-Sumalla *et al.*, 2018; Al-Taweel *et al.*, 2019; Murphy *et al.*, 2019; Eljaoudi *et al.*, 2023
Lack of awareness on the importance of antidotes and on the deficiencies in antidote preparedness	Bailey *et al.*, 2003; Dart *et al.*, 2009; Alhaddad, 2016; Murphy *et al.*, 2019
Physicians not requesting certain antidotes	Al-Taweel *et al.*, 2019
Unclear and inconsistent restocking process	Abu Esba *et al.*, 2022
Inaccessible storage design	Mitchell *et al.*, 2013; Abu Esba *et al.*, 2022
Lack of staff competency	Abu Esba *et al.*, 2022

1.5 International Antidote Guidelines

The United States guidelines established by Dart *et al.* (2018) and the Royal College of Emergency Medicine (RCEM) and National Poisons Information Service (NPIS) guidelines,[5] are globally recognised antidote stocking guidelines which have been adapted in international studies for enhancement in emergency preparedness (Al-Sohaim *et al.*, 2012; AlTamimi *et al.*, 2017; Rodrigues Fernandes *et al.*, 2017; Al-Taweel *et al.*, 2022).

The United States consensus guidelines on antidote stocking were first published in 2000 by Dart *et al.*, and since then these were reviewed twice to reflect changes in antidotes availability and target identified inefficiencies in antidote stocking (Dart *et al.*, 2009; Dart *et al.*, 2018). The consensus guidelines were developed through the structured analysis of existing antidote literature, by a consensus panel consisting of experts from various sectors. The finalised guidelines reflect the minimal amounts of antidotes which need to be stocked for the treatment of a 100kg patient for a period of 8 or 24 hours.

The United Kingdom follows the RCEM and NPIS guidelines for antidote stocking.[5] These guidelines have been first developed in 2006 and were revised on four occasions, the last being in 2021 (Harnett *et al.*, 2021). In agreement with the United Stated guidelines, the RCEM and NPIC guidelines prioritise availability of time critical antidotes. These guidelines divide the antidotes into three time-dependant categories.

[5] Royal College of Emergency Medicine and National Poisons Information Service Guideline on Antidote Availability for Emergency Departments (Version 6, September 2023)[Internet] London: Royal College of Emergency Medicine. [Cited 2024 May 26] Available from: Drug (rcem.ac.uk)

Category A includes drugs which must be available within the Emergency Department for immediate use, Category B includes drugs which are to be available within 1 hour, and Category C drugs includes those antidotes maintained supra-regionally. These guidelines include the minimal quantity of antidotes required for a 24-hour treatment of an adult patient.

In Norway, the national antidote stocking recommendations were established by the poison information centre.[4] These were based on hospital size rather than urgency of antidote availability, and the estimated consumption was based on the treatment of a single 70kg patient with no guideline on the minimum quantity to be maintained. The Norwegian poison information centre indicated that these guidelines may not be applicable to all hospitals in Norway since factors such as geographical location, local poisoning epidemiology and cooperation agreements may influence types and quantities of antidotes stocked. A survey conducted by Lao *et al.*, in 2022 revealed that despite the introduction of national recommendations by the Norwegian authorities in 2007, antidote preparedness is still lacking. When comparing the Norwegian guidelines with US and UK guidelines, the main difference is that the latter are based on the timely availability of the antidote, whereas Norwegian guidelines are based on hospital size (Lao *et al.*, 2022).

[4] Antidoter – anbefalt lagerhold I norske sykehus [Internet]. Norway: The Poisons Information Centre; c2022 [cited 2024 May 26]. Available from: https://www.helsebiblioteket.no/forgiftninger/antidoter-og-eliminasjon/antidoter-anbefalt-lagerhold-i-norske-sykehus

1.7 Pharmacist Role in Antidote and Emergency Preparedness

Pharmacists have a critical role in emergency preparedness and are invaluable healthcare professionals in health crisis due to their centralised community placement and clinical expertise (Aruru *et al.*, 2021; Cadogan and Hughes, 2021). Various public health crises in recent decades including the postal anthrax attacks in 2001, Hurricane Katarina in 2005 and the Influenza A (H1N1) pandemic in 2009, have resulted in the elevation of the pharmacy profession in emergency preparedness and response (Aldrich and Benson, 2008; Committee on Prepositioned Medical Countermeasures for the Public and Institute of Medicine, 2011; Miller *et al.*, 2012; Schwerzmann *et al.*, 2017). The fundamental role of pharmacists in emergency situations was also highlighted globally during the Covid-19 pandemic whereby pharmacists responded through provision of multiple healthcare services including public health advice and education, symptoms surveillance, telehealth visits, medication stewardship, medication logistics, insurance coordination, identification and mitigation of drug shortages, and evidence evaluation to inform clinical decisions for managing COVID-19 infection (Bhat and Kehasse, 2020; Gross and MacDougall, 2020; Ung, 2020; Watson *et al.*, 2021).

In recognition of the vital contributions pharmacists may perform in crisis management, Aruru *et al.*, (2021) developed a Pharmacy Emergency Preparedness and Response Framework. The developed framework, focused on five main areas: (i) emergency preparedness and response, (ii) operations management, (iii) patient care and population health interventions, (iv) public health pharmacy education and continuing professional education, and (v) evaluation, research, and dissemination for impact and outcomes.

Apart from roles in the management of mass casualty events, pharmacists also have a role in the management of acute toxicological cases. Summerlin *et al.*, (2023) show a positive effect in the incorporation of a pharmacist-based toxicology consultant service in the Emergency Department for the management of toxicological cases through lowering of incidence errors.

Despite recognition of the importance of the pharmacy profession in emergency preparedness, lacunae for the integration of pharmacists in the management of emergency crises exists, resulting in the underutilisation of pharmacist competency and skills (Aruru *et al.*, 2021; Cadogan and Hughes, 2021).

1.8 Local Scenario and Rationale of the Study

Unavailability of an antidote in an emergency toxicological situation impacts the patients, healthcare professionals and the national healthcare system. This study recognised a gap in literature on the local management of antidotes in emergency preparedness hindering developments in national emergency preparedness. A risk management study aids in the identification, assessment, and mitigation of risks in the local antidote emergency preparedness.

This study is of national importance since it also seeks to develop guidelines on achieving sustainable preparedness for a national emergency, taking into consideration the limitations of a small island nation. Providing a clear picture of the local situation concerning antidote management can provide motivation and trigger changes which will improve national resilience and robustness in case of threats. The guidelines and

recommendations from this work can serve as a catalyst for local decision makers to take necessary measures to mitigate the risks involved in antidote and emergency preparedness.

1.9 Aims and Objectives

The aims were to review the management of antidote preparedness in Malta and to develop guidelines on emergency preparedness based on risk management principles.

The objectives were to:

- Collect data on local antidote preparedness and identify risks in emergency preparedness from the sourcing till the dispensing of antidotes at patient's end
- Categorise identified risks through qualitative analysis
- Establish a focus group for risk theme validation and perform risk assessments
- Develop guidelines for antidote and emergency preparedness

Chapter 2

Methodology

2.1 Methodology Overview

A thorough literature review on antidote availability and accessibility was conducted and all the necessary approvals to perform this research were acquired. This study was conducted in three distinct phases (Figure 2.1).

Phase one of this study entailed data collection on local antidote availability and accessibility through the collection of data on antidotes employing Dynamic Artificial Intelligence® (Dynamic AI®) software at the Central Processing and Supplies Unit (CPSU), meetings with healthcare professionals working in the field of antidotes, performance of vertical audits of selected antidotes and onsite observations. Thematic analysis between and across all data sets was performed for risk identification and categorisation.

Phase two of this study involved the establishment of an expert focus group for the validation of identified risk themes, and to discuss the local risk management strategies employed for validated risks. Prioritisation of risks was performed through the focus group and colour-coded risk matrices were developed for risk assessment.

Phase three of this research study incorporated the development of guidelines for local optimisation in antidote and emergency preparedness based on risk-management principles. The developed guidelines were presented to expert healthcare professionals for validation.

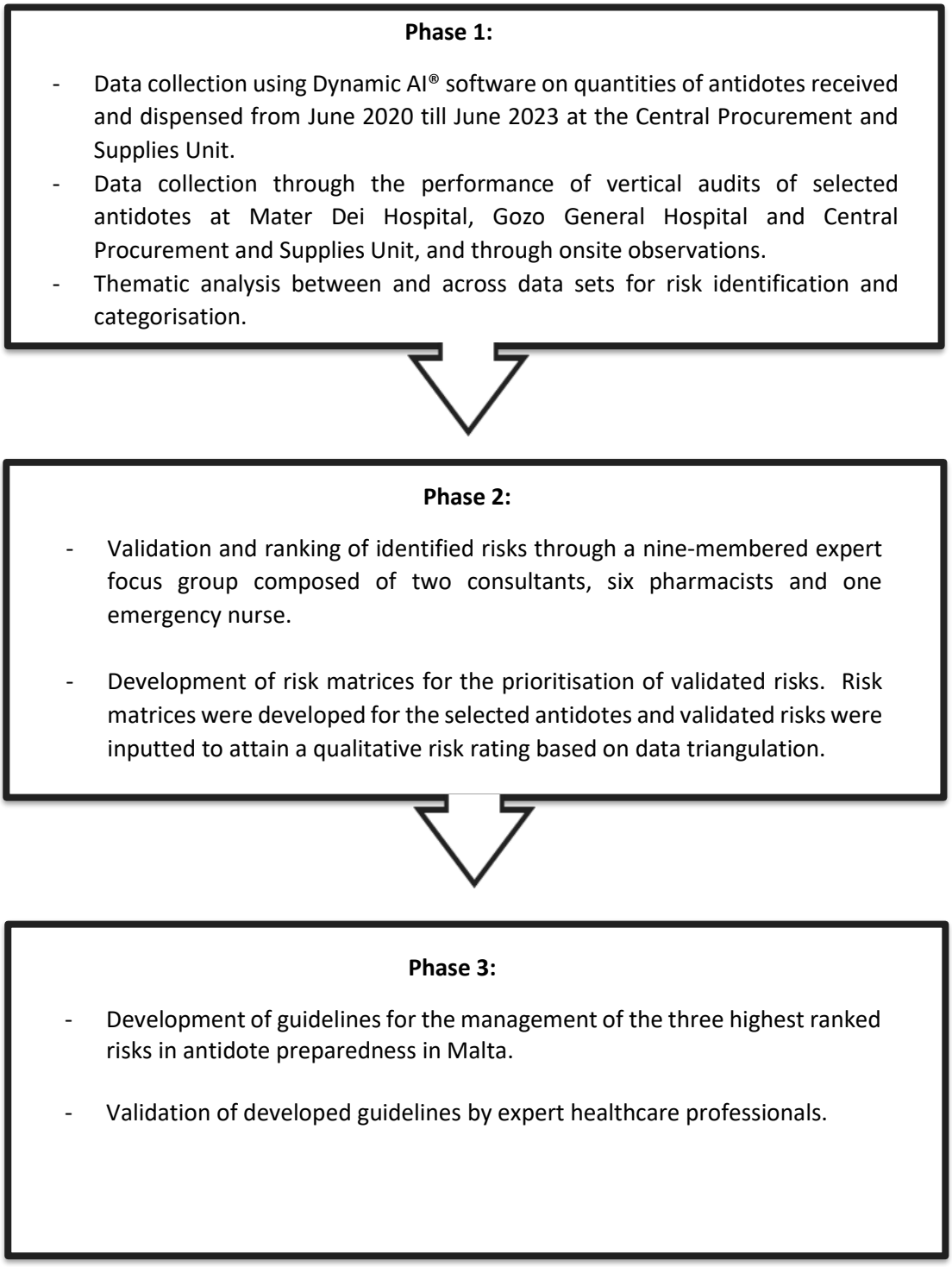


Figure 2.1 Methodology overview flowchart

2.2 Research Design

A qualitative research approach was applied throughout this study. This research approach allowed for pattern analysis of retrospective data collected on antidotes through Dynamic AI® software. The pattern analysis was performed to select antidotes to be taken as examples for this study. Data collection involved the application of different methods: (i) performance of vertical audits, (ii) onsite observations, (iii) meetings with healthcare professionals in the field of antidotes and (iv) discussions within the expert focus group. Thematic analysis of data was incorporated within the research design allowing for an in-depth understanding of decisions and life experiences which cannot be investigated through a quantitative approach. The thematic analysis applied to this research study involved both method and data source triangulation. The incorporation of two different types of data triangulation permitted for enhanced robustness, credibility, and reliability of the qualitative approach through the analysis of data attained from various methods and diverse healthcare professionals from different sections within the healthcare system.

2.3 Study Settings and Approvals

This research study was set at the (i) Central Procurement and Supplies Unit (CPSU), (ii) Mater Dei Hospital (MDH) and (iii) Gozo General Hospital (GGH). CPSU was selected as one of the study sites since it is the Contracting Authority which manages the procurement and supply of materials, works, and services purchased by the Government of Malta, including medicinal products such as antidotes. MDH and GGH were included in the study setting since, as the two acute public hospitals in the Maltese Islands, they are the main consumers of the procured antidotes. Approval to conduct this study was

sought from the Managing Director of CPSU, Chief Executive Officer at MDH, and the Executive Director at GGH. Data Protection Clearance was attained from all the involved study settings. Ethical approval was granted by the University of Malta Faculty of Medicine and Surgery Research Ethics Committee with reference number: MED-2023-00269 (Appendix 1).

2.4 Literature Review on Antidote Availability and Accessibility

A literature review was performed using (i) online databases namely Pubmed®, ProQuest®, and Google Scholar, (ii) Hybrid Discovery (HyDi) search engine of the University of Malta, (iii) European and Maltese laws and (iv) official websites. Keywords utilised for the literature search included: antidote accessibility and availability; emergency preparedness; supply chain risk management; risk management in emergency preparedness; audits on antidotes; antidote stocking guidelines; antidote procurement; poison centre; risk management guidelines.

2.5 Phase 1a: Data Collection on Antidote Availability and Accessibility

A list of antidotes procured in Malta was collected from the Government Formulary List (GFL) and this list was verified by CPSU antidote procurement officer. Dynamic AI® software was utilised to collect data on the quantities of antidotes procured and dispensed. Pattern analysis was performed for the selection of antidotes for the vertical audits.

Eight different antidotes procured in Malta were selected for data collection: atropine sulphate 600mcg/ml injections, pralidoxime 1g injections, hydroxocobalamin kit, sodium

thiosulphate 25% w/v injections, sodium nitrite 300mg injections, digoxin immune Fab 40mg/vial, activated charcoal 50g granules, and acetylcysteine 200mg/ml infusion. A systematic approach was undertaken for the selection of antidotes as to include antidotes which are rarely used, such as those antidotes administered in cyanide toxicity and to include more frequently used antidotes such as acetylcysteine for paracetamol toxicity. This selection of antidotes allowed for data collection on both antidotes which have a high turn-over and those which are less frequently administered, if at all. Given that timely administration of antidotes is a critical determinant of their efficacy, it was ensured that the list of chosen antidotes included items which must be immediately available and others which have a wider timeframe for administration. The selected antidotes were used to perform vertical audits at the Accident and Emergency Department (A & E) at MDH, Pharmacy Department at GGH and CPSU, between September and October 2023 (Table 2.1).

Table 2.1 Schedule and settings of vertical audits conducted between September and October 2023

Audit Setting	Pre-audit Meeting	Audit Date	Number of batches audited	Auditor	Auditee
A & E at MDH	22/09/2023	26/09/2023	15	Researcher	Charge Nurse at A & E MDH
Pharmacy Department at GGH	13/09/2023	14/10/2023	15	Researcher	Pharmacist (Pharmaceutical Service Manager)
CPSU Administration and CPSU stores	10/10/2023	17/10/2023	15	Researcher	Pharmacist (Procurement Officer) Responsible Person (Quality Assurance)

Each department was primarily requested to provide any Standard Operating Procedure/s (SOP) or any other relevant documents which are followed in the handling of antidotes. Following examination of the documentation provided, three different checklists for the different audit settings were prepared to guide the audits (Appendix 2). Vertical audits were carried out as per Figure 2.2. The auditing activities performed within this study were adapted from Section 6 of the Joint Audit Programme for European Economic Area Good Manufacturing Practice inspectorates by the European Medicines Agency (2021), describing the performance of auditing activities.[6] During each of the three audits performed, the auditees were asked to describe the chain of actions which are performed upon receipt till the dispensing of antidotes. In the case of the CPSU audit, given that this is the Contracting Authority, the auditor also dwelled into the sourcing, procurement, and delivery logistics of antidotes. Dynamic AI® software was utilised to identify trends in the flow of selected antidotes.

Two batch numbers from each of the selected antidotes received between June 2020 and June 2023, were taken as representative samples and data available for each of these batches was analysed. The batch numbers chosen for each antidote were selected through systematic sampling whereby the first and last batches received between June 2020 and June 2023 for each antidote were selected for analysis. The selected batches were followed from the ordering of antidotes at CPSU, till the dispensing of antidotes at entities end.

[6] European Medicines Agency (EMA). Joint Audit Programme for EEA GMP inspectorates [Internet]. Netherlands:EMA; 2021 [cited May 26]. Available from: https://www.ema.europa.eu/en/documents/other/joint-audit-programme-eea-gmp-inspectorates-procedure_en.pdf

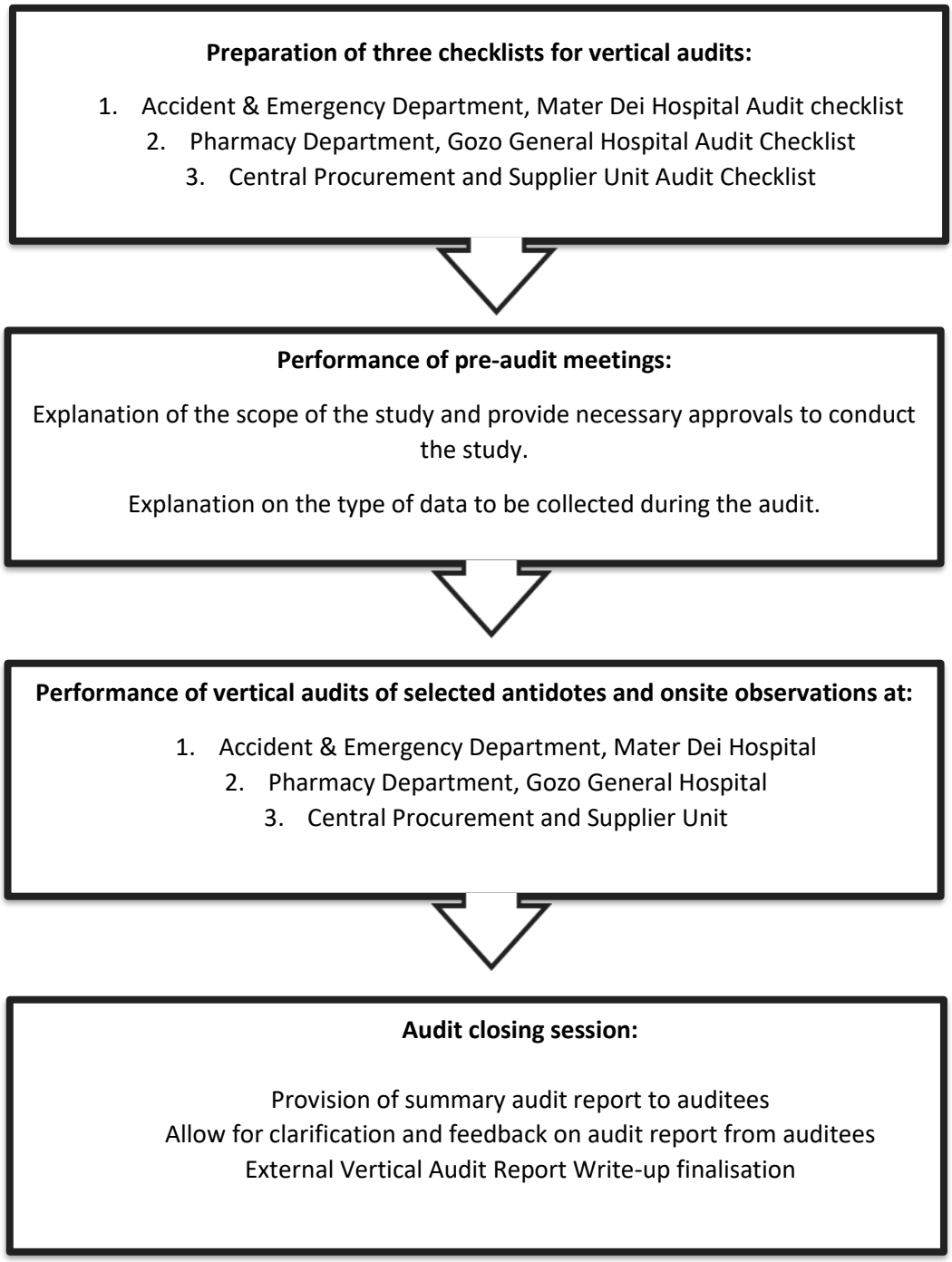


Figure 2.2 Procedure of vertical audits for the assessment of local antidote and emergency preparedness

2.6 Phase 1b: Analysis of Vertical Audits and On-site Observations

The details of each vertical audit and on-site observations were fully transcribed following each visit and qualitative analysis was performed (Figure 2.3). Each record was critically analysed by the researcher and areas of interest were highlighted. Areas of interest were defined as aspects in the data which the researcher deemed as posing a risk in emergency preparedness due to possible hindrance in antidote availability and accessibility. This process was repeated five times for each record, to ensure that no risk was omitted. Each of the highlighted areas was then coded and common codes across and between all data collected were analysed and grouped. This process was repeated three times, allowing for new data to be coded and categorised.

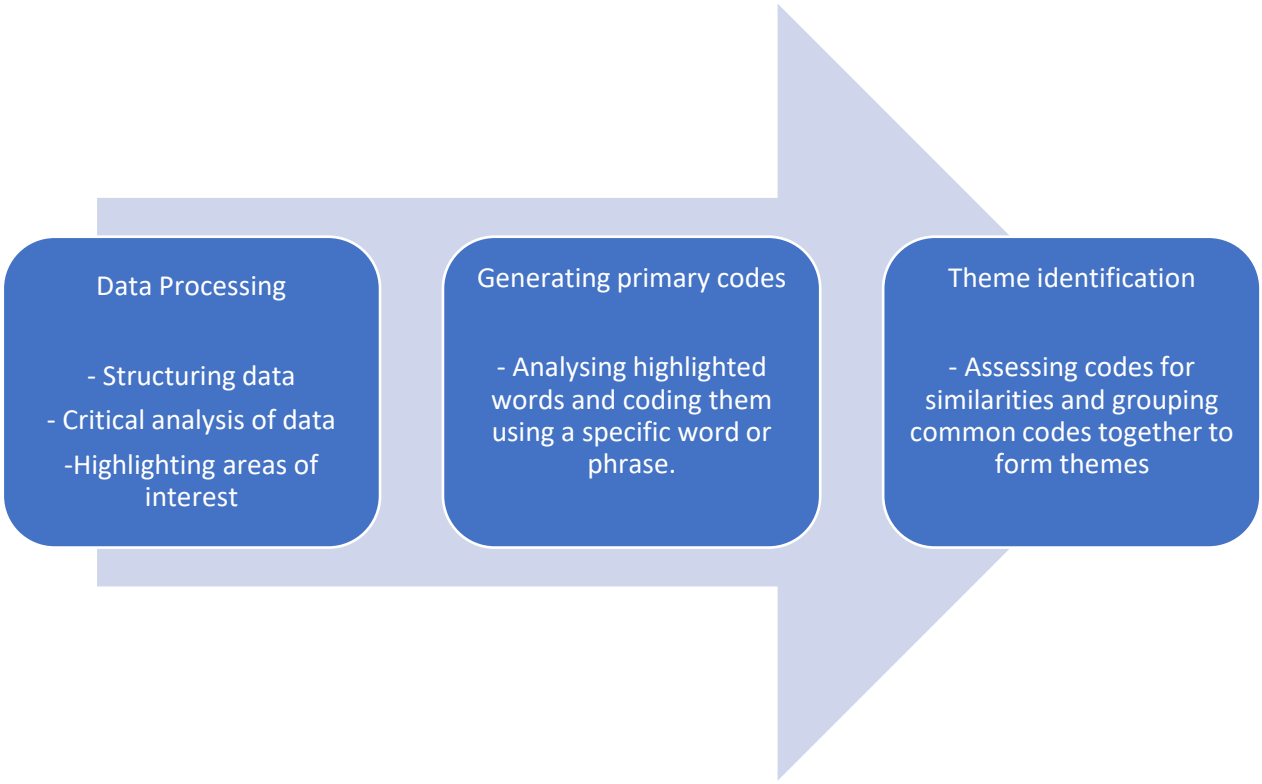


Figure 2.3 The initial process of thematic analysis. Adapted from: Nowell LS, Norris JM, White DE *et al.* Thematic Analysis: Striving to Meet the Trustworthiness Criteria. International Journal of Qualitative Methods. 2017;16(1):1-13. Doi:10.1177/160940691773384

2.7 Phase 2a: Research Focus Group

A research-based focus group composed of nine experts in the field of antidotes and emergency preparedness was established for (i) validation of the identified risk categories in Phase 1 of this study and (ii) for possible identification of further risks through the members' experience and knowledge. Focus group members were recruited by the researcher through convenience sampling from the existing working Antidote Committee in Malta. Participants were invited to take part in this research study by means of an electronic mail communication. All selected participants had previous experience in antidote research or professional experience in the sourcing, procurement, or administration of antidotes.

The researcher presented the identified risk categories to the nine-membered research focus group and requested each member to state whether he/she agreed with the identified risks and to provide any feedback from their end. A discussion was held for further identification of risks in local emergency preparedness with respect to antidotes. Following risk categories validation, participants were asked whether there were any risk management strategies already in place for the identified risks. All the validated risk categories were rated as 'high risk', 'medium risk' or 'low risk' by the focus group members to aid in risk prioritisation. Prioritisation was based on discussion of probability of the risk occurring and the impact it would have if it were to occur. All data collected through the expert focus group was thematically analysed through inductive coding of data.

2.8 Phase 2b: Method and Data Source Triangulation

The data attained from the Dynamic AI® software, the vertical audits, the meetings with healthcare professionals in the field of antidotes, and the expert focus group, were all used to analyse holistically the local situation with regards to antidote and emergency preparedness. Given the minimal publications and available resources on local antidotes and emergency preparedness, application of triangulation offered the possibility to investigate a phenomenon within context to gain a nuanced view from multiple perspectives.

Two different types of triangulations were applied to this research study:

(i) Method Triangulation - This involved the use of multiple methods for data collection. This type of triangulation allowed the researcher to minimise the bias and possible deficiencies associated with a single method use.

(ii) Data source triangulation - This involved the collection of data from different stakeholders and healthcare professionals.

Both method triangulation and data source triangulation allowed for increased validity and reliability of results and aided in the construction of more robust risk matrices through the convergence of findings attained through different stakeholders and methodologies.

2.9 Phase 2c: Development of a Risk Assessment Matrix

A colour-coded 5x5 risk assessment matrix was developed using Microsoft Excel® to assess the severity of identified risks (Figure 2.4). The vertical axis represents the probability of the risk occurring and the horizontal axis represents the impact of the hazard if it were to occur. The qualitative risk assessment matrix was developed where the categories of probability and impact were described using five adjectives: 'Very Low', 'Low', 'Medium', 'High', and 'Very High' (Table 2.2 and 2.3).

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Moderate	Severe	Severe	Critical	Critical
	High	Sustainable	Moderate	Severe	Critical	Critical
	Medium	Sustainable	Moderate	Moderate	Severe	Critical
	Low	Sustainable	Sustainable	Moderate	Severe	Critical
	Very Low	Sustainable	Sustainable	Sustainable	Moderate	Severe

Figure 2.4 Colour-coded risk matrix

Table 2.2 Definition of probability description of qualitative risk matrices. Adapted from: Pascarella G, Rossi M, Montella E, Capasso A, De Feo G, Botti G *et al*. Risk Analysis in Healthcare Organisations: Methodological Framework and Critical Variables. Risk Management and Healthcare Policy. 2021;14:2897-2911. Doi: 10.2147/RMHP.S309098

Probability Description	Definition
Very High	A definite risk that has very high frequency. Incident is expected to occur
High	Incident has occurred more than once
Moderate	Incident has occurred previously
Low	Seldom risk with low probability of occurrence, however, cannot be excluded entirely
Very Low	Unlikely risks which have a rare level of occurrence

Table 2.3 Definition of impact description of qualitative risk matrices. Adapted from: Pascarella G, Rossi M, Montella E, Capasso A, De Feo G, Botti G *et al*. Risk Analysis in Healthcare Organisations: Methodological Framework and Critical Variables. Risk Management and Healthcare Policy. 2021;14:2897-2911. Doi: 10.2147/RMHP.S309098

Impact Description	Definition
Very High	Life-threatening scenario, irreversible health impact, event impacts large number of patients
High	Major health complications with long term impact and prolonged hospitalisation
Moderate	Severe health complication
Low	Minor health impact
Very Low	Negligible health impact

All the identified and validated risks in Phase 1 and Phase 2a, were described using one of the five adjectives: 'Very Low', 'Low', 'Medium', 'High', and 'Very High', with respect to probability occurrence and impact in case of occurrence. This process was repeated for all chosen antidotes.

Once the probability and impact for each risk was described via data triangulation, the risk rating was calculated by inputting the probability and impact into the developed risk assessment matrix.

2.10 Phase 3: Development of Guidelines

The risk themes identified and validated in Phase 2 of the methodology were prioritised according to the risk ratings generated from the colour-coded risk matrices. The top three risk themes identified as posing the highest threat to antidote emergency preparedness by the expert focus group were selected for the development of guidelines.

The developed guidelines tackle both antidotes used for individual acute toxicological cases and the availability of antidotes in case of mass casualties. These guidelines were designed to target different healthcare professionals at different stages of the supply chain. Developed guidelines were forwarded to two clinical toxicology consultants and a pharmacist from the national poison centre for validation.

2.11 Dissemination of Results

Findings from this study were disseminated at the CPSU Annual Conference through abstract publication (October 2023), at the 28th Congress of the European Association of Hospital Pharmacy through a poster presentation (March 2024), and through an article publication in the European Journal of Hospital Pharmacy.

Study findings were accepted to be presented at the 82nd International Pharmaceutical Federation World Congress of Pharmacy and Pharmaceutical Sciences in Cape Town, South Africa (September 2024) (Appendix 6).

Chapter 3

Results

This chapter presents results concerning the management of antidote preparedness in Malta with the objective of reviewing the management of antidotes and developing guidelines on emergency preparedness based on risk management principles.

3.1 Results of Phase 1: Management of Antidote Preparedness in Malta

This section includes results of onsite observations, vertical audits, and meetings with healthcare professionals involved in the handling of antidotes from sourcing stage up to dispensing of antidote for emergency situations.

3.1.1 Sourcing of Antidotes

In Malta, the CPSU is the Contracting Authority responsible for the sourcing and procurement of pharmaceutical products for hospital use including antidotes. Eight hours of onsite observations were performed at CPSU for enhanced understanding of the operations of this body in the management of antidotes. The sourcing and procurement of pharmaceuticals occur through internal collaboration of different officers within the Contracting Authority and external collaboration with suppliers and manufacturers in the pharmaceutical supply chain. Procurement of antidotes is performed according to the Public Procurement Regulations[7], Emergency Procurement Regulations[8] and CPSU Procurement internal policy notes. There are no legislations or policy notes which are specific to antidotes though there is an external stakeholder policy governing the

[7] Public Procurement Regulations, 2016 (LN352/2016) [cited 2024 May 26]. Available from URL: https://legislation.mt/eli/sl/601.3/eng/pdf
[8] Emergency Procurement Regulations, 2016 (LN350/2016) [cited 2024 May 26]. Available from URL: https://legislation.mt/eli/ln/2016/350/eng/pdf

procurement of standby stock items. Antidotes sourced and procured by CPSU are then dispensed to hospitals according to demand.

According to the GFL, thirty-two antidotes are available in Malta for the treatment of toxicological cases. Twenty-nine of these antidotes are sourced by CPSU as per Table 3.1. Atropine sulphate and pralidoxime chloride injection was added to the formulary in 2006 when the British Royal Army gave the antidote to the Government of Malta following Queen Elizabeth II's visit to Malta. This antidote has never been procured by CPSU. Although Botulism antitoxin Types A, B and E is listed on the GFL, this antitoxin was processed for deletion in 2013 due to sourcing issues. At that time, a proposal was sent to the Directorate of Pharmaceutical Affairs (DPA) to consider a change in specifications to facilitate sourcing, however, these were not amended. Malta had participated in the Joint Procurement Agreement (JPA) where antidote was sourced, evaluated, and awarded jointly. However, this antidote was never procured due to lack of demand by MDH and failure to update specifications according to market availability. N-acetylcysteine 600mg effervescent tablets were last procured in 2021 and were being processed for deletion due to lack of demand and problematic sourcing.

Antidotes are sourced and procured by different officers at CPSU, however, most of the antidotes fall under the responsibility of a single officer. In cases whereby the officer is absent from duty, another officer is given hand over of duties to ensure continuation of provision of service.

Table 3.1: Antidotes listed on the Government Formulary, their sourcing and average annual consumption

Antidotes on the GFL	Sourced by CPSU (Yes / No)	Average Annual Consumption in units (June 2020-2023)
Atropine sulphate 500mcg/ml or 600mcg/ml	Yes	20,364
Pyridoxime (vitamin B6) 50mg tablets	Yes	16,795
Phytomenadione (Vitamin K1) 10mg/ml in 0.2ml	Yes	7,065
Glucagon 1mg powder and solvent for solution for injection	Yes	6,246
Phytomenadione (Vitamin K1) 10mg/ml in 1ml	Yes	6,024
Acetylcysteine 200mg/ml	Yes	3,417
Protamine Sulphate 50mg/5ml injection	Yes	2,759
Flumazenil 500mcg in 5ml injection	Yes	1,837
Sodium Bicarbonate 8.4% in 200ml	Yes	1,754
MESNA 100mg/ml in 10ml injection	Yes	1,425
Methylthioninium Chloride (Methylene Blue) 5mg/ml injection IV	Yes	1,409
Naloxone HCl 400mcg/ml injection IV and IM	Yes	822
Parenteral fat emulsion 20% in 100ml emulsion for IV infusion	Yes	510
Fomepizole 5mg/ml concentration for solution for infusion (Replacement of Absolute Alcohol)	Yes	451
Calcium Chloride 0.68mmol/ml infusion	Yes	437
Desferrioxamine mesylate 500mg injection	Yes	337
Sodium Thiosulphate 25% w/v or 50% w/v solution for injection IV	Yes	214
Succimer 200mg capsules	Yes	189
Parenteral fat emulsion LCT 20% in 500ml emulsion for IV infusion	Yes	131
Activated Charcoal	Yes	93
Octreotide 500mcg/ml injection	Yes	80
Dantrolene sodium 20mg powder for solution for injection	Yes	80
Digoxin antibodies 38mg or 40mg powder for solution for injection	Yes	56
Sodium Calcium Edetate 1g Injection	Yes	37
Pralidoxime Mesylate 1g powder for solution for IV injection	Yes	32
Dimercaprol 300mg injection	Yes	30
Sodium Nitrite 300mg (3%w/v) injection	Yes	27
Hydroxocobalamin 5g injection	Yes	19
Phentolamine Mesylate 5mg/ml injection IV and IM	Yes	NA
Atropine sulphate + pralidoxime chloride 2mg+600mg	No	NA
Botulism antitoxin Type A, B and E	No	NA
N-acetylcysteine 600mg capsules/tablets	No	NA

Locally, antidotes are sourced through the issuing of open calls as per Public Procurement Regulations.[7] The types of procurement calls which are issued depend on the urgency of the item and the financial budget available. Five different types of procurement calls are possible as described in Table 3.2.

Table 3.2: Types of procurement calls which may be published for sourcing of pharmaceuticals including antidotes

Type of Call	Financial threshold	Publication Period	Accelerated Publication Period
Call for Quotation	< €10,000	12 days	7 days
Departmental Tender	< €143,000	21 days	15 days
Contract Tender	> €143,000	30 days	NA
Emergency Response Unit Call	NA	6 days	NA
Direct Order Unit Call	NA	Variable	NA

The sourcing process (Figure 3.1) initiates by the validation of antidote specifications by the DPA. Once specifications are confirmed, the procurement officer estimates the quantity required and the financial cost for each respective antidote. The estimated cost of the tender determines the type of call to be issued.

[7] Public Procurement Regulations, 2016 (LN352/2016) [cited 2024 May 26]. Available from URL: https://legislation.mt/eli/sl/601.3/eng/pdf

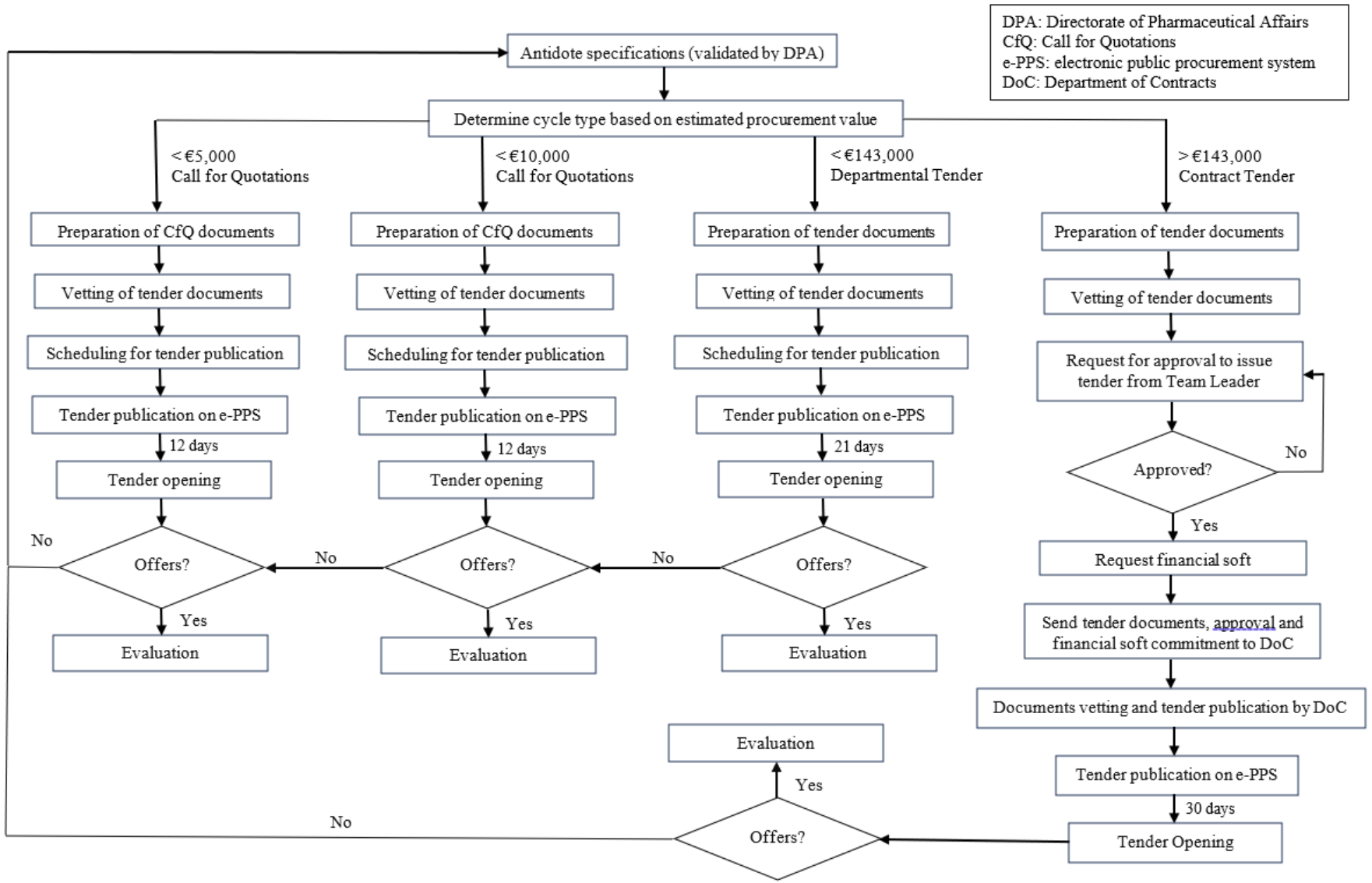


Figure 3.1: Sourcing of antidotes through normal open procedure

Tender documents are prepared by the procurement officer and are vetted by a different officer who gives the go ahead for publication. The tender is then scheduled for publication and is published accordingly in a matter of days. Upon tender publication, the tender process must undergo five official stages: (i) Tender Submission, (ii) Tender Opening, (iii) Tender Evaluation, (iv) Tender Stand-still Period, and (v) Tender Award/Cancellation stage as described in Table 3.3.

Table 3.3 Tender stages in a procurement cycle

Tender Stage	Description
Tender Submission	Suppliers put forward their offers and any requests for clarifications on the tender at publication
Tender Opening	Opening of offers by two officers who are not involved in the evaluation of the tender. This is performed on the same date as the closing date for submission of tenders
Tender Evaluation	Evaluation of submitted offers by the Evaluation Committee. This committee is composed of the secretary, the evaluator, and the chairperson
Tender Stand-still Period	Any call with a value higher than 5,000 euro, allows for an objection period of 10 days, during which any of the bidders may issue an appeal to object against the recommendation made by the Evaluation Committee
Tender Award or Cancellation	Award or cancellation of a call through the electronic public procurement system (e-PPS), following the end of the stand-still period. In case of an appeal, the evaluation of the tender is reviewed by the Public Contracts Review Board prior to awarding or cancelling of tender

Once a tender is awarded, the successful bidder, has within two working days to accept award on e-PPS. A contract agreement is prepared by the procurement officer in case of acceptance of award, vetted by a different officer, and sent to the awarded bidder for endorsement. The successful bidder has ten days to endorse the contract agreement and send it to CPSU. Following acceptance by supplier, this contract agreement is forwarded to CPSU management for endorsement, and this marks the initiation of the contract. If successful supplier refuses award or does not respond to award, a further evaluation is performed and the second cheapest, technically compliant offer is awarded. This can only be performed if more than one eligible quote is received. If the sole supplier rejected award, the tender is referred for cancellation and a new call will have to be initiated for the procurement of the antidote.

The endorsement of the Contract Agreement by both the supplier and the Contracting Authority, allows for the initiation of contract management. Contract management is the process of ordering supply, ensuring delivery by stipulated timeframes, and ensuring abidance to the contract terms and conditions, whilst at the same time ensuring availability of timely treatment for uncompromised patient care. The time frame for delivery of an antidote consignment is according to period stipulated in the published tender dossier. At the time of this study, the tender dossiers were stipulating a first delivery within sixteen weeks with the possibility of monthly staggered orders. Confirmation of orders, thereafter, may be placed with a first delivery of ten weeks and monthly staggered orders. Any medication which is placed on the Maltese market must

be duly registered[9] and delivered by the stipulated timeline, otherwise the Contracting Authority reserves the right to purchase item on the defaulter's account. If an unregistered antidote is awarded, the awarded supplier has ninety days from endorsement of the contract agreement to register the antidote.

In cases of urgent need for procurement of an antidote, CPSU has two teams for such emergency situations, the Emergency Response Unit (ERU) and the Direct Order (DO) unit. The ERU being an emergency unit, does not fall under the normal public procurement regulations but is guided by the Emergency Procurement Regulations, LN350/2016.[8] In case of any issues with the procurement of an item, the ERU team is alerted by the procurement officer through a request for an urgent call for offers using an ERU request template. The ERU team issues an ERU call based on the provided information on the same day that the request is received.

The DO unit intervenes in cases of extreme urgency when need for supply is imminent. In such a case, the procurement officer compiles a detailed case report to request approval from the procurement team leader and/or the Head of Procurement to issue a direct order. The detailed case includes proof of unavailability of supply and justification for urgent delivery. Following approval, the procurement officer fills in a DO request template and sends it to the procurement team leader with a declaration form to be filled in by the team leader. This request form is sent to the DO unit to issue a DO call. The publication period

[8] Emergency Procurement Regulations, 2016 (LN350/2016) [cited 2024 May 19]. Available from URL: https://legislation.mt/eli/ln/2016/350/eng/pdf

[9] Article 20 of Chapter 458 of the Laws of Malta (Medicines Act) [Cited 2024 May 19] Available from URL: https://legislation.mt/eli/cap/458/eng/pdf

of a DO call varies and can be as short as closing within a few hours. Same-day delivery may be requested. In a less urgent situation, where antidote supply is being sourced to maintain stand by stock levels, a call through an open procedure is issued.

3.1.2 Procurement of Antidotes

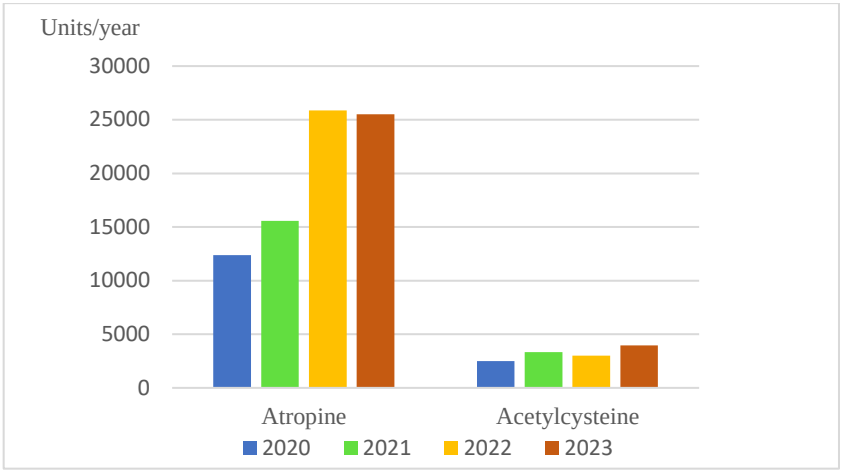
The quantity of antidotes procured often depends on the level of demand made by entities for the specific antidotes. For example, antidotes which have additional indications tend to have higher levels of demand than items used solely as antidotes. The estimated quantity is either based on: (i) antidote approved quantity to be maintained as stand by stock or, (ii) in the case of antidotes for which there is a monthly demand, on the annual expected consumption. Figure 3.2 represents the demand for the eight antidotes monitored in this study for the period of June 2020 to June 2023.

For items which have an ulterior indication other than for use as an antidote, such as atropine, or which have a high and relatively stable consumption such as acetylcysteine, procurement quantities ordered are based according to the average annual consumption calculated through Dynamic AI® software as follows:

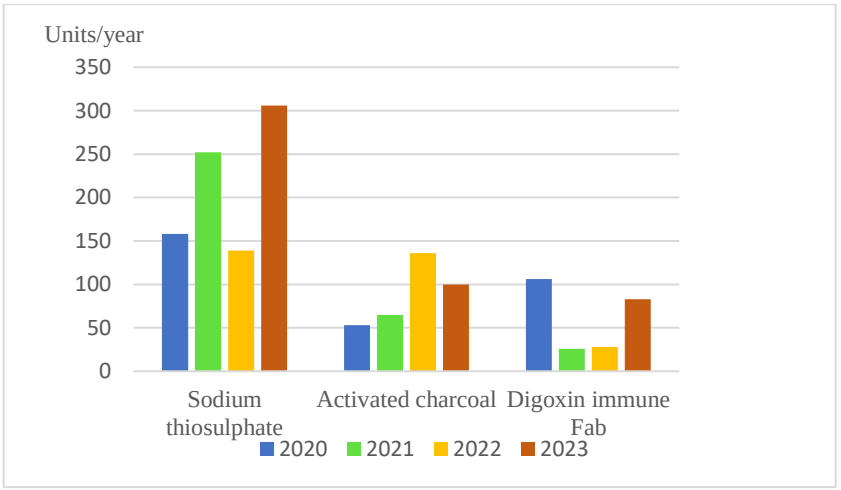
$$\frac{(Previous\ year\ consumption + Past\ 3\ months\ consumption)}{2}$$

Antidotes which do not have a monthly customer demand, are ordered upon notification of stand by stock usage by hospitals. Digoxin immune Fab, activated charcoal, sodium thiosulphate, sodium nitrite, pralidoxime, and hydroxocobalamin kit are all ordered using the standby stock system.

(a)



(b)



(c)

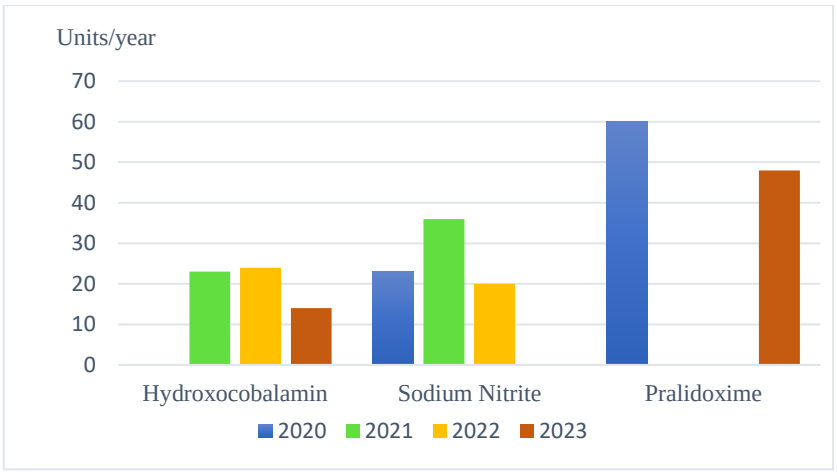


Figure 3.2 Demand levels of (a) atropine and acetylcysteine, (b) sodium thiosulphate, activated charcoal, and digoxin immune Fab, and (c) hydroxocobalamin, sodium nitrite and pralidoxime, by MDH and GGH over a three-year period (June 2020-June 2023)

3.1.3 Handling of Antidotes at CPSU

Procured antidotes are delivered to CPSU stores in San Gwann which is in close proximity to MDH. On delivery to CPSU stores, any refrigerated items are prioritised for checking. Before unloading a consignment, the receiving officer confirms that the antidotes are physically intact and had no temperature excursions during transportation. Any discrepancy is communicated to CPSU Responsible Person who decides whether to accept or refuse the delivered supply. In case of refusal of a consignment the Responsible Person notifies the procurement officer of the rejection with justification. For cold-chain antidotes received from local suppliers, the receiving officer carries out a physical check to ascertain that the cold chain was maintained for that product. In case of ambient antidotes (below 25℃) received from local suppliers, a temperature check is only performed during the months where ambient temperature exceeds 25℃, generally from May till end of October or as advised by the Responsible Person. If a cold-chain antidote is being delivered by a foreign supplier, the Responsible Person verifies that a cold chain verification device (electronic temperature data logger or colour change tag) is present within the consignment and that the correct temperature was maintained throughout transportation. In case that a cold chain verification device is missing, or a temperature excursion has been detected, the Responsible Person makes an informed decision on whether to accept or refuse the consignment. The consignment is accepted only following a declaration by the manufacturer that the temperature excursion has not impacted the quality of the antidotes and is safe for patient use.

Once the necessary checks have been performed the antidotes are unloaded and details of the consignment is entered into the advanced inventory system by the receiving officer or

data entry clerk. A goods received voucher is completed, checked, endorsed, and stamped by the receiving officer. A computer-generated pick list with a unique transfer number is printed and the accepted antidote supply is then transferred to the quarantine area. The pick list, invoice, and other relevant documents, together with a sample of each batch are then forwarded to the quality assurance section to ensure the products' quality before release.

The releasing officer verifies that the antidote supply passed the verification step and is physically intact with the correct labelling and packaging in compliance with the tender conditions, and that any relevant approvals, documents, or certificates have been received. These include registration details and certificate of analysis.

Once all verifications and confirmations are complete, the releasing officer or responsible person at CPSU, authorises the transfer of stock from quarantine depot to the relevant destination in CPSU stores. All relevant data about the antidote including transfer number, batch number, expiry date and Marketing Authorisation Holder (MAH) is entered on the CPSU database for the purpose of audit and traceability.

3.1.4 Handling of Antidotes at MDH

When antidotes are received by MDH Pharmacy, these go through the process of reconciliation. They are checked to ensure that the quantities on order and on invoice tally. Then items are physically checked for any damages in terms of quality. Quantity, batch number, and expiry date verifications are performed. In case of any discrepancies or defects, the supplier is informed. Once antidotes are accepted, they are registered on

Access Dimensions® Software and a Goods Received Note is printed and endorsed. When an ordered antidote does not arrive with the delivered items, this is listed on an 'Out of Stock List', which is then updated accordingly when the antidote is available and delivered to MDH pharmacy.

When a new antidote is delivered to MDH Pharmacy, this is handed to the Quality Assurance section to verify the licensing status. MDH Pharmacy receive antidote requests from MDH wards through the Online Requisition System and these requests are processed through the Access Dimensions® Software.

In case that the antidote is an unlicensed medicinal product (UMP), the dispensing officer ensures that there is a valid UMP approval. If an UMP form is in place, it is ensured that the signature/s on the forms pertain to the authorised prescriber/s. If no UMP form is in place, a new UMP form is requested prior to dispensing. Once all criteria are met, the dispensing officer fills in the required details and prepares standby stock as requested. If stock at the dispensary goes below the approved standby stock, the dispensing officer informs the pharmacist in charge of the depleted stand-by stock at the dispensary to check whether further stock can be ordered from CPSU.

Once the order has been prepared, the dispensing officer registers the transaction in Access Dimensions® Software and the prepared standby stock order is double checked with the request form received from the ward. The antidotes being dispensed are checked for the presence of a visual QR2D code on the outer package and items are

decommissioned as per Falsified Medicines Directive.[10] Antidotes are then dispensed to the officer collecting the medications following the collecting officer's endorsement of the order form.

Following the dispensing of any standby stock item including antidotes, the pharmacist in charge of stand by stock or delegate informs the procurement officer at CPSU, the principal pharmacist in charge of MDH pharmacy stores and the store officers at CPSU. The information forwarded includes the identification code, name and dose of antidote, quantity dispensed, quantity remaining at dispensary, quantity remaining at pharmacy stores, total quantity to be kept at MDH Pharmacy and the quantity to be ordered from CPSU to maintain an adequate quantity of stand-by stock according to the approved quantities. The pharmacist in charge of standby stock then, places an urgent order with MDH Pharmacy stores to replenish the quantities dispensed. In case the required antidote is out of stock, the antidote is listed on the urgent out of stock list.

3.1.5 Handling of Antidotes at GGH

Antidotes are received at GGH Pharmacy Department monthly from CPSU stores and upon receipt these are checked by a pharmacy technician to ensure that the right antidotes have been received in the requested quantity. As per Standard Operating Procedure (SOP) GGH/Pharm/001, received medications are checked to verify that (i) correct antidote formulation and quantity has been received, (ii) packaging is intact, and (iii)

[10] Directive 2011/62/EU of the European Parliament and of the Council amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products [Internet]. Official Journal of The European Union. 2011;L174/74 [cited 2024 May 14]. Available from: https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF

product has an acceptable expiry date. Any antidotes which require refrigeration including digoxin immune Fab, are stored in the refrigerator immediately after delivery. In case that ordered antidotes are not delivered, these are placed on back order and an enquiry is made with CPSU responsible officer regarding the missing antidote and the estimated date of arrival.

3.1.6 Results from Vertical Audits

A total of three vertical audits were carried out between September and October 2023 at A & E MDH, Pharmacy Department GGH and CPSU, each covering the eight antidotes selected for this study. Audit reports were prepared, and each audit report was reviewed with the auditee prior to finalisation. Tables 3.4, 3.5 and 3.6 show the identified deficiencies in antidote emergency preparedness from the vertical audits at GGH, A & E MDH, and CPSU respectively.

Table 3.4: Gaps in operating system and proposed corrective actions following vertical audits at GGH Pharmacy Department

Gap number	Gaps in the Current System	Proposed Corrective Actions
D1	Lack of standard operating procedures to follow during dispensing of antidotes	Develop standard operating procedures for dispensing of antidotes
D2	Lack of guidelines in case of a mass casualty event	Develop guidelines. These should clearly state the responsibilities of each officer. Responsibilities shall be supported by training records
D3	Lack of standard operating procedures on the handling of standby stock items including antidotes.	Develop standard operating procedures for handling of stand-by items including antidotes
D4	Lack of an official antidote standby stock list.	Development of an official Antidote stand-by list
D5	Inefficient ordering system of antidotes	Establish a Stand-by stock ordering system through an agreement with the Central Procurement and Supplies Unit
D6	No policy in place on the potential use of expired antidotes in case of an emergency	Preparation of a policy on the potential use of expired antidotes in case of emergency when non-expired antidotes or alternatives are not available
D7	Poor record keeping	Maintenance of reliable records and secure storage of data
D8	Poor accessibility and identification of antidotes	Antidotes to be placed in an accessible location and clearly labelled
D9	Poor communication between GGH Pharmacy Department, and Central Procurement and Supplies Unit on antidote availability	Identify officers responsible for the handling of antidotes in each department to facilitate communication

Table 3.5: Gaps in operating system and proposed corrective actions following vertical audits at A & E MDH

Gap number	Gaps in the Current System	Proposed Corrective Actions
D1	Lack of standard operating procedures to be followed in case of emergency	Develop procedures including flowcharts
D2	Lack of guidelines in case of a mass casualty event	Develop guidelines. These should clearly state the responsibilities of each officer. Responsibilities should be supported by training records
D3	Lack of labelling/notice to indicate storage location of antidotes	Put up a visible notice indicating location of antidotes for ease of accessibility
D4	Lack of training on handling and use of antidotes for mass casualty events	Schedule training program for staff on antidotes use and related activities especially for mass casualty events. Maintain training records
D5	Poor segregation and labelling of antidote medication	Antidotes to be segregated and labelled for easy identification and accessibility
D6	No records of expiry date monitoring	Maintain records
D7	No records of antidote use, redistribution, and orders	Maintain records
D8	Inadequate stocking of antidotes	Ensure stock is replaced upon use in line with standby stock quantities
D9	Lack of temperature control in the Chemical, Biological, Radiological and Nuclear substances store. No temperature records.	Temperature of antidotes stored in the Chemical, Biological, Radiological and Nuclear substances store must not exceed 25°C. Temperature should be controlled and monitored
D10	Poor accessibility to antidote store - Key positions in key cabinet are not labelled	Organise key cabinet so that keys are labelled and easily identified
D11	Obstruction of Chemical, Biological, Radiological and Nuclear substances store and lack of labelling	Chemical, Biological, Radiological and Nuclear substances store should be clearly labelled and a ‘Do not obstruct’ notice should be in place

Table 3.6: Gaps in operating system and proposed corrective actions following vertical audits at CPSU

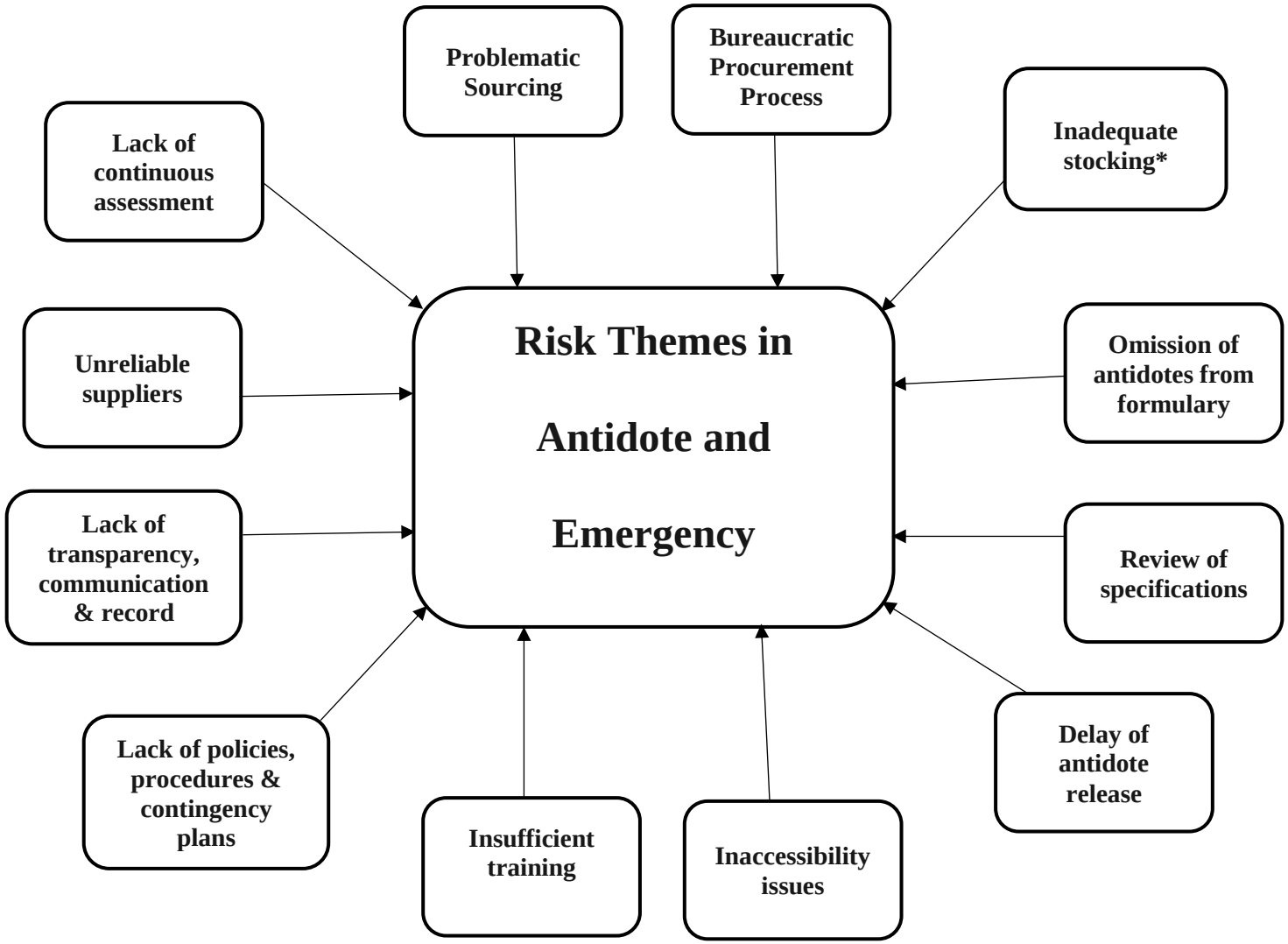
Gap number	Gaps in the Current System	Proposed Corrective Actions
D1	Lack of policy notes on the procurement of antidotes	Develop guidelines on the sourcing, procurement, and maintenance of antidotes
D2	Lack of strategy in place for the sourcing and procurement of (i) large quantities of antidotes for mass casualty preparedness and (ii) antidote not included in the Government Formulary List, in a timely manner	Develop procedures which include logistic arrangements to procure antidotes in a timely manner
D3	Poor accessibility to available policies on antidotes	Officers involved in the handling of antidotes must have access to existing policies relating to antidotes as applicable
D4	Unorganised reviewing of antidote stocks and procurement status	Schedule antidote procurement card review
D5	Lengthy procurement processes which do not respect operational timeframe	Implement deadlines for different stages and monitor adherence
D6	Procurement specifications do not always reflect market availabilities	Undertake a proactive approach in the development of antidote procurement specifications
D7	Poor traceability of orders placed/processed through the urgent route	Generation of orders through procurement software which is traceable
D8	Use of unreliable suppliers – Deadlines not respected, and temperature excursions detected	Perform evaluation of supplier service and grade suppliers according to efficiency and reliability. Use supplier grading in evaluation of tender
D9	Inefficient maintenance of stand by stock	Revise procurement procedures. Procurement timeframe needs to ensure that SBS is replenished as needed

3.1.7 Qualitative Analysis of Vertical Audits, Onsite Observations, and Meetings with Healthcare Professionals

A total of sixty codes were generated through inductive coding of raw data (Appendix 3). Table 3.7 demonstrates some examples of the initial codes generated. Similar codes were grouped together to form twelve risk themes as per Figure 3.3.

Table 3.7 Initial code generation from critical analysis of raw data

Initial code	Number of antidotes affected from selected antidotes (N=8)	Example or raw data
No procedures in place for handling of antidotes	8	There are no policy notes which are specific to the handling of antidotes
Inaccessibility of antidote data	8	'We did not know that antidote was available'
Insufficient quantities in case of mass casualties	8	6 hydroxocobalamin kits available at GGH. 10 hydroxocobalamin available at MDH 10 hydroxocobalamin available at CPSU
Lengthy delivery period	8	16 weeks delivery period on contract
Urgent order not delivered	8	No guarantee of antidote being delivered when ordered through the urgent route
Non-uniform strategy of antidote ordering	6	'CPSU is not always informed when this antidote is dispensed by entities'
Lack of visible notice where antidotes are kept	6	CBRN store is not labelled Emergency trolleys containing antidotes were not fully labelled
Erratic antidote demand	4	Sodium thiosulphate being used in renal wards for cases of calciphylaxis which is increasing its demand
Unlicensed antidote	4	Activated Charcoal was delivered through the urgent route and required Article 20 approval for its release. This took an additional 11 days
Specifications for procurement not updated according to market availability	3	Pralidoxime specifications resulted in no offers during procurement cycles. Following multiple cancellations, specifications were revised to include other oximes and alternative antidote was sourced
Sole manufacturer	2	'Hydroxocobalamin is sourced through a sole manufacturer'
Antidote shortage	1	In June 2023 there was an international shortage of Digoxin immune Fab.



*Includes issues of lack of planning and inadequate demand

Figure 3.3: Identified risk themes in antidote and emergency preparedness

3.2 Results of Phase 2: Risk Identification, Validation, and Assessment

This section includes results of thematic analysis, focus group discussion and risk matrices developed from data triangulation. The following includes a summary of the points highlighted during the focus group meeting and discussions with other healthcare professionals.

All members of the expert panel (N=9) were in full agreement with eleven of the identified risks (Table 3.8). The expert panel emphasised that Malta, being an extremely small country, which is also an island, has its own challenges when it comes to antidote availability. The problems which are faced locally, due to the limitations of a small island are mostly with regards to supply, but not only.

Some of the identified risk themes may even apply to other pharmaceuticals however, their impact tends to be greater in the case of antidotes. Taking problematic sourcing as an example, this is an issue which is unfortunately being encountered with various pharmaceuticals. In the case of antidotes, one of the reasons for problematic sourcing is the limited number of manufacturers which produce specific antidotes. For some antidotes there is only one manufacturer and if something goes wrong with this manufacturer, a critical situation arises.

Table 3.8 Key feedback from focus group on identified risk themes

Risk Theme	Agreement by Focus Group Panel (N=9)	Main Points from Focus Group Discussion
Problematic sourcing of antidotes	9	- Demographics and logistics of Malta - Need to consider each antidote separately
Bureaucratic medicine introduction and procurement processes	9	- Lengthy approval for introduction on GFL - Procurement process has its dedicated timelines as per Public Procurement Regulations and Extended Producer Responsibility Framework Regulations in emergencies
Inadequate stocking of antidotes	9	- Need for a strategy to attain antidotes from available sources in a timely manner - Dilemma on quantities of antidotes to stock - Distinction between regularly used and rarely used antidotes - Problems with inaccurate demand forecasts due to lack of planning especially in case of antidotes used in mass casualties and antidotes with a short shelf life
Omission of antidotes from the Government Formulary List	9	- Management of risk through the addition of new antidotes on the formulary - An exercise was performed to review available antidotes - Lack of MAH and consultant request for introduction of antidotes
Delay of antidote release	9	-Regulatory issues with the release of antidotes from quarantined stock available in Malta
Inaccessibility issues	9	- Antidote Committee has increased the number of antidotes available in A & E MDH, added the types of antidotes available in A & E MDH - Possible issues remain in the movement of antidotes between different bodies
Insufficient training	9	-Acknowledgment of need for increased training especially for paramedics -Need for increase in awareness of importance of training for emergency preparedness
Lack of policies, procedures, and contingency plan	9	Practical example taken using hydroxocobalamin in case of fire to reflect lack of emergency preparedness due to unavailability of guidelines No national plan available in terms of mass poisoning incidences The Antidote Committee is working on guidelines for emergency preparedness to be made available to healthcare professional in the National Health Service
Lack of transparency, communication and record keeping	9	- Importance of expiry date monitoring. Example taken using Naloxone situation in Malta - Deficiencies in decentralised data management system - No national chemical registry, lack of national communication and record keeping
Unreliable supplier	9	-Possibility of blacklisting or whitelisting suppliers
Lack of continuous assessment	9	-Antidote Committee periodically reviews the management of antidotes
Review of specifications	6	-Need for a more proactive approach in the reviewing of antidote specifications for procurement

3.2.1 Risk Theme 1: Problematic Sourcing

Sourcing of pharmaceuticals is becoming increasingly problematic with the highly volatile market situation. Antidotes are even more problematic to source given the smaller quantities which are usually stocked. In addition, the pharmaceutical industry is more willing to invest in other pharmaceuticals which have a wider and more consistent market since this results in greater financial gain. Hydroxocobalamin kit and sodium nitrite are two antidotes which are produced by a sole manufacturer. Despite this, locally there has not been any sourcing or procurement issues concerning hydroxocobalamin. This was also confirmed by healthcare professionals at CPSU, GGH and MDH. A problem could, however, arise in the event that the manufacturer can no longer supply to Malta due to an interruption in the supply chain such as a manufacturing issue, shortage of active pharmaceutical ingredient or an export ban. Sodium nitrite has been very problematic to source since 2017. Procurement calls were being cancelled due to exceeded financial threshold of the published tenders, and more recently, due to no submission of tender offers.

The focus group panel members agreed that problematic sourcing of antidotes is a valid risk and was deemed to pose a 'high risk' in antidote availability. Some suppliers are reluctant to provide antidotes to Malta due to the very low volume procured and the bureaucratic registration process which involves significant time and fees. The fact that the Maltese islands are very small with only two main acute general hospitals, one on each island, does not provide the luxury of sharing of antidotes between multiple close hospitals as occurs in other countries such as Italy, the United Kingdom and the United

States. If a mass incident occurs, sourcing of antidotes will be especially difficult since minimal antidote stocks are available on the island and no contingency plan is available.

3.2.2 Risk Theme 2: Bureaucratic Procurement Processes

The bureaucratic procurement process is an issue which is not only experienced in Malta but occurs internationally. As observed during the audit at CPSU, a procurement cycle takes approximately six to nine months to be completed, starting from the publication of the procurement call till the endorsement of the contract agreement. The focus group panel agreed that the lengthy procurement process certainly poses a risk to availability of antidotes, however, it was also acknowledged that implementing change for improvement in this area is very difficult. The risk theme of 'bureaucratic procurement process' was difficult to categorise with respect to severity of risk. The level of severity depends on the specific case. When an acute case arises and supply is urgently required, this is usually sourced through the urgent route, via a direct order. The bureaucratic procurement process with respect to antidotes mostly interferes with the maintenance of appropriate stand-by quantities and approval through DPA to increase the quantities of antidotes to be maintained as stand-by stock. Another mentioned aspect in the bureaucratic procurement process is the 16-week first delivery period of contract agreements for the supply of pharmaceuticals including antidotes, though this mirrors the manufacturing and production timelines of pharmaceuticals.

3.2.3 Risk Theme 3: Inadequate Stocking of Antidotes

Locally, there is no official document to indicate the quantities of antidotes to be maintained at any of the audited settings. The focus group participants explained that an official antidote list was prepared by the Antidote Committee for both MDH and GGH and that in 2023 the Antidote Committee reviewed the antidote list in the presence of representative from both hospitals. However, this document was not available at GGH Pharmacy Department and CPSU during audits.

A & E at MDH have a document with the quantities of antidotes to be maintained as standby stock. However, during the vertical audits at A & E MDH, very low stock of acetylcysteine was observed (n=3) when compared to the approved quantity to be maintained at the Emergency Department (n=30). Replenishment of antidotes at A & E MDH occurs on a weekly basis and not upon use of medication. Digoxin immune Fab, sodium nitrite and sodium thiosulphate are not maintained at A & E MDH but are stored by MDH Pharmacy Department and this may hinder timely availability. Sodium nitrite is not available at either MDH Pharmacy or CPSU due to problematic sourcing.

MDH Pharmacy has a document listing the quantities of antidotes to be maintained as stand by stock, as developed by the Antidote Committee. The standby stock quantities are not adequately maintained for multiple antidotes as per data attained from MDH Pharmacy. This includes low stocks of atropine sulphate, activated charcoal, acetylcysteine, and digoxin immune Fab, when compared to the approved stand by quantities.

GGH do not have an official antidote list with an approved stand by quantity. At GGH antidotes were included with the yearly customer demand excel sheet provided to CPSU prior to the beginning of the new year. The customer demand excel sheet includes a complete order of pharmaceuticals an entity requires for the whole year. For example, during 2023, GGH ordered 120 vials of digoxin immune Fab with ten vials being sent per month. Given that the actual demand for these vials was less than the forecasted quantities, GGH was overstocked. GGH Pharmacy does not stock sodium nitrite, sodium thiosulphate and pralidoxime.

During the audit at CPSU it was noted that there is no policy note on the quantity of antidotes to be maintained at CPSU stores. Standby stock quantities at CPSU are not officially quantified. Nonetheless, CPSU attempts to maintain standby stock in the equivalent amount to that required by MDH for availability of replacement stock in case of use.

The approved quantities of antidotes at hospitals are not enough to support mass casualties. The expert focus group panel agreed that inadequate stocking is a risk theme which is of relevance and may have a significant impact on antidote availability and accessibility. The severity of this risk varies for antidotes which are frequently used to those antidotes which are rarely used, if ever. In frequently used antidotes, the customer demand is used for the procurement of antidotes. For rarely used antidotes, there is a dilemma on how much antidotes to stock. A practical example was taken using methanol poisoning. In Malta, fomepizole has been introduced in 2022 as an antidote for methanol poisoning to replace dehydrated alcohol. It was noted that cases of methanol poisoning are rare in Malta, with only a single episode in recent years. However, internationally in

countries such as Estonia and Czech Republic, healthcare professionals are faced with mass incidences of methanol intoxications due to cultural and traditional activities involving home alcoholic preparations. The focus group panel expressed concern over the lack of preparedness if such a situation was to occur in Malta due to for instance the importation of contaminated alcoholic beverages.

From a procurement perspective, one of the main concerns which falls under inadequate antidote stocking is that CPSU does not have an accurate demand forecast and the pharmaceutical industry is requesting that the demand is made from two years ahead of time for the allocation of supply for Malta.

Naloxone was taken as an example of local inadequate stocking. This antidote was out of stock in Malta in April 2023 since all stock available on the Maltese islands expired in the same month and available replacement stock was not enough to cater for the increase in demand. Naloxone is a frequently used antidote in Malta as an opioid antagonist in the event of opioid poisoning. Due to its relatively high utilisation compared to other antidotes, its procurement is based on the average monthly consumption derived from the annual consumption data. It was noted that one of the problems in this case was that CPSU was procuring only one formulation of naloxone. This implies that if there is unavailability of this formulation due to supply interruption such as a sourcing issue, the healthcare system will be exposed to an unacceptable risk. Consequently, having different formulations for the same antidote may decrease sourcing issues. However, the need remains to tackle the main issue behind supply unavailability, which in most cases, as with the case of naloxone, is the underestimation of demand by the entities. If more

than one formulation of naloxone had to be procured, one needs to ensure that an accurate demand is maintained for each formulation procured.

3.2.4 Risk Theme 4: Omission of Antidotes from the Government Formulary List

The focus group panel declared that the antidote committee is aware of the need to include additional antidotes to the Government Formulary List and stated that work is in progress on this issue. The focus group ranked the 'unavailability of an official antidote list and that specific antidotes are omitted from the Government Formulary List' risk theme, as a moderate risk given that there is a management strategy already in progress. It was noted that requests for the introduction of novel antidotes on the GFL are being processed and forwarded to DPA.

3.2.5 Risk Theme 5: Lack of Periodic Review of Specifications

During the CPSU audit, procurement officers stated that prior to issuing of any procurement call, the antidote specifications are referred to DPA for validation. Members of the expert focus group confirmed this statement and added that validation of specifications involves the performance of market research to confirm that the provided specifications are still relevant. Sometimes specifications do not require amendments since they would still be relevant. An example of this is the specifications for hydroxocobalamin kit which is produced by a sole manufacturer. In the vertical audit it was noted that specifications did not require amendments since the available product had not been altered. For several antidotes, although specifications were reviewed prior to the publication of a procurement cycle, tender calls kept being cancelled due to lack of

offers or due to technical non-compliance. The procurement officer of atropine sulphate 600mcg/ml injections has shown the auditor how in 2022 calls were being cancelled due to the unavailability of a product which fits with the published technical specifications. This antidote was then sourced following review and modification of antidote specifications by DPA to include acceptance of atropine sulphate 500mcg/ml injections.

A similar situation was observed with pralidoxime injections where multiple calls were being cancelled in 2023 due to lack of offers. Upon cancellation of multiple calls, DPA referred the specifications to the Antidote Committee to review the specifications for the potential inclusion of a different oxime. Following necessary research and literature review it was determined that specifications may be opened to include a different oxime which is considered as being interchangeable with pralidoxime and which is also commercially more readily available. In this case, the sourcing and procurement of this antidote was critical since all stock at the entities had an expiry date ranging from May to June 2023. The revision of specifications allowed for the procurement of obidoxime by the Emergency Response Unit and ensured continued antidote availability.

During the focus group meeting, two members claimed that antidote specifications have always been amended whenever changes were required. However, it was also acknowledged that improvements can be made through a more proactive approach and by reviewing specifications on a more regular basis based on what is available on the market. Three out of nine (33%) of the focus group members disagreed with 'lack of periodic review of specification' as one of the risks in antidote availability. Nonetheless, the researcher deemed that this risk may have a critical impact on antidote sourcing and availability as documented by the case studies and cannot be overlooked. The researcher

amended the risk theme from ‘lack of periodic review of specifications’ to ‘reactive approach in the review of specifications’ in acknowledgment of the fact that antidote specification reviews are performed reactively rather than proactively to avoid delaying the procurement and sourcing process.

3.2.6 Risk Theme 6: Delay of Antidote Release from Quarantine

When antidotes are received at CPSU stores, they are checked for quality assurance and released by the responsible persons prior to items being available for dispensing and use for treatment. This risk theme encapsulates all possible scenarios which may lead to a delay in antidote release from quarantine. These include falsified medicines directive alert, discrepancies between ordered and delivered item, need for relabelling, and temperature excursion.

Activated Charcoal is one of the antidotes which experienced a delay in release from quarantine in April 2023. During the vertical audits at CPSU, the auditee explained that the disruption was due to the fact that the delivered product had a different United Kingdom registration number than that previously indicated by the supplier. CPSU had registered the item based on the initial registration details provided and had to initiate another registration request from the Malta Medicines Authority. This led to an eleven-day delay for release. This delay did not compromise patient treatment but still represented a risk. In case of urgent need this antidote could have been released through the submission of an Unlicensed Medicinal Product form.

Sodium thiosulphate is another antidote which experienced delays in release from quarantine. One of the batches of this antidote for which a vertical audit was performed was released ninety-two days following receipt. This three-month delay was attributed to the need for over-labelling. From the vertical audits performed, it was noted that the lengthiest release processes were in cases where antidotes required over-labelling and the exemptions were not approved by the competent authority.

When there is an issue with batch release due to registration issues, CPSU informs the Superintendent of Public Health and the regulatory sector for approval and to evaluate the possibility of a waiver in case of an emergency. If the antidote is a United Kingdom product, it is more difficult to get the waiver for release and item release from quarantine tends to be delayed. The focus group panel agreed that there is a limit to what can be done to mitigate risks of delay in antidotes from CPSU's end. All members of the focus group panel confirmed that this risk theme is valid since it may lead to antidote unavailability. It was discussed how in the case of an incident whereby an antidote is urgently needed and is yet to be released, the Superintendent of Public Health may issue a waiver for antidote release. Approval by the Superintendent of Public Health is given on a case-by-case basis. In accordance with this, in June 2020, an unlicensed batch of Pralidoxime 1g injections was immediately released on the basis that item was listed on the Superintendent of Public Health exemption list for unlicensed medicinal products.

In certain scenarios such as in the event of antidote experiencing a temperature excursion, item cannot be released prior to documented confirmation from the manufacturer that the temperature excursion has not impacted on the quality of the pharmaceutical product. This confirmation is critical to ensure the safety of the patient being treated.

3.2.7 Risk Theme 7: Inaccessibility of Available Antidotes

Accessibility of antidotes is a critical factor which may have a great impact on the efficacy of time-dependant antidote treatment. This risk theme was developed from local antidote storage deficiencies noted during audits and onsite observations at A & E MDH and GGH Pharmacy. During onsite visits at both A & E MDH and GGH Pharmacy it was noted that the location of antidotes was not clearly indicated. At A & E MDH access to the Chemical, Biological, Radiological and Nuclear material (CBRN) store was obstructed, and the store was not labelled. At GGH Pharmacy, antidotes were stored in different areas with some antidotes located in unreachable areas requiring the use of a ladder to gain access to the antidotes. In addition, antidotes which require immediate administration such as in the case digoxin immune Fab were not stored at A & E MDH and would require ordering from MDH Pharmacy in case of need. The officer in charge at A & E MDH stated that if antidote is available at MDH Pharmacy, the antidote may be delivered within minutes. This time frame agreed with the information obtained from MDH pharmacy. At GGH most antidotes are not maintained at the Emergency Department but must be ordered through GGH pharmacy in case of need. This may hinder timely administration especially for time-dependant antidotes. In case that an antidote which is stocked at MDH, is urgently required at GGH, if weather permits, a helicopter is used for the transfer of the antidote to mitigate possible traffic delays.

Focus group participants fully agreed with the inclusion of this risk theme. In case of a fire incident, hydroxocobalamin kit is not carried on site by the ambulance team until verification of possible cyanide intoxication. When A & E MDH is notified of the emergency, an ambulance with one nurse is immediately dispatched on site to assess the

situation. This ambulance will not be equipped with cyanide antidotes. The onsite nurse will describe the situation to the consultant toxicologist and if the possibility of cyanide poisoning is confirmed, a second ambulance with a second nurse will be dispatched together with the Incident Support Unit van. The second ambulance will carry the cyanide aluminium treatment box from A & E which includes nine hydroxocobalamin kits. The Emergency Physician Response Unit is notified and dispatched on site. These physicians prescribe antidotes in case of need and nurses administer the antidotes. Consequently, immediate administration cannot be performed as intended and the antidote administration is delayed.

3.2.8 Risk Theme 8: Insufficient Training

Insufficient training is a risk which was derived from information collected through communication with various healthcare professionals including officers from A & E MDH. Simulated training exercises involving cases of emergencies requiring the use of antidotes are not regularly performed. During the audit at A & E MDH, it was stated that it had been several years since the staff was involved in some form of simulation exercise involving antidotes. The officer in charge expressed the need for periodic training exercises concerning emergency preparedness for mass intoxication events.

Focus group participants agreed that there is insufficient training on antidotes and a lot can be done for improvement. It was noted that there is a lack of awareness on the need for training and that there needs to be a plan for regular training of staff. Following agreement with all participants, insufficient training was categorised as being of high risk.

3.2.9 Risk Theme 9: Lack of Policies, Procedures, and National Contingency Plan on Antidote Management

Lack of policies and procedures specifically on the handling and use of antidotes was noted at all audits performed. This implies lack of uniformity in service which may lead to various errors. The unavailability of a national contingency plan poses a high risk for mass toxicological cases or in the event where an antidote not listed on the formulary list is urgently required. This risk theme was validated by all focus group participants in recognition of the fact that existing deficiencies of guidelines in antidote preparedness pose a high risk to the national emergency preparedness.

As members of the Antidote Committee, the focus group participants explained that they are working on guidelines for antidote use, and these will be made available to all officers concerned with antidotes in the National Health Services. In 2008, guideline algorithms focusing on the symptoms, treatment and monitoring actions involved in nerve agents and cyanide intoxication were compiled, validated, and published (Anastasi, 2008). Updated guideline documents are to be made available for pre-hospital availability of antidotes in case of, for example, cyanide toxicity due to a fire incident.

3.2.10 Risk Theme 10: Lack of Transparency, Poor Communication and Poor Record Keeping on Local Antidote Availability

Lack of transparency, poor communication and poor record keeping on local antidote availability was included as one of the risk themes as a result of:

(i) Inconsistent notifications to CPSU of when stand by stock is used by entities deviating from the approved process: 'In certain instances CPSU is informed that more stock is required of an antidote, when all stock has been dispensed and not when individual quantities are used up'.

(ii) Lack of data on the use of antidotes by Emergency Departments since no logbooks are maintained.

(iii) No logbooks or other records are kept on expiry of antidotes at A & E MDH

(iv) Data on batches received prior to September 2023 were not available by GGH Pharmacy since 'due to a change in concession agreement, the online stock system was put on hold and previous data was lost'.

(v) Inefficient communication between CPSU and GGH: 'the period GGH Pharmacy Department was out of stock of activated charcoal was due to time wasted hunting stock without being informed that item was unlicensed'.

Focus group participants agreed with these risks and participants suggested that optimisation of the Information Technology System may help resolve these issues. One of the toxicological consultants suggested the development of a colour-coded grading system (green, orange, red), intended to alert the A & E department consultants on any problems in the availability of specific antidotes. If an antidote is marked green, the consultants would know that there is no issue with supply whereas, if an item is marked orange, it may be tackled before it becomes critical (red). Focus group experts fully agreed with alerting the Antidote Committee on any problematic sourcing of antidotes. It was stated that it is important to have an intelligent system which is used by trained personnel. It was emphasised that one should make the best use of the available data and act accordingly.

The focus group panel agreed that the risk theme of lack of transparency, poor communication, and poor record keeping on local antidote availability, also applies to the lack of information available on the maintenance of antidotes in certain companies in Malta. It was mentioned that there is no national chemical register and collated records of national antidote stocks available at both governmental departments and at private companies. The focus group members agreed that there is a lack of transparency, poor communication, and poor record keeping on a national basis. This risk theme was amended to 'Lack of National Strategic Plan' to reflect the need for a national action plan. It was agreed that this risk theme is of high importance as to avoid a 'crisis mode' situation if a mass incident is to occur.

3.2.11 Risk Themes 11: Unreliable Suppliers

'Unreliable suppliers' is a risk theme which emerged through data collected from CPSU and meetings with procurement officers. During the vertical audits it was noted that in multiple cases, antidotes ordered through the ERU and DO unit were not delivered by due date. The procurement officer stated that when an ERU order or a DO is placed, there is no guarantee that the supply will be delivered on time. If the order is not delivered by due date CPSU can cancel the order and reissue a new urgent call. In the case when delivered antidotes are not accepted due to excursion in temperature, the CPSU Responsible Person contacts the supplier to provide a declaration from the MAH on whether the medication is still safe to use. Temperature excursion occurred more than once during the transportation of digoxin immune Fab from supplier's warehouse to CPSU. It was also mentioned that in 2013 CPSU had tried to negotiate with the specific suppliers/manufacturers that delivery of stock is performed within 48-72 hours.

However, this negotiation did not lead to the desired result due to the issues with product demand forecast, and other challenges associated with logistics and transportation services. The approach taken up was to do a Memorandum of Understanding (MOU) with neighbouring countries so that Malta is supplied directly upon an incident. CPSU has a MOU with Italy through the embassy for such assistance in case of urgent need for the supply of pharmaceuticals, depending on the situation. There was also a Pre-Brexit gentlemen's agreement with the UK to assist the Maltese authorities as needed. However, following the experience of Covid-19 all countries are rethinking the feasibility and effectiveness of such agreements. In any case, both MOU and the gentlemen's agreement are non-legally binding.

Unacceptability of delivered antidotes and unreliable suppliers were both validated by the full focus group panel given that these have the potential to impact antidote availability. The possibility of whitelisting or blacklisting suppliers was favourably proposed as a management tool to reduce the risk from unreliable suppliers.

3.2.12 Lack of Continuous Assessment and Review for Improvement in the Management of Antidotes and Emergency Preparedness

Locally there is no strategy in place for the assessment of the management of antidotes. The Antidote Committee meets monthly to discuss antidote related issues and possible improvements for implementation, such as, the need for addition of certain antidotes on the GFL. This committee does not assess existing or prospective deficiencies within the antidote management process for risk mitigation and emergency preparedness. Its primary role is that of an advisory committee.

The risk of 'lack of continuous assessment and review for improvement in the management of antidotes and emergency preparedness' was also validated. The focus group participants stated that although there is place for improvement in the review of antidotes, the existing Antidote Committee is an active working group which is working to optimise antidote availability in the Maltese islands. Lack of continuous assessment and review for improvement in the management of antidotes was ranked as low risk by the focus group panel.

3.2.13 Additional Risks

The focus group panel identified the financial burden of antidote procurement as a possible additional risk theme in antidote availability. Reference was made to the situation in the United Kingdom and Italy where certain antidotes are stockpiled for use in the context of deliberate terroristic attacks or other chemical emergencies. An example is the United Kingdom reserve of emergency stock for major incidents which include chemical and radiological countermeasures. This preparedness does not solely involve the Ministry of Health but also other ministries including the Ministry of Defence and the Ministry of Home Affairs. The collaboration of different ministries allows the provision of financial support and enhanced logistics. Locally, there are funds available for emergency preparedness for different ministries. The issue is that although these ministries have allocated funds for such emergencies, they do not have the necessary expertise. The focus group participants agreed that locally, there is no common plan in emergency preparedness for mass incidences of this nature. It was noted that different entities were working on the same issues separately and this was resulting in confusion and waste of resources and time.

3.2.14 Results from Risk Assessments

A total of 13 risk matrices (Appendix 4) were developed. Risk assessments were based on qualitative data attained from different healthcare professionals through different methods. Eleven of the validated risk themes were inputted into each risk matrix depending on the risk impact and the risk severity allocated to each risk in terms of the respective antidote. The risk theme 'Omission of antidotes from the Government Formulary List' was not inputted in the risk matrix since all selected antidotes are already listed on the GFL.

In the developed qualitative risk matrices, the extent of probability and impact were determined through data triangulation and analysis of expert focus group discussion.

Two risk matrices were developed for atropine sulphate, pralidoxime, hydroxocobalamin, sodium thiosulphate and sodium nitrite:

(1) Risk matrix to assess risk themes in acute individual toxicological cases
(2) Risk matrix to assess risk themes in mass casualty events

A single risk matrix was developed for activated charcoal, digoxin immune Fab and acetylcysteine focusing solely on individual toxicities due to their unlikely use in mass events.

3.3 Results of Phase 3: Development of Guidelines

The top risk themes which were denoted as being of the highest importance in the local scenario through the expert focus group were: (i) Problematic Sourcing, (ii) Inadequate Stocking and (iii) Lack of National Strategy Plan.

Three guidelines (Appendix 5) were developed following focus group discussion and risk matrices assessments to address identified prioritised risks and provide guidance for enhanced emergency preparedness (Table 3.9).

Table 3.9 Developed guidelines for risk management in antidote emergency preparedness

Risk Theme	Developed Guideline
Problematic Sourcing	Guideline for Optimisation in the Procurement of Problematic to Source Antidotes
Inadequate Stocking	Guideline on Stocking of Antidotes
Lack of National Strategy Plan	Guideline for Optimisation in the Transparency, Communication and Record Keeping on Local Antidote Availability

Chapter 4

Discussion

4.1 Risks Identified in Antidote and Emergency Preparedness

Emergencies caused by toxicological material may arise from chemical terroristic attacks, industrial, occupational, residential or transportation accidents, national disasters, and self-harm attempts. These incidences may lead to individual toxicities or even mass casualties depending on the extent of the incidence. Apart from the toxicity of victims, such tragedies may lead to mass psychogenic illness, especially in traumatic cases arousing confusion in the society. Although the occurrence of chemical events is rare, the healthcare system must be prepared to manage such situations since the consequences of unpreparedness may imply catastrophic costs to human life. Healthcare system preparedness must cater for both individual acute poisoning cases and for mass exposure events. A part of emergency preparedness for chemical poisoning cases involves ensuring availability of adequate antidote supply in a timely manner.

The occurrence of various crisis including BREXIT, Covid-19 and the numerous wars such as in Ukraine and Gaza have caused major disruptions and challenges in the global healthcare supply chain. Furthermore, the ever-aggravating climate change implications are also having a disruptive effect on various supply chains including healthcare. Consequently, it is becoming even more difficult to secure healthcare supplies in a timely manner. The availability of antidotes in hospitals tends to be problematic and inadequate stocking has been widely recorded (Abu Esba *et al.*, 2022; Al-Taweel *et al.*, 2022; Pandya *et al.*, 2023). This study has shown inadequate stocking of antidotes also in Malta and poor emergency preparedness especially with respect to mass casualty events requiring antidote treatment.

This research has identified twelve main risk themes which are predominant in the local scenario with regards to antidotes and emergency preparedness. The expert focus group validated all risks and suggested the inclusion of an additional risk, that is the financial constraints associated with procurement of antidotes. The top three risk themes which were determined to be of the highest priority by the expert focus group were (i) Problematic sourcing, (ii) Inadequate stocking and (iii) Lack of a national strategy plan. Guidelines for these three risk themes were prepared based on the findings of this study. However, in the researcher's opinion the other risk themes are equally important and need to be tackled to have a comprehensive response to the identified deficiencies.

Problematic sourcing risk theme is particularly concerning for rarely used antidotes which are procured and maintained in small quantities since these have no other application. Such antidotes represent minimal profitability for suppliers and thus, investment in such medications is not a financially attractive endeavour. Suppliers are further discouraged from providing such antidotes to Malta by the bureaucratic registration procedure and extensive costs involved especially for items which are not manufactured within the European Union.

Inadequate stocking is a risk theme which may be a consequence of problematic sourcing but not only. Poor planning, inefficient communication and lack of reliable data also contribute to inadequate antidote stocking. The entities cannot accurately predict the required amounts of rarely used antidotes since their use is unforeseeable and cannot be calculated on past record use. The developed risk matrices (Appendix 4) reflect how inadequate stocking mostly impacts preparedness for mass casualties in the local scenario. In some countries such as Japan, the United Stated and Thailand, the government

maintains a stockpile of antidotes from which urgent supply may be obtained in case of a chemical mass casualty incident (Srisuma *et al.*, 2018; Antoniello *et al.*, 2023; Koido *et al.*, 2023). Large, developed countries such as the United States, Germany, France, and the United Kingdom have a healthcare system composed of multiple acute hospitals. These have the advantage of the possibility of pooling resources, thus allowing the sharing of antidote stocks among hospitals, resulting in a reduced financial burden and greater efficiency (Dart *et al.*, 2018; Harnett *et al.*, 2021; Kaiser and Dart, 2022). In Malta, there are only two national acute public hospitals: Mater Dei Hospital and Gozo General Hospital, which stock limited quantities of selected antidotes and there is no stockpile system in place. It is difficult to justify an increase in antidote stocking especially if there is no increase in demand due to perceived lack of requirement by the clinicians. Replacement stock for the standby quantities is maintained by CPSU however, there is no national policy or procedure in place for antidote maintenance and management. In addition, there is no functional contingency plan in place to ensure that the required antidotes are made available in a strategic and timely manner especially in case of a mass casualty event.

The unavailability of standard operating procedures or policies on the handling and management of antidotes, is a critical risk theme since such procedures are fundamental to maintaining a reliable and efficient operational system. Such documents are also important for assessment and evaluation of emergency preparedness. The developed risk matrices indicate that the lack of policies is deemed as critical for both individual acute cases and mass casualty preparedness. This risk theme was identified by the expert focus group as being of moderate impact solely for those antidotes which have a high consumption rate. Such antidotes generally follow the same procurement procedures as

other medications due to their higher demand in contrast to other rarely used antidotes. Standardised procedures should be adopted by all National Bodies involved in the management of antidotes. An important missing protocol which can have an impact on antidote availability, concerns the potential use of expired antidotes in case of a crisis situation.

A lack of national strategy plan for antidote management is a risk theme which is the root cause of several deficiencies including lack of planning, poor communication, lack of transparency and poor record keeping of antidote availability and use. This risk theme was described as a critical or severe risk theme for most of the monitored antidotes during this study as per developed risk matrices, for both individual cases and mass casualty events. The two antidotes which were deemed to be less sensitive to this risk theme were those with a higher demand and this is mainly so in an individual toxicological case scenario since the impact would be greatly magnified in case of a mass casualty event.

Inaccessibility of antidotes is a risk theme which was recognised in all audit settings however, this issue can be resolved by locating the antidotes in a segregated, easily accessible, and well-labelled location. Murphy *et al.*, (2019) increased accessibility of antidotes through the placement of two highly visible antidote kits in the Emergency Department, one for room temperature antidotes and the other for refrigerated antidotes. This can also be easily applied in A & E of local hospitals since it involves minimal financial investment. In case of certain antidotes which require immediate administration such as hydroxocobalamin, these should be also available for pre-hospital use for example in the paramedic mobile unit to ensure more efficient utilisation.

The risk theme of insufficient training concerns all staff responsible for antidote handling but is most applicable to officers involved in emergency crisis in relation to antidote administration. Training exercises and simulation drills are a vital component of emergency preparedness especially for mass casualty events. Although knowledge is essential, it is not sufficient on its own to ensure optimal performance during an actual crisis event. Such activities will provide the trainee with the necessary operational experience confidence and familiarity with procedures and equipment utilised in case of emergency. Untrained personnel are more likely to experience a psychic trauma which can have a detrimental impact on their operational efficacy in a critical and stressful situation.

The bureaucratic procedures for the introduction of medicines on the GFL and for antidote procurement is a risk theme which has an impact on all antidotes but is more concerning for low demand antidotes and for unexpected urgent delivery requirements. This risk theme also recognises the lengthy process for the introduction of novel antidotes on the GFL. Presently departmental tenders take on average of 6 months to reach the contract agreement and endorsement stages, whereas delivery can take up to an additional 4 months under normal circumstances. Fast track procedures are available through the Emergency Response and the Direct Order units but these are not robust or reassuring either. Contract agreements for antidotes need to cater for the exceptional requirements of antidote need for timely availability. The other alternative is to increase the stocking quantity, but this would imply greater financial costs and probably more wastage due to expired antidotes stocks.

Unreliable suppliers is a risk theme based upon retrospective observations of suppliers' services. Unreliable service includes failing to deliver after awarding of a tender, late deliveries, and temperature excursions of antidotes during transit to CPSU stores. This issue can be mitigated by grading suppliers' service following an assessment and evaluation of past performance especially in the case of antidotes. Grading should be evidence-based on documented state of efficiency and reliability using clear undisputable benchmarks. Such grading should be given due weight when awarding tender offers. This grading can also be used to blacklist suppliers which do not comply with good practice. A similar approach, was tentatively suggested by CPSU and by the Chamber of Commerce where a failing supplier would have been disqualified from participating in tendering process for two years, but this proposal was rejected by the Department of Contracts.

Delay of antidote release is a risk theme which recognises the possibility of delay in treatment availability due to bureaucratic procedures. This may be a consequence of registration issues, issues associated with the Falsified Medicines Directive and over-labelling requirements. In case of an emergency, a waiver may be issued to release the antidote however, measures need to be put in place to ensure rapid processing without delays.

Review of specifications was the only identified risk theme to which not all the focus members agreed upon. However, the researcher deemed it as a critical risk theme which should be given due consideration since this had been the cause of delayed procurement in multiple instances. This study revealed that a reactive approach in the review of specifications is being applied and this restricts the sourcing spectrum which results in

unnecessary delays. A more proactive approach needs to be adopted to ensure that procurement specifications are reviewed regularly to reflect the actual market antidote availability.

Lack of continuous assessment is a risk theme which impacts negatively on the general performance of the management of antidotes and emergency preparedness. The absence of a reliable monitoring and assessment process does not allow management to identify system deficiencies and implement the necessary quality improvements. Without actual assessment of reliable benchmarks, the level of preparedness and competence cannot be evaluated correctly.

4.2 Risk Management for Individual Toxicological Emergencies Preparedness

Locally, twenty-nine antidotes are procured by CPSU for antidote preparedness in the event of individual acute toxicological cases requiring antidote treatment and these are distributed to hospitals according to demand. Available approved standby stock is enough to support initial treatment of a minimum of two acute patients. Atropine sulphate 600mcg injection which is listed as an antidote in case of organophosphate toxicity is also used in cardiology cases involving bradycardia. Due to the multiple clinical indications, atropine sulphate tends to have a higher demand than other antidotes thereby there is an adequate stockpile and if the entities use stocks as per first expire first out system, wastage could be minimised. Acetylcysteine injections are solely indicated as antidotes in paracetamol overdose. Despite having a sole indication, this antidote has a high consumption in Malta due to the relative frequent paracetamol overdose cases presented at A & E MDH. Digoxin immune Fab, activated charcoal, and sodium thiosulphate may

be categorised as having medium consumption level. Although they do not have a constant demand, they have a relatively high turnover compared to other antidotes such as pralidoxime, hydroxocobalamin and sodium nitrite since these are rarely used antidotes.

Expert healthcare professionals from the study focus group noted that there has not been a local case whereby patient care was compromised due to antidote unavailability. Nonetheless, data collected revealed inadequate stocking of five out of the eight (62.5%) monitored antidotes. In the case of digoxin immune Fab, one of the hospitals had an excess of supply while the other hospital needed additional supply. Neither of the two hospitals nor CPSU was aware of the situation since the stocking data records software used by CPSU and the hospitals are not interlinked. This incidence did not lead to compromised patient care however, it did result in costly wastage of many digoxin immune Fab vials. This could have been averted if stocking data was available and used for the redistribution of this antidote, thus allowing utilisation by the other hospital. This highlights the need for better information system management for optimal use of available resources. In 2017, iSTK software was approved by the Government of Malta for stock management and all entities had to employ this software. However, MDH Pharmacy did not use this system and GGH Pharmacy could not use the system as they had a privately owned database. Consequently, the benefits of using iSTK software for the management of pharmaceuticals, could not be reaped.

A basic requirement for optimised management of antidote stocks is the establishment of a common database for information relating to antidotes availability which is accepted and implemented by all parties. This will provide real-time information on stock

availability and better communication between all players. Threshold stock limits and expiry date alarms can be included in the software to minimise room for oversight errors. In addition, where possible operating procedures on the handling and management of antidotes should be simplified, streamlined and common to all users such that procedures are standardised. Presently this is not the case.

Another risk theme identified which is of great concern for management of individual toxicities, is the possibility of requiring an antidote which is not approved and procured in Malta. There is no existing plan of action on how to deal with such a scenario. Given the geographical isolation of Malta, ideally a minimum quantity of all antidotes which require immediate administration are to be stocked and maintained at the two main hospitals. This study recognised three main reasons for not stocking certain antidotes in Malta, (i) lack of antidote requests by physicians, (ii) sourcing issues as in the case of sodium nitrite, and (iii) financial constraints and over bureaucratic processes. These reasons have also been recognised in previous international studies, in addition to other explanations including short shelf life and reliance on nearby hospitals (Eljaoudi *et al.*, 2023). The high expenses of certain antidotes must be weighed against other possibly more significant costs incurred if poisoning is not rapidly reversed with an antidote due to unavailability. In the absence of an antidote, the patient may experience further complications such as organ damage or failure which may result in prolonged hospitalisation as well as additional treatments and follow ups. This will amount to increased patient suffering, higher costs and poorer hospital statistics relating to patient morbidity and mortality.

Antidotes which have been identified by expert healthcare professional as requiring introduction on the GFL and for which they had to fill in applications for introduction, include, cyproheptadine for the management of serotonin syndrome, levocarnitine for the management of severe sodium valproate toxicity, andexanet alpha for the management of apixaban/rivaroxaban toxicity, uridine triacetate for the management of 5-Fluorouracil or capecitabine overdose, and botulinum antitoxin for the management of botulism. Presently, only two of these antidotes, levocarnitine and uridine triacetate are in the process of introduction to the GFL.

4.3 Risk Management for Mass Chemical Casualty Event Preparedness

The occurrence of a mass chemical event is a rare unforeseen and overwhelming situation for which any healthcare system must be prepared to reduce the devastating outcomes through the immediate management of the situation. In Malta, there are different bodies which have a role in emergency preparedness including the Civil Protection Department, the Armed Forces of Malta, the Malta Police Force, and the Ministry for Health and Active Ageing. Despite the availability of all these resources, there is a lack of national strategic plan which incorporates the collaboration of these different bodies in case of a mass toxicological emergency. The availability of different units to tackle emergency preparedness is not enough to ensure efficient performance unless their activities are finely tuned and co-ordinated.

Malta has no active national strategy planning involving a chemical register and a strategic mechanism of action in case of a national toxicological emergency requiring antidote treatment. This study highlights the need for the collaboration of different

sectors within the national public health system to address the deficiencies in the current emergency preparedness and develop a national strategy plan. 'Guideline for Optimisation in the Transparency, Communication and Record Keeping on Local Antidote Availability' was developed to provide a working document on how antidote preparedness can be enhanced through the collaboration of national bodies. In addition to optimised communication of antidote availability, the national strategy plan should include other aspects in emergency preparedness such as logistical and transportation details, decontamination strategies and details on availability of safety equipment including personal protective equipment. A highlighted deficiency in the management of the Tokyo subway sarin attack in 1995 was the uncoordinated response whereby the concerned organisations acted independently from one another with minimal communication involved. According to Okumura *et al.* (1998), this occurred since although existing disaster plans were available, a practical system was not in place. In a mass casualty chemical emergency, time is of the essence. Ensuring preparedness of each organisation involved in emergency management, is crucial to be able to operate under the overwhelming situation in an efficient manner.

4.4 Continuous Assessment for Antidotes and Emergency Preparedness

In Malta, the Antidote Committee meets monthly to discuss emerging antidote issues and since the establishment of this Committee, improvements have been achieved in the availability of antidotes especially with regards to the introduction of new antidotes. However, to have a sustainable effective level of emergency preparedness, it is critical to establish a system which allows for the periodic assessment of antidote management and emergency preparedness in practice. A tool for continuous risk assessment and

evaluation of emergency preparedness must be implemented to optimise the local preparedness situation and work towards a sustainable and more resilient healthcare system.

Israel is regarded as one of the most well-prepared countries in case of a chemical or biological terrorist attack due to its experience in previous and ongoing conflicts. The Israeli healthcare system developed an evaluation tool for emergency preparedness based on measurable and objective parameters including the appraisal of Standard Operating Procedures efficacy, training and field exercises, staff's knowledge, and infrastructure and equipment (Adini *et al.,* 2012). Such an evaluation is performed at each hospital in Israel at least once every two years and a limited evaluation process is performed each year (Siman-Tov *et al.*, 2020). A similar tool for the evaluation of emergency preparedness can be adapted to the local scenario to identify new areas of improvements and to ensure efficient implementation and optimisation of strategies. This requires the establishment of measurable benchmarks which need to be assessed and evaluated objectively over time. Implementation of such a tool may require a radical culture change where the assessor is viewed as a facilitator and helper in the optimisation of efficiency of the operational systems and not as an examiner checking on individual performances of the workforce. Audits act as an eye opener to view the actual state of matters. Audit reports, non-compliances, observations, and recommendations present a clear picture of existing gaps in the system and serve to make improvements and stimulate proactivity.

This research study applied basic elements of SCRM to address the local situation concerning antidote availability and related emergency preparedness. However, a more holistic approach involving both internal and external implementation of tools, techniques

and strategies is needed as well as cooperation with the various supply chain components (Fan and Stevenson, 2018). This approach, if sustained over a time period ensures a more comprehensive and co-ordinated risk management response.

4.5 Recommendations

This study recommends the formalisation of an official antidotes list which includes the name of the antidotes available in the national health system, identity of the bodies stocking the antidotes, the quantities maintained at each site, storage conditions, and timeframe for antidote administration. This information must be available to all relevant National Bodies.

It is recommended that a National Antidote Database is established for the enhanced transparency, communication and record keeping on local antidote availability as per developed guideline (Appendix 5). Restricted access to this database is provided according to need and to safeguard national security.

Common procedures specific for the handling and management of antidotes should be developed and adopted by each body involved in the management of antidotes. This ensures a uniform operational system which simplifies assessment and evaluation by the monitoring entity. Responsibility and authority of bodies need to be clearly defined to ensure no ambiguity, or misunderstanding. Documents should be controlled and reviewed regularly and preferably form part of a quality system. It is recommended to set up a regular training program for all key personnel involved in the handling of antidotes

and other personnel involved in case of a mass emergency event. Training records of participants need to be recorded and maintained for assessment and evaluation.

It is recommended that a National Poison Centre acts as a mediator of toxicological information from point of reporting of intoxication case/event to the management of treatment, which includes decontamination strategies, prevention of secondary exposures and antidotes usability. The National Poison Centre should have a strategic communication plan in place on how and to whom to disseminate information in the event of an emergency.

This study suggests the development of an evaluation tool incorporating measurable benchmarks to aid hospitals to build a sustainable and effective level of emergency preparedness in Malta. In addition, this study recommends the setting up of an assessment team to periodically review and audit the management of antidotes in practice and provide feedback to the Antidote Committee for improvement.

International cooperation agreements at European and global level should be established to facilitate the availability and accessibility of antidotes in a timely, organised manner especially in events of mass exposure. Such agreements can allow the pooling and redistribution of resources especially in cases of mass events. Co-operation may also be possible through international agencies such as the Organisation for the Prohibition of Chemical Weapons which also covers technical assistance in cases of contamination by chemical warfare agents and related toxic chemicals. Agreements need to be robust and preferably backed up by legal means.

4.6 Limitations of the Study

This study reviewed and assessed the management of antidotes at the CPSU, MDH and GGH and did not include other National Bodies which may also be involved in emergency preparedness. These include the Civil Protection Unit, the Police Force, and the Armed Forced of Malta. Such bodies may have additional antidotes available which were not accounted for in this study. No local chemical registry was found to be available, and the Antidote Committee are unaware of the quantities and types of antidotes maintained by different National Bodies, if any. The lack of knowledge of availability of antidotes on a national level, was identified in this study as being a risk and a guideline was developed for increased transparency between different bodies with a role in emergency preparedness.

The vertical audits performed in this research study as part of the risk identification methodology, focused solely on eight antidotes. The data collected for the selected antidotes was limited to only two batches from deliveries over a period of three years. These batches were taken as a representation for all antidotes procured in Malta. The inclusion of more antidotes over a larger timeframe, may have led to the identification of additional risks.

An onsite audit at the main national acute hospital in Malta could not be performed due to lack of cooperation. Instead, data on antidote management was collected through analysis of the Standard Operating Procedures and communication with an intermediary from the hospital's Pharmacy Department. Consequently, information provided could not be verified. Audit reports are not presented in this study due to confidentiality issues.

4.7 Conclusion

Findings from this study indicate local limitations in planning and approving availability of antidotes, and challenging emergency preparedness especially in case of a mass toxicity event. The lack of a contingency plan to source and attain antidotes in a timely manner, makes the situation even more critical and highlights the need for healthcare system optimisation for emergency preparedness. This can be achieved by an ongoing evaluation and assessment process of the management and operational activities aimed at encouraging effective improvement. This study also indicated a willingness by the different actors within the process to improve and strengthen the system at all levels. This is encouraging but must be sustained by concrete action such as adequate training and effective monitoring of progress. Although chemical terrorism and chemical incidents can be said to have a rare occurrence, preparedness is fundamental given the time dependant efficacy of antidotes and the grave implications of system failure.

The three guidelines developed in this study targeted three of the most concerning risk themes identified in this research on the local scenario and seek to harmonise the processes involved in managing emergency preparedness through a risk-based approach. The guidelines and recommendations from this work can serve as a catalyst for local decision makers to take needed measures to mitigate the risks involved in antidote in relation to emergency preparedness. A complimentary study can be conducted to assess and evaluate the actual performance in simulated real life events through an emergency exercise.

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Appendices

Appendix 1

Ethics Approval

L-Università ta' Malta

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Ref No: MED-2023-00269

18 August 2023

Ms Paula Gambin
129 Main Street,
Zabbar
ZBR1200

With reference to your application submitted to the Faculty Research Ethics Committee in connection with your research entitled:

Risk management for Antidote and Emergency Preparedness

The Faculty Research Ethics Committee is granting ethical approval for the above-mentioned application.

Professor Anthony Serracino Inglott
Chair
Faculty Research Ethics Committee

Appendix 2

External Audit Checklists

External Audit Checklist

Accident and Emergency Department Mater Dei Hospital

No.	Question	Response of Auditee and Observations
1	Are there any SOPs available in the handling of antidotes?	
2	Is there an unofficial strategy in place to deal with mass causalities in need of antidotes?	
3	Can you provide a list of antidotes maintained in ED with their Stand-by quantities and storage locations?	
4	Case Scenario: A combustion occurs in the Malta Freeport and there is possibly mass cyanide poisoning. What is the action plan to secure antidote supply?	
5	Do you perform a simulated exercise in case of emergencies requiring antidotes?	

Item 1: Atropine Sulphate 600mcg/ml injection

Batch Numbers: 908010 and A0438A01

No.	Question	Response of Auditee and Observations
1	What quantity of Atropine Sulphate is maintained as Stand- by stock for use as an antidote in organophosphate toxicity?	
2	Actual quantity available?	
3	Where is Atropine sulphate stored? (Request to view site) - What does each treatment box contain? - How many patients does each box treat?	
4	Is temperature monitored? (where are the records kept)	
5	Who is authorised to administer treatment? How many people are authorised?	

6	Who is aware of where this antidote is kept? (is this documented somewhere?)	
7	Who has access to the antidotes? - Is the CN office locked? - Are the keys labelled and where?	
8	Is the expiry date monitored? - See expiry date sheet - Are there any records kept on replacement stocks?	
9	Is there an agreed upon limit by when expiring stock is to be replaced?	
10	When is replacement stock ordered? - Is the note left on a sticky note? - Or is it documented somewhere and stored (logbook)?	
11	Are there any records kept of when an antidote is released and used?	
12	Can you provide an estimate timeframe between the ordering and delivery of supply to ED?	
13	Who orders and delivers the antidote to the ED?	
14	What happens if urgent stock is required? How long does it take for this to be delivered?	
15	Who receives and stores the item at ED?	
16	Did you receive any quantities of Atropine sulphate with batch numbers 908010 and A0438A01 from MDH pharmacy?	
17	Can I see records maintained of: - Receipt - Storage - Expiry date records - Stock replacement/ Disposal Associated with these batch no. if available?	
18	Is redistribution performed for Atropine Sulphate 600mcg/ml injections? If yes, when and how? (any records)	

Item 2: Pralidoxime 1g injections

Batch Number: 933462

No.	Question	Response of Auditee and Observations
1	What quantity of Pralidoxime is maintained as Stand- by stock for use as an antidote?	
2	Actual quantity available?	
3	Where is this item stored? (Can I see the storage area) - Check what is inside the treatment kit	
4	Is temperature monitored? (where are the records kept)	
5	Who is authorised to administer treatment? How many people are authorised?	
6	Who is aware of where this antidote is kept? - (is this documented somewhere? Maybe a chart of ED)	
7	Who has access to the antidotes? - Is the CN office locked? - Are the keys labelled and where?	
8	Is the expiry date monitored? - See expiry date sheet - Are there any records kept on replacement stocks?	
9	Is there an agreed upon limit by when expiring stock is to be replaced?	
10	When is replacement stock ordered?	
11	Are there any records kept of when an antidote is released and used?	
12	Can you provide an estimate timeframe between the ordering and delivery of supply to ED?	
13	Who orders and delivers the antidote to the ED?	
14	What happens if urgent stock is required?	
15	Who receives and stores the item at ED?	
16	Did you receive any quantities of Pralidoxime 1g injections with batch number 933462 from MDH pharmacy?	
17	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	

Item 3: Hydroxocobalamin kit

Batch Number: 1914-02 and 2111-01

No.	Question	Response of Auditee and Observations
1	What quantity of Hydroxocobalamin kit is maintained as Standby stock?	
2	Actual quantity available?	
3	Where is this item stored? How many cyanide poisoning treatment boxes are there? - Every cyanide treatment box has how many Cyanokits? Each kit can treat how many patients?	
4	What is the cyanide poisoning treatment box composed of?	
5	Is temperature monitored? (where are the records kept)	
6	Who is authorised to administer treatment? How many people are authorised?	
7	Who is aware of where this antidote is kept? (is this documented somewhere?)	
8	Who has access to the antidotes? - Is the CN office locked? - Are the keys labelled and where?	
9	Is the expiry date monitored? - See expiry date sheet - Are there any records kept on replacement stocks?	
10	Is there an agreed upon limit by when expiring stock is to be replaced?	
11	When is replacement stock ordered?	
12	Are there any records kept of when an antidote is released and used?	
13	Can you provide an estimate timeframe between the ordering and delivery of supply to ED?	
14	Who orders and delivers the antidote to the ED?	
15	What happens if urgent stock is required?	
16	Who receives and stores the item at ED?	
17	Did you receive any quantities of Hydroxocobalamin kit with batch numbers 1914-02 and 2111-01 from MDH pharmacy?	
18	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	

Item 4: Activated charcoal

Batch Number: 20K04B and 22J14A

No.	Question	Response of Auditee and Observations
1	What quantity of Activated Charcoal is maintained as Stand- by stock?	
2	Actual quantity available?	
3	What quantity is ordered to treat 1 adult patient?	
4	Where is this item stored? (Can I see the storage area)	
5	Is temperature monitored? How? Where are records kept?	
6	Who is authorised to administer treatment? How many people are authorised?	
7	Who is aware of where this antidote is kept?	
9	Is the expiry date monitored? - See expiry date sheet - Are there any records kept on replacement stocks?	
10	Is there an agreed upon limit by when expiring stock is to be replaced?	
11	When is replacement stock ordered?	
12	Are there any records kept of when an antidote is released and used?	
13	Can you provide an estimate timeframe between the ordering and delivery of supply to ED?	
14	Who orders and delivers the antidote to the ED?	
15	What happens if urgent stock is required?	
16	Who receives and stores the item at ED?	
17	Did you receive any quantities of Activated Charcoal with batch numbers 20K04B and 22J14A from MDH pharmacy?	
18	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	
19	Is redistribution performed for Activated Charcoal? If yes, when and how?	

Item 5: Acetylcysteine 200mg/mL injections

Batch Number: T245 and Y241

No.	Question	Response of Auditee and Observations
1	What quantity of Acetylcysteine 200mg/mL injections is maintained as Stand- by stock?	
2	Actual quantity available?	
3	What quantity is ordered to treat 1 adult patient?	
4	Where is this item stored? (Can I see the storage area)	
5	Is temperature monitored? How? Where are records kept?	
6	Who is authorised to administer treatment? How many people are authorised?	
7	Who is aware of where this antidote is kept? (is this documented somewhere? Maybe a chart of ED)	
9	Is the expiry date monitored? - See expiry date sheet - Are there any records kept on replacement stocks?	
10	Is there an agreed upon limit by when expiring stock is to be replaced?	
11	When is replacement stock ordered?	
12	Are there any records kept of when an antidote is released and used?	
13	Can you provide an estimate timeframe between the ordering and delivery of supply to ED?	
14	Who orders and delivers the antidote to the ED?	
15	What happens if urgent stock is required?	
16	Who receives and stores the item at ED?	
17	Did you receive any quantities of Acetylcysteine 200mg/mL injections with batch numbers T245 and Y241 from MDH pharmacy?	
18	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	
19	Is redistribution performed for Acetylcysteine 200mg/mL injections? If yes, when and how?	

Item 6: Sodium Thiosulphate

Batch Numbers: 1927411 and 2223511

No.	Question	Response of Auditee and Observations
1	What quantity of Sodium Thiosulphate is maintained as Stand- by stock?	
2	Actual quantity available	
3	What quantity is ordered to treat 1 adult patient?	
4	Has this item ever been requested by ED?	
5	Who is authorised to administer treatment? How many people are authorised?	
6	If needed, how is it obtained?	
7	How long does it take for an item to be delivered to ED following ordering?	
8	Where is this item stored if delivered?	
9	If item is delivered to ED but not used, what is done with the item? (Or not all delivered quantity is used)	
10	Did you receive any quantities of Sodium Thiosulphate with batch numbers 1927411 and 2223511 from MDH pharmacy?	
11	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	

Item 7: Digoxin immune Fab

Batch Numbers: BN201506C and BN201604D

No.	Question	Response of Auditee and Observations
1	What quantity of digoxin immune Fab are kept as SBS at ED?	
2	Actual Quantity available?	
3	What quantity is ordered to treat 1 adult patient?	
4	Has this item ever been requested by ED?	
5	Who is authorised to administer treatment? How many people are authorised?	
6	If needed, how is it obtained?	
7	How long does it take for an item to be delivered to ED following ordering?	
8	Where is this item stored if delivered? (Can I see the storage area)	
9	Is temperature monitored? How? Where are records kept?	
10	If item is delivered to ED but not used, what is done with the item? (Or not all delivered quantity is used)	
11	Did you receive any quantities of digoxin immune Fab with batch numbers BN201506C and BN201604D from MDH pharmacy?	
12	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	

Item 8: Sodium Nitrite 300mg injections

Batch Numbers: 2098-128A and 2098-137B

No.	Question	Response of Auditee and Observations
1	What quantity of Sodium Nitrite injections are kept as SBS at ED?	
2	Actual quantity available?	
3	What quantity is ordered to treat 1 adult patient?	
4	Has this item ever been requested by ED?	
5	Who is authorised to administer treatment? How many people are authorised?	
6	If needed, how is it obtained?	
7	How long does it take for an item to be delivered to ED following ordering?	
8	Where is this item stored if delivered?	
9	Is temperature monitored? How? Where are records kept?	
10	If item is delivered to ED but not used, what is done with the item? (Or not all delivered quantity is used)	
11	Did you receive any quantities of Sodium nitrite 300mg injections with batch numbers 2098-128A and 2098-137B from MDH pharmacy?	
12	Can I see records maintained of: - Receival - Storage - Expiry date records - Stock replacement/ Disposal associated with these batch no., if available?	

External Audit Checklist

Pharmacy Department Gozo General Hospital

No.	Checklist	Response of Auditee and Observations
1	Is there a policy/standard operating procedure (SOP)/guideline on the receival, storage, dispensing, disposal or redistribution of antidotes?	
2	Which are the antidotes maintained at GGH? Can you provide a list with the quantities maintained as SBS?	
3	Are all antidotes at GGH ordered in the same manner? If yes, how? If no, what is the difference and reason?	
4	In the scenario of an antidote being dispensed, is replacement stock immediately ordered?	
5	Who orders the antidotes? Is there a specific officer assigned? Is the same officer responsible for normal, urgent and extra orders?	
6	Can I see an order request of an antidote?	
7	Who is the order sent to?	
8	Are pre-ordered antidotes on three-monthly basis delivered with other medications between the 3rd week and end of month?	
9	Who receives the antidotes? Is there an officer assigned for the acceptance of supply after hours?	
10	What is checked upon receipt of antidotes?	
11	According to the policy (GGH/Pharm/001), during transportation, a temperature data logger must be present. Refrigerated items must be monitored	

Item 1: Atropine Sulphate 600mcg/ml injection

Batch Numbers: 908010 and A0438A01

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials were delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these two batches: 908010 and A0438A01	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three-monthly basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 2: Pralidoxime 1g injections

Batch Number: 933462

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For this batch: 933462	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How?Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 3: Hydroxocobalamin kit

Batch Number: 1914-02 and 2111-01

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these batches: 1914-02 and 2111-01	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 4: Activated charcoal

Batch Number: 20K04B and 22J14A

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these batches: 20K04B and 22J14A	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three-months basis through the CD list?	
10	Is redistribution performed for this item? When? How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 5: Acetylcysteine 200mg/mL injections

Batch Number: T245 and Y241

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these batches: T245 and Y241	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 6: Sodium Thiosulphate

Batch Numbers: 1927411 and 2223511

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these batches: 1927411 and 2223511	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 7: Digoxin immune Fab

Batch Numbers: BN201506C and BN201604D

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: - Ordering - Receipt - Storage - Dispensing - Disposal For these batches: BN201506C and BN201604D	
4	Where is it stored? Is it in a temperature monitored area? (Store between 2 and 8°C. Do not freeze. Keep vial in outer carton in order to protect from light.)	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

Item 8: Sodium Nitrite 300mg injections

Batch Numbers: 2098-128A and 2098-137B

No.	Checklist	Response of Auditee and Observations
1	Do you keep SBS for use as an antidote? If, yes what quantity is maintained as standby stock?	
2	How many vials where delivered between June 2020 and June 2023?	
3	Can you kindly provide any documentation of: □ Ordering □ Receipt □ Storage □ Dispensing □ Disposal For these batches: 2098-128A and 2098-137B	
4	Where is it stored? Is it in a temperature monitored area <25°C?	
5	Have you ever been out of stock of this item between June 2020 and June 2023? Reason?	
6	Was an urgent order performed for this item between June 2020 and June 2023? Why?	
7	Was an extra order performed for this item between June 2020 and June 2023? Why?	
8	How long does it take for an urgent order to be delivered in case of an emergency? (approximately)	
9	How is this item generally ordered? On a three months basis through the CD list?	
10	Is redistribution performed for this item? When How? Why?	
11	Can you kindly provide data on the quantity of the is item discarded between June 2020 and June 2023, and batch numbers?	
12	What is done in case of mass casualties requiring the use of this antidote? Any contingency plan?	

External Audit Checklist

Central Procurement and Supplies Unit

No.	Checklist	Response of Auditee and Observations
1	Are there any SOPs/policies/guidelines or other relevant documents available in the procurement of antidotes?	
2	Are all antidotes procured by the same officer?	
3	Are all antidotes procured in the same manner?	
4	Can you describe the procurement process of antidotes?	
5	Are antidotes problematic to source? Why?	
6	Are antidotes problematic to procure? Why	
7	Is there a contingency plan in case of mass casualties requiring antidote use?	
8	Is there a contingency plan in place, in case of an acute case requiring the use of antidote which is not procured?	

Item 1: Atropine Sulphate 600mcg/ml injection

Batch Numbers: 908010 and A0438A01

No.	Checklist	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores? If no, why?	
2	Is item problematic to source? Why?	
3	Have there been any past issues with the sourcing and procurement of this item?	
4	Is item sourced from a sole manufacturer? If yes, why?	
5	How long does it take for a cycle to be established? Approximate time frame.	
6	When is a new call issued?	
7	What happens if no offers are received for a call?	
8	When is a new order placed?	
9	How long does it take for supply to arrive when an order is placed?	
10	Any disruptions in delivery of procured items? (request examples)	

11	Do you recall whether this item was ever OOS at CPSU and entities?	
12	What records are kept of Batch no. 908010 and A0438A01?	
13	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
14	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 2: Pralidoxime 1g injections

Batch Number: 933462

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues between June 2020- June 2023 with the sourcing and procurement of this item?	
5	Is item sourced from a sole manufacturer? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items? Check Batch no. 933462.	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	Do you monitor expiry dates of this antidote?	
13	When is a new order placed? (Check time period between placing dispensing to entities and placing of order between June 2020- June 2023)	
14	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
15	What records are kept of Batch no. 933462?	

16	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
17	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 3: Hydroxocobalamin kit

Batch Number: 1914-02 and 2111-01

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole manufacturer? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items? (Check 1914-02 and 2111-01)	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	Do you monitor expiry dates of this antidote?	
13	When is a new order placed?	
14	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
15	What records are kept of Batch no. 1914-02 and 2111-01?	
16	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
17	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 4: Activated charcoal

Batch Number: 20K04B and 22J14A

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole Manufacturer? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items? (20K04B and 22J14A)	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	Do you monitor expiry dates of this antidote?	
13	When is a new order placed? (20K04B and 22J14A)	
14	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
15	What records are kept of Batch no. 20K04B and 22J14A?	
16	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
17	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 5: Acetylcysteine 200mg/mL injections

Batch Number: T245 and Y241

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole supplier? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items?	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	When is a new order placed?	
13	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
14	What records are kept of Batch no. 18L10A and 22J14A?	
15	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
16	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 6: Sodium Thiosulphate

Batch Numbers: 1927411 and 2223511

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole supplier? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items?	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	When is a new order placed?	
13	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
14	What records are kept of Batch no. 1927411 and 2223511?	
15	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
16	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 7: Digoxin immune Fab

Batch Numbers: BN201506C and BN201604D

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole supplier? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items?	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	When is a new order placed?	
13	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
14	What records are kept of Batch no. BN201506C and BN201604D?	
15	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
16	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Item 8: Sodium Nitrite 300mg injections

Batch Numbers: 2098-128A and 2098-137B

No.	Question	Response of Auditee and Observations
1	Is this item treated as a Standby Stock (SBS) item? If yes, what quantity is maintained as SBS at CPSU stores?	
2	What quantity is currently available at CPSU stores?	
3	Is item problematic to source? If yes, why?	
4	Have there been any past issues with the sourcing and procurement of this item?	
5	Is item sourced from a sole supplier? If yes, why?	
6	What was done in case of problematic sourcing?	
7	Is there an active cycle for this item?	
8	How long does it take for a cycle to be established? Approximate time frame.	
9	Any disruptions in delivery of procured items?	
10	When is a new call issued?	
11	What happens if no offers are received for a call?	
12	When is a new order placed?	
13	How long does it take for supply to arrive when an order is placed? (ask for examples from specific batch no.)	
14	What records are kept of Batch no. 2098-128A and 2098-137B?	
15	If supply is being urgently requested by entities, and nil stock or not enough stock is available at CPSU stores, is there a contingency plan in place to attain supply? What is the timeframe?	
16	In case of mass casualties requiring the use of this antidote, is there a contingency plan for sourcing and procurement of antidote?	

Appendix 3

Raw Data Thematic Analysis

Risk Theme	Codes	Raw data
Problematic Sourcing	Sole Manufacturer	'Sodium Nitrite has always been procured from a sole manufacturer' and 'item is problematic to source since no offers are being received' 'Hydroxocobalamin kit is produced by a sole manufacturer' 'All past tenders of pralidoxime 1g injections were of a sole manufacturer'
	Antidote shortage	There has been an international shortage of digoxin immune Fab in 2023 due to an increase in demand. Sodium nitrite 300mg injections – no supply available at MDH and CPSU.
	Sourcing issues due to demographics	'Malta is a very small country which is also an island, hinders further the sourcing of antidotes'
	Limited manufacturers	'limited number of manufacturers produce antidotes, making these medicinal products problematic to source' 'may be problematic to source since it is attained from a sole manufacturer'
	No quotes on published procurement calls	Pralidoxime 1g injections – 'nil offers were received for multiple procurement calls' Sodium Nitrite 300mg injections - 'specifications were recently amended in view that no offers were received', 'last contract was awarded in 2017 and this was abandoned' Activated charcoal – 'there were sourcing issues since nil offers were being quoted for this antidote'
Bureaucratic Procurement Process	Lengthy delivery period	Pralidoxime 1g injections – 'this batch was delivered 16 weeks following the placement of order' Contract conditions do not cater for urgent deliveries
	Lengthy process to issue a procurement cycle and secure a contract	'a procurement cycle takes approximately six to nine months', 'it varies depending on the type of procurement call issued, whether offers are received, and the amount of hastening performed'
	Bureaucratic process for antidote introduction	'Approval to increase the quantities of standby stock and approval for the introduction of new antidotes is a very lengthy process'

Risk Theme	Codes	Raw data
Inadequate stocking	Incorrect demand forecast	'Entities cannot provide an accurate demand of antidotes given that the use of antidotes is unforeseeable.' 'do not have the right demand' 'The industry is requesting a forecasted demand two years prior'
	Insufficient SBS in case of a mass event	6 hydroxocobalamin kits available at GGH. 10 hydroxocobalamin available at A & E MDH 10 hydroxocobalamin available at CPSU This equates to a single dose treatment of 26 adult patients 48 Obidoxime vials available in case of organophosphate poisoning
	Standby stock is not maintained	The quantity of Acetylcysteine found in the drawer was noted to be 3 vials of Parvolex® 200mg/ml Concentrate for Solution for Infusion – Standby stock is of 30 units MDH had inadequate stocking of atropine 600mcg/ml injections, activated charcoal, acetylcysteine, sodium nitrite and digoxin immune Fab. CPSU had inadequate stocking of activated charcoal, atropine sulfate, acetylcysteine, and sodium nitrite. 'The auditee stated that it is very difficult to maintain stand by stock of sodium thiosulphate due to the increase in demand' 'In case of urgent need for an antidote (antidote is not available/ more quantities are required), GGH Pharmacy Department contacts CPSU to check whether stock is available. If item is available at CPSU stores or may be redistributed, stock will arrive within the same day or even within a few hours.'
	Unofficial standby stock quantities	'does not have an official antidote list with an approved amount of stand by quantities' 'stocks maintained are not officially quantified' 'always try to keep a total quantity of five Digoxin Antibody' 'has no official stand by list, it is ensured that 80 units of atropine are always available'
	Inadequate stocking due to multiple indications	'demand of this antidote is erratic since it is not only used as an antidote'

Risk Theme	Codes	Raw data
Inadequate stocking	Inconsistent notification when standby stock is used	'CPSU is not always informed when antidotes are dispensed by entities leading to untimely orders and inadequate stocking. This has occurred for example with activated charcoal, digoxin immune Fab and sodium thiosulphate injections. 'supply is not ordered upon use'
	Demand variations	'item is not solely used as an antidote but it is being increasingly prescribed in renal wards for the prevention or treatment of renal calciphylaxis. The auditee stated that it is very difficult to maintain stand by stock of this item due to the increase in demand'
	Untimely restocking	'Ordering is done weekly through the Emergency Department pharmacist and if stock is low or unavailable, it is done on a necessary basis by the Emergency Department charge nurse'
	Overstocking	'Large quantities of digoxin immune Fab wasted due to overstocking'
Unreliable suppliers	Transportation issues	'sometimes pharmaceuticals may be delivered late due to a courier missing the scheduled transportation'
	Temperature excursions	'temperature excursions during transportations may result in either delayed antidote availability of unavailability in the case that antidote is no longer safe to use'
	Failure to register antidote	'If a supplier through a normal tender delivers an unregistered antidote, this item cannot be released and made available prior to registration'
	Supplier not accepting award on e-PPS	'there is loss of time in establishing a tender in cases whereby the successful bidder fails to abide to timeframes especially when it comes to accepting award on e-PPS and endorsing the contract agreement'
	Urgent order not delivered	'no guarantee that the antidote will be delivered when ordered through the urgent route' 'order was placed but never received'
	Failure to deliver by due date	'supplier was late in delivery'
Omission of antidotes from formulary	Antidote not listed on the formulary	New antidotes require introduction on the Government Formulary List
Lack of continuous assessment	Lack of antidote assessment	'no schedules assessment of antidotes'
	No evaluation strategy in place for antidotes	'Antidote Committee is an advisory committee'

Risk Theme	Codes	Raw data
Inaccessibility issues	Lack of visible notice where antidotes are kept	'None of these cupboards were labelled' 'The CBRN storage cupboard was not labelled' 'These were located on the top shelf of a shelved cupboard with other antidotes. This shelf was not labelled' Emergency trolleys containing antidotes were not fully labelled.
	Inefficient segregation	'no segregation between different drugs' 'These were stored on a different shelving cupboard than the other antidotes'
	Time wastage due to storage location	'If for some reason the Charge Nurse is unavailable, the senior nurses must contact security to gain access' 'Obstruction of CBRN cupboard' 'Item not maintained in the Emergency Department' 'require a ladder to reach the antidotes'
	Inaccessibility of antidote data	'We did not know that antidote was available'
	Inaccessibility to key for CBRN storage area	'Keys of the CBRN cupboard were kept in the Charge Nurse office which is electronically access controlled using a swipe card held by the Charge Nurses. If for some reason the Charge Nurse is unavailable, the senior nurses must contact security to gain access.' 'The CBRN cupboard key included four keys, each with a different colour but none of which were labelled' Key positions in key cabinet are not labelled
	Unavailability of antidotes	'Pralidoxime, sodium nitrite and sodium thiosulphate were never stocked' 'If item is available at CPSU stores or may be redistributed, stock will arrive within approximately two hours by ferry.'

Risk Theme	Codes	Raw data
Insufficient Training	Lack of simulated training exercises	'couple of years ago a form of simulation exercise was performed in conjunction with the Civil Protection Department in Malta however, this is not done regularly'
	Lack of knowledge	'very few know what the antidotes are used for, let alone how they are administered'
	Training interest	'auditee expressed interest in having such simulations and stated that training is required specifically with regards to antidotes'
	Time wasted in searching for technique of antidote administration	'the nurse checks on TOXBASE® for directions on administration (D4). If directions are not clear or unavailable at that moment, they will contacts the Pharmacy Department for assistance on administration procedure.'
Delay of antidote release	Registration issues	'The ordered item was of registration number AA565/37701 PL18157/0020. Item received was PL51463/0098. This item is not registered by CPSU. Item could not be released immediately and CPSU had to incur further costs for the release of the item through article 20.'
	Temperature excursion	'Batches of digoxin immune Fab experienced temperature excursions'
	Over-labelling	're-labelling - took 92 days for antidote to be released' 'antidote delivered in a foreign language'
	Batch Specific Release required	'Product comes from Germany- relabelling or a batch specific release is required'
	Delayed release	'delayed release of antidotes from quarantine may be due to registration issues, Falsified Medicines Directive non-compliance, temperature excursions, damaged item delivered, incorrect item delivered'
Review of specifications	Specifications for procurement not updated according to market availability	'in 2022 calls were being cancelled due to unavailability of technical compliant product. Specifications were opened to include acceptance of 500mcg/ml injections. Item was sourced following review of specifications'
	Specifications updated following calls cancellation	'Following cancellation of 2 consecutive calls due to no offers, Directorate of Pharmaceutical Affairs were notified of sourcing issues and specifications were updated.'

Risk Theme	Codes	Raw data
Lack of Policies, Procedures and Contingency plans	No policy in place for expired antidotes	'Any expired medication are segregated and placed in the Charge Nurse office. No logbook is maintained' 'Expired antidotes are not removed from the shelf unless replacement stock is available (D6). A notice is placed on the medication to alert that the antidote is expired.' 'Expired antidotes are not discarded prior to better dated supply is available'
	Lack of procedures on antidote procurement in case of mass casualties	'available antidote stocks are not sufficient for mass toxicological events' 'an international agreement is needed to attain antidotes fast'
	Lack of temperature control	'CBRN storage cupboard was located in a non-air-conditioned corridor close to the Charge Nurse office'
	Lack of procedures notes for management of standby stock	'no notification system in place for a change in officer responsible for antidotes' 'lack of consistency in ordering strategy of antidotes' Lack of procedures in place specifically for antidotes in any of the audited settings
	Non-uniform strategy of antidote ordering	'CPSU is not always informed when this antidote is dispensed by entities'
	Lack of policy notes	'no policy notes specific to the procurement of antidotes'
	No procedures in place for handling of antidotes	There are no policy notes which are specific to the handling of antidotes 'no procedure in place for handling stand-by stock items'
	Inefficient ordering system	Policy notes are not organised and easily accessible
	No official contingency plan for the timely procurement of unavailable antidotes	'In real urgent cases CPSU could post-Exceptional Medicinal Treatment Committee approval issue urgent cycles' 'No contingency plan is in place for the procurement of antidotes in case of a mass event or for the urgent procurement of an antidote which is unavailable in Malta'

Risk Theme	Codes	Raw data
Lack of transparency, poor communication and record keeping	Inefficient coordination	‘There is inefficient coordination between different bodies’ ‘time wasted hunting stock without being informed that item was unlicensed’ ‘not always informed when antidotes are dispensed by entities’ ‘no notification system in place for a change in officer responsible for antidotes’
	Lack of reliable data storage	‘Due to a change in concession agreement, the online stock system was put on hold and previous data was lost’
	Lack of traceability	No date of when orders were placed for these batches was found on the procurement card
	Poor accessibility to policy notes	‘external stakeholder policy governing the procurement of antidotes’ – not available to procurement officer
	Lack of records	‘Available records did not contain the batch numbers of medications. Available records including batch numbers were only of batches which were received since September 2023’ ‘Traceability of batches of selected antidotes could not be performed due to lack of batch numbers records.’ ‘No records of antidote use, redistribution and orders’ ‘No temperature records’
	Lack of knowledge on national antidote availability	‘are the private companies stocking antidotes?’ ‘we are unaware of which antidotes other national bodies have, if any’
	No chemical registry	‘there is no national chemical registry available’
	Lack of data on antidote use	‘Records of antidote usage are not kept’

Appendix 4

Risk Matrices

Risk matrix of atropine sulphate 600mcg/ml injections for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Lack of policies				
	High	Bureaucratic procurement process			Review of Specifications	
	Medium	Inadequate stocking	Unreliable suppliers	Lack of national strategy plan		Problematic Sourcing, Inaccessibility issues
	Low					Insufficient training, Lack of continuous assessment
	Very Low	Delay of antidote release				

Risk matrix of atropine sulphate 600mcg/ml injections for mass casualty events

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High					Lack of policies, Inadequate stocking
	High					Review of Specifications Bureaucratic procurement process
	Medium					Problematic Sourcing, Unreliable suppliers, Lack of national strategy plan, Inaccessibility issues
	Low					Lack of continuous assessment, Insufficient training
	Very Low					Delay of antidote release

Risk matrix of pralidoxime 1g injections for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Insufficient training, Lack of continuous assessment	Inaccessibility issue, Lack of policies			Lack of national strategy plan
	High		Problematic sourcing, Bureaucratic procurement process	Review of specifications		
	Medium			Inadequate stocking		
	Low		Unreliable Suppliers			
	Very Low		Delay of antidote release			

Risk matrix of pralidoxime 1g injections for mass casualty events

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High		Inaccessibility issue			Inadequate stocking, Insufficient training, Lack of policies, Lack of national strategy plan, Lack of continuous assessment
	High			Review of specifications		Problematic sourcing, Bureaucratic procurement process
	Medium					
	Low					Unreliable Suppliers
	Very Low		Delay of antidote release			

Risk matrix of hydroxocobalamin kit for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Inadequate stocking, Lack of continuous assessment	,			Insufficient training, Lack of policies, Lack of national strategy plan,
	High		Bureaucratic procurement process			Inaccessibility issue
	Medium					
	Low	Review of specifications, Unreliable suppliers	Problematic sourcing			
	Very Low					Delay of antidote release

Risk matrix of hydroxocobalamin kit for mass casualty events

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High					Problematic sourcing, Inadequate stocking, Insufficient training, Lack of policies, Lack of national strategy plan, Lack of continuous assessment, Delay of antidote release
	High					Bureaucratic procurement process, Inaccessibility issue
	Medium					
	Low	Review of specifications				Unreliable Suppliers
	Very Low					

Risk matrix of sodium thiosulphate for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Problematic sourcing, Lack of continuous assessment	,		Inadequate stocking	Insufficient training, Lack of policies, Lack of national strategy plan,
	High		Bureaucratic procurement process			Review of specifications, Inaccessibility issue
	Medium		Delay of antidote release			
	Low	Unreliable suppliers				
	Very Low					

Risk matrix of sodium thiosulphate for mass casualty events

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High					Problematic sourcing, Inadequate stocking, Insufficient training, Lack of policies, Lack of national strategy plan, Lack of continuous assessment
	High					Bureaucratic procurement process, Review of specifications, Inaccessibility issue
	Medium					Delay of antidote release, Unreliable Suppliers
	Low					
	Very Low					

Risk matrix of sodium nitrite for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Problematic sourcing, Lack of continuous assessment	Inadequate stocking			Insufficient training, Lack of policies, Lack of national strategy plan,
	High	Bureaucratic procurement process	Inaccessibility issue			Review of specifications
	Medium					
	Low		Delay of antidote release, Unreliable suppliers			
	Very Low					

Risk matrix of sodium nitrite for mass casualty events

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High					Problematic sourcing, Inadequate stocking, Insufficient training, Lack of policies, Lack of national strategy plan, Lack of continuous assessment
	High					Bureaucratic procurement process, Review of specifications, Inaccessibility issue
	Medium					
	Low					Delay of antidote release, Unreliable Suppliers
	Very Low					

Risk matrix of digoxin immune Fab for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High		Lack of continuous assessment		Lack of policies, Insufficient training	Lack of national strategy plan
	High		Bureaucratic procurement process, Inadequate stocking,			Unreliable suppliers
	Medium		Inaccessibility issue			
	Low	Review of specifications	Problematic sourcing,			Delay of antidote release
	Very Low					

Risk matrix of activated charcoal for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High		Lack of policies	Lack of national strategy plan, Lack of continuous assessment		Problematic sourcing
	High		Bureaucratic procurement process	Inadequate stocking, Unreliable suppliers		
	Medium		Delay of antidote release			
	Low	Review of specifications	Problematic sourcing, Insufficient training			
	Very Low		Inaccessibility issue			

Risk matrix of acetylcysteine for individual acute cases

Impact		Very Low	Low	Medium	High	Very High
Probability	Very High	Lack of policies, Lack of national strategy plan		Insufficient training		Problematic sourcing
	High		Lack of continuous assessment			
	Medium			Inadequate stocking	Bureaucratic procurement process	
	Low		Delay of antidote release, Unreliable suppliers	Inaccessibility issues	Review of specifications	
	Very Low					

Appendix 5

Guidelines

Guideline for Optimisation in the Procurement of Problematic to Source Antidotes

Date of Issue: April 2024

1.0 Scope

1.1 The aim of this guideline is to provide healthcare professionals with strategies for optimisation of local antidote emergency preparedness with respect to problematic sourcing.

2.0 Definitions

2.1 Problematic to source antidotes: antidotes which could not be sourced through the publication of open procedures following the issuing of at least two open calls for procurement of the antidote.

2.2 Market Research: an ongoing process involving the screening for local and international antidote availabilities for the optimisation of formulary antidote specifications and identification of potential new antidotes.

2.3 Horizon Scanning: systematic process for the identification of emerging medicinal products and assessment of possible threats and opportunities to the healthcare system.

2.4 Stand by stock: a defined quantity of antidotes which must be always present and solely used for specified toxicological emergencies.

2.5 Central Processing and Supplies Unit: Contracting Authority responsible for acquiring cost-effective and quality supplies, materials and works for the Ministry of Health. This includes the sourcing and procurement of pharmaceutical products including antidotes.

2.6 Directorate of Pharmaceutical Affairs: directorate responsible for the establishment of the Government formulary list and implementation of sustainable pharmaceutical policies.

2.7 Antidote Committee: An interprofessional working group responsible for the management of antidotes in Malta.

2.8 Malta National Poison Centre: local specialised unit in the prevention, diagnosis, and management of poisoning.

2.9 Procurement officer: officer responsible for the purchasing of antidotes on the government formulary list in line with the procurement regulations currently in force and maintaining appropriate stock levels through reviewing and ordering of antidotes.

3.0 List of Abbreviations

3.1 SBS: Stand by stock

3.2 CPSU: Central Processing and Supplies Unit

3.3 DPA: Directorate of Pharmaceutical Affairs

4.0 Responsibility

4.1 It is the responsibility of the procurement officer to notify the Head of Procurement and Directorate of Pharmaceutical Affairs (DPA) on any problematic to source antidotes, available quantities and expected availability of new consignment.

4.2 It is the responsibility of pharmacists within the DPA to perform extended Market Research on problematic to source antidotes, communicate findings with the Antidote Committee, amend specifications accordingly, and inform the procurement officer.

4.3 It is the responsibility of DPA to notify medical practitioners in the Emergency Department of problematic to source antidote.

4.3 It is the responsibility of the Antidote Committee to address mitigation strategies for problematic to source antidotes.

5.0 Guideline

5.1 Performance of Market Research and Horizon Scanning to identify antidote or alternative/s availability in other Member States/other countries (Appendix 1). In the case that:

(i) **An antidote with different specifications or a suitable alternative is available**: amend specifications accordingly to include all possible formulations available. Forward amended specifications to the Antidote Committee for approval.

(ii) **No alternative is available**: inform Antidote Committee and Malta National Poison Centre. Include antidote on 'CPSU Problematic to source items list`. Intensify the market research effort for sourcing of antidote or alternative and consider arrangements of joint procurement through the European Union. Establish a list of international hospitals for the possibility of supplying the antidote in case of urgency.

(iii) **An alternative is already being procured**: increase quantity to be maintained as stand by stock (SBS) accordingly.

5.2 Check stock available and expiry of antidote at all entities (Appendix 2) to assess availability and be able to relocate antidotes if necessary. In the case that:

(i) **Entities are adequately stocked** as per approved SBS quantity, procurement officer is to issue a new call with amended specifications.

(ii) **Entities are inadequately stocked** as per approved SBS quantity, procurement officer is to issue an order to top up SBS quantity and issue a new call with the amended specifications.

(iii) **Entities are overstocked**, perform re-distribution of antidote between entities and procurement officer is to issue a new call with amended specifications.

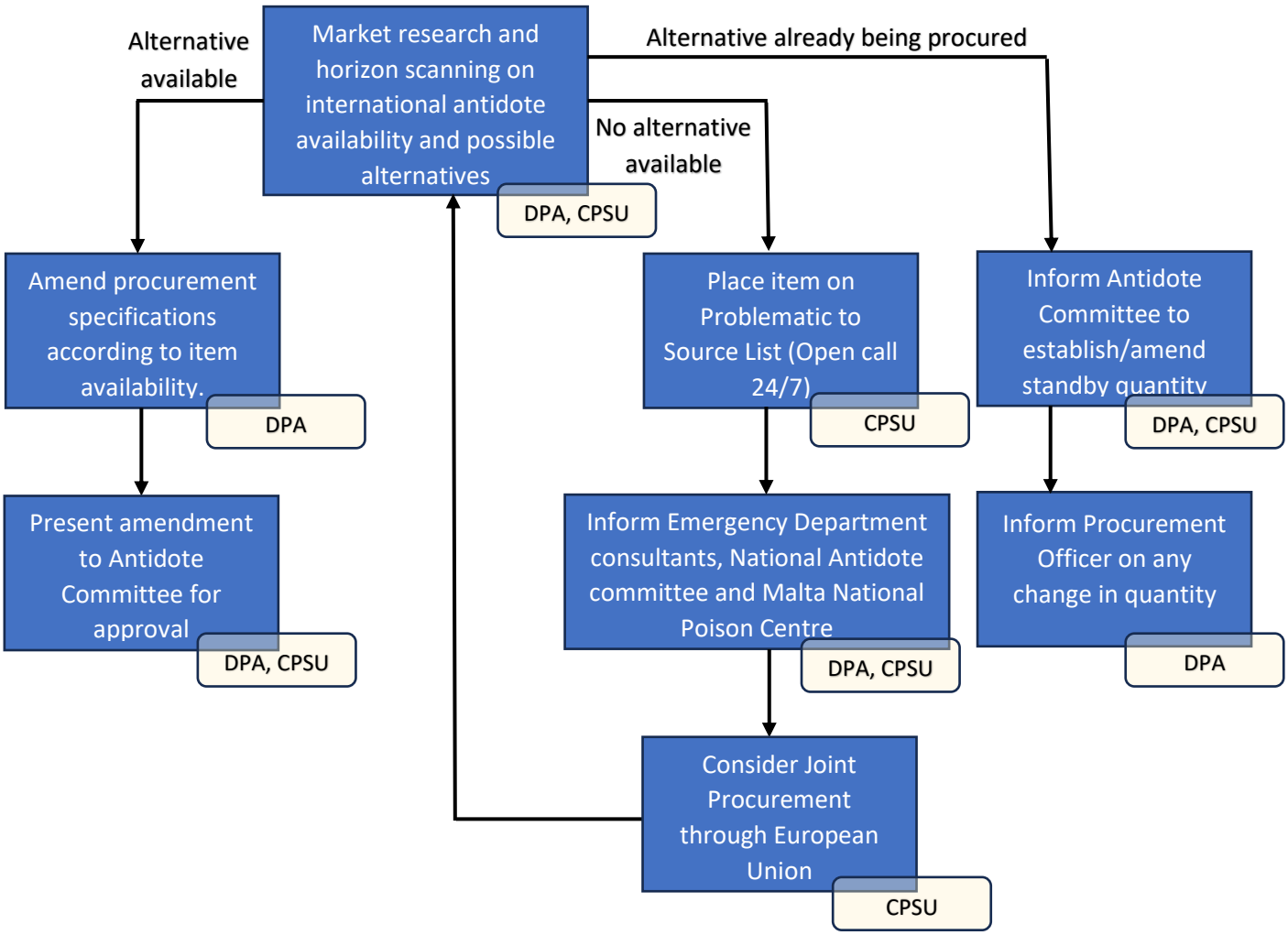
5.3 Communication with end user: Notify Malta National Poisons Centre, emergency consultants and Emergency Department medical practitioners on problematic sourcing of antidote, present available quantities and expected availability of new consignment. Problematic to source antidote is to be prescribed only for emergency cases.

6.0 Appendices

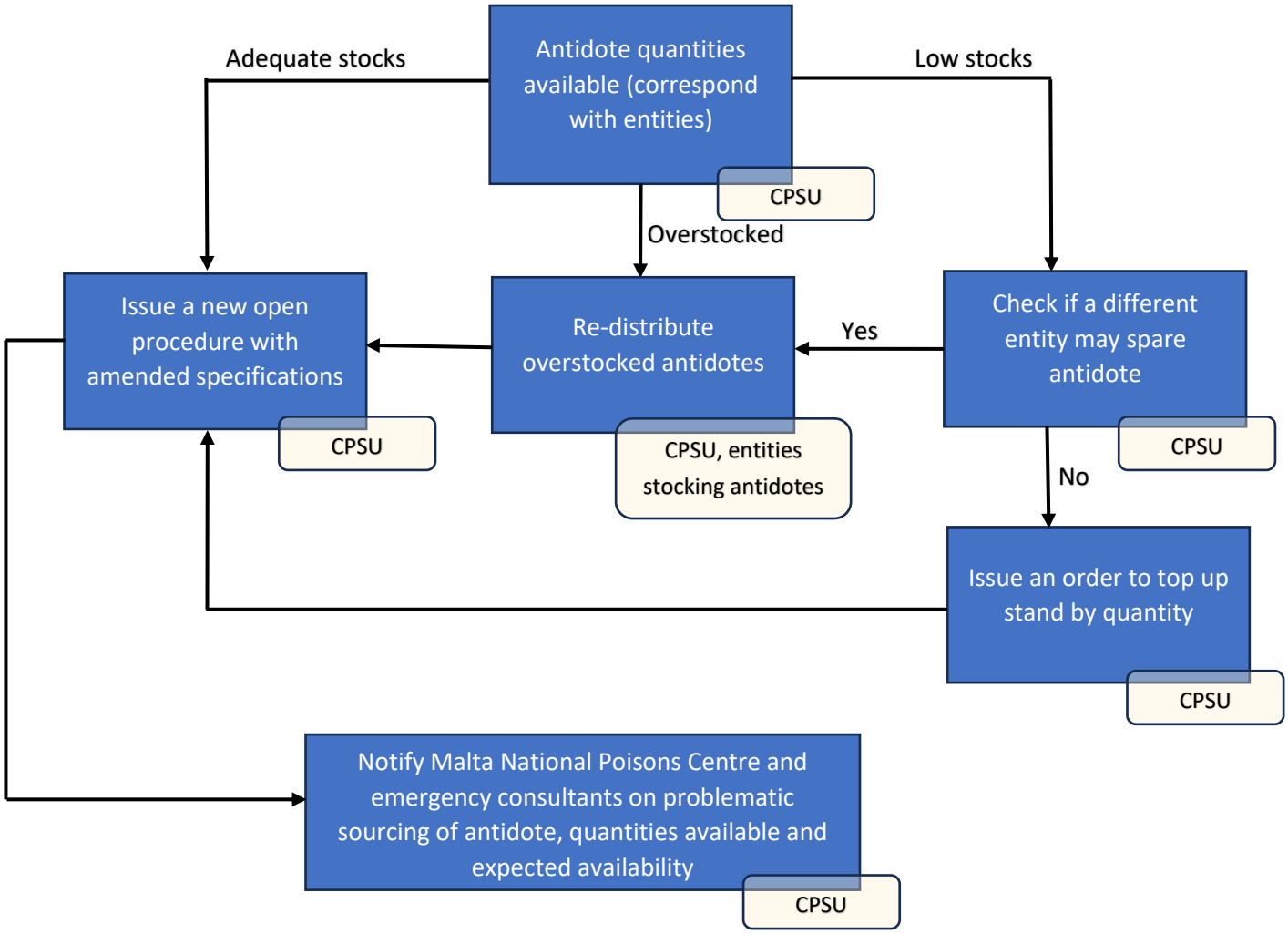
Appendix 1 Action plan according to market research for problematic to source antidotes

Appendix 2 Action plan according to stock position, in problematic to source antidotes

Appendix 1 - Action plan according to market research for problematic to source antidotes



Appendix 2 Action plan according to stock position, in problematic to source antidotes



Guideline on Stocking of Antidotes

Date of Issue: April 2024

1.0 Scope

1.1 The aim of this guideline is to provide healthcare professionals with strategies for optimisation in the stocking of antidotes. This guideline is divided into two sections to provide antidote stocking guidance for two possible scenarios:

(i) Individual acute cases

(ii) Mass casualty events

2.0 Definitions

2.1 Individual acute cases: is a one-off toxicological case which is not a representation of any general pattern.

2.2 Mass casualty: an event which results in the toxicity of several number of patients.

2.3 National list of antidotes: a list of antidotes stocked at a national level which must be available at any moment in time in the approved quantity.

2.4 Standby stock items: antidotes which are maintained as stand by and solely used in case of a toxicological emergency.

2.5 Central Processing and Supplies Unit (CPSU): Contracting Authority responsible for acquiring cost-effective and quality supplies, materials and works for the Ministry for Health and Active Ageing. This includes the sourcing and procurement of pharmaceutical products including antidotes.

2.6 Government Formulary List (GFL): a list of medicinal products including antidotes which have been approved for use in the national healthcare services.

2.7 Antidote Committee: an interprofessional working group responsible for the management of antidotes in Malta.

2.8 Directorate of Pharmaceutical Affairs: directorate responsible for the establishment of the Government formulary list and implementation of sustainable pharmaceutical policies.

3.0 List of Abbreviations

3.1 SBS: Stand by stock

3.2 CPSU: Central Processing and Supplies Unit

3.3 DPA: Directorate of Pharmaceutical Affairs

3.4 GFL: Government Formulary List

4.0 Responsibility

4.1 It is the responsibility of the Antidote Committee to raise request for a National list of antidotes.

4.2 It is the responsibility of the Contracting Authority (CPSU) to procure adequate quantities of antidotes and advise DPA in case of problematic sourcing.

4.3 It is the responsibility of each Pharmacy Department which stocks antidotes to ensure adequate amounts of antidotes are maintained as per approved quantity and to order replacement stock from CPSU in a timely, organised manner.

4.4 It is the responsibility of each entity which stocks antidotes used for multiple indications, to ensure that a strategy is in place for stock rotation with the aim of maintaining stock with the longest expiry date as SBS.

4.5 It is the responsibility of the Antidote Committee to ensure periodic review of antidotes included in the Government Formulary list and of quantities to be maintained as SBS.

5.0 Guideline on stocking of antidotes for individual acute cases (Appendix 1)

5.1 Establish an official National list of antidotes to be procured for individual acute cases, including the minimum quantities to be maintained of each antidote. This list is made available to the Antidotes Procurement Section, Pharmacists and Pharmacy Technicians responsible for handling antidotes and stand by stock items at each entity stocking antidotes and to Emergency Department consultants and medical practitioners.

5.2 A monthly internal antidote stock take is to be performed by each department stocking antidotes to ensure that antidotes are well stocked as per approved quantities and to ensure that items are within shelf-life. In case that quantities do not tally with the approved quantities, the Contracting Authority (CPSU) should be notified for necessary actions (replenishment in cases of low stock or redistribution in case of overstocking). If quantity of antidotes does not tally with official approved quantities, discrepancy should be investigated, and necessary action taken to avoid recurrence.

5.3 CPSU is to stock replenishment supply equating to the same quantity to be maintained as SBS by all entities.

5.4 For antidotes used for other indications, rotate stock to ensure that the SBS always has the longest expiry date. Store antidote SBS in an accessible, clearly labelled location

separate from the other stock for use in other indications. This ensures that antidote SBS is solely utilised for toxicological emergencies and that the appropriate quantities are maintained.

5.5 For antidotes which need to be included to the Government Formulary List:

(i) Malta National Poisons Centre, and/or Clinical Toxicologists, and/or Emergency Department consultants, and/or any other relevant consultants are to propose the inclusion of required antidote to the Antidote Committee.

(ii) Antidote Committee reviews proposal and if approved, committee is to submit necessary documentation to DPA to raise request to procure the antidotes.

(iii) DPA to secure funding to support required quantities.

(iv) Following receipt of necessary approvals, CPSU is to initiate procurement cycle for double the estimated quantity to ensure availability of replacement stock.

5.6 An annual review of the National list of antidotes included in the GFL for individual acute cases must be performed by the Antidote Committee to assess need for amendments to the list.

6.0 Guideline on stocking of antidotes for mass casualty event:

6.1 Establish an official National list of antidotes to be procured for mass casualty events, including the minimum quantities to be maintained for each antidote, and the estimated number of patients the SBS would cater for in case of an emergency. This should be based upon a Hazard Vulnerability Analysis performed for the local scenario.

6.2 Establish a stockpile for antidotes which must be immediately administered in case of emergencies. Where possible, the financial burden can be lessened by applying a shelf-life extension program which allows for the extension of a medication's shelf life of properly stored items. This requires close liaison with manufacturer/supplier and possibly may also require periodic stability testing.

6.3 Storage of antidote stockpile must be in a protected and secure location within a controlled environment. Location must be easily accessible and clearly labelled.

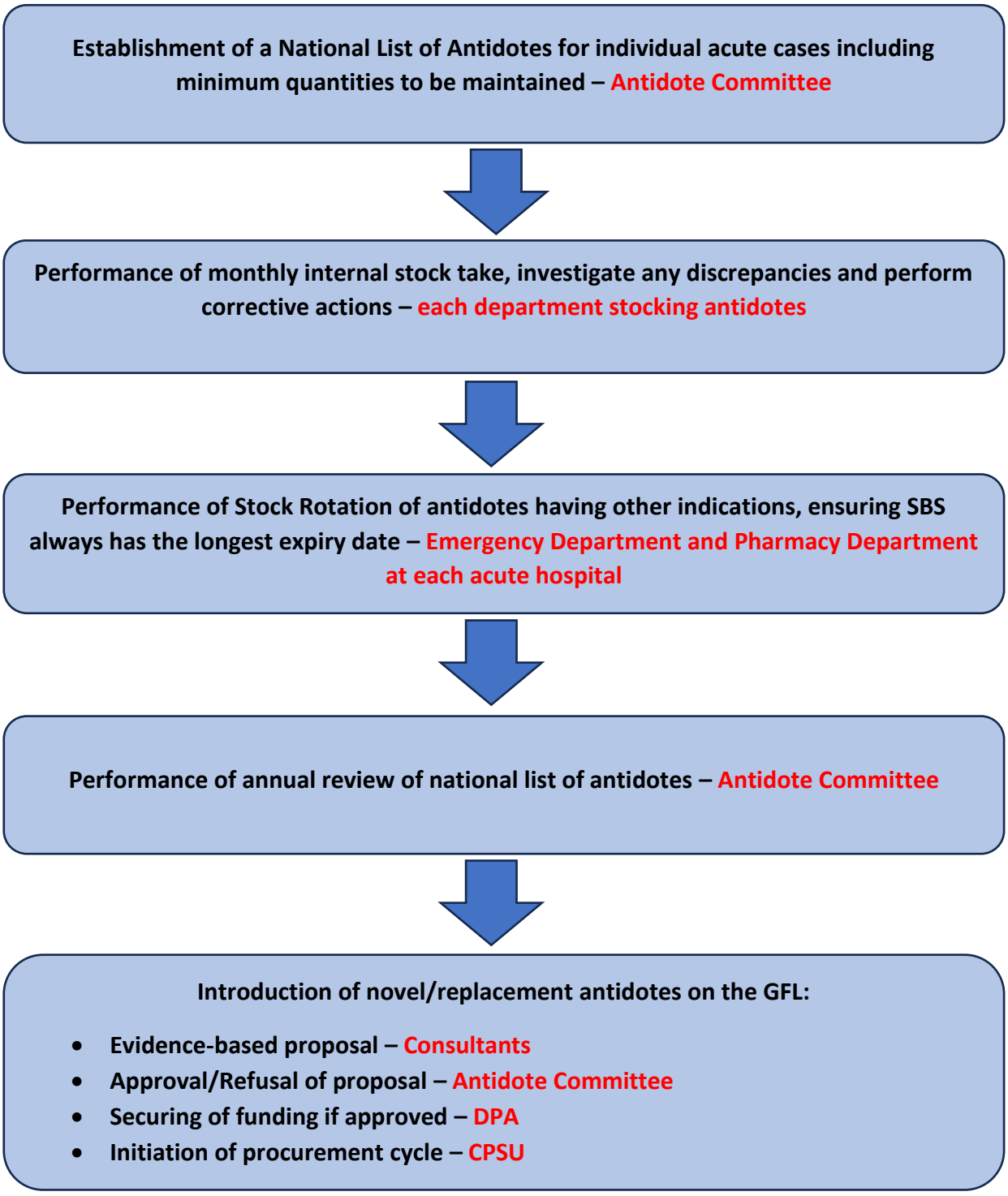
6.4 For antidotes which may be administered within 1 hour or later, establish international cooperation agreements for the facilitation of antidote availability, accessibility, and usability. Such agreements must include the development of an emergency logistical plan to ensure the delivery of antidotes in a timely and effective manner.

7.0 Appendices

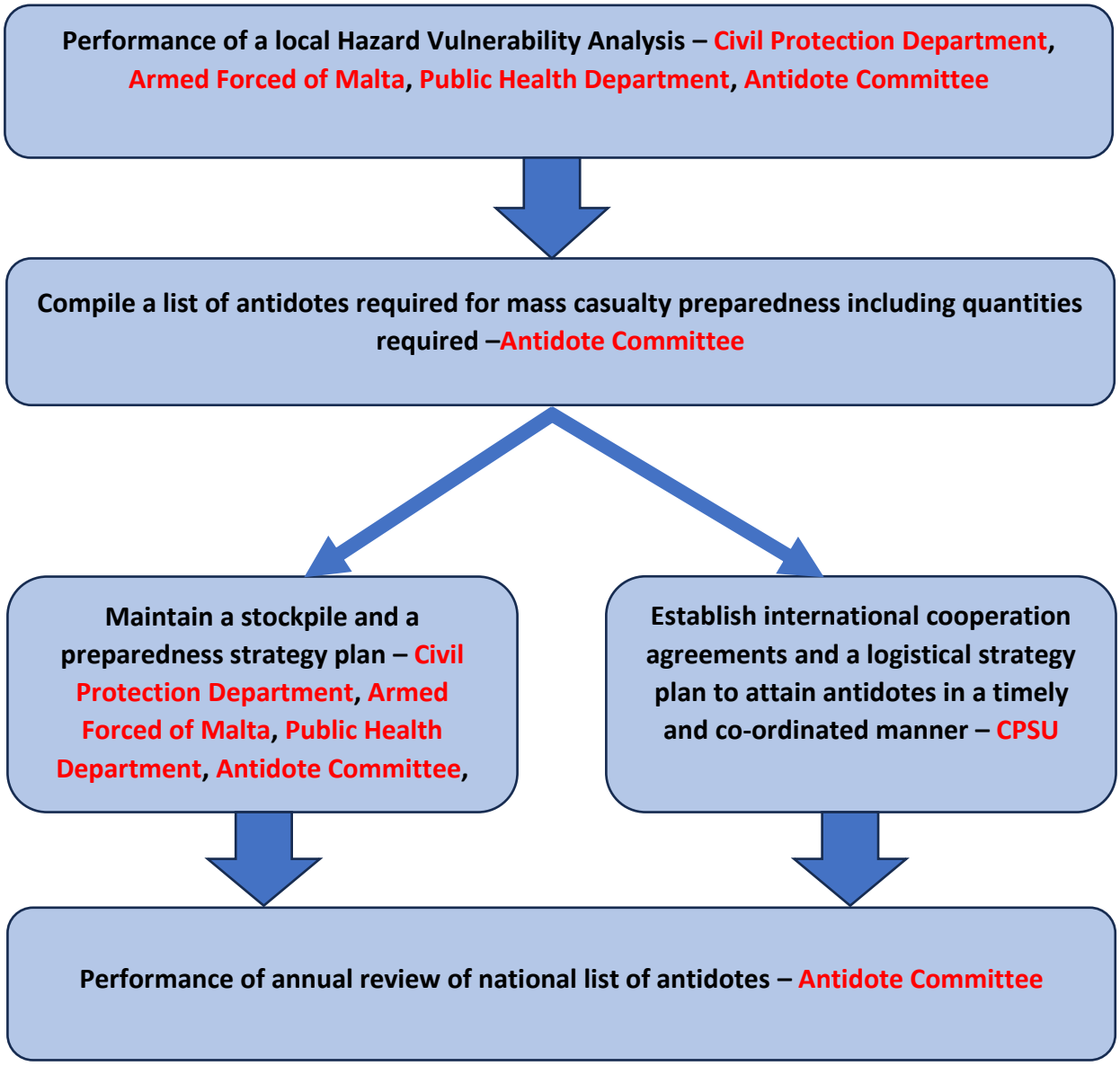
7.1 Appendix 1 - Summary flowchart for stocking of antidotes for individual acute cases

7.2 Appendix 2 – Summary flowchart for stocking of antidotes for mass casualties

Appendix 1 – Summary flowchart for stocking of antidotes for individual acute cases



Appendix 2 – Summary flowchart for stocking of antidotes for mass casualties



Guideline for Optimisation in the Transparency, Communication and Record Keeping on Local Antidote Availability.

Date of Issue: April 2024

2.0 Scope

1.1 The aim of this guideline is to provide healthcare professionals with strategies for optimisation of local antidote emergency preparedness through the optimisation in transparency, communication and record keeping on local antidote availability.

2.0 Definitions

2.1 National Antidote Database: a database of antidotes stocked at a national level which must be available at any moment in time in the approved quantity.

2.2 Antidote Committee: an interprofessional working group responsible for the management of antidotes in Malta.

2.3 Mass exposure: an event which results in the toxicity of several number of patients.

2.4 Audit team: a team of pharmacists trained in auditing who determine compliance with policies and procedures with respect to antidotes availability, emergency preparedness and overall management.

3.0 Guideline

3.1 Establish a single antidote database (National Antidote Database) which includes all the critical data concerning antidotes available to the health authorities and to the emergency/protection response bodies. Utilise this database for the procurement, stocking, dispensing and disposal of antidotes. This database must be reliable, secure,

validated and includes data processing facilities. Access to this database is to be restricted with different users having different level access rights. Such database will provide a real time picture of antidote availability and will give an alarm if thresholds are reached.

3.2 National Bodies which need to be informed on the availability status of antidotes and those involved in the use of such antidotes, need to be identified and a list of contact persons for each body is prepared. Access to the National Database on Antidotes is given according to need.

3.3 National Bodies are to take responsibility of ensuring that: (i) all documents relating to antidote procurement, storage, dispensing and disposal are regularly reviewed, amended and communicated as necessary and, (ii) regular training programmes are planned and executed for all personnel involved in the management and use of antidotes, including in case of a mass exposure event.

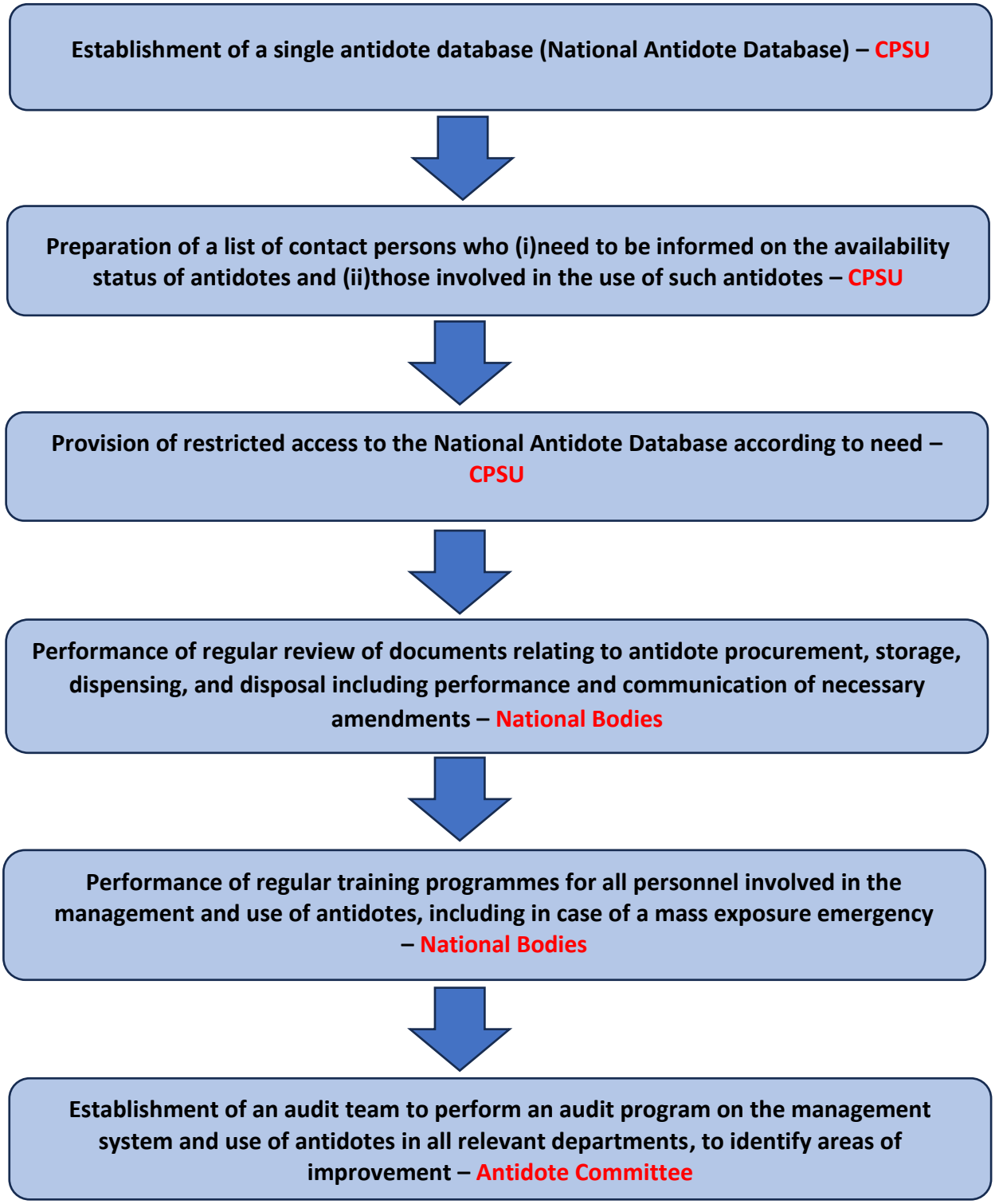
3.4 Establish an audit team consisting of pharmacists and other relevant professionals, which will have the facility, authority, responsibility to perform an audit program on the management system and use of antidotes in all relevant departments. Audit reports are to be forwarded to the Antidote Committee for their action.

3.5 Antidote Committee is to provide advice to National Bodies as necessary.

4.0 Appendix

4.1 Appendix 1 - Summary flowchart for optimisation in the transparency, communication and record keeping on local antidote availability.

Appendix 1: Summary flowchart for optimisation in the transparency, communication and record keeping on local antidote availability.



Appendix 6

Dissemination of Study Findings

Article published in the CPSU annual conference abstract book 2023: Gambin P, Attard Pizzuto M, Anastasi A. Availability and Accessibility of Antidotes in the Maltese Islands. Anastasi A., editor. Proceedings of the CPSU Annual Conference 2023: The Edge Annual 10th CPSU Conference; 2023 Oct 26-27; St. Julian, Malta. Malta: Central Procurement Supplies Unit Ministry for Health;2023.p.17.

CPSU Annual Conference 2023 - The Edge

TITLE

AVAILABILITY AND ACCESSIBILITY OF ANTIDOTES IN THE MALTESE ISLANDS

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AIM

The aim of this study is to evaluate antidote availability and accessibility for emergency preparedness in the Maltese islands.

OBJECTIVES

- Perform a thorough literature review on available international guidelines on antidote stocking.
- Collect data on antidote availability and accessibility from the Central Procurement and Supplies Unit (CPSU), Mater Dei Hospital (MDH) and Gozo General Hospital (GGH).
- Analyse local findings on the availability and accessibility of antidotes and identify possible areas for improvement.

METHOD AND DESIGN

A thorough literature search was performed to identify previous research on antidote stocking and to review existing guidelines on antidote preparedness. Vertical audits of eight chosen antidotes (Atropine 600mcg/ml injections, Pralidoxime 1g injections, Hydroxocobalamin kit, Sodium Thiosulphate, Sodium Nitrite, Digoxin Antibodies, Activated Charcoal and Acetylcysteine) were performed at CPSU, MDH and GGH, to assess local emergency preparedness.

ANALYSIS OF FINDINGS

Thematic analysis of data attained from this study was performed to identify patterns between and across the entire data sets. The problematic sourcing of antidotes and, the inadequate lengthy policy approval and procurement process for urgent situations, were two prominent themes which emerged across the dataset in view that timely availability of antidotes is a major determinant of antidote efficacy.

CONCLUSION

This research highlights the critical need for optimization in the local emergency preparedness especially with regards to sourcing and procurement strategies, and in the development of national contingency plans. Whereas larger countries have the advantage of borrowing antidotes from nearby hospitals[1], Malta is solely dependent on the availability and accessibility of antidotes in two acute hospitals. Action from multiple stakeholders is necessary to ensure national resilience for the Maltese Islands. Risks associated with availability can be mitigated through the establishment of international cooperation agreements.

REFERENCES

[1] Antoniello AA, Pauls P, Awad NI, Sobolewski K, Fernandez D, Bridgeman P. Optimization of antidote stocking, availability, and administration practices for a large multihospital organization. American Journal of Health System Pharmacy. 2023;80(1):S1-S10. Doi:10.1093/ajhp/zxac191

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2SPD-017 **RISK IDENTIFICATION IN ANTIDOTE AND EMERGENCY PREPAREDNESS**

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Background and Importance Globally, antidote preparedness has been identified as a major challenge (Antoniello et al, 2023). The healthcare system must be able to ensure antidote availability and effective management for both individual poison cases and for mass casualties, whilst weighing in the financial burden. This study recognised a gap in literature on the local situation of emergency preparedness with regards to antidotes and the risks in local antidote availability and accessibility. Identification of risks is crucial for the development of risk management strategies to ensure no disruptions in the antidote supply chain.

Aim and Objectives The aim of this study was to identify risks in the availability and accessibility of antidotes in a small nation.

Material and Methods Vertical audits of eight antidotes (pralidoxime, atropine sulphate 600 mcg/ml injections, hydroxocobalamin kit, sodium thiosulphate, sodium nitrite, digoxin immune fab, activated charcoal and, acetylcysteine) were performed at the procurement unit and two acute general hospitals, to identify risks starting from the sourcing to the dispensing of antidotes for patient use. A clinical expert focus group was established for validation and prioritisation of identified risks.

Results Five of the antidotes were noted to have problematic sourcing due to restricted availability on the open market. Logistics and costs of antidotes had a major influence on antidote availability and accessibility. Other identified risks include inadequate stocking of antidotes, lack of periodic review of procurement specifications, delay of antidote release from quarantine due to regulatory barriers, insufficient training, lack of guidelines and national contingency plan, unreliable suppliers and bureaucratic procurement processes.

Conclusion and Relevance This is the first study of this nature to take place in this small nation. Findings indicate critical need for healthcare system optimisation in emergency preparedness. Risks associated with availability can be mitigated through the establishment of international cooperation agreements at European and global levels. The risks identified will be utilised in the development of guidelines and recommendations on the optimisation of emergency preparedness based on risk management principles.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. Antoniello AA, Pauls P, Awad NI, Sobolewski K, Fernandez D, Bridgeman P. Optimization of antidote stocking, availability, and administration practices for a large multihospital organization. *American Journal of Health System Pharmacy*. 2023;**80** (1):S1-S10. doi:10.1093/ajhp/zxac191.

Conflict of Interest No conflict of interest.

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RISK IDENTIFICATION IN ANTIDOTE AND EMERGENCY PREPAREDNESS

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BACKGROUND AND IMPORTANCE

Globally antidote preparedness for both acute cases and mass casualties has been identified as a major challenge.[1] Small nations especially islands, tend to face additional risks due to logistics and size.

The identification of risks in antidote availability and accessibility is crucial for the development of risk management strategies to ensure uncompromised patient care in emergency situations.

AIM AND OBJECTIVES

To identify risks in the availability and accessibility of antidotes in Malta.

Objectives: To assess the local scenario of antidote preparedness through (i) meetings with experts in the field and, (ii) performance of vertical audits of eight antidotes.

To identify risks in the local antidote preparedness and, to validate identified risks through an expert focus group.

METHODS

Vertical audits of eight antidotes – Pralidoxime, Atropine Sulphate, Hydroxocobalamin kit, Sodium Thiosulphate, Sodium Nitrite, Digoxin Immune Fab, Activated charcoal and, Acetylcysteine, were performed at the central procurement unit and two acute general hospitals.

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Data Transcription – Collected data was transcribed for thematic analysis including onsite observations and discussions with healthcare professionals.

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Data Processing – Data from observations, vertical audits and meeting with experts was structured and areas of interest were highlighted.

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Code Generation – Each highlighted area of interest was denoted a code which gave context to raw data.

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Risk Themes Identification – Similar codes were grouped together to form risk themes.

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Risk Themes Validation – Identified risk themes were validated by a nine-membered expert focus group.

RESULTS

- Thirteen risk themes were identified, and all were validated by a nine-membered expert focus group. Seven risk themes were ranked as high priority.
- Table 1 shows the high priority risk themes and the number of antidotes impacted by each risk theme as per vertical audits.
- Three main recommendations were developed from the thematic analysis:
  - ✓ setting up a team to assess and review the management of antidotes in practice and provide a regular feedback report for improvement to the working Antidote Committee.
  - ✓ setting up a training program for all key personnel involved in the handling of antidotes and mass casualties.
  - ✓ establishing cooperation agreements at local, European and global level to facilitate the availability, accessibility and, usability of antidotes in a timely and organised manner.

Table 1: Quantity of antidotes impacted by prioritised, validated risk themes

High Priority Risk Themes	Number of Antidotes
Lack of national strategic plan	8
Inadequate stocking of antidotes	8
Insufficient training	8
Lack of policies, guidelines or procedures	8
Problematic sourcing of antidotes	5
Unacceptability of delivered antidotes	1
Unreliable suppliers	1

CONCLUSION AND RELEVANCE

Findings indicate need for healthcare system optimisation in emergency preparedness. Risks associated with availability can be mitigated through the establishment of international cooperation agreements at European and global levels. Identified risks are utilised in the development of guidelines and recommendations on the optimisation of emergency preparedness based on risk management principles.

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REFERENCES

[1]Antoniello AA, Paula P, Awad NI, Sobolewski K, Fernandez D, Bridgeman P. Optimization of antidote stocking, availability, and administration practices for a large multihospital organization. American Journal of Health System Pharmacy. 2023;80(1):81-810. Doi:10.1093/ajhp/zxac191

Poster Presentation, University of Malta Research Expo (UMRE), May 2024: Gambin P, Attard Pizzuto M, Anastasi A. Risk Assessment on Local Antidote Availability: Are we prepared?

L-Università ta' Malta | Research Expo 2024

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Risk Assessment on Local Antidote Availability: Are we prepared?

Project brief

Aims & objectives

Globally, antidote preparedness has been identified as a major challenge. The healthcare system must ensure antidote availability and effective management for both individual poison cases and for mass casualties, with consideration to financial aspects. This study recognised a gap in literature on the local situation of emergency preparedness with regards to antidotes and deficiencies in local antidote availability. Identification of risks is crucial for the development of risk management strategies. The aim was to perform a risk assessment of antidote availability and accessibility in Malta.

Methodology

Data was collected after ethics approval on antidote availability and accessibility through: (i) vertical audits of eight antidotes (pralidoxime, atropine sulphate injections, hydroxocobalamin kit, sodium thiosulphate, sodium nitrite, digoxin immune Fab, activated charcoal and acetylcysteine) at the Central Procurement Unit and two acute general hospitals, (ii) onsite-observations and (iii) meeting with healthcare professionals in the field of antidotes.

Thematic analysis (Figure 1) of data collected was performed for risk identification through data triangulation.

A focus group was established for the validation and prioritisation of identified risks. Validated risks were inputted into a colour-coded qualitative risk matrix (Figure 2) developed for each antidote.

Figure 1: Process of Thematic Analysis

Figure 2: Developed Risk Matrix

Table 1: Validated Identified Risk Themes

Risk Themes	
Problematic sourcing	Inadequate stocking
Bureaucratic procurement process	Omission of antidotes from formulary
Review of specifications	Lack of policies
Lack of national strategy plan	Review of specifications
Inaccessibility	Insufficient training
Lack of continuous assessment	Unreliable suppliers

Results & Conclusions

All identified risk themes (Table 1) were validated by a nine-membered expert focus group. The top three risk themes were: (1) Problematic sourcing of antidotes, (2) Inadequate antidote stocking and, (3) Lack of national strategic plan.

Findings indicate inadequate antidote availability in Malta especially for mass casualty emergency preparedness. The unavailability of a contingency plan to source and attain antidotes in a timely manner, makes the situation even more critical. The prioritised risk themes were utilised to develop guidelines to enhance local emergency preparedness based on risk management principles.

Abstract Acceptance for 82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences 2024, Cape Town, South Africa, September 2024: Gambin P, Attard Pizzuto M, Anastasi A, Serracino-Inglott A. Optimisation of Antidote Emergency Preparedness: A Risk-Based Approach.

Title: Optimisation of Antidote Emergency Preparedness: A Risk-Based Approach

Background information: Antidotes are key products in acute poisonings in life threatening situations which are globally recorded for suboptimal availability. Antidote availability needs to be balanced against rationale economic funding within a pharmaceutical budget. Within this context, there is an element of risk identification and mitigation within an antidote emergency preparedness programme. Small nations, especially islands, tend to face additional risks due to difficulties associated with logistics and size.

Purpose: To perform a risk assessment of antidote availability and accessibility in Malta and provide guidelines and recommendations for optimisation of antidote emergency preparedness.

Method: Phase 1: Data was collected on antidote availability and accessibility through: (i) vertical audits of eight antidotes (Pralidoxime, Atropine Sulphate, Hydroxocobalamin kit, Sodium Thiosulphate, Sodium Nitrite, Digoxin Immune Fab, Activated Charcoal and, Acetylcysteine) at the central pharmaceutical procurement unit of the national health service and two acute general hospitals, (ii) onsite-observations and (iii) meeting with experts in the field. Thematic analysis of all data collected was performed for risk identification. Phase 2: A focus group was established for the validation of identified risks. Validated risks were inputted into a colour-coded qualitative risk matrix developed for each antidote for risk theme prioritisation. Phase 3: Recommendations and guidelines for optimisation of antidote preparedness were developed and validated.

Results: Thirteen risk themes were identified and validated by a nine-membered expert focus group. The top three risk themes were: (1) Problematic sourcing of antidotes, (2) Inadequate antidote stocking and, (3) Lack of national strategic plan. Guidelines were developed, using flow charts, to address the top three risk themes identified and to optimise local antidote emergency preparedness. The guideline for problematic sourcing of antidotes was targeted towards the central procurement unit and the Department of Health Policy. The guideline on stocking of antidotes was divided into two to account for both individual toxicological cases and mass casualty events. This guideline was directed towards the Antidote Committee, the Contracting Authority, and healthcare professionals responsible for the stocking and handling of antidotes. The guideline for the lack of national strategic plan addressed national bodies for the development of a single national antidote database giving access to real-time, reliable, secure, and validated data which is accessible to authorised personnel.

Conclusion: Findings indicate critical need for healthcare system optimisation in emergency preparedness to ensure timely availability of antidotes. This study

recommends (i) setting up of an audit team to periodically review and assess the management of antidotes in practice and provide feedback to the Antidote Committee for improvement, (ii) setting up of a training program for all key personnel involved in the handling of antidotes and other personnel involved in case of a mass event and, (iii) establishing international cooperation agreements at European and global levels to facilitate the availability and accessibility of antidotes in a timely, organised manner especially in cases of mass exposure. The developed guidelines seek to harmonise the processes involved in managing emergency preparedness through a risk-based approach.