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Barriers to the Implementation of a Unique Identifier and a Track and Trace System in the Lebanese Pharmaceutical Sector

By

Stephanie Joseph Rached

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THESIS APPROVAL FORM

Student Name: Stephanie Rached I.D. #: 200703031

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The undersigned certify that they have examined the final electronic copy of this thesis and approved it in Partial Fulfillment of the requirements for the degree of:

Master of Science in the major of Pharmaceutical Development and Management

Thesis Advisor's Name: Dr. Hani Dimassi

Signature: [redacted] Date: 23 / 05 / 2022 (Day / Month / Year)

Committee Member's Name: Dr. Rasha Hamra

Signature: [redacted] Date: 23 / 05 / 2022 (Day / Month / Year)

Committee Member's Name: Dr. Roy Kanbar

Signature: [redacted] Date: 23 / 05 / 2022 (Day / Month / Year)

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Barriers to the Implementation of a Unique Identifier and a Track and Trace System in the Lebanese Pharmaceutical Sector

Stephanie Joseph Rached

ABSTRACT

Globalization of the pharmaceutical supply chain introduced many new challenges requiring innovative technologies to ensure patients' access to safe and effective medicine. Adding a unique identifier and implementing a track and trace system on pharmaceuticals allow the traceability of products across the supply chain, ensuring quality by reducing counterfeit products, facilitating the recall process, increasing transparency and on the long run speeding up the reimbursement process by third party payers. There are several barriers preventing the implementation of the track and trace system in Lebanon. The aim of this operational research is to identify these barriers in local pharmaceutical institutions mainly local manufacturers and pharmacies; and providing recommendations to policymakers. Through a three-steps operational research, data was collected from local manufacturers through structured or semi-structured interviews, data was also collected form a purposive sample of pharmacies through focus groups and interviews, and finally key informants and policy makers were interviewed for a presentation of results and providing recommendations. Descriptive statistics were used to analyze quantitative results, while thematic analysis was used for qualitative data followed by exploratory data analysis. Different themes were identified for the barriers to implementation: financial, logistic, regulatory, internal planning/human resources and infrastructure issues/context specific.

Keywords: Pharmaceutical Industry, Unique Identifier, Track and Trace, Serialization, Pharmaceutical Supply Chain, Counterfeit, Implementation Barriers, Recommendations, Policymakers.

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List of Abbreviations

2D Two dimensional

AI Application Identifier

DSCSA Drug Supply Chain and Security Act

DTTS Drug Track & Trace System

EU European Union

FDA Food and Drug Administration

FMD Falsified Medicines Directive

GMP Good Manufacturing Practice

GSDP Good Storage and Distribution Practice

GSL General Sale List

GTIN Global Trade Item Number

IMPACT International Medical Products Anti-Counterfeiting Taskforce

INTERPOL International Criminal Police Organization

IRB Institutional Review Board

MAA Marketing Authorization Application

MOHAP Ministry of Health and Prevention

NDA New Drug Application

NDC National Drug Code

OPL Order of Pharmacists in Lebanon

RFID Radio Frequency Identification

SCM Supply Chain Management

SFDA Saudi Food and Drug Administration

SNI Standardized Numerical Identification

SSCC Serial Shipping Container Code

SPIL Syndicate of Pharmaceutical Industries in Lebanon

WHO World Health Organization

Chapter One

Introduction

1.1.Overview

1.1.1. The pharmaceutical product and its development process

A pharmaceutical product is defined by the World health Organization (WHO) as a special preparation used in medicine for the prevention or treatment of diseases (WHO EMRO | Pharmaceutical Products | Health Topics, n.d.). It is identified through the drug discovery process. This process includes the identification of a drug candidate, its synthesis, characterization, validation, optimization, and assays for therapeutic efficacy. If these investigations yield satisfactory results, the process of drug development then starts (Deore et al., 2019). The drug development is divided into the pre-clinical evaluation followed by the clinical evaluation (figure 1).

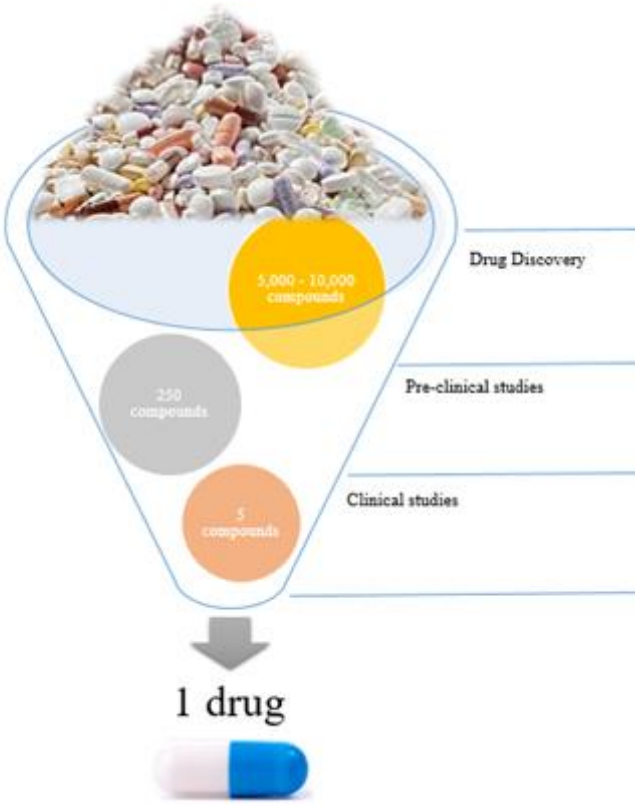


Figure 1 Drug discovery and development process

In the pre-clinical phase, the drug's safety and efficacy are evaluated in animal models. This phase is divided into pharmacological studies exploring the absorption, distribution, metabolism, and elimination of the drug; and toxicological studies addressing toxicity of a drug in different cases (single-dose or acute toxicity, repeated-dose toxicity, genotoxicity...) (European Medicines Agency, 2008). This is followed by the clinical evaluation collecting data about the clinical safety and efficacy of drugs. There are four phases in clinical trials and the details are summarized in figure 2.

Once all pre-clinical and clinical studies are concluded, and the drug is deemed safe and effective for its intended use, manufacturers file a New Drug Application (NDA) to the FDA or a Marketing Authorization Application (MAA) in the EU (Kashyap et al., 2013). Following the approval of the drug product, the focus turns to marketing and distribution through the pharmaceutical supply chain.

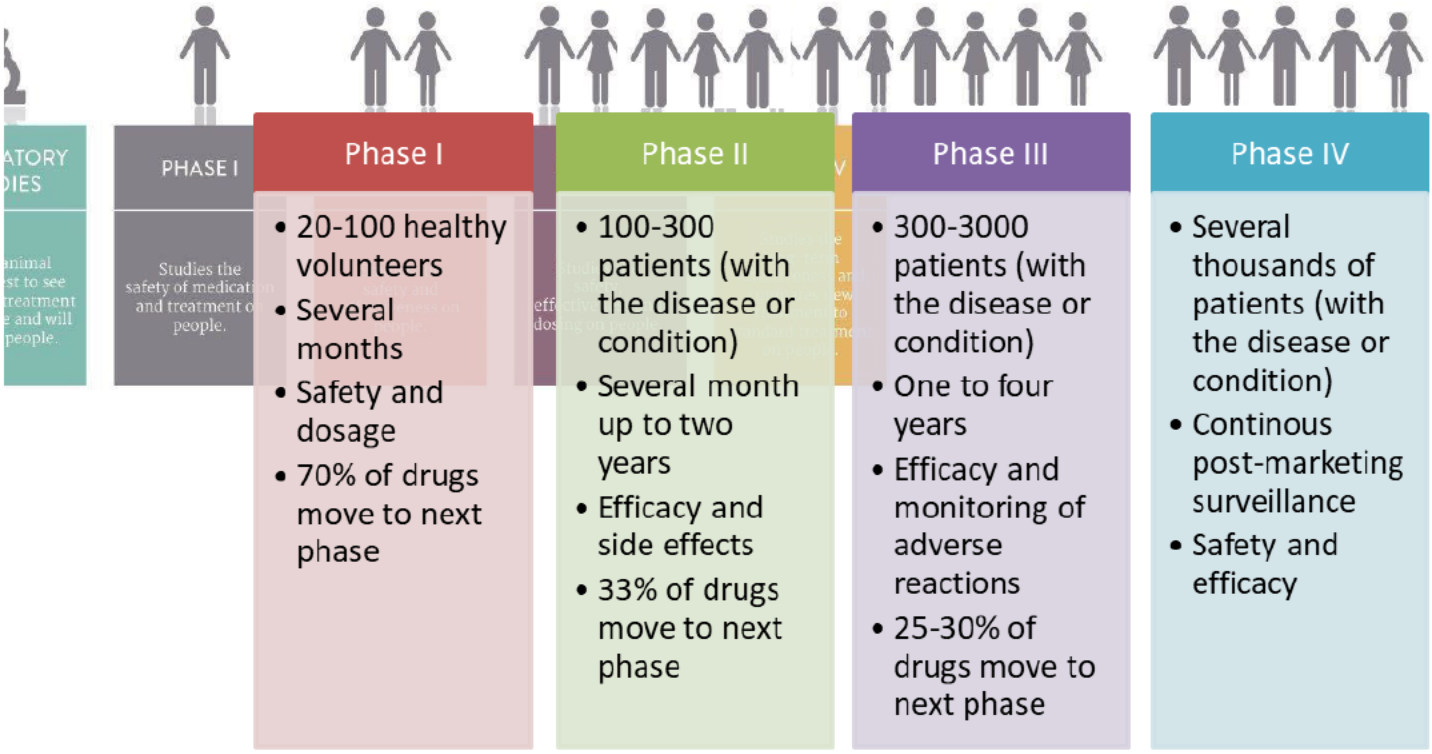


Figure 2 Clinical trial phases (U.S. Food and Drug Administration, 2018)

1.1.2. The supply chain

The pharmaceutical supply chain is the means through which drugs are manufactured and delivered to patients. The term supply chain refers to planning, sourcing, production, and distribution of products (Yousefi & Alibabaei, 2015). It is a highly complex process, which involves several stakeholders such as manufacturers, wholesalers, and pharmacies; and many steps are taken to ensure that counterfeit products don't find a way into the market and that drugs become accessible to patients. Globally, pharmaceutical companies are facing challenges such as quality standards, healthcare reform, and increased requirements by regulatory authorities (Rossetti et al., 2011). The complexity of the supply chain is increasing and managing it has become essential especially with the expanding variety of drugs distributed, increased outsourcing, and the advances in technology (Lee, 2002; Singh et al., 2016). Supply chain management (SCM) helps companies overcome these complexities by ensuring flexibility and constant innovation. It involves the development of strategies taking into consideration the needs of patients and customers, an appropriate approach to supply and demand to each market and using effective and legal marketing tools to reach the highest number of customers. Successful SCM gives companies a competitive advantage over competitors and allows faster incorporation of products in new markets (Lee, 2002).

1.2. Globalization of the supply chain

1.2.1. The challenges in manufacturing and global distribution

New challenges are emerging as a result of globalization of the pharmaceutical supply chain. These challenges include technical, economic, social, political, and legal considerations. The manufacturing and distribution of pharmaceutical products are becoming more difficult with time, which requires innovative technologies to ensure patient safety and access to medicine (Mackey & Nayyar, 2017). According to Wang et al. (2005): "the crucial aim of SCM in pharma industry is to make the right product, for the right customer, in the right amount, at the right time" (Moosivand et al., 2019).

Pharma companies are facing the challenge of incorporating their products across different regulatory regimes and meeting the quality standards across different countries. The best strategy to adopt is harmonization, which is meeting the highest standards among different markets, enabling pharma companies to be ready when moving to smaller and less developed markets in the future (Cordon et al., 2016). This harmonization across the different regulatory regimes and adoption of common standards is the most cost-effective strategy. With growing demand in existing and emerging markets, flexibility alone is no longer enough; companies must adopt a new approach to distribution as well; improving their supply chain performance is critical in order to maintain a competitive advantage (Cordon et al., 2016; Moosivand et al., 2019). Furthermore, companies need to enhance their supply chain to ensure customer satisfaction, accurate forecasting, and lowering of the total supply chain costs. An information technology platform, combined with a flexible and dynamic supply chain ensures the quality and safety of drugs and reduces operational costs (Cordon et al., 2016).

Additionally, pharmaceutical companies must comply with the Good Storage and Distribution Practice (GSDP). This is especially challenging with products sensitive to temperature fluctuation. Cold chain management is therefore essential, as any deviation from the required storage conditions can lead to major problems and jeopardize the safety of the patients (Hosseini Bamakan et al., 2021). Transportation temperature must be monitored, and data should be reviewed as each stakeholder receives the products to ensure the recommended storage conditions were maintained during transport and storage (WHO Expert Committee on Specifications for Pharmaceutical Preparations, 2020).

Another major challenge facing pharmaceutical companies is counterfeit drugs. As defined by the WHO, a counterfeit is a product that is “deliberately and fraudulently mislabeled with respect to source and/or identity”(Kopp, 2010). This definition can be applied to both brand and generic products. Therefore, counterfeit refers to any of the following: products with the correct ingredients, products with the wrong ingredients, products without active ingredients, products with incorrect quantities of

active ingredients, or products with fake packaging (Cordon et al., 2016). Because unqualified personnel usually produce these products under suboptimal conditions, they have the potential to cause harm to patients and fail to treat the disease they were intended to treat. They can also lead to antimicrobial resistance in certain cases. Furthermore, these products are usually designed to appear exactly like the genuine products and therefore are often difficult to detect (Substandard and Falsified Medical Products, n.d.). The pharmaceutical industry ranks among the top 10 counterfeited goods (Cordon et al., 2016). Counterfeit drugs pose a global threat to the healthcare sector since it is not limited to less developed countries. While it is more pronounced in less developed countries, it is also a concern in developed countries as well. In fact, it is estimated that 1% of pharmaceutical products available in developed countries are likely to be counterfeit, and this number rises to 10% in developing countries (Kon & Mikov, 2011). In 2015, data suggested that 128 countries were found to be impacted by counterfeit products, which accounted for a 38% increase in worldwide incidence compared to previous years. Additional data also suggest a growing rate of illegal sales of prescription medicine online, threatening the health and lives of consumers globally. It is estimated that at any given time there are approximately 40,000 active online sellers of medical products, and 93-96% of them are illegal (Isles, 2017).

All the previously mentioned problems and challenges are endangering the patients' rights to access safe and effective medicine, leading them to settle for substandard products and endangering their lives. Therefore, it is essential to have a better supply chain management enabling the traceability of products across the supply chain to minimize these risks.

1.2.2. Optimization of the supply chain

Due to the increasing risk of counterfeits, several organizations published ways for patients to identify these products and highlighted some of the signs to watch out for when purchasing a pharmaceutical product such as (Substandard and Falsified Medical Products, n.d.):

- Examine the condition of the outer packaging and compare it to previous packs received
- Examine the packaging for any spelling mistake, the manufacturing and expiry date, and make sure all the data on the outside matches what is inside
- Ensure the medicine looks correct, is not degraded, or discolored or has any unusual characteristics
- Refer to the pharmacist, doctor, or any healthcare professional if the product is suspected to be a counterfeit, if product is not working properly, or any new side effects appear

In 2006, the WHO launched a taskforce to put a stop to counterfeit products focusing on patients' safety and public health. The International Medical Products Anti-Counterfeiting Taskforce (IMPACT) increased the public's awareness to the problem of counterfeits and encouraged everyone involved in the supply chain in addition to the general population to inform the authorities about any suspicious activity or any doubt in a product's authenticity (WHO Launches Taskforce to Fight Counterfeit Drugs, 2006). IMPACT members included drug regulatory authorities and law enforcement agencies and any international organization involved in combating counterfeit drugs. Due to the criminal aspect in the production of counterfeit products, an agreement was signed in 2008 between the WHO and The International Criminal Police Organization (INTERPOL) enhancing the collaboration between the two organizations (WHO Open Forum: IMPACT Frequently Asked Questions, 2010). Operation Pangea is an international effort coordinated by INTERPOL to stop online sales of counterfeit products and raise awareness on the risks of buying medicinal products from unregulated websites. Since its launch, Operation Pangea has made more than 3,000 arrests and prevented over 105 million units of pharmaceutical products from reaching unsuspecting customers (Operation Pangea – Shining a Light on Pharmaceutical Crime, 2019).

Several initiatives were taken by different countries on a national level in their efforts to counteract the emergence of counterfeit products in their markets. The manufacturing and distribution of pharmaceutical products is usually governed by a

set of laws and regulations where only licensed institutions can distribute drugs (manufacturers and distributors) and ultimately pharmacies (which represent the end of the supply chain) are allowed to dispense these products to patients. In the U.S., the FDA in collaboration with the U.S. Customs and Borders Protection ensure that all borders and areas that represent the most threat on the supply chain are monitored closely since most counterfeit products are made abroad and then smuggled into the U.S. endangering their local supply (Counterfeit Medicine | FDA, n.d.). Furthermore, the U.S. also works with other governments to close illegal operations involving the production and distribution of counterfeit drugs globally. Similarly, the European Union (EU) recently adopted a new directive, the Falsified Medicines Directive, to prevent counterfeit products from entering the supply chain and protect patients. This directive introduced new safety measure and enhanced control across Europe using four main pillars: Safety features of medicines, supply chain and good distribution practice, active substance and excipients, and internet sales (Falsified Medicines: Overview | European Medicines Agency, 2020). Different countries have adopted different measure to combat counterfeit products whether by having a closed supply chain, issuing new legislations, or adopting new identification and safety features and measure.

As for cold chain management, pharmaceutical companies can use different temperature monitoring systems; either chemical, mechanical, or electronic, depending on the amount of information required. The most widely used technique is the data logger, which is an electronic device that measures and stores data using external or built-in sensors (Bishara, 2006; TempMate, n.d.). Data loggers should be validated and calibrated regularly and, depending on their type and quality, they can monitor a wide range of parameters such as temperature, relative humidity, light intensity, differential pressure… (Cas DataLoggers, n.d.). The incorporation of other technologies such as traceability, with the monitoring systems, could enhance the cold chain management by preserving the history of the product, keeping record of all the stakeholders involved and the location of the product at any time. This can be achieved by real time information flow between all stakeholders involved in the

supply chain, resulting in a much more effective control of the critical parameters of cold chain (Hosseini Bamakan et al., 2021).

Furthermore, pharmaceutical products may need to be recalled at any given time from the market. A recall may be issued if the product is found to have questionable quality, safety or efficacy and might be potentially harmful on patients. In this case, the manufacturer must notify all the stakeholders and recipients of the product in question that it's being recalled and to stop its sale immediately (Sadhna & Nagaich, 2015). Optimization of the supply chain would ensure that products can be recalled from the market in a timely manner when required, ensuring patient safety.

The following section will focus on the new technologies that can be implemented allowing for the identification and traceability of pharmaceutical products across the supply chain. These technologies can reduce the risk of counterfeit products entering the market, facilitate the recall process and increase the transparency of the supply chain.

1.3.The technologies available for pharmaceutical industry

There are several technologies available that have shown great benefit when used in the pharmaceutical industry. The combination of product identification and an electronic track and trace system or an e-pedigree would increase the security of the supply chain (Bansal et al., 2013). Since the pharmaceutical industry deals directly with human lives, all pharmaceutical products manufactured and distributed must meet certain standards. The most important characteristic of a pharmaceutical product is its identity (U.S.Department of Health and Human Services et al., 2021). This identity encompasses all the history of the product starting from the raw materials and equipment used until the finished product is distributed and reaches the patient. There are several technologies available to preserve the identity of products and allow their traceability throughout the supply chain. The main technologies available and used worldwide will be described in this following section.

1.3.1. Radio frequency identification (RFID)

This technology consists of digital data, which uniquely identifies a product, and is encoded in RFID tags. These tags hold a small microchip to store the data required which is transmitted and captured wirelessly by an RFID reader. Then, the data captured is transmitted to a computer database where it can be stored and evaluated (Potdar et al., 2006). This process is illustrated in figure 3 below.

Figure 3 RFID technology components and how it works

RFID was invented in the 1970s and used in several industries to identify products, animals, and people (Coustasse et al., 2010). An increasing number of industries are relying on RFID technology. The application of RFID tags to pharmaceutical products allows their traceability during their journey in the supply chain by scanning the tags with RFID readers and transmitting the data to a computer database. In order to allow full traceability, RFID tags must be placed on each product entering the market, and these tags must be scanned at every level in the supply chain. However, the cost of the tags is considered to be high compared to other options, especially when factoring in the possibility of having damaged tags that, if not replaced, could lead to loss of full traceability. In 2005, the FDA created a committee for the assessment of the value of using RFID in the pharmaceutical industry. Furthermore, Purdue Pharma L.P. launched a pilot study on the narcotic product Oxycontin, with the two main distributors of this product. The main objective of this pilot was the restriction of illegal versions of this pain reliever. All four doses of oxycontin were labeled with RFID tags, and then tracked from the manufacturing plant to the distributors (Bollampally & Dzever, 2015). The cost of each RFID tag added to the bottle ranged between $0.3 to $0.5. In addition to the

tags, expenses covered handheld scanners, which cost $500-$1,000 each, and essential equipment such as PCs and software at both the manufacturing and shipping level. In total, the company's initial investment cost $2 million. Despite the promising start, a major concern emerged during this pilot, a high number of tags experiencing read failures pushed the manufacturer to test all tags before and after applying them. Other issues faced included the short distance for data scanning and reading due to the small size of the tags placed based on the space available on the bottles, and the challenge of tagging drugs in liquid form since liquids can obstruct high frequency signals (Purdue Pharma RFID Enabled Packaging - Packaging Gateway, 2005).

Similarly, in 2006, Pfizer announced the addition of RFID tags to one of its most counterfeited drugs: Viagra. In fact, Pfizer spent around $5 million to implement RFID on this product alone (Otoshi et al., 2007). The company's goal for using RFID was to enhance patient safety and increase patients' confidence in the product. However, unlike Purdue Pharma, Pfizer's pilot did not include all stakeholders in the supply chain of Viagra. Therefore, full traceability of the product was not possible since it required all parties to invest in specific technologies to capture and share information about the movement of products. These efforts made by leading companies such as Pfizer and Purdue Pharma among others (table 1) on their most counterfeited products highlighted the importance of governmental support when it comes to the implementation of similar technologies involving multiple stakeholders. Government issued regulations could ensure traceability occurs at the level of each intermediary in the supply chain.

There are several benefits for the implementation of RFID in pharmaceutical industry such as real-time visibility of products in the supply chain and the difficulty to duplicate RFID tags. However, there are also several drawbacks mainly the high costs of implementation, the concerns about the return on investment especially on low priced drugs, and the difficulty for implementation on drugs in liquid form.

Table 1: Pharmaceutical companies who conducted pilots on RFID (Coustasse et al., 2010)

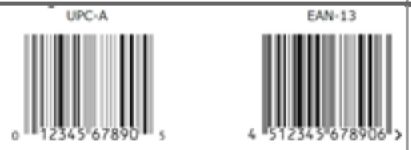
Manufacturer	Product	Year
Purdue Pharma	Oxycontin®(Narcotic)	2005
Pfizer	Viagra®	2006
GlaxoSmithKline	Trizivir® (HIV drug)	2006
Johnson & Johnson	All products	2007

1.3.2. Serialization

Serialization is the process of assigning a unique number to each package of a pharmaceutical product. It requires each stakeholder to implement an authentication process and validate products at each step. This allows for traceability and visibility across the supply chain, reducing the risk of counterfeit products(Cordon et al., 2016). This process is known as the track and trace technology.

Serialization starts with the implementation of common standards on all pharmaceutical products. The most commonly used standards in the pharmaceutical industry are GS1 standards. GS1 is a non-profit organization that develops global standards, they started using unique product codes since 1971 (How We Got Here | GS1, n.d.). Identification starts by assigning a Global Trade Item Number or GTIN to each product. The manufacturer, through GS1, assigns this GTIN, and it usually contains 14 digits composed of the company prefix (assigned by GS1), the item reference number, and a check digit (GS1, 2021). As for the serial number, it is either numeric or alphanumeric and can be composed of up to 20 characters. Although the GTIN is unique by product, the combination of GTIN and serial number is unique per pack of pharmaceutical product. This is followed by the selection of the data carrier. A data carrier is the graphical representation of the data in a computer or machine-readable format. There are several types of barcodes issued by GS1 and used as a data carrier. Each type is widely used in a specific industry and summarized in table 2 (GS1, 2021).

Table 2: Types of GS1 barcodes used in different industries (GS1, 2021)

Barcode name	Symbol	Industry
EAN/UPC symbology family Examples: UPC-A, UPC-E, EAN-13, and EAN-8 barcodes		Trade items at point-of-sale
Data Matrix		Healthcare retail
QR code		Advertising marketing, invoices, and billing

GS1 data matrix carrier is the ISO/IEC recognized and the standardized implementation of Data Matrix. GS1 Data matrix is a two-dimensional (2D) barcode made up of individual dots organized into a grid in the shape of a square. This grid is usually bordered by a finder pattern used to specify the orientation of the barcode (Figure 4). The data matrix can hold the largest amount of information compared to other barcodes (3,116 numbers or 2,335 alphanumeric characters) and remains legible even when printed in a small size (GS1, 2018).

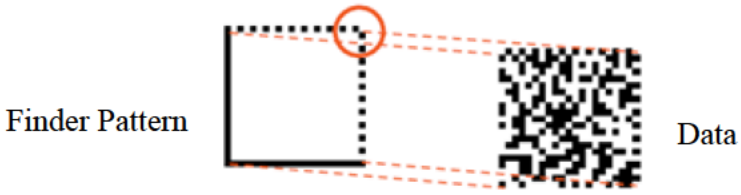


Figure 4 Finder Pattern and data (GS1, 2018)

The encoding of the data in the data matrix is a structured process where an application identifier (AI) always precedes the data encoded. AIs are usually composed of two digits, and they identify the data that follows them. Table 3 shows the most common AIs used in the pharmaceutical industry.

Table 3: GS1 elements (GS1, 2018)

Application Identifier (AI)	**Data definition**	**AI and Data format**
01	GTIN	N2+N14*
10	Batch/Lot number	N2+X...20
11	Production date (YYMMDD)	N2+N6
17	Expiry date(YYMMDD)	N2+N6
21	Serial number	N2+X…20
*N = numeric, N2 is fixed length 2 numeric digits, X…20 is alphanumeric up to 20 characters		

Once encoded, the data matrix can be printed on the package, it is recommended to have human readable data printed in addition to the 2D data matrix. The human readable data is usually printed next to the barcode with the AIs between parentheses followed by the data (figure 5). It also must be clear and legible.

Figure 5 Example of a 2D data matrix
with human readable data (GS1, 2018)

Once printed, the data matrix requires a special 2D imager-based reader/scanner to capture the encoded data. Using this reader, the barcode is first scanned then processed to decode the data and identify the product in question.

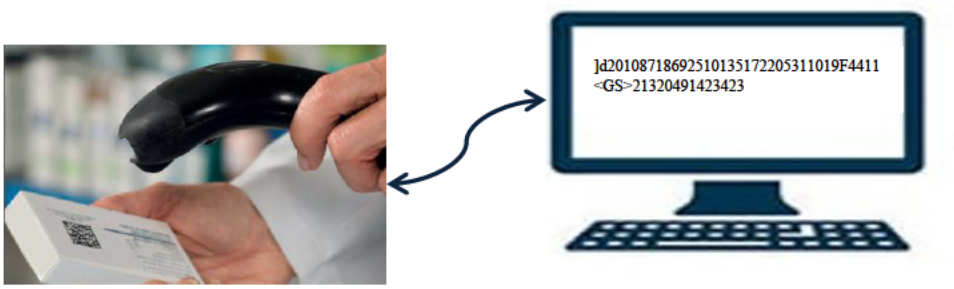


Figure 6 Serialization technology components and how it works

In 2012, Pfizer discovered that around 40% of Viagra sales in Hong Kong were counterfeit (Griffen, 2019). To combat the presence of counterfeit and increase the sales of the original product, Pfizer decided to implement serialization on this product. The aim of this implementation was to protect their blockbuster drug while tracking its distribution and ensuring patients' loyalty by providing authentic products to the market. Due to the circumstances at the time, a fast solution was needed which led Pfizer to bypass the printing of barcodes at the manufacturing level and turn to labelling packages already available in their distribution centers (figure 7). The labels were printed and placed on the packages within a few weeks. Once in place the barcodes allowed all stakeholders to verify the authenticity of the product simply by using a barcode reader, in addition to full traceability through the supply chain. Patients were also able to scan the same barcode using smartphones to ensure authenticity of the products. Within 12 months of implementation, the problem with the fake Viagra disappeared and sales increased substantially (Kezzler Speaks Counterfeit Drugs with Healthcare Packaging | Kezzler, n.d.). The implementation of serialization and the appropriate traceability system won Pfizer a commercial innovation award at the time and drove them to expand serialization to other products as well.

This technology has been widely studied and evaluated in several countries and has shown several advantages over other technologies. The effectiveness of the implementation of mass serialization depends on the stakeholders and the countries involved in the supply chain. The advantages of using a 2D data matrix is that this

type of barcodes can hold more information than other barcodes (such as linear barcodes), it can be printed directly on the products and remains legible even when printed in small size (Practical when there is little to no space remaining on the secondary packaging of pharmaceutical products). It also has an error correction algorithm in case the data matrix is damaged, the barcode can still be scanned despite being damages, torn, or printed poorly (GS1 DataMatrix A Tool to Improve Patient Safety through Visibility in the Supply Chain, 2013). Furthermore, this technology has a relatively lower cost for implementation compared to others (table 4) (Bansal et al., 2013).

Figure 7 Viagra pack showing label added for serialization in Hong Kong (Griffen, 2019)

Table 4: RFID vs Data matrix (Bansal et al., 2013)

Features	RFID	2D data matrix
Direct line of sight required with reader	No	Yes
Readability **Interference with liquids and metals** **Effect of tag orientation**	 High Low	 Low Low
Difficult to duplicate	Yes	No
Cost of tag	High	Low
Technology set up cost	High	Low
Data storage	High	High compared to other barcodes Low compared to RFID
Requires specific reader	Yes (RFID reader)	Yes (but same reader is able to read other barcodes as well)

1.3.3. **Blockchain technologies**

All previously discussed technologies require a centralized system where transactions can be stored, which possess certain vulnerabilities especially to hacking and data manipulation. Therefore, the use of a decentralized system of networks is essential going forward to provide the ultimate security to the supply chain. This is known as blockchain technology (Hosseini Bamakan et al., 2021).

Blockchain is an emergent technology that consists of a peer-to-peer network to record and store data using advanced encryption techniques. Encrypting data renders it tamper-proof and provides stakeholders with increased security and data privacy. Each stakeholder would create and record their transactions to a ledger, which is a database shared with other users of a blockchain. Then the set of transactions is accumulated into a block, which is then put into an algorithm to create a unique code related to this data set. This creates the first piece of data, and then the next stakeholder would go through the exact same process creating the next block. Each

block added by a stakeholder contains several transactions in addition to the previous stakeholder's block (Hosseini Bamakan et al., 2021).

There are three categories of blockchain: public, private, and consortium. A public blockchain allows anyone to take part in another party's transactions while still using specific algorithms to keep the chain safe. A well know application of a public blockchain is Bitcoin. A private blockchain only allows access to authorized users. It usually has an owner (or a central authority) who provides different access levels of information to each stakeholder and has high privacy and safety mechanisms. Finally, consortium blockchain is very similar to private blockchain except it does not have a single owner. It is also known as federated blockchains. It allows all users to view data while only some of them are allowed to actually write to the block. These categories are used to refer to a user's ability to write information to blockchain. When it comes to the user's ability to read data, it is referred to as either open or closed blockchain. The open blockchain is accessible to end-users, providing a level of trust in the process, while closed blockchain makes data less accessible limiting the end user's trust.

When implemented in the pharmaceutical supply chain, which involves several stakeholders, all parties must have the ability to share and update data. Stakeholders include manufacturers, wholesalers, logistics companies, shipping partners, and pharmacists. Furthermore, many pharmaceutical products are sensitive to environmental factors such as temperature, humidity, and light. Any fluctuation in these parameters whether due to equipment failure, electricity shortage or transport conditions; may affect the quality of the product either by reducing its efficacy or by causing undesirable effects in patients. Cold chain management, a low-temperature controlled supply chain, is therefore essential and is one of the areas where blockchain technology is being investigated (Hosseini Bamakan et al., 2021). The main importance of this technology is because each step depends on the previous one and affects the next. Blockchain would allow stakeholders to check on the status of the product and ensure its quality at any moment preventing loss of quality and additional costs.

As pharmaceutical products move throughout the supply chain, each stakeholder would create and record all transactions and as each block is formed, they accumulate eventually into a blockchain (Rogerson & Parry, 2020). Blockchain technology is very secure as data is encrypted, therefore, the blockchain would be operated by an organization who limits the visibility to the data recorded and only allowed parties would have access to any data. The organization in charge would either allow or restrict access as needed. Therefore, the ideal solution would be a private blockchain to avoid data manipulation and any illegal access due to the sensitivity of the data shared. This data would reflect the quality of the product and any deviation from the recommended storage conditions (temperature, humidity, or light exposure). Furthermore, blockchain would allow the traceability of each product starting from the manufacturer in the country of origin, through the supply chain, until it reaches the patient (Hosseini Bamakan et al., 2021).

Due to its novelty, there are very few applications of blockchain technology in the pharmaceutical supply chain (Hosseini Bamakan et al., 2021). However, its implementation is being studied in several countries and multiple sectors. One example is a blockchain start-up by a company in San Francisco called Chronicled, who created a solution in response to the Drug Supply Chain and Security Act (DSCSA) (discussed in the next section) by the FDA. This solution is meant to make the supply chain more reliable and efficient. In 2017, the FDA launched the MediLedger pilot project in collaboration with 25 pharmaceutical companies. The objective of this pilot was to explore the feasibility of using blockchain technology to meet the requirements of the DSCSA (drug supply chain security act). The participants represented a variety of stakeholders usually included in the pharmaceutical supply chain such as brand and generic manufacturers, distributors, and pharmacy chains among others (table 6) (Sample, 2020) .

Table 5: Participants in the MediLedger Pilot

Company Name	Type
AmerisourceBergen	Wholesale Distributor, Third party logistics
Amgen	Manufacturer
Cardinal Health	Wholesale Distributor, Third party logistics
Center for Supply Chain Studies	Consulting
Dermira	Manufacturer
Eli Lilly	Manufacturer
Endo	Manufacturer
FedEx	Third party logistics
FFF Enterprises	Wholesale Distributor
Chronicled	**Solution provider**
Genentech	Manufacturer
Gilead	Manufacturer
GS1	Global industry standards
Glaxo Smith-Kline	Manufacturer
Hikma	Manufacturer
Inmar	Third party logistics
Maor	Dispenser
McKesson	Wholesale Distributor, Third party logistics
Novartis	Manufacturer
Novo Nordisk	Manufacturer
Pfizer	Manufacturer
Sanofi	Manufacturer
Vaxserve	Distributor
Walgreens	Dispenser
Walmart	Dispenser

The blockchain-based system developed for this pilot maintained complete privacy of transactions recorded ensuring traceability back to the manufacturer and allowing for faster recalls when required. The main work approach was based on several key principles highlighted in Figure 8 and included the following components:

- The use of a blockchain distributed ledger system to exchange data for prescription medicine between stakeholders.
- Identification of the standards that would benefit this implementation
- Development of a financial model for stakeholders.
- Identification of potential issues with the system performance and challenges.
- Identification of how the MediLedger solution could be interoperable with other solutions in place.

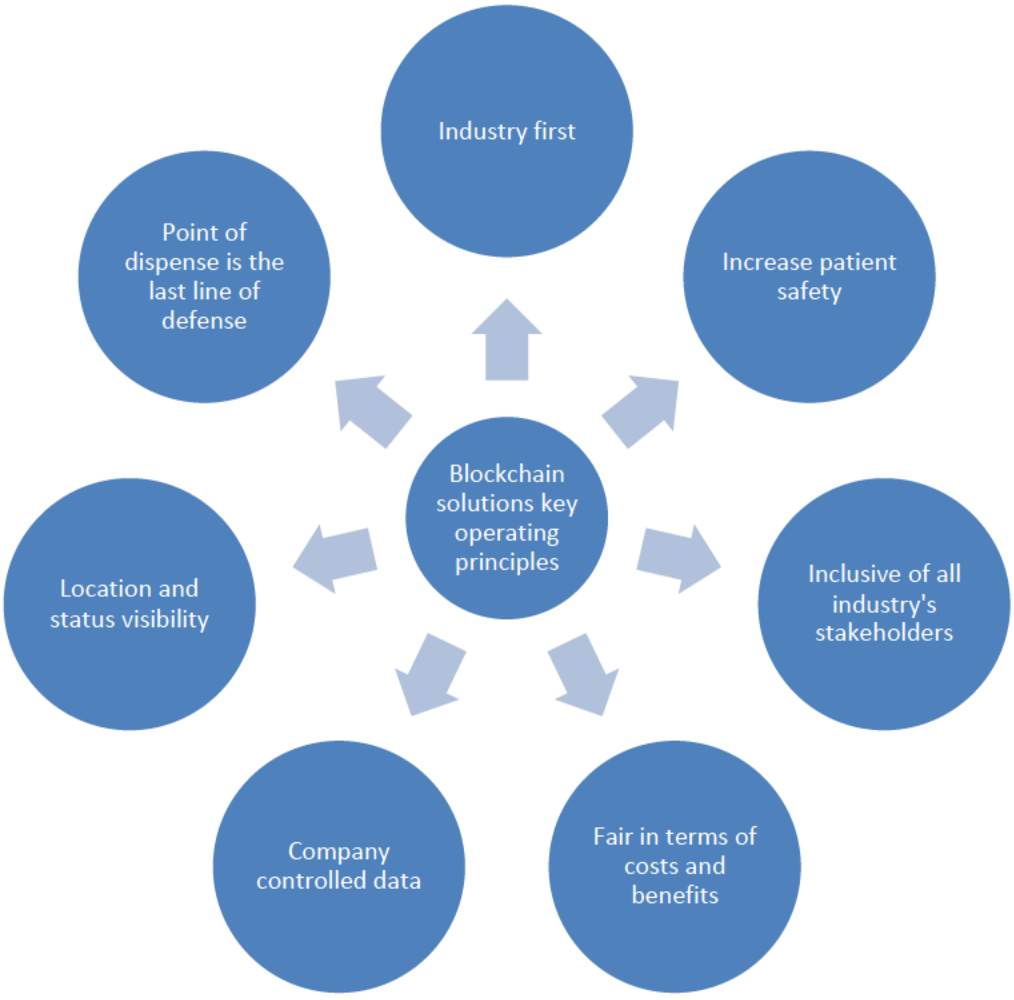


Figure 8 Key principles of Blockchain technology

The advantages of having high-level system requirements ensure that only authorized companies in the pharma industry can connect to the system, provide complete privacy of data committed to a blockchain, it can process more than 2000 transactions per second, and can complete verification requests in less than a second. The advantage of blockchain technology over other solutions is its ability to handle and manage exceptions. As products move in the supply chain from an upstream partner to a downstream partner, any small mistake can cause a disruption in the flow of information. Although impossible to change data on a blockchain, it is possible to create new transactions to correct for past mistakes. The exceptions encountered in the MediLedger pilot were either missing transactions, discrepancies between quantities ordered and received, or errors in the serial numbers. An example of handling an exception is summarized in table 5 below with the actions taken to counteract the errors.

Table 6: Example of an exception encountered in the MediLedger pilot (Sample, 2020)

Exception	**Description**	**Handling on MediLedger**	**Result**
Missing file at Receipt	Product received physically but the file was missing on MediLedger	• File must be corrected before processing. • Send a peer-to-peer message to seller and request the missing file	• Proceed if products verified. • Treat product as suspect if not verified

Since the DSCSA aims at combatting counterfeits, the MediLedger pilot also addressed the issue of products suspected as counterfeits. These suspects were identified as either having a duplicate serial number, having a GTIN that doesn't exist, or with a known status as destroyed or recalled (Sample, 2020).

The results of this pilot showed that this solution requires the participation of all the industry's stakeholders for the long-term success of such implementation. The lack of full participations would result in incomplete data, breaking the chain of custody of the products. Furthermore, it highlighted the importance of a governance body that would be responsible of policymaking, enforcing rules and operating procedures, and would ensure the interests of all stakeholders are met. However, there are many challenges facing the implementation of this track and trace solution. The main challenges are the lack of a worldwide approach to the verification process by different authorities, lack of appropriate standards that would allow the multiple systems in place at the level of each stakeholder to become interoperable, in addition to concerns related to safety and ownership of data shared, and the cost to smaller stakeholders. However, despite all these challenges, the adoption of this new technology could offer many benefits such as safety and security of the supply chain, patient safety, and complete traceability of pharmaceutical products. Ultimately, the implementation of blockchain would ensure the ability to track pharmaceutical products simply by scanning the barcode printed on the pack at any time and locate products in question in the case of any public health crisis. This would increase the patient's trust since they would be able to see the history of each products ensuring drug identification and verification (Schöner et al., 2017).

1.4. Implementation in different countries

1.4.1. The **European Union (EU) regulations**

(COMMISSION DELEGATED REGULATION (EU) 2016/161 - of 2 October 2015, 2016)

The Falsified Medicines Directive (FMD) is a legal framework by the European Union (EU) that introduces measures to fight fake medicines and ensure patient safety by preventing the entry of counterfeits into the supply chain. The FMD was published in July 2011, comprising 50 articles, and it included the required safety measures, rules for importation, and record keeping requirements by stakeholders. The unified requirements between EU countries aim at reducing the costs of

implementation and allowing the full circulation of products across the EU. The necessary rules are set to be implemented on medicinal products subject to prescription with a few exceptions (refer to annex 1). The safety features selected and described in the regulation were found to be the most cost-effective option.

The safety measures consist of placing safety features, mainly a unique identifier and an anti-tampering device, on the packaging of pharmaceutical products for human use. These safety features allow the identification and authentication of products. The unique identifier, which is a sequence of numeric and alphanumeric characters, should include the product code, the national reimbursement and identification number (if required by the member state), the batch number, and the expiry date. This data would be encoded using standardized data structure mainly a two-dimensional barcode, specifically a machine-readable data matrix, which must be printed clearly on the package allowing for fast verification. The printing parameters to take into consideration include the contrast between light and dark parts, axial non-uniformity, grid non-uniformity, unused error correction, and fixed pattern damage. The choice of the 2D barcode is mainly due to its ability to store a large amount of data. In addition to the printed barcode, the manufacturer must print the product code, serial number, and national reimbursement number in human readable format in case the barcode is damaged or unreadable at any stage.

The repositories system used for identification of products by an end-to-end verification by stakeholders the entire time the product is on the market allow its authentication and facilitate recalls and withdrawals. The end-to-end verification also helps in the prevention of falsified medicines from reaching the patient thus ensuring patient safety. Furthermore, once products dispensed to patients, their unique identifiers (combination of product code and serial number) can be decommissioned. Each national repository system should be interoperable and connected to supranational repositories to exchange data. data entry starts at the level of the marketing authorization holder, then by wholesalers, pharmacies, and other suppliers of pharmaceutical products.

Manufacturers should retain the information and records of all operation for each product for a minimum of one year after the expiry date or five years after its release to the market. Therefore, the combination of product code and serial number must be unique for the same period of time to allow verification of products as long as they are circulating in the supply chain. Once the product leaves the supply chain, the unique identifier can be decommissioned to avoid its reuse by traffickers. So, another pack with the same unique identifier would never be successfully verified.

The directive entered into force in 2011 and selected February 9, 2019, as the implementation date except for certain countries like Belgium, Greece, and Italy who already had their own systems in place for verification of products. The FMD stated that these countries could have an additional transitional period to adapt their systems to the requirements and at the latest February 9, 2025.

1.4.2. The Food and Drug Administration (FDA) regulations for the United States (U.S.)

Since 2013, the FDA started issuing new requirements to ensure the quality of prescription drugs and safeguard the integrity of the pharmaceutical supply chain. The aim of these new requirements is to prevent illegitimate products from entering the market and facilitate their detection in case they reach the supply chain. All stakeholders involved in the manufacturing, distribution, or dispensing (i.e., retail pharmacies or hospital pharmacies) of pharmaceutical products must abide by these requirements (figure 9). Several guidance documents were issued to facilitate the implementation and the transition phase for stakeholders. The guidance documents detail the standards for the exchange of data between stakeholders and the type of transactions to be recorded. The required information stored should include the transaction information, transaction history, and transaction statement to the purchaser of a product with the lot information of the product exchanged.

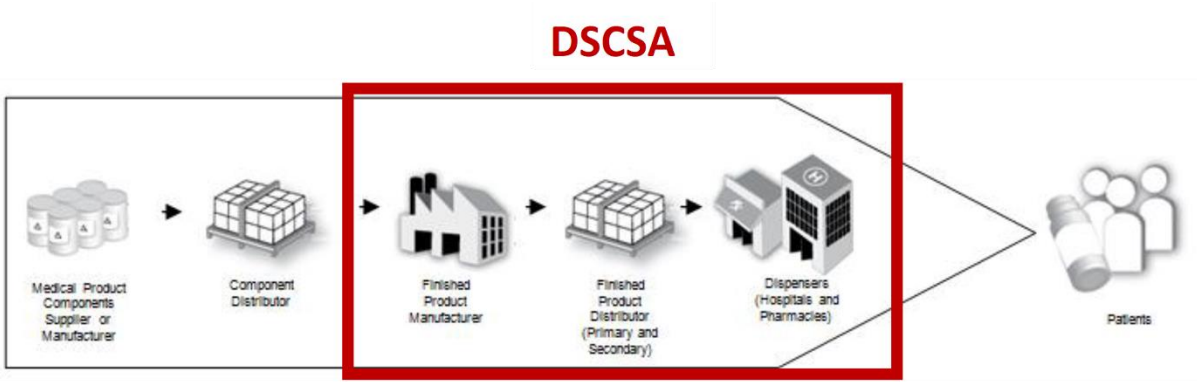


Figure 9 Scope of the DSCSA (Bernstein, 2017)

The products covered by this act refer to products in their finished dosage forms of administration, excluding the following (Drug Quality and Security Act, 2013):

- Blood or blood components intended for transfusion
- Radioactive drugs or biological products
- Imaging drugs
- Certain intravenous products (i.e., intended for replenishment of fluids and electrolytes or dialysis products)
- Medical gas
- Homeopathic drugs

The product identifier is to be placed on the package of prescription drugs and should contain the National Drug Code (NDC), the serial number (numeric or alphanumeric), the lot/batch number, and the expiry date. The combination of the NDC and serial number form the Standardized Numerical Identification (SNI). The SNI, which is unique per products, is then used to identify, authenticate, and track and trace prescription drugs, facilitating the detection of counterfeits (U.S. Food and Drug Administration, 2010). The product identifier should be available in both human and machine-readable formats. The selected data carrier for the machine-readable format is the 2D data matrix barcode (U.S. Food and Drug Administration, 2021).

Data printed on the packages and collected upon scanning of the 2D data matrix should be linked and stored in a database allowing traceability of products. In fact, by 2023, all stakeholders involved in the supply chain must develop interoperable systems to facilitate the exchange of information ensuring identification and full traceability of products as they move through the supply chain. This in turn will facilitate the detection of counterfeit products (Bernstein, 2017).

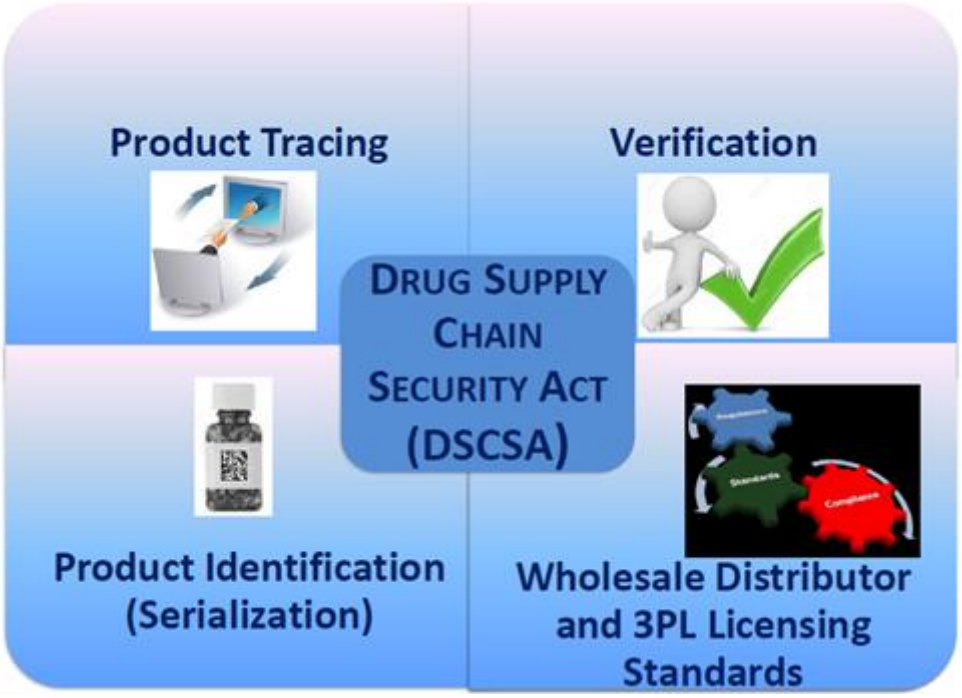


Figure 10 Benefits of DSCSA (Bernstein, 2017)*)*

The goal of the implementation of the DSCSA is an enhanced drug distribution system which provides increased public health benefits, ensure diligence and vigilance by all partners, be adaptable and flexible, and finally be compatible with the health care system and the global marketplace.

1.4.3. **Regulations in MENA (Middle East and North Africa) countries**

In addition to the previously mentioned cases, several countries are issuing their own regulations to comply with international standards when it comes to pharmaceutical products

1.4.3.1. The case of Saudi Arabia

In 2013, the Saudi FDA (SFDA) started issuing regulations to all drug manufacturers and importers with new requirements for the identification and traceability of pharmaceutical products for human use. The regulations issued stated that GS1 standards would be adopted since they were the most widely used standards globally. The first stage of implementation required all manufacturers to acquire a 14-digit GTIN for each product and to upgrade all barcodes from the linear one to the 2D data matrix barcode. The data matrix must hold the following information at least: the GTIN, Expiry date (6-digit format, i.e. YYMMDD), Lot/Batch number, and the serial number. Each of these will be preceded by its AI to facilitate the decoding of data. In addition to the barcode printed on the secondary packaging level, companies are required to use aggregation at the tertiary packaging level to facilitate distribution of packages throughout the supply chain. Aggregation allows the traceability of each pack of a drug without scanning each individual barcode. Simply scanning the barcode on the whole box would record the serial numbers of the units inside, in addition to the lot number and expiry date (Saudi Food & Drug Authority, 2019).

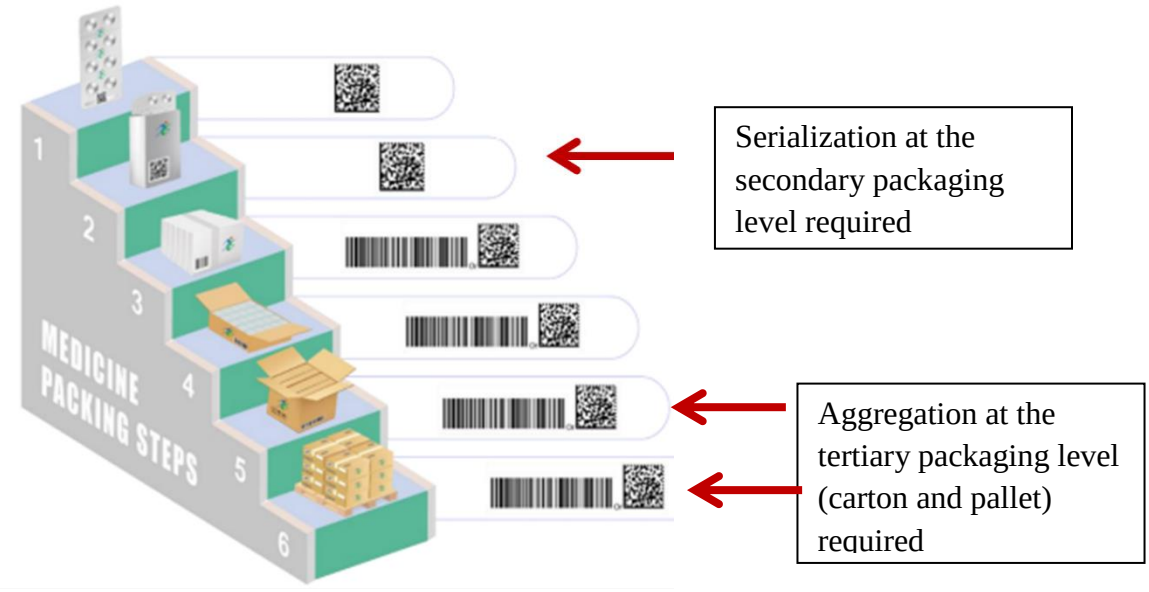


Figure 11 Serialization requirements at Saudi Arabia (Saudi Food & Drug Authority, 2019)

Following the initial regulations by the SFDA, several other guidelines were issued describing their traceability solution, the Drug Track & Trace System (DTTS) and explaining how stakeholders can share their information among each other and with regulators and payers. In general, simply by scanning the barcode, stakeholders record transactions and products information as they move within the supply chain until it reaches the patient (Saudi Food & Drug Authority, 2018).

1.4.3.2. The case of the United Arab Emirates (UAE)

The UAE announced in 2020 the launching of its new track and trace platform "Tatmeen" that will allow the identification and traceability of pharmaceutical products in the UAE supply chain using GS1 serialization standards (The Ministry of Health and Prevention UAE, 2020). The objectives of launching this platform include product security, patient safety, and supply chain visibility. There are three components for this traceability system, it starts by identifying the product, capturing the data, and sharing of information. According to the serialization guide issued by the Ministry of Health and Prevention (MOHAP) in the UAE, the identification of products will occur using a GTIN, a serial number, the expiry date, and the batch/lot number. This data should be encoded in a GS1 data matrix and printed on the secondary packaging in addition to the human readable data. For shipping and distribution, all units must be aggregated and identified with a Serial Shipping Container Code (SSCC) (Figure 12).

As per the regulations, these requirements must be implemented on all pharmaceutical products that are either sold, distributed, or stored in the UAE. The products exempt from the serialization regulations are free samples, products imported for personal use, medical devices, and products belonging to the General Sale List (GSL) such as dietary supplements, antiseptics, and disinfectants (MOHAP, 2021). The timeline for implementation starts with the issuing of the serialization decree which happened in June 2021 (Sochacki, 2021). Manufacturers were then given a six-month grace period for printing the 2D data matrix on the secondary packaging, and 18 months for aggregation and for starting data on the traceability platform Tatmeen.

Packaging Unit	Encoded Data	Application Identifier	Mandatory Symbology	Mandatory Optional
- Secondary Packaging 	GTIN Serial Number Expiry Date Batch Number	(01) (21) (17) (10)	GS1 DataMatrix	Mandatory
- Trade Item - Example: Bundle 	GTIN Serial Number Expiry Date Batch Number	(01) (21) (17) (10)	GS1 DataMatrix	Optional
- Trade Item - Example: Shipper Case - Preferred Option for UAE 	GTIN Serial Number Expiry Date Batch Number	(01) (21) (17) (10)	GS1 DataMatrix	Mandatory
- Homogeneous Logistic Unit - Example: Shipper Case 	SSCC	(00)	GS1-128	Mandatory
- Heterogeneous Logistic Unit and/or Partial Logistic Unit 	SSCC	(00)	GS1-128	Mandatory
- Homogeneous Logistic Unit - Example: Pallet 	SSCC	(00)	GS1-128	Mandatory
- Heterogeneous Logistics Unit - Example: Pallet 	SSCC	(00)	GS1-128	Mandatory

Figure 12: Serialization and aggregation requirements in the UAE (MOHAP, 2021)

1.4.3.3. The case of The Kingdom of Bahrain

The Kingdom of Bahrain is also on the way to full implementation of serialization. In 2017, a legislative decree was issued enforcing the implementation of a track and trace system in the pharmaceutical supply chain (bin Abdullah Al Khalifa, 2017). Following the decree, the guidelines were published in 2019 detailing the requirements regarding the unique identifier and the traceability system. The guidelines stated that a 2D data matrix should be printed on the secondary packaging of all registered products and non-registered products with a valid temporary importation license. The data matrix should contain the GTIN, expiry date, batch number, and serial number. This same data that is encoded in the barcode must be printed next to it in human readable format. Finally, the guidelines explained how data must be shared between stakeholders for full traceability of pharmaceutical products (al Jalahma & al Abbasi, 2019).

1.4.3.4. The case of Turkey

Another example of a full implementation of a track and trace system is Turkey. Just like the previously mentioned cases, Turkey also chose the GS1 Data Matrix as the data carrier to be printed on the secondary package of pharmaceutical products. The barcode must contain the GTIN, serial number, Lot/Batch number and expiry date. The requirements of the data printed and encoded is the same as explained above. In addition, a track and trace system is implemented which has three main functions: 1) Identification of products in the system, 2) Tracking the product in the supply chain, 3) Assist stakeholders to find recalled or expired in a timely fashion (Altunkan et al., 2012). Phase I of implementation started in 2010 by using the unique identifier, followed by phase 2 in 2012 with the full implementation of serialization and aggregation (Cordon et al., 2016). The benefits of such a solution in Turkey is that it connects more than 40,000 stakeholders from manufacturers to wholesalers, pharmacies, exporters, and reimbursement institutions (GS1, 2015). There are many other examples of countries who are on the road for the implementation of track and trace solutions for pharmaceuticals. Figure below shows the current situation of different counties.

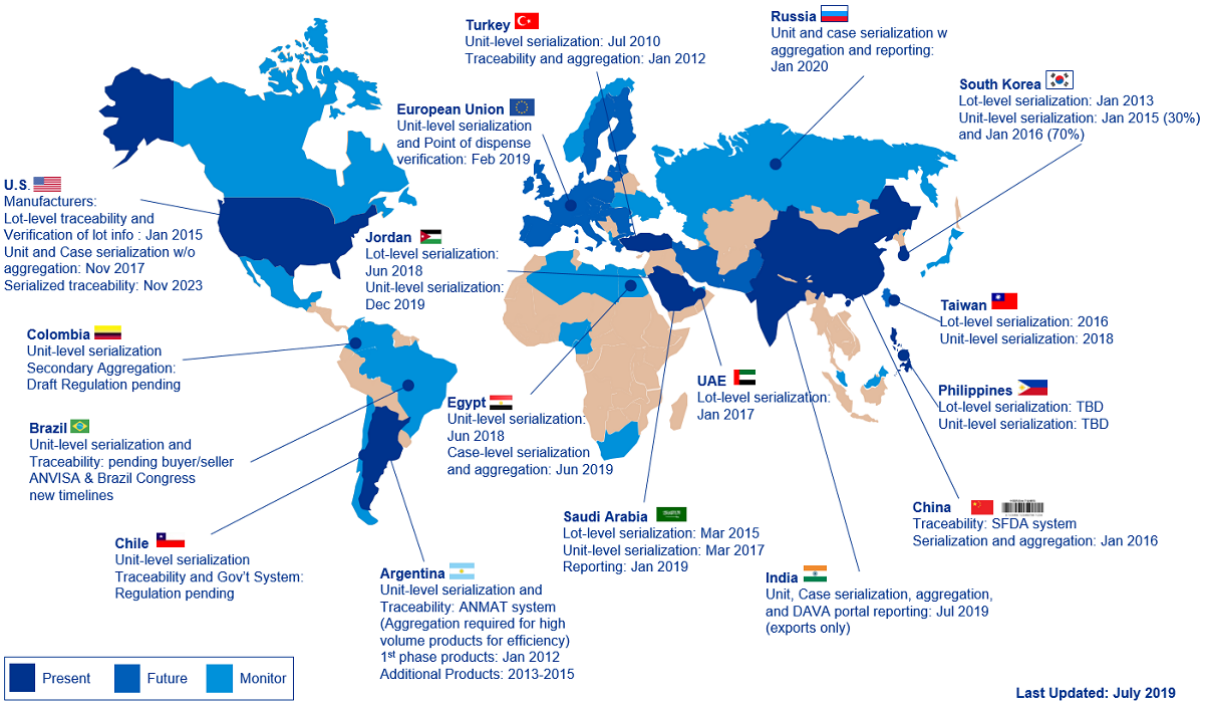


Figure 13 Serialization and traceability requirements in different countries (Colombo et al., 2019)

1.5.Regulations in Lebanon and the current situation

Following the global trend, Lebanon is currently on the path of a full track and trace solution implementation for pharmaceuticals. The Ministry of Public Health started issuing decisions regarding the requirements since 2017. The first decision issued required all manufacturers to adopt the GS1 2D data matrix for all pharmaceutical products. The decision excluded samples and IV products intended for replenishment of fluids and electrolytes from this implementation. The barcode must contain the GTIN, Lot/Batch number, and expiry date. The GTIN used is the 14-digit GTIN issued by GS1, the lot number is up to 20 alphanumeric characters, and the expiry date in the barcode should be in the format YYMMDD (Decision 2405/1 on the Adoption of the 2D Data Matrix on Pharmaceutical Products, 2017). In addition, manufacturers can add a serial number (up to 20 alphanumeric characters) but this is not required until now. The data encoded should also be present in human readable format preferably next to the barcode if the size of the pack allows it (figure 13). The data encoded must be preceded by its AI to allow the decoding of the data upon scan. As for the printed expiry date it should be in a format easily identified by patients with a visual separator between the month and date. The allowed formats include any of the following: MM YYYY, MM.YYYY, MM/YYYY, or MM-YYYY (the month can also be referred to by the first three letters, i.e. JAN for January) (*Decision 2291/1 on the Printed Expiry Date on Secondary Packaging*, 2019).

Figure 14 An example of a 2D data matrix and the human-readable information

Table 7: Data encoded in the 2D data matrix and its AI

Application Identifier (AI)	Data	Example
01	GTIN (14 digits)	06251234560011
17	Expiry date (YYMMDD)	210931
10	Lot/Batch (AB-123)	ABC234
21	Serial number (X1-X20)	SN0123456789

Furthermore, the Ministry of Public Health (MoPH) in Lebanon developed a centralized web-based application, MediTrack, where all stakeholders involved in the supply chain can connect and record their transactions. Some of the functionalities of MediTrack include recording transactions when products change ownership (sales or return), notifying stakeholders of products expired or near expiry, sending notifications about recalled products and flagging them on the system when they are used in transactions, extracting reports when required and identifying the location of products when required. Stakeholders include licensed institutions like manufacturers, importers, wholesalers, and pharmacies. Once licensed, each stakeholder would receive credentials to access MediTrack and start recording their transactions allowing the traceability of pharmaceutical products in the supply chain until they reach the patient (Figure 15).

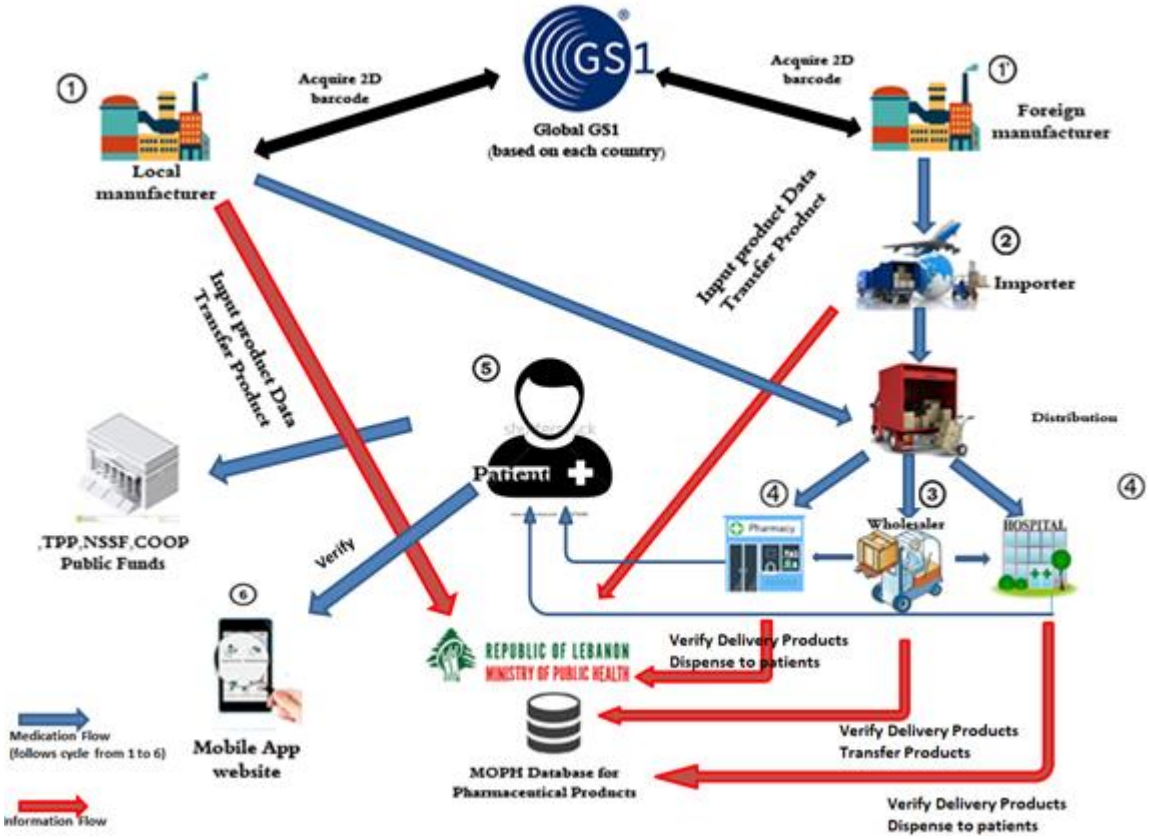


Figure 15 Workflow of the Track and trace system in Lebanon (Abou Mrad et al., 2020)

MediTrack database of registered medication and the list of contacts are regularly updated to ensure all registered medication and institutions are found and verified. Furthermore, stakeholders are responsible of informing the MoPH of all GTINs for their products to ensure products are verified upon scan.

In 2018, the MoPH launched a pilot phase with representatives from the different stakeholders that would be involved in the supply chain, including 6 importers, 1 local manufacturer, 17 community pharmacies, and 2 hospital pharmacies (table 8).

Table 8: Pilot members

Type	Name
Importer	Droguerie de l'union
Importer	R.G.Abou Adal & Co
Importer	Mersaco
Importer	Omnipharma
Importer	Pharmamed
Importer	Sadco – Sami Dandan & Co S.A.R.L
Local manufacturer	Algorithm
Pharmacy	Sili (Jdeideh)
Pharmacy	La Marina (Dbayeh)
Pharmacy	Layal (Aley)
Pharmacy	Anipharm (Damit, Chouf)
Pharmacy	Raja (Chiah)
Pharmacy	Meridien (Baouchrieh)
Pharmacy	Waked (Zouk Mosbeh)
Pharmacy	Ratco (Al Ayroun)
Pharmacy	Diab (Haret hreik)
Pharmacy	Jamal (Nakkache)
Pharmacy	Barbar (Jounieh)
Pharmacy	Al Asria (Zahleh)
Pharmacy	Maarakeh (معركة) (Tyre)
Pharmacy	Damerji
Pharmacy	Pharmacy Zgharta El Zawye
Pharmacy	El Farmacia (Ain w Zein - El Chouf)
Pharmacy	Mazen pharmacy
Hospital pharmacy	Haroun Hospital
Hospital pharmacy	Mount Lebanon Hospital

Each importer provided a list of products that already held a 2D barcode to be used during the pilot phase. Then, all pilot members were invited to the ministry to receive training sessions on the developed system. They were also issued individual account and provided with their credentials to access the database.

The system provides 3 different work options for stakeholders:

- Work on the web-based application (MediTrack) developed by MoPH
- Upload an excel file with all the movements to MediTrack
- Systems integration

The duration of the pilot phase was a whole year, and throughout 2018 all pilot members reported the problems they encountered and their recommendations to enhance the platform. When the pilot ended, the MoPH developed a full implementation plan and announced that the traceability system would be implemented in January 2020 at the level of importers, followed shortly by implementation in pharmacies, and giving local manufacturers a grace period till the end of 2022. Simultaneously, the Guidelines on the implementation of the national barcode system for pharmaceuticals in Lebanon were developed and published in 2020. However, the outbreak of the coronavirus affected the timeline set, and training sessions were delayed till the last quarter of 2020, with the implementation at the level of importers starting in 2021. The training was performed by the e-health department at the MoPH, specifically by the pharmacists in charge of the implementation of the track and trace system in Lebanon. There were 155 importer and distributor involved in this first phase of the implementation. These stakeholders are now active users of MediTrack, meaning they are recording all the transactions performed and updating the system on the location of their products as per the issued regulations. Concurrently, the MoPH was also working on a plan for implementation in pharmacies which was posing a challenge due to the large number of licensed pharmacies (approximately 4,000 registered pharmacies). The final plan involved the integration with the software providers in pharmacies to avoid increasing the workload on pharmacists. Therefore, all software providers must be compliant with MediTrack, enabling pharmacies to share the required data through the software they

already use to perform daily transactions. Furthermore, as the deadline for implementation for local manufacturers is approaching, many preparations should be made. However, the current crisis in the country is affecting all stakeholders. Due to the financial and economic crisis, many basic needs are becoming hard to find. Individuals and institutions are unable to access their local bank accounts, there are prologued electricity cuts, the internet connection is unreliable, and most importantly many medications are no longer available in the market including essential and lifesaving products. In addition to the pandemic and the economic crisis in Lebanon there are many other challenges preventing the full implementation in pharmacies and in local manufacturers.

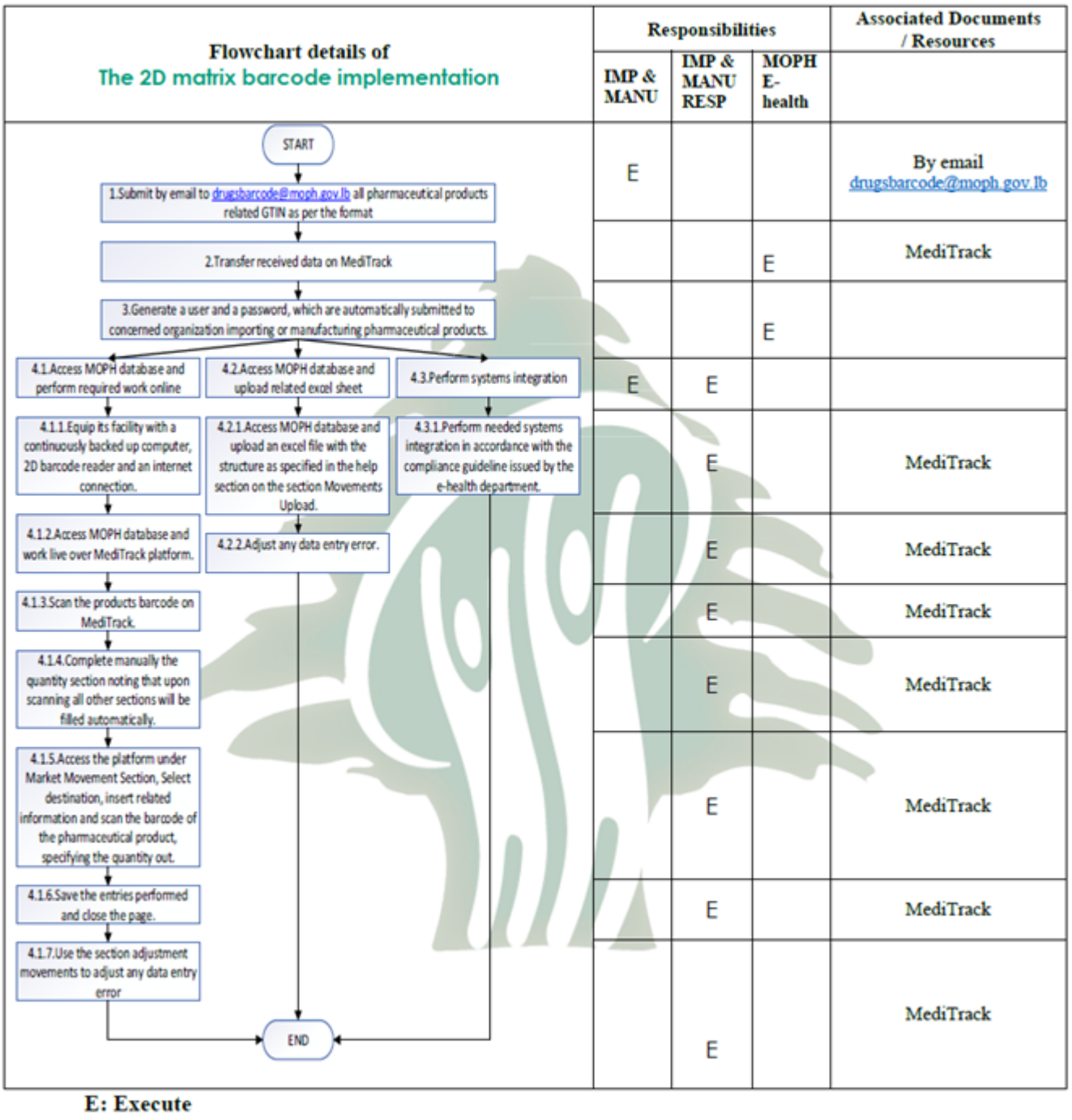


Figure 16 Flowchart of MediTrack implementation (Abou Mrad et al., 2020)

1.7.Specific aims of this research

The aim of this research is to identify, through mixed methods research, the barriers for the implementation of the track and trace system in local pharmaceutical institutions in order to find possible ways to overcome them. This will be a three-steps operational research; the first step will involve interviewing local manufacturers, the second step will involve a focus group of community pharmacies, and finally the third step will be approaching policymakers with the findings and providing recommendations.

Chapter Two

Methodology

This study consists of a mixed methods operational research. It involves the use of quantitative and qualitative data to help provide solutions for implementation problems in healthcare (Monks, 2016). In this research, data will be collected from multiple stakeholders in order to assess their current situation and identify the possible barriers standing in the way of implementation. Following the identification of barriers, recommendations will be presented to assist decision makers and facilitate the implementation on the different stakeholders.

2.1. Ethical issues

2.1.1. IRB approval

This study was approved by the Lebanese American University (LAU) Institutional Review Board (IRB) prior to initiation of the interviews.

2.1.2. Consent forms

Informed consent was obtained from each participant before data collection. The form contained all the details of the research relevant to the participant to make the decision, specifying that participation is voluntary and that results will be reported anonymously. When participants agreed to participate in this research, they received a copy of the signed informed consent form, and the original was kept in the research records. A separate consent form was given to participants for the focus group, assuring them that all the necessary measures to protect their privacy and confidentiality were taken. Names were only recorded on the consent form and were not shared either with other participants or while reporting the results. Participants also selected their preference to recording of the session. Since participants were divided between those who agreed to the recording and

those who did not, the focus group was divided to accommodate the preferences of participants. Other participants were also interviewed separately as per their preference. Participants also agreed in the consent form to respect the privacy of other participants and not to repeat what was shared during the focus group to others.

2.1.3. Record keeping

All research related documents and information were accurate and completed, and available at any time if required. Documents included the IRB approved protocol, original signed copies of all consent forms, data collected, and any other research related documents. All research records were stored under lock by the PI to be kept for at least 3 years from the time the research was completed. After the 3 years have elapsed, and if no longer required, all confidential research data will be destroyed.

2.2. Step 1 of research: Interviews with representatives from local manufacturers of pharmaceutical products

Research question 1: What are the different barriers to the implementation of a unique identifier (2D barcode) and a track and trace system on pharmaceuticals for local manufacturers?

2.2.1. Population and sample

Target population was local manufacturers of pharmaceutical products in Lebanon. There are 12 registered local manufacturers in Lebanon. The inclusion criteria were local manufacturers with marketed product, either fully manufactured or under license, and the products should be subject to the decision 2405/1 issued on 11/12/2017 by the Ministry of Public Health (MoPH) related to the implementation of the 2D barcode and the track and trace system. Manufacturers of intravenous solutions were excluded since these products are exempt in the decision issued. In total there were four

manufacturers excluded, three are manufacturers of serums and IV solutions and one that doesn't have products on the market yet. Table 9 shows the manufacturers that were approached to be interviewed, and the number of products manufactured and marketed in Lebanon by each, and the representation of each one in terms of market size (Ministry of Public Health, 2021b). In total, these local manufacturers represent 22% of registered pharmaceutical products.

Table 9: Local manufacturers in Lebanon and the number of registered products (Number of products and Percentage are calculated based on the last published list on the MOPH website where the total number of registered products is 5481)

Manufacturer's name	Number of products marketed	Percentage of registered products (%)
Algorithm	155	2.83
Arwan	51	0.93
Benta (BPI)	358	6.53
Chapha	13	0.24
Mediphar	168	3.07
Mephico	52	0.95
Pharmadex	155	2.83
Pharmaline	255	4.65

This research covers all the target population of local manufacturers since all the manufacturers subject to the decisions issued were approached and interviewed.

2.2.2. Data collection

A letter was sent to each company requesting an interview along with a letter of support from the MoPH. All participants provided their consent prior to the interview. Data was collected through structured or semi-structured interviews with representatives from local manufacturers. Interviews were recorded (when permission was granted form the participant) to provide record of what was discussed. The participants were from different departments such as production, quality, regulatory or the owner of the company. The interviews were conducted with one or more representative form each company. Examples of data collected: lines already implementing the track and trace system, quantities produced, time added to production, the cost of machines used to print the barcodes, the number of machines needed, additional personnel needed, difficulties acquiring additional equipment or personnel, other possible barriers that can delay the implementation, methods to ensure quality of products is not affected, what might facilitate the process, …

2.2.3. Data analysis

Descriptive statistics was used to analyze quantitative results, while qualitative data was transformed using Braun & Clarke's six steps thematic analysis (Clarke et al., 2015). This thematic analysis starts with familiarizing ourselves with the data, meaning transcribing it, reading the transcripts several times, and noting down the initial ideas. The second step is generating initial codes, where all interesting features of the entire data set are given codes. This is followed by searching for themes, where a combination of codes relevant to each other is collated in a potential theme. Then, the identified themes will be reviewed and analyzed to determine if they are coherent. This is usually done over two phases; first themes are checked in relation to the coded extracts then for the overall data set. This will lead to the generation of a thematic map of the analysis. Once the map is generated, the fifth step of the thematic analysis is defining and naming

the themes, where themes are redefined, and potential subthemes are identified within the data. The sixth and final step is producing the report where all the analysis is transformed into a scholarly report using a selection of examples that relate to the themes, research questions and literature.

Advantages of thematic analysis:

- Highly flexible approach that can be modified according to the needs of the study
- Does not require theoretical knowledge of other qualitative approaches
- Useful method for highlighting the similarities and differences in the perspectives of participants

Credibility is achieved by peer debriefing (also known as analytic triangulation), which provides an external check on the research process (Nowell et al, 2017).

Thematic analysis of the results was done by the principal investigator and no saturation was reached because it wasn't in the scope of this research.

2.3. Step 2 of research: Focus group with community pharmacies

Research question 2: What are the different barriers to the implementation of a track and trace system on pharmaceuticals for community pharmacies? (done in parallel with step 1 mentioned above)

2.3.1. Population and sample

The target population was owners of licensed community pharmacies for a focus group. There are 3920 licensed pharmacies distributed all over Lebanon. Out of these 3920, there are 189 hospital pharmacies and 3731 community pharmacies. Figure 17 shows their distribution by governorate (Ministry of Public Health, 2021a). For the scope of this research, the aim was to explore potential barriers at community pharmacy level and thus a

purposive sample of pharmacies in Lebanon was selected. The inclusion criteria for the focus group consisted of 1-2 community pharmacies from each governorate, both large or small pharmacies, computerized or non-computerized.

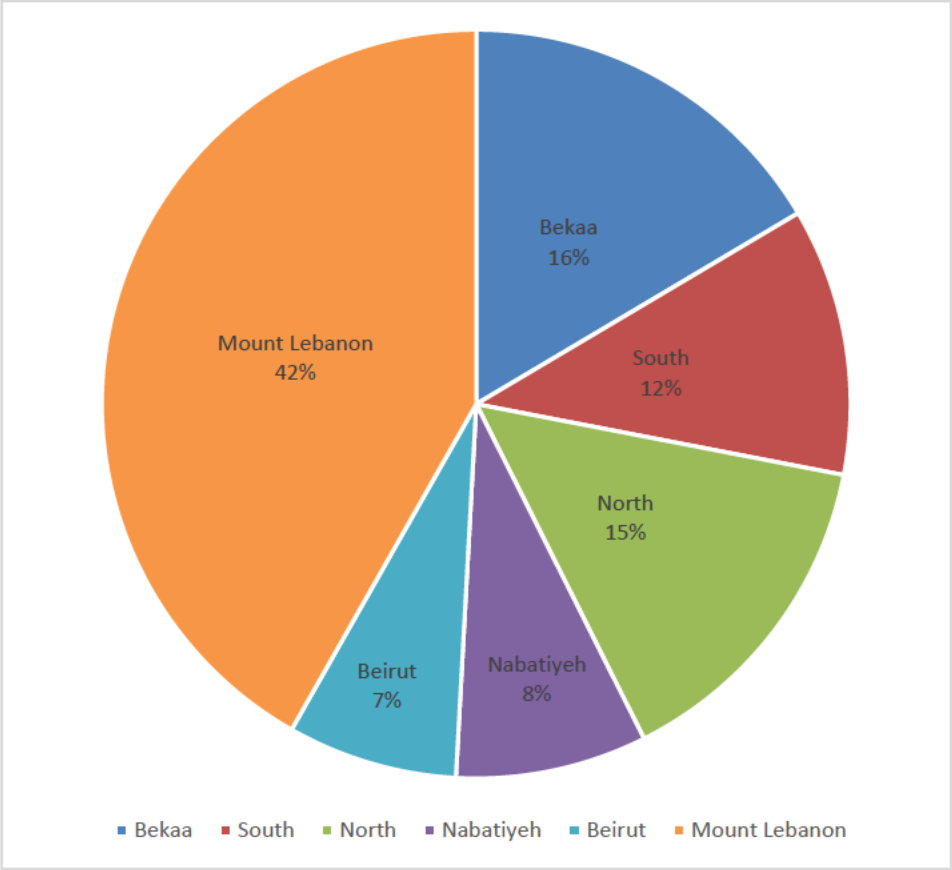


Figure 17: Distribution of pharmacies in Lebanon by governorate

2.3.2. Data collection

Data was collected after receiving consent through a focus group of pharmacists. Participants who expressed their wish not to be recorded were interviewed separately. The group interview allowed for data collection from several people simultaneously while using the group interaction and communication as part of the method. Semi-structured interviews were used to guide the group discussion focusing on their knowledge of the regulation issued by the MoPH and the timelines for the implementation, in

addition to the barriers they think will hinder this implementation and their expectations from regulators and policymakers to assist in this process. Participants were encouraged to talk to each other while answering questions and commenting on the other's experience and point of view. This setting was mainly beneficial when open-ended questions were used, and participants were encouraged to explore the important aspects related to their work. This process led to more questions during the discussion by the pharmacists, which highlighted their priorities and the areas to focus on. Focus group sessions were recorded after receiving consent to provide record of what was discussed.

2.3.3. Data analysis

Since this question also included qualitative data, the same methods of analysis mentioned in Research question 1 were applied here.

2.4. Step 3: Key informants' interviews with policymakers /stakeholders

Research question 3: How can the regulatory authorities assist, facilitate, or speed up the implementation of the track and trace system on pharmaceuticals?

2.4.1. Population and sample

The target population was key representatives from the major regulatory authorities and policymakers. The inclusion criteria is for regulators involved directly in decision-making or influencing decision making in Lebanon such as the Ministry of Public Health (MOPH), the World Health Organization (WHO), the Order of Pharmacists (OPL), the Syndicate of the Pharmaceutical Industries in Lebanon (SPIL).

2.4.2. Data collection

Following the completion of questions 1 and 2, interviews were conducted with key informants from regulatory authorities. During the interviews, the

preliminary findings from questions 1 and 2 were discussed and feedback was collected to guide in the formulation of recommendations after the conclusion of the research.

2.4.3. Data analysis

Refer to data analysis in Research question 1.

All the data collected from the interviews were closely examined and compared; then the concepts collected were grouped to come up with theories and generalize the findings. Finding common concepts and coding was done manually.

Chapter Three

Results

3.1.Manufacturers response about the unique identifier (2D barcode)

In total, eight manufacturers were approached, and all agreed to participate in this research. After signing the informed consent, an interview was set up with representatives from each manufacturing company. The participants interviewed were regulatory affairs specialists, production managers, site managers or owners of the company. Some interviews included one person able to answer all the questions, while others included multiple representatives from the same company. Interviews were recorded when participants gave consent, otherwise the answers to the questions were written directly during the interview. The interviews took between 30-40 minutes each. All the questions were designed to assess the readiness of manufacturers, the challenges faced, and the barriers to the implementation of the requirements set by the MoPH regarding the printing of the 2D barcode on the outer package and the use of a local traceability system. Results of the questions are reported in the below sections.

Multiple questions were asked during the interview directly or indirectly related to the use of the 2D barcode and the implementation of the traceability system MediTrack in Lebanon. The results of the interviews showed that all participants are aware of the regulations issued and the timeline set for local manufacturers and that there are different levels of readiness from those that are fully prepared for implementations to those that are still in the planning stage. In total, four out of eight manufacturers (50%) said that they have been preparing for this implementation for a while. The preparations include the planning, purchasing of machines and equipment, reviewing the design of the package of all registered products, and preparing the staff for implementation. Three out of eight manufacturers (37.5%) said that they already have products with the 2D barcode (figure 18), and one already implemented it on all its products.

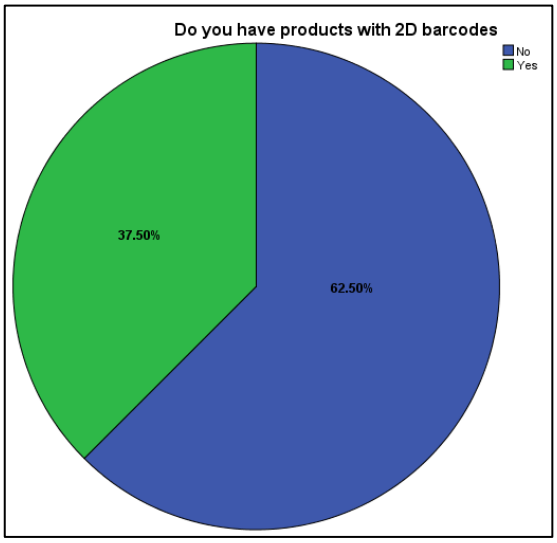


Figure 18: Participants answers on whether
they already have products with the 2D barcode

The interviews provided two perspectives when it comes to such an implementation. One group was able to provide additional insight to the challenges faced since they already started implementing the 2D barcode on their products either partially or fully, and another group focused only on the barriers that are currently standing in the way of implementation. All participants who already implemented or started the implementation agreed that it needs a lot of planning and preparation. In fact, one participant said that "it was a lengthy process; we had to stop the production line by line in order to install the machines", another participant mentioned that "it took some time to get used to the new process and get the production back on track". They also agreed that it's very costly to implement especially if they include serialization, participant 5 said "It was a big investment for the company since we had to purchase 1 machine for each production line to prevent any delays in production…It would have been much more challenging to implement now". Cost was the most important barriers to all participants. Each manufacturer needs to purchase several machines that can print the 2D barcode. In fact, there should be one machine per production line in order to cover all products manufactured. When asked about the price of each machine, participants stated that each would cost around 30,000 Euros for the regular machine that prints at the lot level, while

serialization machines can cost around 150,000-200,000 Euros. Participant 1 mentioned that “small manufacturers don’t have the capacity to purchase several lines of 2D printing machines, and serialization is even more expensive”. Especially with the inability to secure loans from local banks due to the financial crisis in the country. Participant 1 said “we are unable to get loans from banks, we are securing loans from abroad”, this was also emphasized by participants 3 and 6 who also mentioned that because of the difficulties with acquiring loans, not all companies will be able to cover the cost of the machines and be ready for implementation.

Other challenges mentioned include the cost of other equipment (barcode readers, running cost of machine, maintenance, servers…) and increasing cost of packaging material. Participant 8 said “we need more equipment such as barcode readers for production department, the quality department, and the warehouse to check the printed barcodes; the machines also need maintenance”, while participant 4 said “there are other costs as well such as the running cost of the machines”. The running cost includes the cost of ink, maintenance, and electricity. Participant 6 focused on the increasing cost of packaging material, mentioning that all the products used from the plastic, the bottles and cartons, are imported from other countries.

Furthermore, three out of eight manufacturers (37.5%) also mentioned the need to change the design or dimensions of the outer package in order to accommodate the printing of the 2D barcode and human readable data. This would require the submission of variations to the MOPH at the level of each product. Other challenges mentioned include the change in the production process, training staff, hiring new personnel, absence of a reliable internet connection and other situational problems related to the current crisis in the country. In fact, seven out of eight participants (87.5%) mentioned the lack of infrastructure required for this implementation such as constant electricity supply and a reliable internet connection. Participant 1 mentioned during the interview that “we don’t have the infrastructure for such implementation especially with the current financial situation and electricity cuts” and participant 6 said “it’s hard to implement in Lebanon now due to electricity cuts

and connection problems". Figure 19 shows the response of all participants to the different barriers mentioned.

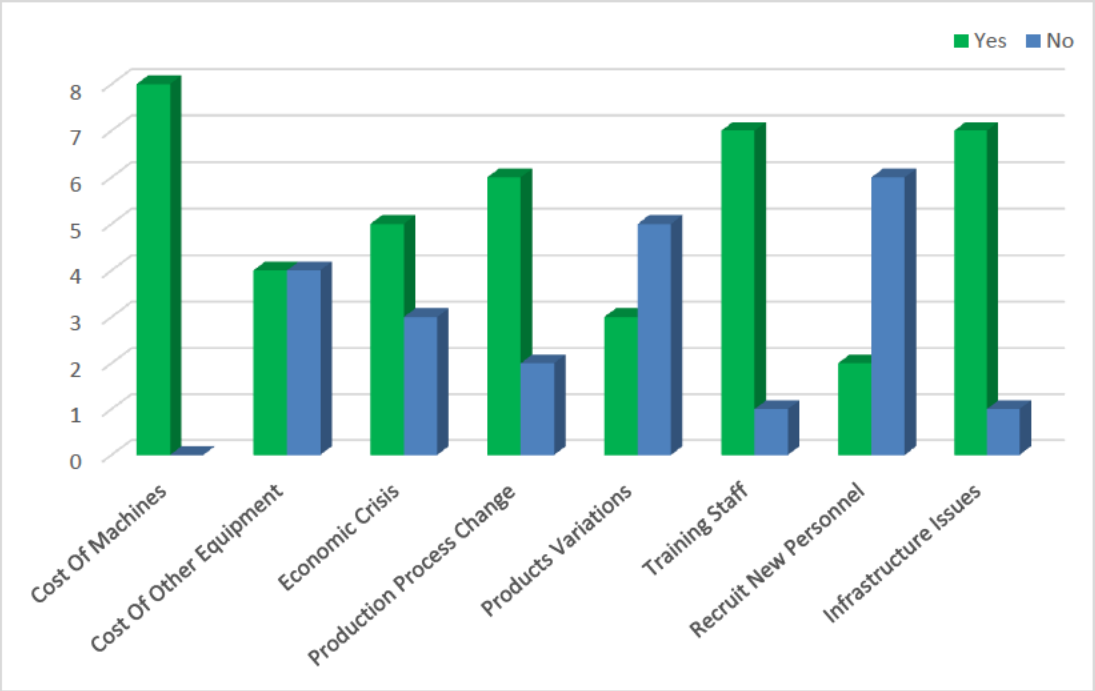


Figure 19: Challenges and barriers identified by manufacturers

Another topic tackled during the interview was whether each manufacturer exports to other countries. Six out of the eight manufacturers (75%) interviewed mentioned that they do export and two are not currently exporting to other countries (Figure 20). The export countries are mainly gulf countries such as Saudi Arabia, UAE, Kuwait, Qatar, and other countries like Syria, Jordan, and Yemen. The different destinations for export mentioned by all participants can be seen in figure 21. Several of these export destinations are also either implementing traceability or are planning for future implementation. Therefore, by meeting the local requirements, local manufacturers ensure the continuity of their export and gives them access to new markets.

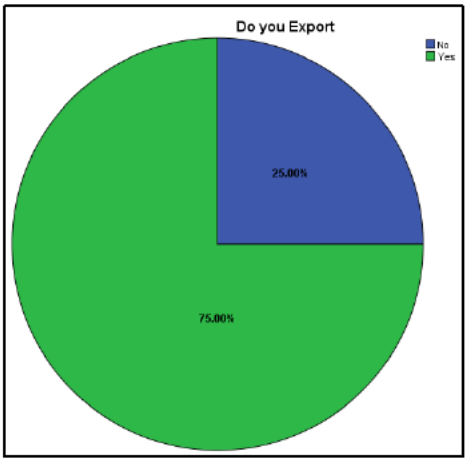


Figure 20: Participants answers on whether they export their products

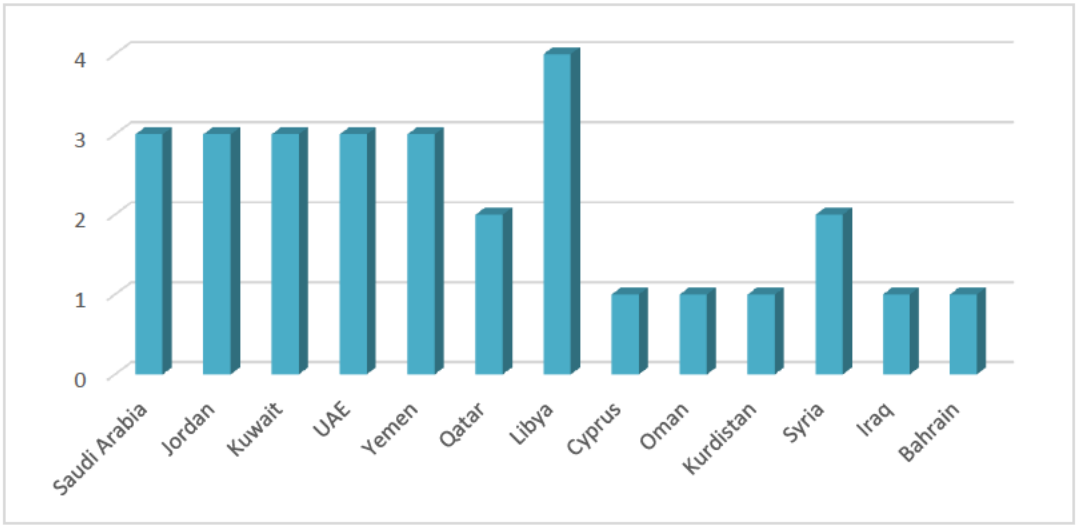


Figure 21: Main destinations for export

3.2.Manufacturers response about the track and trace system

Participants were also asked whether they have a computer system in place. All participants stated that they have their own systems where they enter the different transactions and are able to track their products at the lot level. One participant also mentioned their traceability reaches serialization and aggregation. However, they all agreed that the main concern is the unstable and unreliable internet connection when it comes to connecting to the MoPH developed traceability system. One participant said, “we don’t have the infrastructure required for such implementation especially with the current situation in the country specifically the electricity cuts and internet connection problems”.

When asked about the traceability system MediTrack developed by MoPH, four out of eight manufacturers (50%) said that they don’t expect any problems when they start working on MediTrack, however they all agreed that they need training sessions on the system and a testing phase before the deadline.

Despite all the challenges and barriers mentioned by the participants, they all agreed that such implementation is very beneficial especially given the current crisis in the country and shortage of medicines. Table 10 shows the major benefits mentioned by all participants. In fact, due to its importance, five participants (62.5%) said that implementation should include pharmaceutical-like products at a later stage. As for the drawback, there were two major drawbacks mentioned, the cost of this implementation and the risk of not reaching the full benefits of traceability if not all the stakeholders (distributors and pharmacies) are connected to MediTrack. Two participants expressed their concerns regarding other stakeholders’ inability to work on Meditrack due to electricity cuts and internet connection problems. Participant 2 also mentioned that some pharmacies in remote area may not even be computerized and if they are computerized, they don’t have access to the internet due to their location.

Table 10 : Benefits and drawbacks identified by manufacturers on the implementation of traceability in Lebanon

Benefits	Drawbacks
Ensure patient safety	High cost of implementation
Follow Global trends of serialization and traceability	The implementation will not have a full impact if not all stakeholders are connected
Regulate the pharmaceutical sector in Lebanon	
Unique feature printed on the box	
Prevent medication stockpiling	

Finally, when asked whether they will be ready to meet the deadline set by the MoPH, December 31st, 2022; 50% responded that they have been preparing for the implementations and will be ready by the end of the deadline, while the rest stated that they will not be ready for full implementation on time (Figure 22). Participant 4 said "we may not be ready for implementation since we don't have the printing machines yet" while participant 8 said "we only have one machine for printing however we need at least three to cover all our production lines".

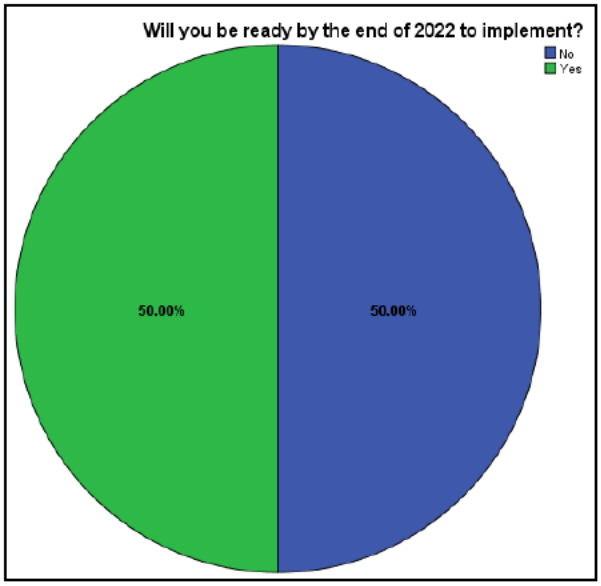


Figure 22: Participants answer about their readiness for implementation by the end of 2022

3.3.Pharmacies feedback from the focus groups

In total, 12 pharmacies from different governorates were approached to participate in this research (Figure 23). Three were unable to participate either due to interruption in the electricity or the internet or due to last minute engagement at work. The focus groups consisted of a total of 9 pharmacies, with 4 agreeing to being recorded while the rest requested not to be recorded. Participants who did not join the recorded focus group were interviewed separately and individually. The sample from community pharmacies was a limited and purposive sample and not representative of the regional variations

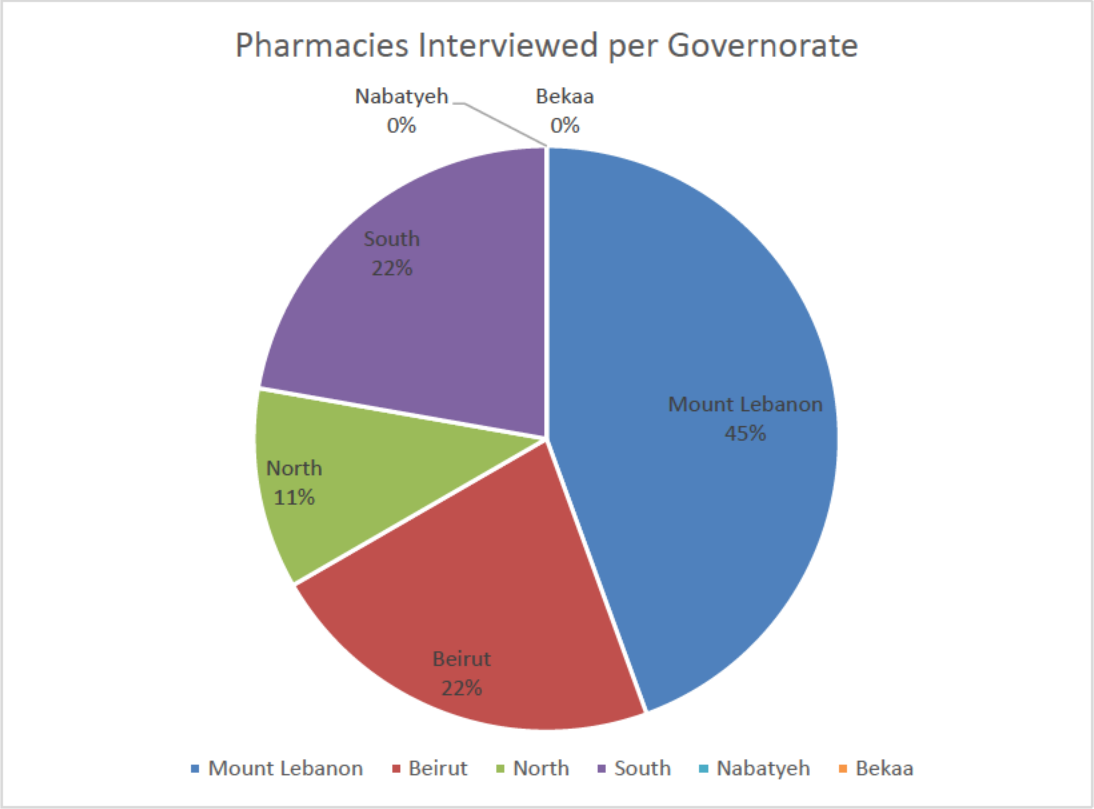


Figure 23: Distribution of pharmacies interviewed per governorate

All the pharmacies included stated that they were computerized, and all have a barcode reader. However only one of them have a barcode reader able to read the 2D barcode, while the rest can only read a linear barcode. The software used in these pharmacies varied between SoftPharm and Apothicare. Seven out of nine pharmacies (77.78%) use SoftPharm, while two (22.22%) use Apothicare. Figure 24 shows the pharmacists response to some of the questions asked.

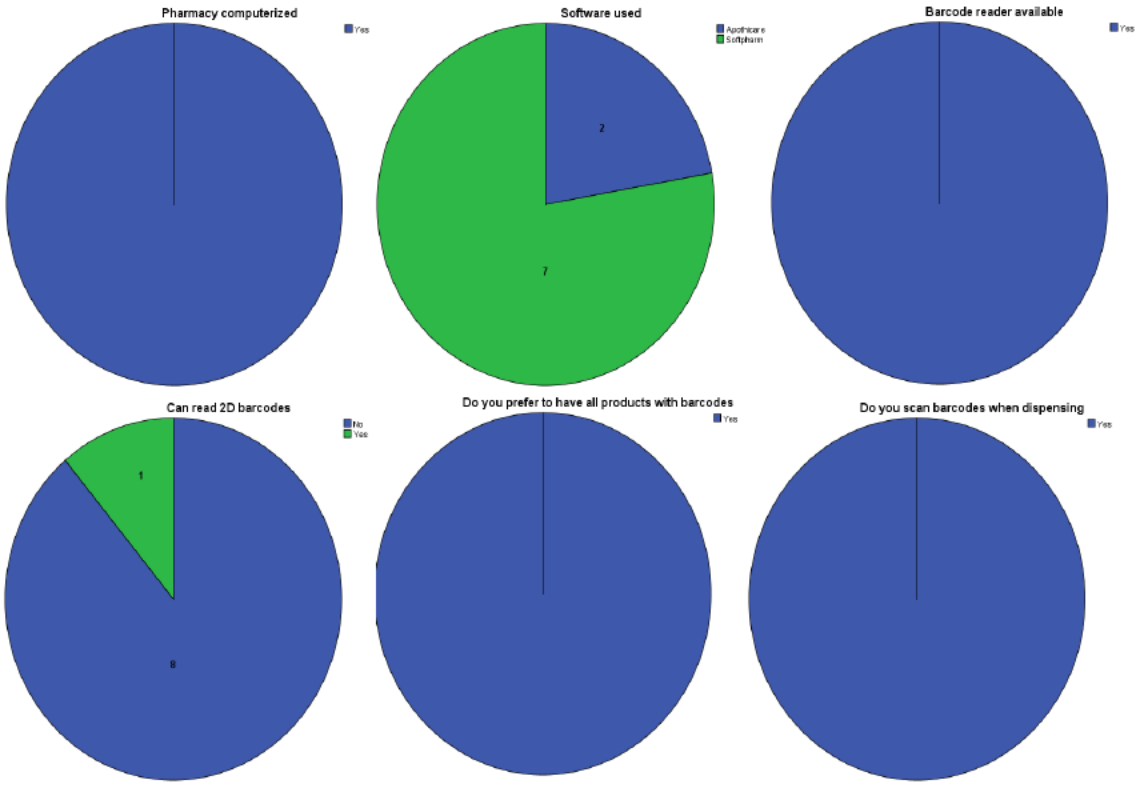


Figure 24: Pharmacies answers to the questions asked during the focus group

Pharmacists were then asked whether they use the barcode while dispensing or search by products names. All answered that they use the barcode when available however not all products have barcodes and sometimes, they have to search manually for the products which can lead to errors. They agreed that it would be better to have barcodes on all products since it allows for faster dispensing, makes it

easier to find products, and reduce the risk of errors (Figure 25). Participant 1 said "having the barcode would allow for faster dispensing" while participant 6 said "sometimes we have many patients coming at the same time, so it is easier to scan barcodes and less time consuming". Participant 8 also said that "scanning a barcode instead of searching for the product manually reduces the risk of error especially when we are in a hurry with many patients waiting in the pharmacy".

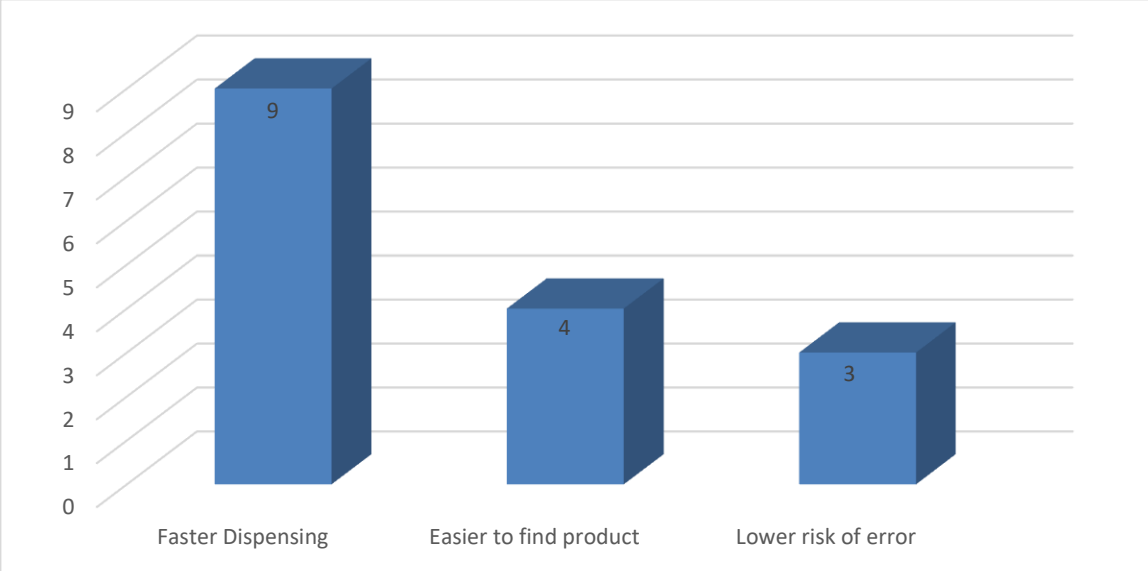


Figure 25: Advantages of using the barcode for dispensing

When asked about their knowledge about the local regulations, only three pharmacies (33.33%) were aware that there are local regulations in place for the traceability of pharmaceutical products, however they didn't know about the details of the regulations or how far into the implementation it currently is (Figure 26).

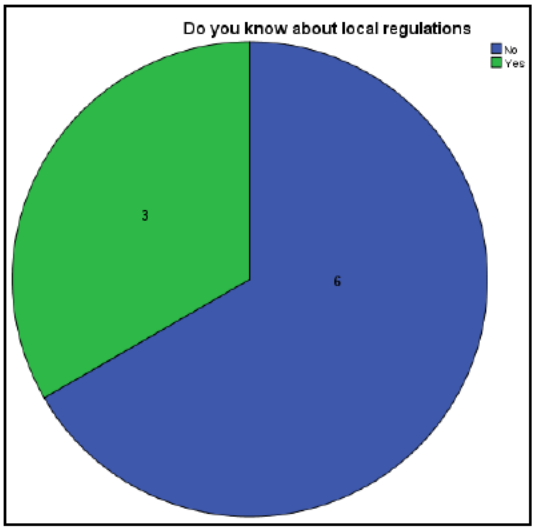


Figure 26: Pharmacists answer about their knowledge of the local regulations issued

Once they heard about the regulations, all pharmacists agreed that it would be beneficial to have such a system in place however there are some barriers currently that prevent such implementation. Table 11 shows the response regarding the benefits and barriers.

Table 11: The benefits and barriers to traceability implementation identified by pharmacists

Benefits of Traceability	**Barriers to implementation**
Helps to reduce counterfeits in the market	Economic Crisis and inability to purchase 2D barcode readers
Increase patient safety	Electricity cuts
Prevent smuggling of drugs outside the country	Unreliable internet connection
Better visibility for refilling prescriptions	Additional costs for software maintenance
Prevent medication stockpiling	Pharmacies in remote areas are not connected to the internet

3.4. Interviews with regulators and policymakers

Following the conclusion of the interviews with local manufacturers and the focus groups and interviews with pharmacies, regulators were approached in order to discuss the findings of this research. The interviews were conducted in the form of presentation of findings and results and providing the recommendations. These interviews included representatives from the MoPH, the main regulatory body for the pharmaceutical sector in Lebanon, and representatives from the SPIL. During the interviews, the barriers identified were discussed in detail and the recommendations were provided in order to facilitate the implementation for local manufacturers and pharmacies. No direct feedback was received on whether any of the recommendations would be considered.

Chapter Four

Discussion

4.1.Barriers identified for local manufacturers

The aim of this research was to identify the barriers for the implementation of the track and trace system in local pharmaceutical institutions in order to find possible ways to overcome them. Based on the interviews' transcripts, five major themes could be derived for the different barriers and challenges to implementation. The five themes are the following:

- Financial/Economic
- Logistics and production
- Regulatory
- Internal planning / Human resources
- Infrastructure issues / Context specific

Following the initial analysis of the transcripts, additional patterns were identified allowing the extraction of several excerpts related to each theme (Annex 2) and the identification of several sub-themes creating a hierarchical frame (Figure 27).

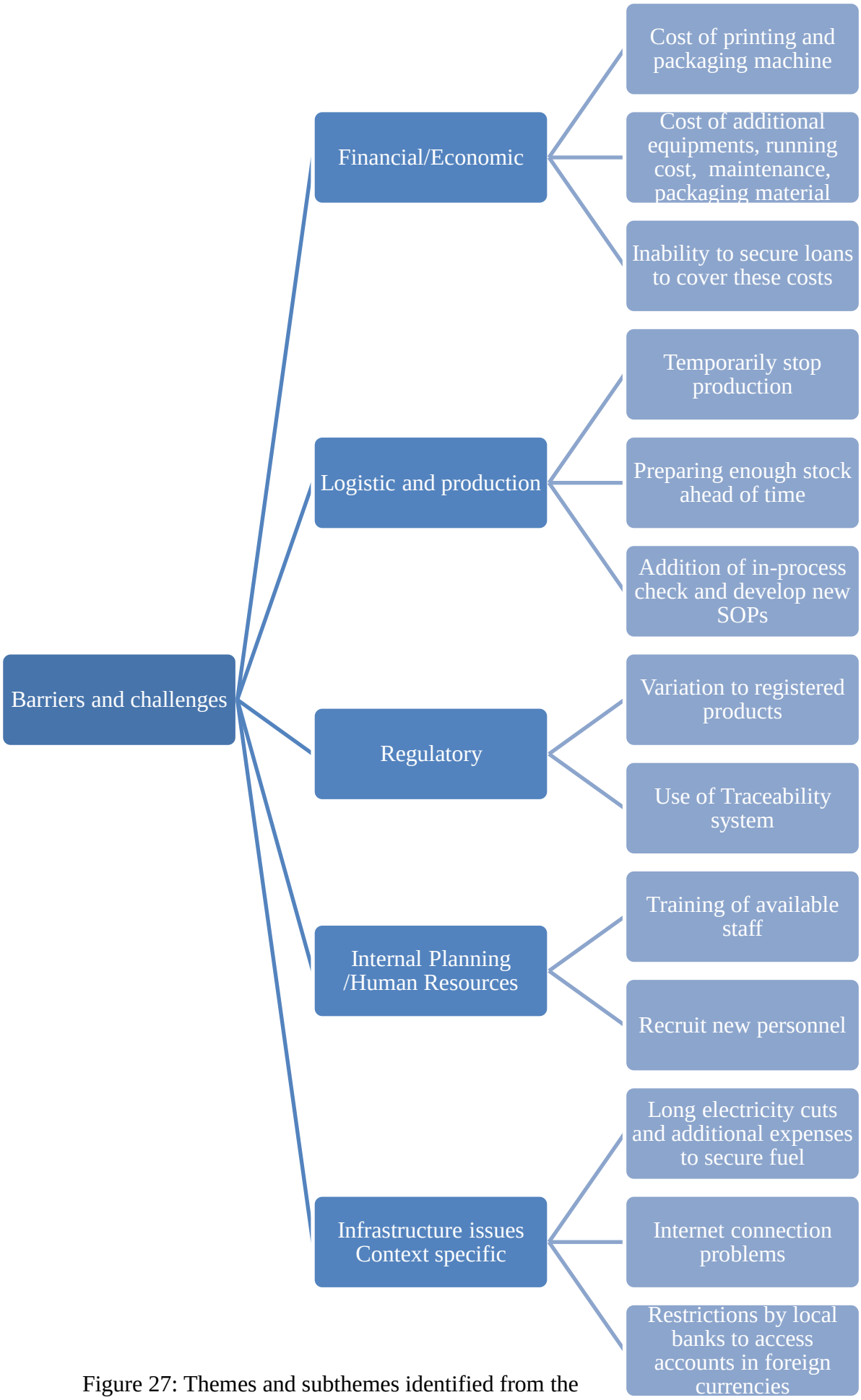


Figure 27: Themes and subthemes identified from the interviews with local manufacturers

4.1.1. Financial/Economic barrier

The financial barriers have multiple aspects starting with the cost of purchasing the printing machines and the traceability software, it also includes the running cost of the machines such as maintenance, ink, spare part, and required packaging material; and finally, the problems encountered at banks to secure loans to cover these costs. In fact, the financial barrier is the major concern for all participants. As seen in figure 19, all participants mentioned the cost as a challenge or barrier for the implementation. In fact, cost was a big concern for pharmaceutical industries globally during the implementation of serialization, especially with the pressure from governments to reduce the prices of pharmaceutical products (Botta, 2017). Small manufacturers have limited resources and might not be able to fully dedicate them to the implementation of traceability especially given the current situation and crisis in the country; therefore, they might have to withdraw from the market either partially or completely if they don't meet the set deadline. A survey conducted in the US prior to the deadline for implementation of the DSCSA showed that only 54% of pharmaceutical companies were ready for implementation. Most of the participants thought that compliance was difficult but achievable given enough time is provided to understand the requirements and to plan the implementation (Understanding Serialization Challenges, 2016). Therefore, comparing the results of the survey conducted in the US to the survey conducted with the local manufacturers, the findings look very similar. Given the fact that global companies found such implementation challenging, the results of the local survey are not surprising especially taking into consideration the current economic crisis in the country.

4.1.2. Logistic and production barriers

The second barrier identified is the logistic barriers and the challenges at the production level. This includes the decreased production efficiency and

even the complete halt of production while machines are installed and tested. If manufacturers don't take the necessary measures and build up their stock ahead of time this might lead to decrease in the sales since installation may take up to several weeks. In fact, many companies look for ways to counteract the decrease in production efficiency during the first stages of implementation by increasing their staff, improving the overall packaging effectiveness of the machines, and by finding ways to utilize the serialization data as return on investment (Shanley, 2018).

4.1.3. Regulatory barriers

When it comes to the regulatory challenges, there are two main subcategories in this theme. The first one deals with the variations needed in case the manufacturer must change the design of the box to accommodate the printing of the 2D barcode and the human readable data. As per the participants, this doesn't pose a huge problem since the same variation would be submitted to multiple products. Furthermore, since this variation would occur to meet the set requirements, this shouldn't create a big challenge from the regulatory side. The variation process related to the change in the design consists of filling an application that can be found on the MoPH website and submitting it to the service of pharmacy for approval (Ministry of Public Health, n.d.). The second main challenge is the use of the traceability system MediTrack. The MoPH needs to schedule multiple training sessions for all users and explain how the system works and all the options available. In addition, companies will require time to assess the best way to proceed and have a testing phase during which they can integrate with their own system and assess how feasible the integration is. In their efforts to comply with serialization regulations, global pharmaceutical companies had to invest in new software and processes to be able to be able to identify, track, share, and manage the required information (TraceLink, n.d.). Implementing serialization is therefore not

only about printing the unique identifier; it is about changing the whole process of manufacturing and data sharing. It requires the adoption of 2D barcode, purchasing the required scanning equipment, warehouse management, upgrading available software or switching to different ones that allow the automation of the whole process (TraceLink, n.d.). Local Companies should seize this opportunity to start planning for serialization since the current requirements only ask for traceability at the lot level. This can be considered as a steppingstone before the implementation of serialization, they can use this period to best analyze their situation and discover the best way for them to benefit from the implementation of serialization instead of considering it a hindrance due to its cost.

4.1.4. Internal planning / Human resources barriers

The fourth barrier identified is human resources which is divided into two parts, first the training of present staff and second recruiting additional personnel to cover new tasks in the new production and distribution process. As per the Good Manufacturing Practice (GMP) guidelines, all personnel must receive the appropriate initial training along with continuous training to ensure products are manufactured according to the appropriate standards (WHO Expert Committee on Specifications for Pharmaceutical Preparations, 2014). The same applies regarding the training of staff handling the storage and distribution according to the Good Storage and Distribution Practices (GSDP). The training should be provided to all employees involved in the manufacturing and traceability process, as for the new personnel recruited, they should be qualified in the area they are asked to fill (WHO Expert Committee on Specifications for Pharmaceutical Preparations, 2020). Although this may delay implementation for a certain time, once adequately trained all processes should return to normal with time. It might also help if some visual aids

related to equipment and diagrams of the new processes are added in the work area (Maldonado & Torres, 2016).

4.1.5. Infrastructure issues / Context specific

Finally, another complicated barrier for the implementation, is the current crisis Lebanon is going through. Due to the financial and economic crisis in the country, some of the basic daily needs are hard to access. First of all, due to shortage of fuel, the electricity supply is practically non-existent. This is specifically concerning in the pharmaceutical sector for manufacturers, importers, and pharmacies. Without a constant supply of electricity manufacturers would not be able to run their production machines or get any of their hardware or software running and warehouses and pharmacies wouldn't be able to meet the GSDP requirements especially for products that require refrigeration or be able to connect to traceability systems. Consequently, in order to maintain good practices, companies are searching for alternative options to provide electricity that are much more expensive. Furthermore, the use of the traceability system requires an uninterrupted internet connection, which is also a major problem in the country. There are several problems related to the internet connection, and pharmaceutical companies cannot control this issue since it originates from the internet service providers. Therefore, using a web-based traceability system may be challenging for real time data, the possible solution is accounting for a certain lag in the updated data between stakeholders, however this may pose an issue once pharmacies are connected as well. Finally, the last issue is the problem with the banking sector which adopted a certain form of capital control preventing individuals and institutions from accessing their accounts in foreign currencies all the while the Lebanese Lira is losing its value. Furthermore, banks also ceased all loans and companies have no other option than to look for loans from abroad which makes this implementation problematic during these times.

Despite the initial challenges and thinking beyond the initial investment, this implementation could provide several benefits such as giving companies access to other markets and opportunities to export their products to markets that require serialization and traceability. In fact, many of the countries to which local manufacturers currently export is either in the process of implementation or have already implemented serialization such as Saudi Arabia and Jordan (Colombo et al., 2019). Therefore, meeting the local requirements will also provide them with the means to maintain their export to these countries; giving them access to more consumers and allowing them to benefit from diverse markets in face of the current financial challenges in the country.

4.2. Barriers identified for pharmacies

As for pharmacies, there are some barriers similar to the barriers identified for local manufacturers to a certain extent while others are different. There are three major themes for the barriers to implementation at the level of pharmacies:

- Financial/Economic
- Regulatory
- Infrastructure issues / Context specific

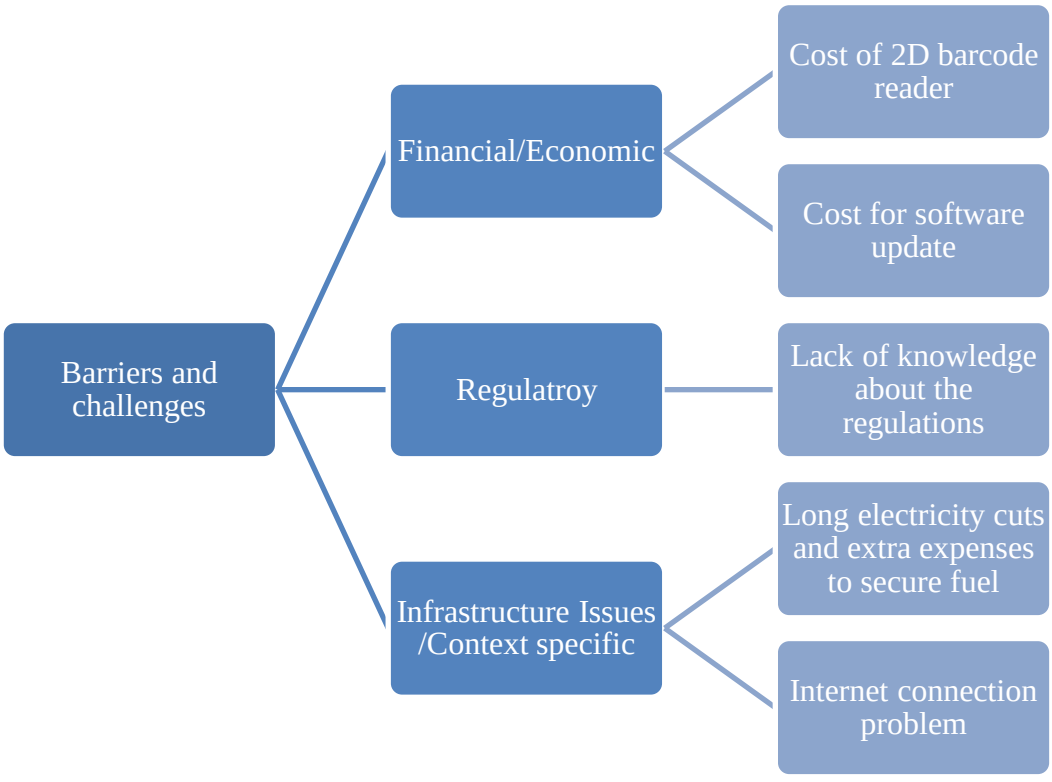


Figure 28: Themes and subthemes identified from the focus group and interviews with pharmacies

4.2.1. Financial/Economic barriers

All pharmacists expressed their concern regarding the additional costs related to purchasing a 2D barcode reader and the additional costs for software maintenance. The cost of a 2D barcode reader starts at 200 Dollars and can go up to 600 Dollars or higher based on its capabilities and specifications (Camcode, 2022). As for the software available in pharmacies, SofPharm is used in more than 90% of the pharmacies in Lebanon (Professional Computer Association of Lebanon, 2019). This could facilitate the implementation in pharmacies since the software can directly integrate with MediTrack and facilitate data transfer, preventing double work and reducing the pharmacists' workload while meeting the requirements set by MoPH. Other software companies can perform the same integration with MediTrack and prevent the additional workload on the pharmacist or the need to hire additional staff to work on the system.

Although this same barrier was identified for manufacturers, it affects each stakeholder differently. While the impact to manufacturers is at a larger scale due to the very high cost of machines and equipment, for pharmacies this is mainly related to the purchase of barcode readers and software update.

4.2.2. Regulatory: Lack of knowledge about the regulations

The focus group and interviews showed that many pharmacists are not yet aware of the issued regulations. Efforts need to be made to advertise and raise awareness to the pharmacists on this implementation since it affects all stakeholders involved in the supply chain as well as the patient. The survey conducted in the US, previously mentioned above, also included hospitals and retail pharmacies and it also showed that 32% of hospitals and 41% of retail pharmacies were not familiar with the requirements of serialization and the traceability system (Understanding Serialization Challenges, 2016).

4.2.3. Infrastructure issues / Context specific

Finally, regarding the electricity cuts and the internet connection, this is a problem at the national level, and it may not be as easy to solve. Pharmacists are spending extra costs to maintain constant electricity in their pharmacies; however they cannot fix the internet connection problems and therefore the only possible solution is for the regulatory authorities to allow a certain level of delay instead of real time data transfer until a more practical solution is reached.

Chapter Five

Recommendations

All the findings and results of the interviews and the focus groups provide a detailed image of all the barriers standing in the way of the implementation of the unique identifier (2D barcode) and the traceability system MediTrack in the Lebanese pharmaceutical sector. These findings also allow the presentation of possible recommendations to regulators and decision makers to facilitate the implementation. The recommendations can be divided in three categories:

5.1. Recommendations at the regulatory level

- Provide a grace period or an extension for manufacturers unable to fully implement the 2D barcode and traceability by the end of 2022
- Allow for gradual implementation of the 2D barcode on products
- Seek funds from donors to provide incentives for stakeholders
- Raise awareness of pharmacists on the whole traceability project
- Ensure the security and confidentiality of shared data
- Schedule multiple training sessions on MediTrack

5.2. Recommendations at the level of local manufacturers

- Increase the price of some registered products that are very inexpensive
- Provide a suitable testing period (at least 2-3 months) on MediTrack

5.3. Recommendations at the level of pharmacies

- Provide 2D barcode readers for pharmacies by securing funds from donors or by arranging for an acceptable deal with a local provider to negotiate the price
- Encourage pharmacies software providers to provide facilitations for payment and maintenance

In addition to the above, there are several other recommendations that are beyond the scope of the health sector, and therefore beyond the scope of this research. Whether the proposed recommendations would be taken into consideration or not by policy makers remains to be seen. However, the success of such an implementation requires the cooperation of all concerned parties including the policy makers especially given the current economic crisis in the country and the loss of many pharmaceutical products from the market as a consequence.

Chapter Six

Conclusion

The implementation of the unique identifier and a track and trace system brings a lot of benefits to the pharmaceutical sector by enhancing the supply chain, increasing patient safety, preventing counterfeits, and facilitating the recall process. This is especially beneficial in Lebanon, given the problems encountered over the past year from medication stockpiling and smuggling outside the country. There are many positive outcomes to serialization and companies must think of it as a return on their investment. Some of these benefits include visibility of products as they move through the supply chain, management of expiration date and reducing product loss, and improving inventory practices (Maldonado & Torres, 2016). The long-term benefits outweigh the initial drawbacks and challenges, and it could also save the supply chain further costs by improving the forecasting as data starts flowing in real time in the supply chain and by creating innovative packaging solutions (Botta, 2017). One of the strengths of this research is that it focuses on the barriers of the implementation by local manufacturers in Lebanon, which is the first of its kind to best of our knowledge. It is also comprehensive research including all local manufacturers. The interviews identified the major problems faced by manufacturers and the major barriers to implementation. The research also explores the perception at the level of pharmacies through focus groups and interviews. It included a collection and triangulation of multiple perspectives by all the different stakeholders involved in the implementation of such a system. Furthermore, this operational research allowed the development of concrete recommendations which were presented to regulators and policy makers in the pharmaceutical sector. It can also be used as an example and transferred to other countries considering a similar implementation. Any of these recommendations can facilitate the implementation on the stakeholders involved and encourage them to speed it up. As for the limitations of this research, in the focus group setting some members may have been hesitant to express their thoughts and opinions if they opposed the opinion of another member

in the group, it also affects confidentiality of data shared in the session (due to the group setting vs individual). Furthermore, non-computerized pharmacies were not represented in the sample population. Another limitation is the inability to target all the policymakers due to time limitations and inability to reach some of them and the inability to conduct interactive interviews with regulators/policy makers due to the fact that the participants are not the sole decision makers. Additionally, one of the disadvantages of thematic analysis is that due to its flexibility, it can lead to some inconsistency when deriving themes from the data.

Future studies would be beneficial to identify and find possible solutions for remote pharmacies that may not be computerized or might have problems connecting to the internet due to their remote locations. Other studies may also focus on the implementation at the unit level in the hospital setting to further enhance patient safety.

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Annex1

List of medicinal products or product categories subject to prescription that shall not bear the safety features, referred to in Article 45(1)		
Name of active substance or product category	**Pharmaceutical form**	**Strength**
Homeopathic medicinal products	Any	Any
Radionuclide generators	Any	Any
Kits	Any	Any
Radionuclide precursors	Any	Any
Advanced therapy medicinal products which contain or consist of tissues or cells	Any	Any
Medicinal gases	Medicinal gas	Any
Solutions for parenteral nutrition having an anatomical therapeutical chemical ('ATC') code beginning with B05BA	Solution for infusion	Any
Solutions affecting the electrolyte balance having an ATC code beginning with B05BB	Solution for infusion	Any
Solutions producing osmotic diuresis having an ATC code beginning with B05BC	Solution for infusion	Any
Intravenous solution additives having an ATC code beginning with B05X	Any	Any
Solvents and diluting agents, including irrigating solutions, having an ATC code beginning with V07AB	Any	Any
Contrast media having an ATC code beginning with V08	Any	Any
Tests for allergic diseases having an ATC code beginning with V04CL	Any	Any
Allergen extracts having an ATC code beginning with V01AA	Any	Any
List of medicinal products or product categories not subject to prescription that shall bear the safety features, referred to in Article 45(2)		
Omeprazole	Gastro-resistant capsule, hard	20mg
Omeprazole	Gastro-resistant capsule, hard	40mg

Annex 2

Manufacturers barriers and challenges		Excerpts from the interviews
Financial barriers	Cost of machines	Cost of the machines is a concern especially in the current financial crisis, It was a big investment for the company since we had to purchase 1 machine for each production line, small manufacturers don't have the capacity to purchase several lines of 2D printing machines, serialization is even more expensive, the cost is too high to upgrade or buy additional machines, can't leave any line without installing the track and trace system because it will mean decreasing the output of the manufacturing site
	Cost of additional equipment (barcode readers, servers, running cost, and maintenance)	we must consider the running cost of machines like the cost of printing (inkjet), we don't have the infrastructure for such implementation (like servers) especially with the current financial situation, we also need to consider the costs for the maintenance of the machines, we need more equipment such as barcode readers for production department to check the printed barcode, QC, and the warehouse
	Increasing costs of packaging material	all materials used in production are imported and need to be paid in fresh cash including the packaging material like bottles and boxes
	Increasing costs of fuel for electricity	We are paying a lot monthly just to buy fuel for electricity to keep everything running
	Inability to secure loans from local banks	The machines are purchased from abroad, the cost before was acceptable it was integrated with the financial cost of the manufacturing site, however now it is a difficult time, we are getting loans from abroad, provide facilitations to get credit in order to buy machines, not all will be able to cover the costs with the financial crisis

Logistic and Production challenges	Temporarily stop production to install new machines	the major problem will be during the installation of the machines since we will need to stop the production for a while, additional challenges include finding enough space to install the new machines at the end of each packaging line, It was a lengthy process and we had to stop production to do the testing, production slowed down initially until staff was trained, there is always a learning curve, It needs a lot of planning and time to implement, it will slow down production because there is only one machine, we will need to reorganize the way of work
	Prepare enough stock ahead of time to cover market needs	the company will need to have stock prepared in advance to prevent shortage of medication on the market
	Addition of in-process check for the barcodes	new personnel needed to check on the 2D barcode after printing, initially it took some time to get used to the new process, another challenge was adding the in process checks on the 2D barcode which has to happen every 30 minutes
	Develop new SOPs	Installing new equipment requires developing new SOPs and updating the guidelines
Regulatory challenges	Traceability system MediTrack	we need more details including training and a testing phase to study all the options available, the testing phase should be at least 2-3 months, The deadline should be realistic and achievable to all, Need technical help during implementation, we need more information and technical support with the implementation, training sessions offered by the ministry would be a good idea (for MediTrack), the distribution process has to be modified and we might experience difficulties in distribution while using the traceability system, provide training for a smooth transition for work on MediTrack, guarantee confidentiality and security of data shared
	Variations to change design of some products	For some products a change in the design was necessary to accommodate the new barcode and printed data, otherwise we just submitted a notification of implementation of serialization, the design of the box might need change, or the dimensions, or the quality of the paper of the carton, some products need a change in the design to be able to accommodate a 2D barcode either due to the small size of the box or due to the absence of secondary packaging (there are special products that consist only of a bottle and the label doesn't have enough space or it's not possible to print the 2D barcode directly on it)

Internal Planning/ Human resources	Training of staff	The team will need new training of course, we need some time to train the staff to the new process, it will only take some time to adjust to the new process of production, there is always a learning curve
	Recruiting new personnel	new personnel needed to check on the 2D barcode after printing, we would need additional IT personnel to work on the traceability system, no need for new personnel, the same people that are positioned at the end of each line will just shift their position to the new end at the new machine installed
Infrastructure issues/ context specific	Electricity cuts	we don't have the infrastructure for such implementation especially with the current financial situation and electricity cuts (no electricity, no internet), Not all stakeholders will be able to connect especially with the electricity cuts and connection problems
	Internet connection problems	we don't have the infrastructure for such implementation especially with the current financial situation and electricity cuts (no electricity, no internet), Not all stakeholders will be able to connect especially with the electricity cuts and connection problems
	Difficulties with local banks	we are unable to get loans from banks, we are securing loans from abroad, we are experiencing delays in production due to delays in approvals from the central bank