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Track & Trace System in the Pharmaceutical Industry

نظام التتبع والتعقب في الصناعة الدوائية

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by

Marlen Asbih

Supervisor: Dr. Hani Shtaya

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Prepared by: Marlen Asbih

Registration number: 1155410

Supervisor: Dr. Hani Shtaya

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The names and signatures of the examining committee are as follows:

1. Dr. Hani A Shtaya Head of Committee Signature:_____
2. Dr. Amjad Abusalha External Examiner Signature:_____
3. Dr. Moammal S Qurt Second Examiner Signature:_____

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List of Abbreviations

Abbreviation	Definition
1D	One Dimensional
2D	Two Dimensional
3PL	Third Party Logistic
AI	Application Identifiers
ATTP	Advanced Track and Trace for Pharmaceuticals
CDC	Centres for Disease Control and Prevention
CFDA	Chinese Food and Drug Administration
cGMP	current Good Manufacturing Practices
CMO	Contract Manufacturing Organization
DB	Data Base
DCVMN	Developing Countries Vaccine Manufacturers Network
DQ	Design Qualification
DQSA	Drug Quality and Security Act
DSCSA	Drug Supply Chain Security Act
DTTS	Drug Track and Trace System
EDMC	Electronic Drug Monitoring Code
EMVO	European Medicines Verification Organisation
EMVS	European Medicines Verification System
EPC	Electronic Product Code
EPCIS	Electronic Product Code Information Services
EPTTS	Egyptian Track and Trace System
ERP	Enterprise Resource Planning
EUIPO	Europe Intellectual Property Office

Abbreviation	Definition
EWM	Extended Warehouse Management
FAT	Factory Acceptance Test
FD&C	Food, Drug and Cosmetic Act
FDA	Food and Drug Administration
FMD	Falsified Medicines Directive
GCP	Global Company Prefix
GDP	Good Distribution Practice
GLN	Global Location Number
GS1	Global Standards One
GTIN	Global Trade Item Number
HIS	United States' Homeland Security Investigations
ID Key	Identification Key
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations
IMPACT	International Medical Products Anti-Counterfeiting Taskforce
INTERPOL	International Criminal Police Organization
IQ	Installation Qualification
IRACM	International Institute of Research Against Counterfeit Medicines
ISA	International Society of Automation
IT	Information Technology
ITS	İlaç Takip Sistemi – Turkish words for "Drug Tracking System"
JFDA	Jordan Food and Drug Administration
MAH	Marketing Authorization Holder
MB	Megabytes

Abbreviation	Definition
MOH	Ministry of Health
MoPH	Lebanese Ministry of Public Health
MPA	Methylprednisolone Acetate
NDC	National Drug Code
NECC	New England Compounding Center
NHRA	National Health Regulatory Authority
NMPA	National Medical Products Administration
NMVO	National Medicines Verification Organisation
NMVS	National Medicines Verification System
OECD	Organisation for Economic Co-operation and Development
OQ	Operational Qualification
OTC	Over the Counter
PDMA	Prescription Drug Marketing Act
PHC	Primary Healthcare Centers
PIATS	Product Identification, Authentication and Tracking System
PM	Project Management
PoD	Point-of-Dispense
PQ	Performance Qualification
PTS	Package Transfer Service
PwC	PricewaterhouseCoopers
Q3	Quarter
QA	Quality Assurance
QP	Qualified Person
RA	Regulatory Affairs

Abbreviation	Definition
RFID	Radio Frequency Identification
ROI	Return On Investment
SAP	Systems Applications and Products in Data Processing
SAT	Site Acceptance Test
SFDA	Saudi Food and Drug Authority
SGTIN	Serialized Global Trade Item Number
SME	Subject Matter Expert
SOP	Standard Operating Procedure
SSCC	Serial Shipping Container Code
T&T	Track and Trace
UAE	United Arab Emirates
URS	User Requirements Specification
USA	United States of America
WHO	World Health Organization
XML	Extensible Markup Language

Abstract

Drug counterfeiting has been there for almost the last 20 years, posing a serious risk on public health. Consumption of counterfeited drugs could cause infections, diseases and it could even lead to death. This is why governments together with supply chain stakeholders joined forces to find a solution for combating drug counterfeiting and ensuring patient safety. This solution is called Track and Trace or Serialization, which is one of the most recent and advanced technologies to fight of drug counterfeiting that prevent the entrance of fake medicines into the supply chain. This is achieved by using Global Standards (GS1) such as Global Trade Item Number (GTIN) to identify a drug product, a 2D Data Matrix Code to carry specific product information (e.g., GTIN, batch number, expiry date and serial number) and an EPCIS (Electronic Product Code Information Service) message to share product information between supply chain stakeholders and the government. This allows having a highly secure system with full visibility of drug movement along the supply chain from the manufacturer all along the way until it is dispensed to the patient.

More governments and countries are recently introducing the Track and Trace regulation into their systems, like Europe and Saudi Arabia, while others are still in the process of developing their own regulations, like Lebanon and Egypt. Implementing a Track and Trace system carries with it several challenges, investments, efforts and time. To reveal different regulations in different countries and to study challenges associated with implementing a Track and Trace system and its impact on the companies and in fighting drug counterfeiting, 6 different surveys were distributed to pharmaceutical companies, wholesalers and pharmacies both in Palestine and Europe. According to the collected data, Palestine is not ready yet to implement a Track and Trace system and the Palestinian Ministry of Health did not enforce any regulation. Whereas in Europe, the Track and Trace has been already enforced as a regulation since 09.02.2019 and is being effectively used across European countries and any other country that

is exporting its products into Europe. Having a Track and Trace system in place is very crucial to ensure patient health, especially in critical times of a pandemic like the one that we are living at the moment, where many drug counterfeiters are taking advantage of people's fear, weakness and vulnerability to produce and sell fake COVID-19 vaccines.

ملخص

كان تزييف الأدوية موجودًا منذ ما يقرب من 20 عامًا وما زال موجودًا حتى اليوم ، مما يشكل خطرًا كبيرًا على الصحة العامة. يمكن أن يتسبب استهلاك الأدوية المزيفة في حدوث عدوى وأمراض وقد يؤدي إلى الوفاة. هذا هو أحد الأسباب الرئيسية لتوحيد الحكومات مع أصحاب المصلحة في سلسلة التوريد لإيجاد حل لمكافحة تزييف الأدوية وضمان سلامة المرضى. يُطلق على هذا الحل اسم نظام التتبع والتعقب أو التسلسل الرقمي، وهو أحد أحدث التقنيات وأكثرها تقدمًا لمكافحة تزييف الأدوية ومنع دخول الأدوية المزيفة إلى سلسلة التوريد. يتم تحقيق ذلك باستخدام المعايير العالمية (GS1) مثل رقم عنصر التجارة العالمية (GTIN) لتحديد المنتج الدوائي ، ورمز مصفوفة بيانات ثنائية الأبعاد لحمل معلومات منتج محددة (على سبيل المثال ، رقم GTIN ورقم الدفعة وتاريخ انتهاء الصلاحية والرقم التسلسلي) و رسالة EPCIS (خدمة معلومات رمز المنتج الإلكتروني) لمشاركة معلومات المنتج بين أصحاب المصلحة في سلسلة التوريد والحكومة. يتيح ذلك وجود نظام آمن للغاية مع رؤية كاملة لحركة الأدوية على طول سلسلة التوريد من الشركة المصنعة طوال الطريق حتى يتم الاستغناء عنها للمريض.

تقوم المزيد من الحكومات والدول مؤخرًا بإدخال أنظمة التتبع والتعقب في أنظمتها ، مثل أوروبا والمملكة العربية السعودية ، بينما لا يزال البعض الآخر في طور تطوير اللوائح الخاصة به ، مثل لبنان ومصر. يحمل تطبيق نظام التتبع والتعقب العديد من التحديات والاستثمارات والجهود والوقت. للكشف عن اللوائح المختلفة في الدول المختلفة ودراسة التحديات المرتبطة بتطبيق نظام التتبع والتعقب وتأثيره على الشركات ومكافحة تزييف الأدوية ، تم توزيع 6 استطلاعات مختلفة على شركات الأدوية وتجار الجملة والصيدليات في كل من فلسطين وأوروبا. وبحسب البيانات التي تم جمعها ، فإن فلسطين ليست مستعدة بعد لتطبيق نظام التتبع والتعقب ، كما أن وزارة الصحة الفلسطينية لم تطبق أي لائحة. بينما في أوروبا ، تم تطبيق نظام التتبع والتعقب بالفعل كقانون منذ 09.02.2019 ويتم استخدامه بشكل فعال في جميع البلدان الأوروبية وأي دولة أخرى تقوم بتصدير منتجاتها إلى أوروبا. يعد وجود نظام التتبع والتعقب أمرًا بالغ الأهمية لضمان صحة المريض ، خاصة في الأوقات الحرجة لوباء مثل ذلك الذي نعيشه في الوقت الحالي ، حيث يستغل العديد من مزيفي الأدوية خوف الناس وضعفهم لإنتاج وبيع لقاحات COVID-19 مزيفة.

1. Chapter One – Introduction

1.1 Research Overview

This study is structured into the following six chapters:

1. Introduction: Purpose of the study and the objectives are described. Additionally, a short background is given about counterfeit products.
2. Literature review: Detailed research and information is provided related to the purpose of the study and the objectives.
3. Methodology: The process of achieving the objectives of this study is described.
4. Results and Discussion: The results of the objectives are detailed, explained and discussed.
5. Conclusion*:* The research is concluded against each objective.
6. Recommendations and Future Work: Further areas and work are detailed.

Overall, the research is documented in a structured approach to ensure that the reader has a clear and sequential understanding about Track and Trace in the pharmaceutical industry.

1.2 Counterfeit Pharmaceutical Products and their impact on patient's health

Counterfeiting of drugs and medical devices is not a new topic, it has been there for almost the last 20 years. What is a counterfeit product? How did it evolve throughout all these years? And which impact does it have on public health? [1]

The World Health Organization (WHO) defines a counterfeit medicine as "one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products. Counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging" [2].

The United States Food and Drug Administration (US FDA) tends to use 2 terminologies: suspect product and illegitimate product. It defines them as follows:

- "Suspect Product: a reason to believe that a product is potentially:
  - Counterfeit, diverted, stolen
  - Subject of fraudulent transaction
  - Intentionally adulterated or appears otherwise unfit for distribution such that would result in serious adverse health consequences or death to humans.
- Illegitimate Product: credible evidence that the product actually is any of the above" [3]

Regardless of the terminology used (counterfeit, suspect, fake, diverted, substandard etc.), eventually all of them have the meaning of a non-genuine product which is posing risk to public health.

When reading the word "counterfeit", you might automatically think of tropical areas like India or developing countries like Africa, which is to a certain extent true, but it is not restricted only to these areas. Unfortunately, counterfeiting is a global issue, where even developed countries are impacted, especially with the rise of internet and the so called "lifestyle drugs" [1]. 1% of pharmaceutical products used in developed countries are counterfeit, whereas the percentage significantly rises to 30 – 40 % in developing countries, representing a total value of $75 billion to $200 billion and growing [4]. Criminals all around the world have been able to counterfeit almost all kinds of pharmaceutical products. Not only have they counterfeited lifestyle drugs, but they were able to counterfeit antibiotics, pain killers, diabetes medicaments, central nervous system medicaments and much more. Most dangerously, they were able to counterfeit drugs for serious illnesses such as malaria, cancer and HIV/AIDS. Figure 1 shows most counterfeit types of pharmaceutical products [5].

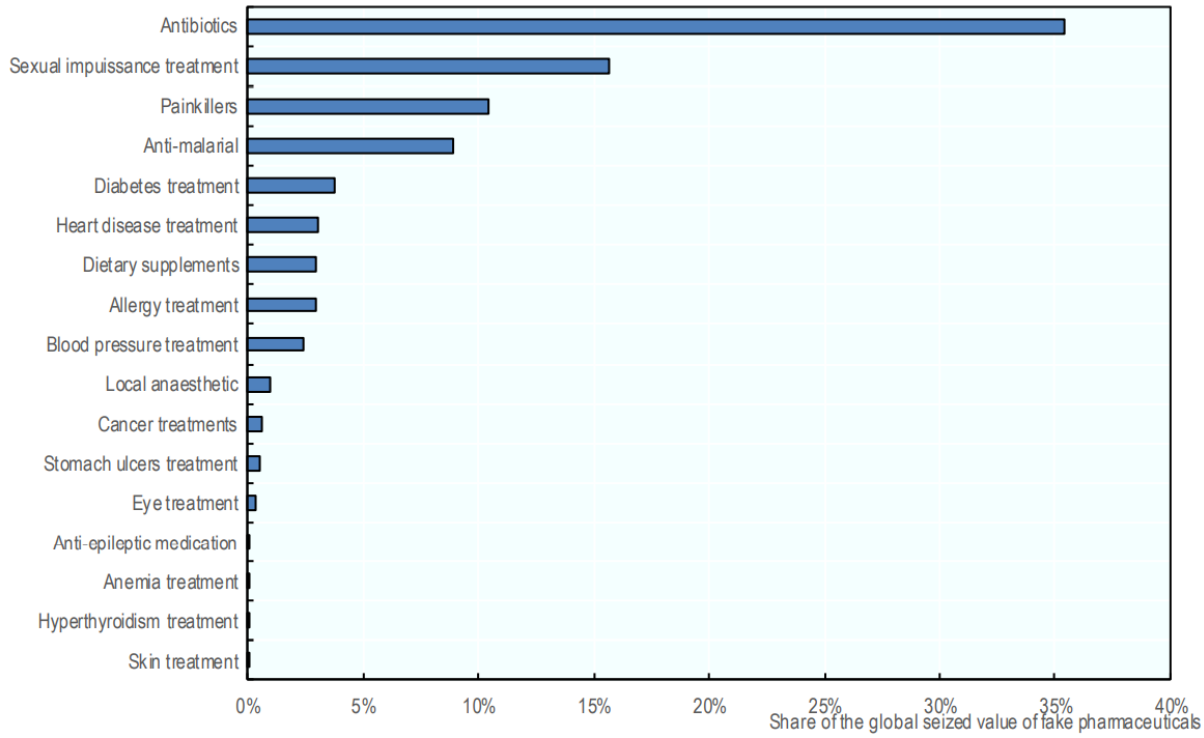


Figure 1: Most counterfeit types of pharmaceutical products [5]

From one side, fake drugs are killing poor people in developing countries such as counterfeit anti-malarial drugs, which is estimated to kill 200,000 people (20%) of the one million people dying from Malaria every year worldwide according to the WHO [6]. On the other hand, fake drugs are also harming and/or killing non-poor people who seek to buy their medicines or lifestyle drugs from online pharmacies due to health conditions which they might find embarrassing such as erectile dysfunction or obesity [1]. Whether it's a life-threatening or non-life-threatening pharmaceutical product, whether it's in a developed country or developing country, whether it's affecting poor people or rich people, counterfeiting is considered a CRIME and a global issue which should be tackled by joining forces, enforcing strict legislations and applying increased penalties worldwide.

Due to the increasing incidents of drug counterfeiting and the serious risks that are imposed on patients' health in all parts of the world, especially in South East Asia, WHO decided to take an act and fight this phenomenon. Thus, an international conference was organized by the WHO in Rome in February 2006 that was attended by 160 participants from different international

organizations, representatives of national medicines regulatory authorities and international associations of patients, health professionals, pharmaceutical manufacturers and wholesalers. This conference resulted in the Declaration of Rome on 18th of February 2006, which stated that the WHO should establish a taskforce responsible for protecting public health by fighting drug counterfeiting. This taskforce is called International Medical Products Anti-Counterfeiting Taskforce (IMPACT) and is defined as an alliance of stakeholders which voluntarily arranges international activities aimed at fighting forging medicinal products in order to protect public health [7].

In 2016, international trade in counterfeit pharmaceuticals reached USD 4.4 billion, causing threat on public health and safety, while enriching criminals and organised crime [5]. In 2017, the market of counterfeit medicines was found to be one of the most profitable types of counterfeited goods with an estimation of $163 billion to $217 billion per year, according to a report conducted by PricewaterhouseCoopers (PwC). While, the WHO estimates that counterfeit medicaments account for 10% of the market globally and more than 30% in some countries [8]. Table 1 shows some of the cases where counterfeit drugs were seized in different countries [9].

Table 1: Some of the counterfeit drugs and their black-market value detected in different countries worldwide [9].

Black Market Value	Counterfeited Drug Detected	Country	Date
US $25 million	244 containers of Viagra	Nigeria	20-Mar-15
Between US $600,000 and US $700,000	170,000 fake drug based on talc, flour and cement (anti-cholesterol drugs)	Colombia	19-Mar-15

Black Market Value	Counterfeited Drug Detected	Country	Date
US $1,292,000	Viagra	Senegal	06-Feb-15
US $238,000	More than 7,000 units of erectile dysfunction tablets (Viagra and Cialis)	United States	05-Dec-14
US $100,000	Anti-cancer medicines and food supplements	Bangladesh	18-Dec-14
£ 200,000	Over 20,000 units of cognitive enhancers	United Kingdom	24-Nov-14
US $600,000	135,000 fake products of anti-cancer, anti-psychotic, erectile dysfunction and weight loss pills	Canada	20-May-14
TL 10 million	Cancer drugs	Turkey	Dec-13

According to a research done by the Organisation for Economic Co-operation and Development (OECD) together with European Union Intellectual Property Office (EUIPO), China and India are taking the lead in drug counterfeit business as they were found to be the main producers of fake medicines. Hong Kong (China), Singapore and India are also considered to be a main drug counterfeiter. While the above-mentioned countries have a reputation of being a primary producer of fake drugs, other countries like the United Arab Emirates (UAE), Singapore, Hong Kong (China), Yemen and Iran have a reputation of serving as transit economies. From the

aforementioned locations, counterfeit medicines are being shipped to any country in the world. However, they primarily target Africa, Europe and the United States [5].

Between 2014 and 2016, the share of the United Arab Emirates and Singapore increased in the global trade of fake pharmaceuticals compared to the time between 2011 and 2013. However, other Middle Eastern countries such as Yemen, Iran and Lebanon have disappeared from the ranking of the top economies that are most likely to export fake medicines. On the other hand, Egypt and some Far East Asian Economies such as Pakistan, Philippines and Indonesia have entered the top 10 and are now main provenance of fake pharmaceuticals in global trade as shown in figure 2 [5].

Provenance economy	GTRIC-e
Hong Kong (China)	1.000
India	1.000
China (People's Republic of)	1.000
United Arab Emirates	0.947
Egypt	0.838
Philippines	0.674
Singapore	0.657
Viet Nam	0.631
Indonesia	0.388
Pakistan	0.332
Cameroon	0.332
Turkey	0.309

Figure 2: The 10 economies most likely to be a provenance of counterfeit pharmaceutical products [5].

Note: GTRIC-e (General Trade-Related Index of Counterfeiting for economies) for pharmaceuticals; average 2014-2016. A higher score on the GTRIC Index indicates a greater likelihood that the economy in question is a source of counterfeit goods [5].

In Kuwait, the government decided to fight drug counterfeiting by increasing both the penalty and fine related to drug counterfeiting. In 2014, the penalty for drug counterfeiting has been increased from only 3 months to 3 – 6 years. As for the fine, it has been increased to reach 5 – 10 thousand Kuwaiti dollars [10].

In 2018, the Pharmaceutical Security Institute (PSI), which is a non-profit global organization, reported double the number of fake medicines and illegal theft incidents compared to 2014. The

PSI also reported that the biggest number of seizures (1,750) was found in North America followed by Asia (1,426).

Europe was the only region which did not experience an increase since 2017 in criminal activities related to drug counterfeiting and illegal theft. The total number of countries which were affected by pharmaceutical criminal activities is 145 [5].

Drug counterfeiting has many negative impacts on us from different perspectives. These impacts include:

1. The most important impact is on the safety of human health. Consuming fake medicaments could fail in treating our medical conditions or could damage our health or even worse, could cause death. It is estimated that between 72,000 and 169,000 children may die from pneumonia every year from fake medicines, and that fake anti-malarial medication might be responsible for an additional 116,000 deaths.
2. Costs of treating patients who received counterfeit drugs and as a consequence are suffering from severe adverse health conditions.
3. Pollution of the environment due to the use of potentially toxic chemicals within an unregulated criminal activity.
4. Social costs in terms of an increase in organised crime and job losses.
5. Loss of sales and damage to the reputations of licit manufacturers.
6. Costs and lost revenues to governments and economies [5].

1.3 Purpose of Study

Lack of regulation encourages drug counterfeiters and gives them the green light to proceed with their drug counterfeiting activities. In order to fight this type of crime and activities, it is crucial for governments to develop and enforce an anti-drug counterfeiting regulation i.e., Track

and Trace. Implementing a highly secure Track and Trace system within a pharmaceutical supply chain facilitates in combating drug counterfeiting, by making it more difficult and complicated for counterfeiters to introduce fake medicinal products into the supply chain, thus ensures patient safety. However, implementing such a system is usually complicated and challenging.

This study is comprised of a quantitative research, where six different surveys were distributed to pharmaceutical companies, wholesalers and pharmacies in Palestine and in Europe (only one of these surveys was distributed to a wholesaler in Saudi Arabia). The collected data about their awareness and/or readiness for different Track and Trace/Serialization regulations, depending on different country's requirements were revealed and compared. Additionally, the challenges faced with implementing a Track and Trace system and its impacts were revealed and discussed in depth.

1.4 Objectives

1. Reveal different technologies available to fight drug counterfeiting, while focusing on the Track and Trace technology, defining what it is, how it works, why is it important and explaining its advantages and disadvantages. The importance of a Track and Trace system is also specifically explained and linked to the current COVID-19 pandemic.
2. Study Track and Trace regulatory requirements for pharmaceutical supply chain stakeholders i.e., pharmaceutical companies, wholesalers and pharmacies, in different countries worldwide and reveal the timelines for implementing this regulation in each country.
3. Reveal the challenges that lie behind implementing a Track and Trace regulation in terms of time, cost, resourcing, planning, system complexity, activities that are required to be fulfilled, etc. in order to comply with the regulation.

4. Collect data from three different surveys (Appendix 1 – Appendix 3) that were distributed to supply chain stakeholders i.e., pharmaceutical manufacturers, wholesalers and pharmacies, in Palestine. Objectives from this set of surveys include:
    a. To study whether Palestinian supply chain stakeholders were aware of serialization and whether they received any regulation from the Palestinian MoH in regards with serialization implementation and expected timelines.
    b. To reveal whether Palestinian supply chain stakeholders export their products to countries where serialization is a requirement and therefore whether they implemented already or have any plans to implement serialization.
    c. To check what is the current status of Palestinian supply chain stakeholders in terms of readiness for serialization and based on that to evaluate the effort needed to implement such a system.
    d. To understand the opinions of Palestinian supply chain stakeholders about serialization and its importance and whether they experienced any drug counterfeiting / stealing incidents.
5. Collect data from three different surveys (Appendix 4 – Appendix 6) that were distributed to supply chain stakeholders i.e., pharmaceutical manufacturers, wholesalers and pharmacies, in Europe (only one of these surveys was distributed to a wholesaler in Saudi Arabia).

    Objectives from the surveys of pharmaceutical manufacturers and wholesalers are:
    a. To reveal which countries, do supply chain stakeholders export their products to and based on that to evaluate which types of serialization systems do they have in place or will have to implement according to different country's regulations.
    b. To understand and reveal challenges (both internal and external) that supply chain stakeholders faced during the implementation of serialization (e.g., regulatory requirements, system complexity, trainings, new hire, etc.).

c. To study what the main driver was for supply chain stakeholders to implement a serialization system i.e., regulatory or other reason.
d. To evaluate the effects and benefits of implementing a serialization system on supply chain stakeholders from different perspectives (during and after implementation) and on patient's health.
e. To check how satisfied / not satisfied were supply chain stakeholders with implementing serialization and to check as well their personal opinion about serialization and its importance.

Objectives from the survey of pharmacies are different and include:

a. To reveal how did pharmacies get informed about serialization and who was responsible for implementing the system and covering the costs of it.
b. To understand how the introduction of serialization affected the daily operations of pharmacists and how are they getting along with it (e.g., system errors, negative verifications, exception cases, etc.).
c. To check how satisfied / not satisfied were pharmacists with implementing serialization and to check as well their opinion about serialization and its importance.

2. Chapter Two – Literature Review

2.1 Technologies for Combating Drug Counterfeiting

There are many different technologies available to prevent drug counterfeiting. These technologies could be either visible, non-visible or digital. Visible and non-visible technologies depend on the physical features or properties of the product itself or of the packaging material whereas digital technologies depend on the linkage of the product with a unique set of pre-defined information. Visible technologies are added on the packaging material and non-visible technologies are included as part of the formulation of the drug product itself. These several technologies could be used at different levels of packaging depending on different situations. This section will describe these different types of technologies to combat drug counterfeiting [1].

2.1.1 Overt Technology

Overt (visible to the eye) technology includes adding visible markers on the packaging or on the label that can help in verifying the authenticity of a drug product. These markers or verifiers can include a hologram (as shown in figure 3), special stickers or integrating inks with changing colours [11].

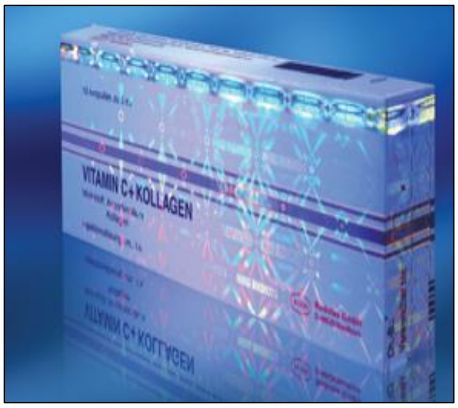


Figure 3: a Hologram on a vitamins package [12]

Another overt technology includes verifying the authenticity of the product by inspecting or analysing its intrinsic features such as the shape and tooling, the texture and granularity, embossing and debossing, and the printing and coating of the primary dosage form. For example, manufacturers should consider investing money in a highly advanced, good quality tablet press with an embossing (adding a stamp or design that stands out) and debossing (adding stamp or design into the inner surface) features, which then makes it difficult and more complex for counterfeiters to afford and to copy the exact tablet shape [1].

2.1.1.1 Advantages of overt technology:

1. By adding overt features on the package / label or on the primary dosage form, it will become more complicated, more difficult and more expensive for counterfeiters to copy it and to produce it with same exact physical features.
2. It will allow manufacturers to verify and authenticate their own products and to distinguish it from fake products.
3. It can be used for real-time verification.
4. Overt features on the package or on the label also help end users to verify whether a drug product is genuine or not [11].
5. In case the product has digital means of verification and the wireless access to database is challenging (in some countries) or not available (in some locations such as in sea ports), then the physical properties and features on the package might be helpful to distinguish whether the product is genuine or not [1].

2.1.1.2 Disadvantages of overt technology:

1. There are various types and amounts of overt features therefore it is not practical that the patient or pharmacist keeps checking which overt feature exists on which product and it is not realistic to expect them to know all these overt features on all the products.
2. It might add an additional cost on the manufacturer depending on the complexity of the features that they decide to introduce.
3. The chosen feature (whether it is a holographic image or a specific primary dosage form) need to be changed every 12 to 18 months otherwise, counterfeiters can find out what the materials are and can start copying them. It is similar to counterfeit-resistant technologies that are incorporated in bank notes, where special ink with changing colours, threads and micro printing are embedded. In order to prevent money faking, the government changes the counterfeit-resistant features every 7 to 10 years.
4. In general, it is relatively easy to copy overt features and produce a fake drug product.
5. If the counterfeiter decides to fake the drug by repacking it then overt features are useless in this case and the drug cannot be verified [11].

2.1.2 Covert Technology

Covert (non-visible/hidden) technology includes adding materials or extra ingredients into the drug product itself, either as part of the drug formulation or as part of the coating material, by using special tools and equipment. These materials can include special inks, threads or chemical taggant to help identify the drug product and they are known only to the manufacturer. The verification of the chemical taggant can be achieved by conducting a chemical analysis, which is performed by the manufacturer [11].

2.1.2.1 Advantages of covert technology:

1. By adding covert features into the drug product, it will become more complicated, more difficult and more expensive for counterfeiters to copy it and to produce it with the same chemical materials incorporated in it.
2. It will allow manufacturers to verify and authenticate their own products and to distinguish it from fake products [11].

2.1.2.2 Disadvantages of covert technology:

1. It might add an additional cost on the manufacturer depending on the complexity of the features that they decide to introduce.
2. Like in overt technology, the chosen feature (whether it is a chemical taggant added to the drug formulation or an extra ingredient added to the coating material) needs to be changed every 12 to 18 months otherwise, counterfeiters can find out what the materials are and can start copying them.
3. It does not allow real-time verification of the drug product, because usually special equipment is needed to test the drug and it can only be done by the manufacturer. In addition to that, these tests may take some time (up to several days) in order to decide whether the drug is fake or genuine [11].

2.1.3 Track and Trace Technology

Track and Trace falls under the digital type of technology, where it adds even more complexity for counterfeiters to fake medicinal products compared to overt and covert technologies. It allows product authentication by scanning a code, which links between the product and a unique set of pre-defined information thus telling us whether a product is genuine or not. The details of how exactly a Track and Trace system works and how the regulation differs from one country to another will be discussed in sections 2.2 and 2.3 [1].

2.2 Track and Trace in the Pharmaceutical Industry

Almost in the last 11 years, especially in recent 3 years, Track and Trace has become the latest technological trend to fight drug counterfeiting. Not only that it has become a trend, but it has also become a regulation enforced by many governments and countries worldwide. In my opinion, it is a very crucial regulation that can increasingly help in ensuring patient safety and combat counterfeiters and criminals that pose serious and dangerous risk to the health and safety of all of us. In general, the idea of Track and Trace is to be able to track a pharmaceutical product along the supply chain and know at any point what is that product, where is it, where did it come from, what event happened to it (e.g., packing, shipping, recalling) and when did that event happen. This is achieved by having a barcode on the product for identification, which captures and carries specific information about the product such as serial number, product barcode, expiry date and lot number. The specific product related information and events are shared and exchanged between supply chain partners and with the government, allowing full visibility and transparency of the drug movement within the supply chain until it reaches the patient. Before a product is dispensed to the patient, the pharmacist or doctor or any other authorized personnel can check the authenticity of that product thus ensuring that the medicinal product being given to the patient is genuine [13]. In this section, the exact definition of Track and Trace system will be revealed, describing how it works, what are the advantages and benefits of implementing such a system and what are the challenges and disadvantages related to it.

2.2.1 GS1 Global Standards

2.2.1.1 Background

What is GS1, what are GS1 standards and how are they related to Track and Trace?

GS1 (Global Standards) is an international non-profit organization, with headquarters in Brussels, that develops and maintains global standards for business communication. Barcodes are the most well-known standards which were introduced by GS1. The history of GS1 goes back to 1971 when industry leaders agreed to use a "universal product code" for product identification. This identification code is known as the Global Trade Item Number (GTIN), which we all know today. It is printed on almost every product all around the world, which helps us to identify different products. In June 1974, a packet of chewing gum (see figure 4) became the first barcoded product to be scanned in a supermarket [14].

Figure 4: The first barcoded product to be scanned in store [14]

In 1995, GS1 expanded their work into the healthcare sector and as a result the first healthcare standards were created. Figure 5 shows the growth and development of GS1 starting from 1971 until 2013. As of today, GS1 has 115 offices worldwide with more than million members [14].

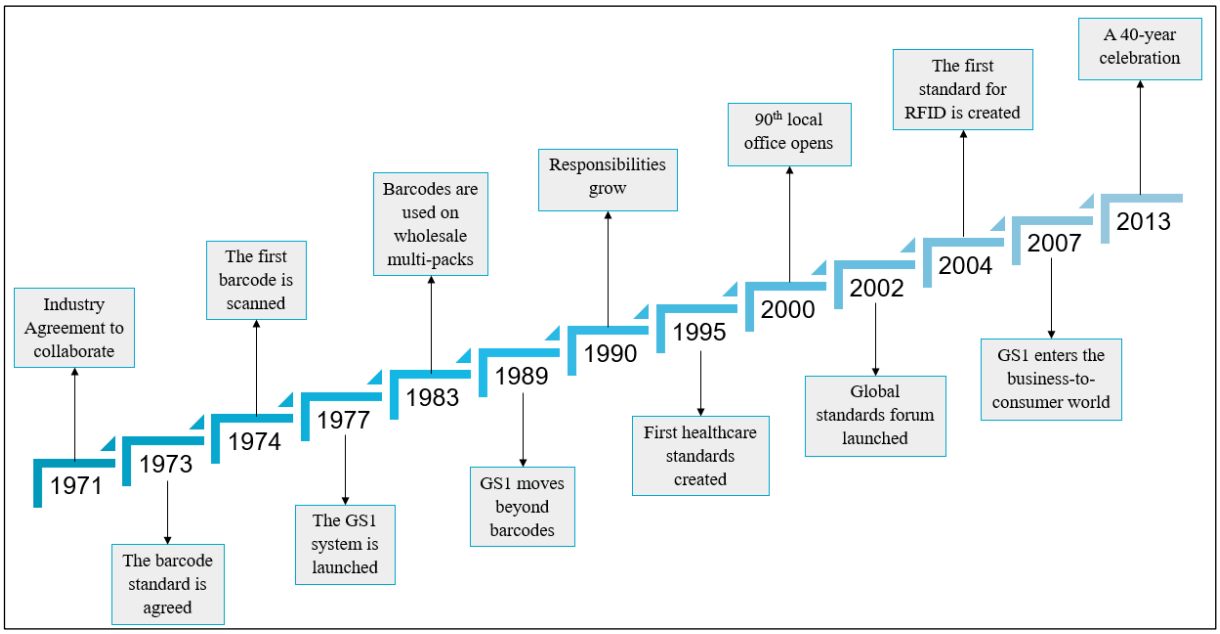


Figure 5: Growth and development of GS1 throughout the years [14]

GS1 healthcare standards were created with the mission to increase:

- ✓ Patient safety
- ✓ Supply chain security and efficiency
- ✓ Traceability and accurate data synchronisation in healthcare systems [15]

2.2.1.2 How do GS1 standards work?

GS1 Standards are divided into 3 groups: 'Identify', 'Capture' and 'Share' as seen in figure 6.

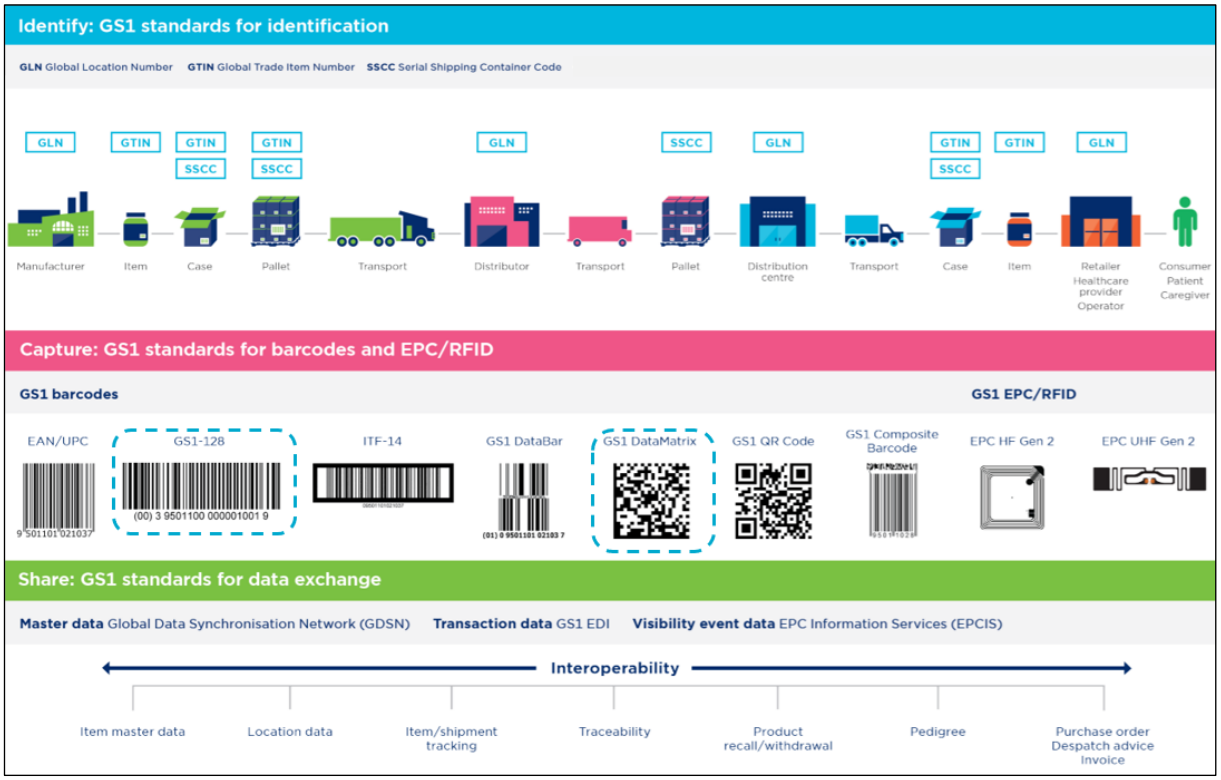


Figure 6: Three different groups of GS1 Standards and their usage along the supply chain [16]

Before proceeding with the explanation of the 3 GS1 groups, it is important to clarify the types and names of packages available in the pharmaceutical industry as shown in figure 7.

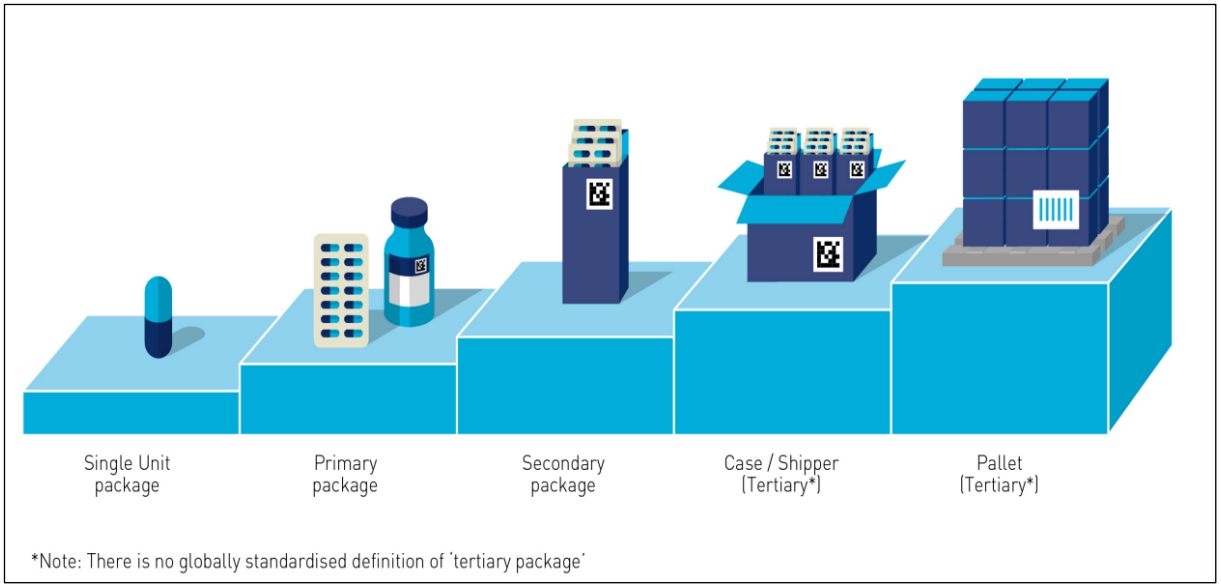


Figure 7: Levels of packaging [17]

Here is the definition of the 3 GS1 groups:

1. **Identify:** Globally unique identification codes called GS1 Identification (ID) Keys are used by companies and organizations to identify trade items, logistics units, physical locations, documents, service relationships and much more. GS1 ID Keys provide companies efficient ways to access information about items in their supply chains and share this information with trading partners thus increasing supply chain visibility.

   The first step to do for a company in order to be able to create and assign GS1 ID Keys, is to become a member of GS1 and obtain a GS1 Company Prefix (GCP). The GCP will be part of the ID Keys when created. There are 12 different GS1 ID Keys depending on what you want to identify. The ID Keys which are of our interest and related to healthcare systems are:

   - Global Trade Item Number (GTIN), which is used to identify products. It can be used for primary packages, secondary packages and cases.
   - Global Location Number (GLN), which is used to identify plants and locations. If for example a pharmaceutical manufacturer has several production plants and several warehouses, then each plant and each warehouse will have its own GLN.

- Serial Shipping Container Code (SSCC), which is used to identify logistics units. It can be used for pallets and in some scenarios for cases as well [18] [19].

2. **Capture:** GS1 Standards provide automatic data capturing by using either barcodes or Electronic Product Code (EPC) / Radio Frequency Identification (RFID), which are data carriers that allow GS1 ID Keys and supplementary data to be affixed directly to a physical object, therefore creating the link between physical things and electronic information [18]. Our focus will be on barcodes since they are mainly used within a pharmaceutical Track and Trace system.

   Barcodes, as mentioned above, are simply vehicles that carry data. They are used to encode information such as product code (e.g., GTIN), serial number, batch number and expiry date. They can be electronically scanned thus enabling supply chain partners like manufacturers, hospitals, pharmacies etc. to automatically identify and track products along the supply chain.

   There are several types of barcodes depending on the purpose of use and depending on different business scenarios. In our case, the most widely used barcodes in the healthcare industry and in the Track and Trace system are:

   - One-dimensional (1D) barcodes: They are widely used in general distribution, healthcare and logistics. The 1D barcode mostly used in healthcare industry is called GS1-128, which enables items to be tracked through global supply chains. GS1-128 is a linear barcode that can include up to 48 alphanumeric characters and can be encoded with any of the GS1 ID keys, in addition to information like serial number, expiry date and more. The SSCC is usually built in a GS1-128 format.
   - Two-dimensional (2D) barcodes: They have the capability to carry a high capacity of information such as GTIN, serial number, batch number and expiry date, and they mostly remain readable even when printed in a small size. 2D

barcodes can have either a rectangular or a square shape with many individual dots. They are used in a wide range of industries, from manufacturing and warehousing to logistics and healthcare. There are 3 types of 2D barcodes: GS1 2D DataMatrix Code, GS1 QR Code and GS1 DotCode. For regulated healthcare trade items, GS1 DataMatrix is the only allowed 2D barcode [20].

In order to identify data encoded within barcodes, GS1 has introduced Application Identifiers (AI), which are a series of numbers between brackets that represent a particular Data Element, as shown in table 2.

Table 2: List of some of the Application Identifiers as defined by GS1 [21].

AI	Data Content	Data Title
00	Serial Shipping Container Code	SSCC
01	Global Trade Item Number	GTIN
10	Batch or lot number	BATCH/LOT
11	Production date	PROD DATE
13	Packaging date	PACK DATE
15	Best before date	BEST BEFORE or BEST BY
16	Sell by date	SELL BY
17	Expiration date	USE BY or EXPIRY
21	Serial number	SERIAL
37	Count of trade items or trade item pieces contained in a logistic unit	COUNT

AI	Data Content	Data Title
240	Additional product identification assigned by the manufacturer	ADDITIONAL ID
254	Global Location Number extension component	GLN EXTENSION COMPONENT
415	Global Location Number of the invoicing party	PAY TO
416	Global Location Number of the production or service location	PROD/SERV LOC
710	National Healthcare Reimbursement Number (NHRN) – Germany PZN	NHRN PZN
ABC*	National Healthcare Reimbursement Number (NHRN) – Country "X" NHRN	NHRN XXX

*Different AI numbers available for other countries

Example: When scanning a 2D DataMatrix code which has the following encoded data:

GTIN "01234567987293",

Expiry Date "231231",

Batch Number "XYZ22334",

Serial Number "MAS0403f2p", then the string that a scanner would return is:

(01)01234567987293**(17)**231231**(10)**XYZ22334**(21)**MAS0403f2p

3. **Share:** GS1 Standards provide the means to exchange data and share information between trading partners within the supply chain and internally within own organization, which is defined as interoperability. The exchanged data includes master data (e.g., GCP, GLN etc.), business transaction data, physical event data and much more. The most common way of sharing data between supply chain partners in the

pharmaceutical industry is by using GS1 Electronic Product Code Information Services (EPCIS). EPCIS allows interoperability between supply chain partners and provides the ability to track and trace products as they move through the supply chain and includes a set of interfaces (capture and query) for obtaining and sharing data about unique items both within and across organizations. EPCIS defines the format in which data is transacted (by a series of Events) by defining 4 dimensions:

- **What**: What is the product? It gives information about what is the trade item and/or shipping container (GTIN, SSCC);
- **When**: When was the product manufactured/shipped/received etc.? It gives information about date and time of when a specific event happened;
- **Where**: Where was the product manufactured/shipped/received etc.? It gives information about the location where a specific event took place (GLN);
- **Why**: Information about the business context including:
    - What is the business Step? E.g., product was shipped or received or recalled etc.
    - What is the current business condition or status of the item/product (also known as disposition)? E.g., “in transit” which means that the product was shipped from location A and is in the progress of reaching location B.
    - Who are the shipping and receiving parties? E.g., it shows who was the former owning party and who is the current owning party.
    - To which business transaction documents is the event linked? E.g., Delivery Number, Purchase Order, Despatch Advice (also known as Advance Ship Notice ASN), etc. [22]

2.2.1.3 Summary

In summary, tracking, traceability and supply chain visibility can be achieved by using GS1 technical standards of the 3 groups: identifying, capturing and sharing. GS1 makes it easier for supply chain partners to interact and to exchange data by providing a standard global business language, which can be used and implemented by any party. This is basically the skeleton for building a Track and Trace system, which will be discussed in the next section (2.2.2). Figure 8 summarizes the main GS1 standards used in the pharmaceutical industry [22].

Figure 8: Main GS1 standards in the pharmaceutical industry [18]

2.2.2 Definition of Pharmaceutical Serialization / Track and Trace

2.2.2.1 Background

After understanding what GS1 Standards are and how they work, this section will explain what Pharmaceutical Serialization / Track and Trace system is and how is it related to GS1 Standards.

As technology is constantly becoming more and more advanced with time, regulators and pharmaceutical supply chain partners must continuously look for innovative technological

solutions and make sure that they are one step ahead of counterfeiters, especially during the current difficult times which the whole world is experiencing due to the covid-19 pandemic. In such critical times, counterfeiters are making use of people's weaknesses and vulnerabilities, not only by trying to steal their data with fraud e-mails and links but also by offering them fake online vaccines. In poor countries where they cannot afford medicaments and vaccines, counterfeiters are finding their ways to distribute and sell fake vaccines. This increases even more the importance of protecting the supply chain from the entrance of any kind of counterfeit medicaments thus increases the necessity of having a Track and Trace system in place [23]. So, what is exactly Serialization, what does Track & Trace mean and what is the difference between them?

Before starting with the definitions, I would like first to clarify that this section will consider the description and definition of a Track and Trace system in general as a concept and not specific to any country. Therefore, whatever is described in this section does necessarily apply to all countries. The different regulations of some chosen countries will be further described in section 2.2.3.

2.2.2.2 Track and Trace Definition

The word **'Tracking'** means to monitor forward movement of finished goods / pharmaceutical products through the entire supply chain, from the manufacturer all through the way until the patient [13].

The word **'Tracing'** means to work backwards through the entire supply chain to be able to trace the product lifecycle and see at which point the genuine product was diverted out of the legitimate supply chain. Tracing also makes the recalling process easier, faster and more efficient by simply going back to the history of the product lifecycle [13].

Therefore, both terms Track and Trace complete each other and have full capability of providing specific information about a pharmaceutical product through the supply chain. This specific information includes batch number, manufacturing date, expiry date, ingredients, specific events that occurred such as shipping or recalling and much more [13]. The most acceptable, achievable and efficient way to fulfil the purpose of a Track and Trace system is by using GS1 Standards (identify, capture and share) since it is a global business language that links between different supply chain partners and the governments no matter where they are or which internal systems they are using. Additionally, using GS1 Standards reduces the cost and complexity of implementing a Track and Trace system. The link between supply chain partners is achieved by using GS1 Identification Keys like GLN to identify locations, GTIN to identify products, GS1 barcodes (e.g., 2D DataMatrix code) to carry GS1 ID Keys and other data (batch number, expiry date, serial number) and finally by using EPCIS messages to share all this data internally within own organization and externally between supply chain partners and with the government [17].

In general, "Track and Trace" is also often referred to as "Serialization" or "Traceability". These 3 terms refer eventually to the same topic, which is to track and trace a drug product throughout a legitimate supply chain.

2.2.2.3 How is Track and Trace system actually achieved?

The first step towards the achievement of Track & Trace is serialization. **'Serialization'** means to make each single product unique by placing an item identifier on it. This item identifier is usually a 2D Data Matrix Code incorporating GTIN paired with a serial number, also known as Serialized GTIN (SGTIN), batch number and expiry date as shown in figure 9. The serial number can be up to 20 digits (it is usually made up of 13 or 14-digits) that can be either numeric (only numbers) or alphanumeric (numbers and letters) and it is usually a randomized non-sequential numbering, which makes it very difficult for counterfeiters to predict [13].

Each country has the right to decide on its own information incorporated in a Data Matrix Code, however a minimum requirement of a GTIN paired with a serial number must be achieved. This way the product becomes a vehicle for carrying information needed for Track and Trace and can be identified individually at any time and at any point within the supply chain. It is also then possible to store further product related information in a database linked to this unique ID. Serialization takes place directly at the production lines and requires in most cases new printing and scanning technologies and software [13].

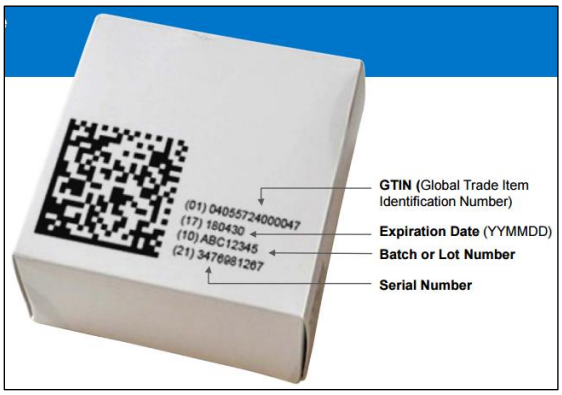


Figure 9: 2D GS1 Data Matrix code printed on a box [24]

Aggregation is the next step after achieving serialization. The meaning of **'aggregation'** is the process of building packaging hierarchies and storing this relationship in a database. Packaging hierarchy is built when a single item (referred to as child) is packed into a higher level of packaging hierarchy (referred to as parent) i.e., a bundle or a shipper case, which is subsequently packed into a higher level of packaging hierarchy (also referred to as parent) i.e., a pallet. Any new packaging level (e.g., cases, pallets etc.) added to the packaging hierarchy, must have a serial number (unique identifier) applied to it [13]. Aggregation however is an optional step, not all regulators enforce aggregation, even though it is very much recommended to have it in place. By having aggregation, one can simply scan the top-level hierarchy (parent) to get data of all packed items (children). For example, in a warehouse, when receiving a shipment with 50,000 items of a certain drug product, it is enough for the warehouse worker to

scan the code on the pallet to get details and list of serial numbers of all the packed items, instead of scanning 50,000 single packs. This reduces time and cost therefore aggregation is recommended. In EU's regulation for example, aggregation is still considered optional. Whereas in Saudi Arabia's regulation, aggregation is mandatory. As previously mentioned, each country has the right to decide on its own requirements and regulations [13] [25] [26]. In section 2.2.3, different regulations of different countries will be described. Figure 10 illustrates the sequence of serialization and aggregation according to different levels of hierarchy and figure 11 illustrates how it looks like in a packaging line.

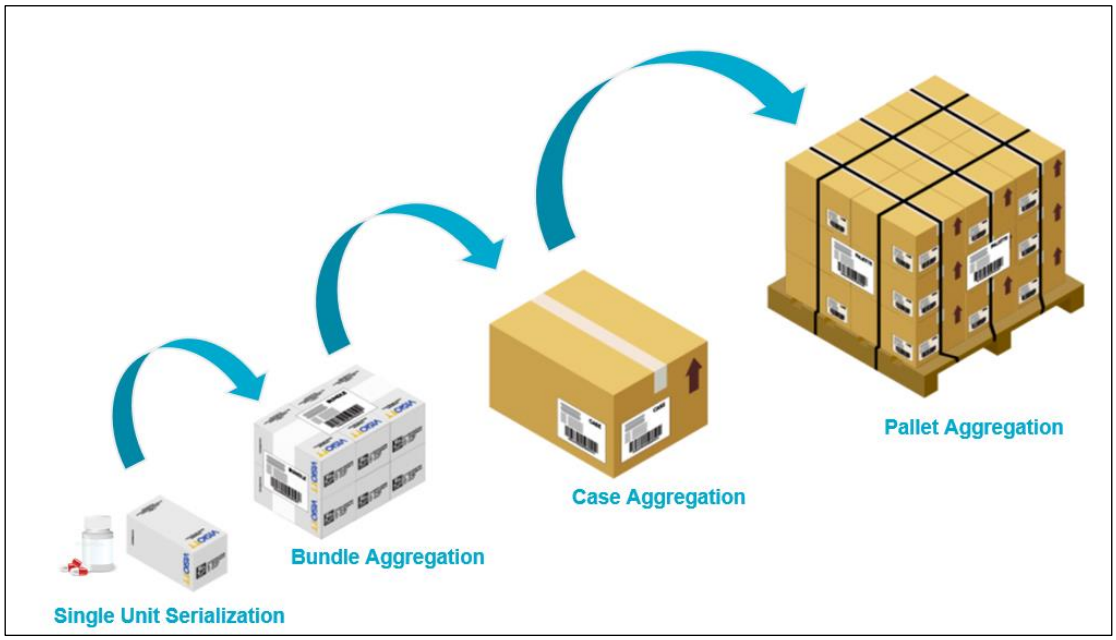


Figure 10: Sequence of serialization and aggregation according to different levels of hierarchy [27]

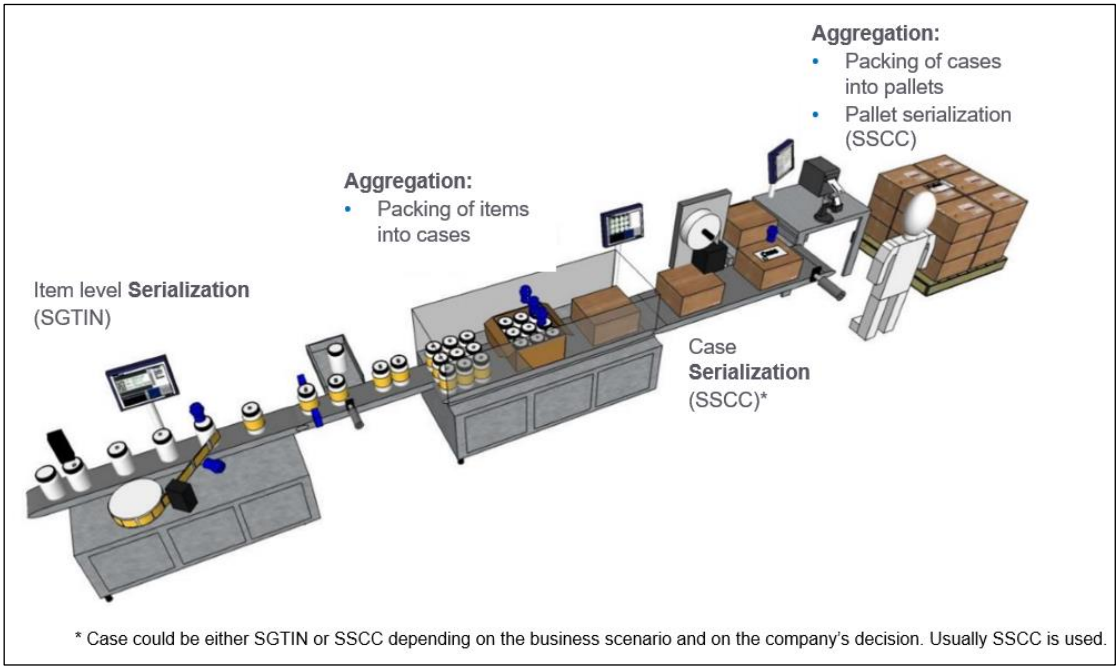


Figure 11: Serialization and aggregation in a production line [28]

Up to this point, "Identify" and "Capture" have been achieved; the product is identified by having a GTIN and the GTIN and other data such as serial number, expiry date and batch number are captured within a 2D Data Matrix Code.

The next step would be "Sharing". As mentioned in section 2.2.1, EPCIS is a GS1 Standard that allows data sharing and facilitates to achieve the following:

- ✓ Sharing real-time information about physical events in the supply chain between supply chain partners.
- ✓ Providing information about physical events related to products within the supply chain such as commissioning, packing, shipping, receiving etc.
- ✓ Allowing organizations to share data about the location of products (GLN) within their own organizations and between other supply chain partners.
- ✓ Facilitating in understanding what is happening in the physical world i.e., which product was produced / shipped, where did it come from and to whom is it being shipped.

- ✓ As previously mentioned, EPCIS data comprises a series of "events". Each EPCIS file documents an event that happened in the physical supply chain and it has four dimensions of information: what (SGTIN/SSCC), where (GLN), when (date and time) and why (commissioning, shipping, receiving, recalling, sampling, inspecting, decommissioning, dispensing, etc.). Example: when an item is serialized and commissioned then an EPCIS event is created, when an item is packed and aggregated then another EPCIS event is created, when an item is decommissioned and sampled then another EPCIS event is created and so on. For every event along the supply chain from the manufacturer until the patient, EPCIS messages are created including the above mentioned 4 dimensions of information [29].

Therefore, EPCIS is vital for the exchange of data between packaging lines and corporate systems, between business partners or supply chain partners, like Contract Manufacturing Organizations (CMOs), 3rd Party Logistics (3PLs), and with the regulators (e.g., government) [29].

Reporting of data to the government is the next important step, which could be considered as part of "Sharing". In general, a notification of serialized items and related events is reported to the governmental Data Base (DB). However, each government has the right to decide which report it wants to receive, with which information and at which point [29].

Finally comes product authentication. The pharmaceutical product is scanned and verified at the point of dispense (pharmacy or hospital) before it is given to the patient. When a product is scanned, the system verifies whether the drug is registered or not, whether it's authenticated or not, whether it's expired or not, whether it's recalled or not, etc. and based on that, the pharmacist / doctor / authorized personnel decides whether the drug can be decommissioned and dispensed to the patient or not. Product authentication can be done by the patient as well using their mobile device and a dedicated application provided from the government /

authorized representative. This allows the patient to scan the 2D Data Matrix Code printed on the package and verify whether the medicinal product is authenticated or not [13]. Figure 12 gives an overview of a T&T system from the manufacturer until the patient.

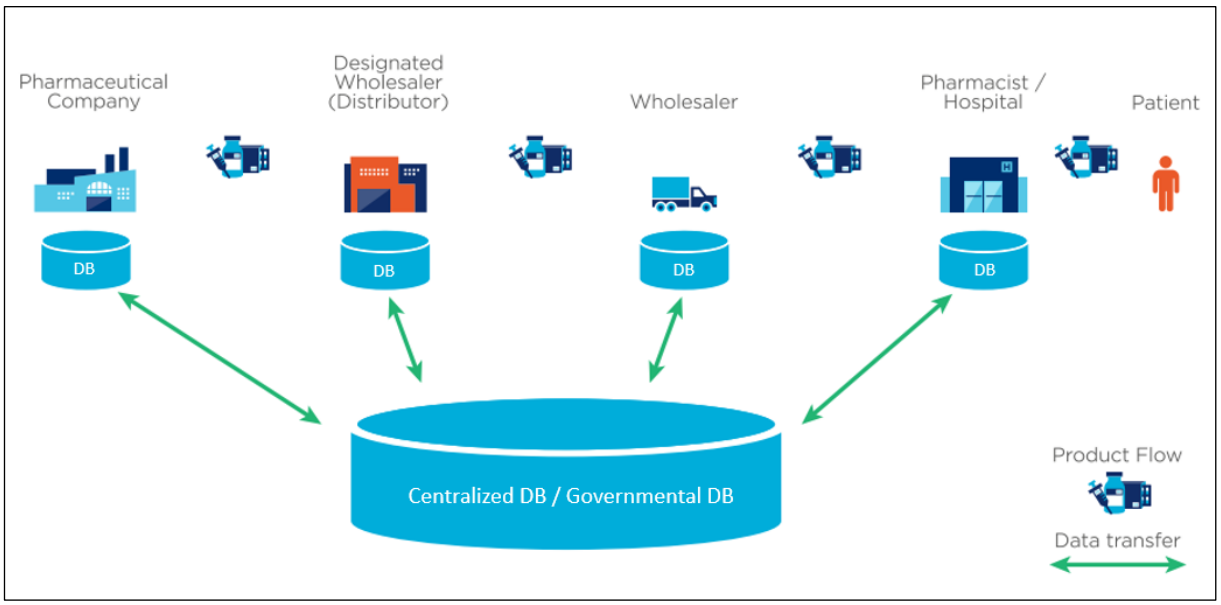


Figure 12: An overview of a T&T system from the manufacturer until the patient [17]

Now comes the question, how are all these systems connected?

There are a few available systems that support the Track and Trace regulation. The most common ones are: SAP ATTP and TraceLink. In this piece of work, SAP ATTP will be considered as the system supporting T&T and will be described accordingly.

In September 2015, the software company SAP (Systems Applications and Products in Data Processing) launched a new software called Advanced Track and Trace for Pharmaceuticals (ATTP) for the purpose of meeting the Track and Trace regulation to combat drug counterfeiting [30]. ATTP was built in a way that it can handle large volumes of data and regulatory reporting required by the new regulation. It provides serialization repository, serial number generation and management, transfer of these serial numbers to the packaging lines and compliance with country-specific regulations and reporting. In addition, it allows the track and

trace of serialized items internally within own organization and externally with supply chain partners and with the government [31].

SAP ATTP has the capability to connect between different systems and parties that are involved in a supply chain. This includes the systems of Marketing Authorization Holders (MAHs), CMOs, wholesalers, distributors, 3PLs and governments. In addition, it connects to the packaging line systems, to the Enterprise Resource Planning (ERP) systems and to the Extended Warehouse Management (EWM) systems as seen in figure 13 [32]. To get a full understanding of the involved systems, here is a definition of ERP and EWM systems.

An ERP system is characterized by being divided into modules for specific functional areas. These functional areas include business management, planning, manufacturing, sales, marketing, distribution, accounting, financial, human resource management, project management, inventory management, service and maintenance, transportation and e-business, which are all supported by an ERP system. To look at an ERP system from an architectural perspective, the ERP software typically facilitates the transparent integration of the functional modules, providing flow of information between the different functions of an enterprise in a consistently visible manner [33].

An EWM system is a flexible warehouse management system, which supports planned and efficient processing of all logistics processes within a warehouse. Additionally, it provides automated support for processing movement of goods and for stock management within a warehouse. Most importantly, it facilitates in Track and Trace as it allows users to determine the exact location of any material even on a storage bin level [34].

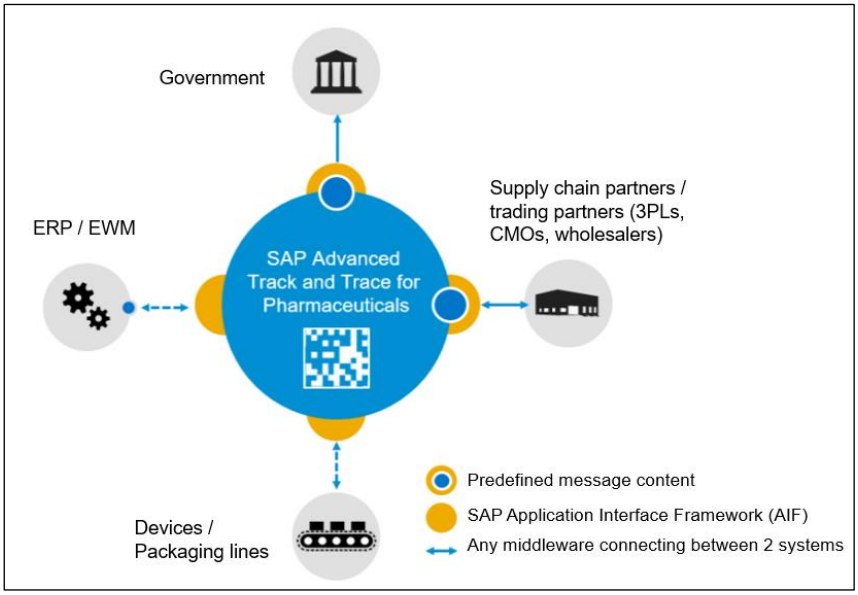


Figure 13: Overview of possible connections with SAP ATTP [32]

The exact way of connection between all these different systems differs from one organization to another depending on their infrastructure, the systems that they have in place and their willingness to introduce new systems if required. In general, a connection between an ATTP system and a non-ATTP system (like TraceLink or other systems) is possible [29].

In a typical serialization solution, there are 5 levels of functional layers according to ISA-95. By setting up the correct layers and systems and connecting between them, a track and trace system can be achieved. Figure 14 describes these 5 layers, their components and the connections between them. Between level 3 and level 4, and between level 4 and level 5, there are usually middlewares. A middleware is responsible for allowing 2 different levels to connect and speak the same language by mapping and translating between the various components of the overall solution [29].

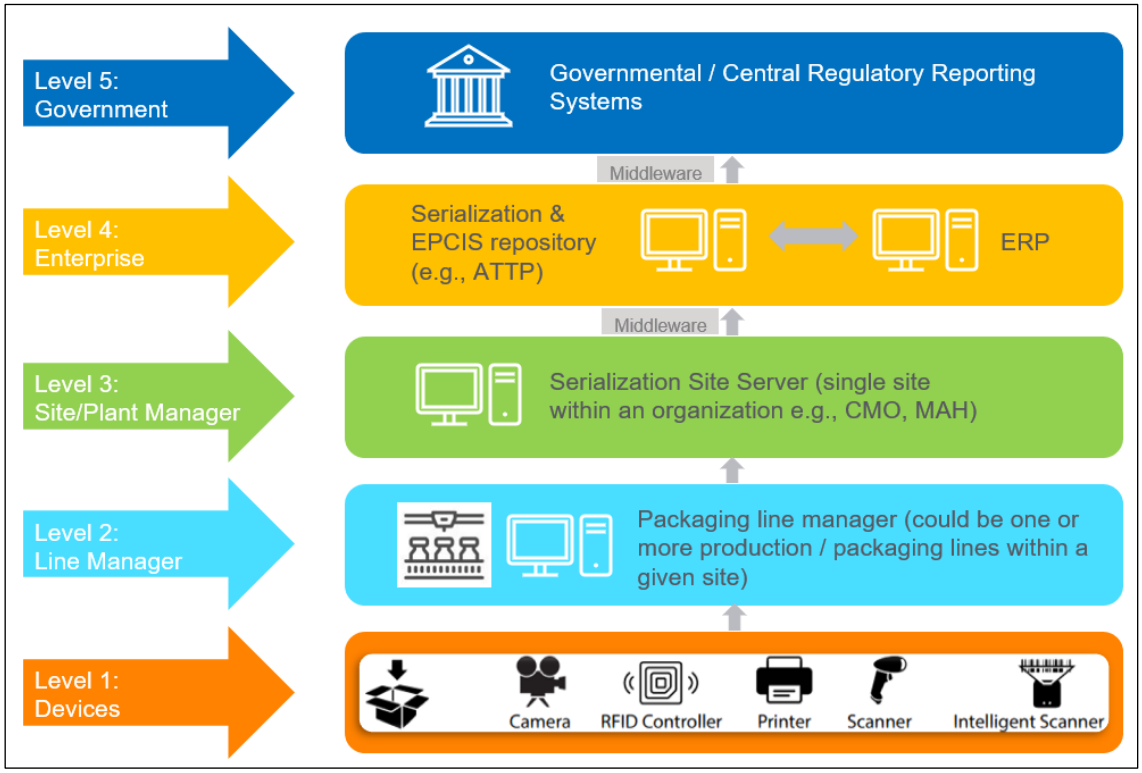


Figure 14: Functional layers of a typical serialization solution according to ISA-95 [35].

Note: ISA-95 is the 95th standard generated by the International Society of Automation (ISA), which defines a standard way of connecting different business systems to the automation control systems and devices. It is widely used when implementing serialization at the packaging line levels [35]

As seen in figure 15, the packaging line in a pharmaceutical company is connected to ATTP system that manages serial numbers and data exchange between the manufacturer and the packaging line and between the manufacturer and supply chain partners and/or governmental systems. When producing a certain batch or product, the packaging line requests a defined range of serial numbers (depending on the size of the batch) from ATTP and ATTP in return creates and sends back these serial numbers to the packaging line. The serial number and other data (i.e., GTIN, batch number and expiry date) are then printed on each single pack. Once packaging is finished, EPCIS events are created with all serial numbers that have been utilized, batch number, expiry date and GTIN, which is saved in the system and shared with the intended supply chain partner and/or government. This allows tracking of the product once it's shipped from the manufacturer till it reaches the dispensing point [32].

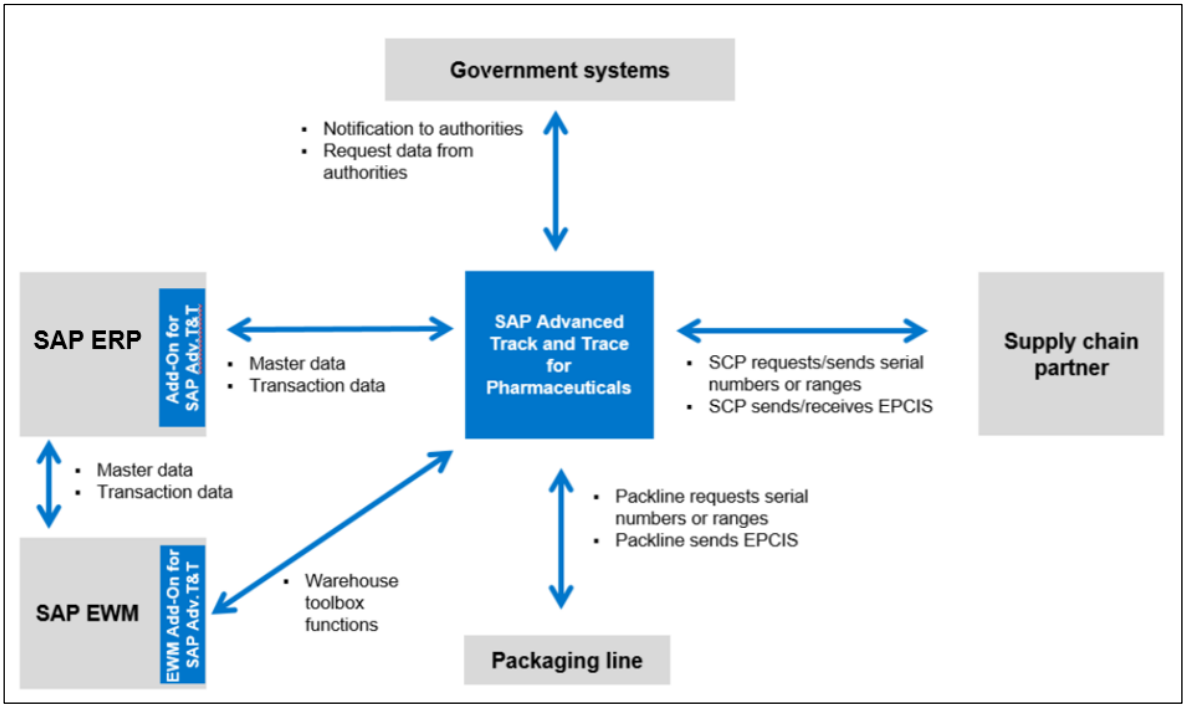


Figure 15: Landscape overview and connections between different systems [32]

Below are some screenshots (figures 16 – 19) of how SAP ATTP system looks like. These screenshots have been taken from the internal ATTP system of my current employer Movilitas, which requires access to be able to login. Therefore, the reference will be shown as the official website of Movilitas [36].

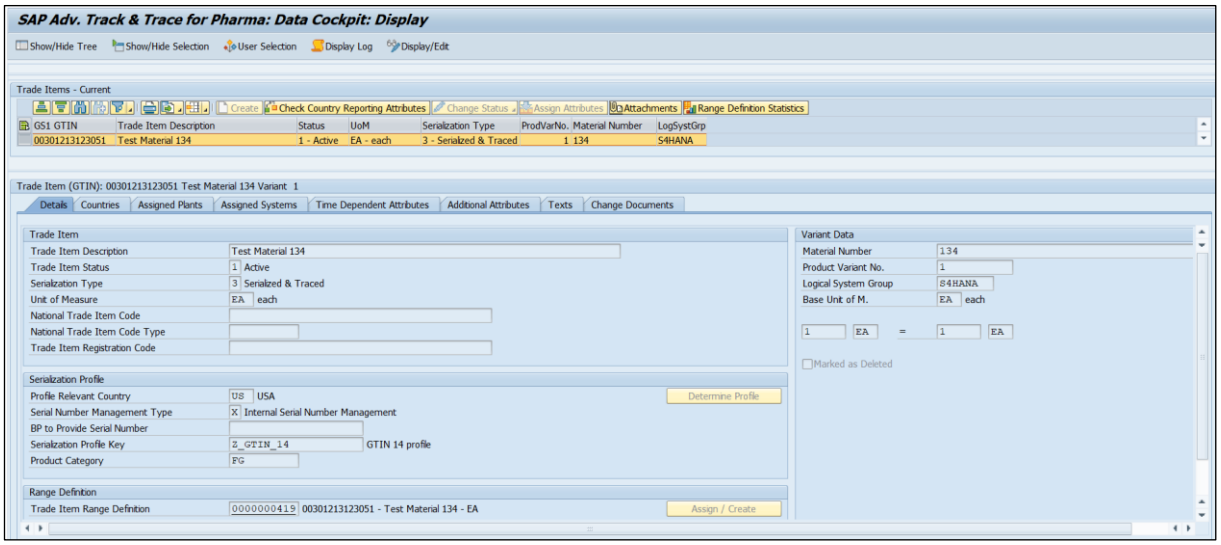


Figure 16: SAP ATTP – Data Cockpit – Trade Item (our pharmaceutical product) details [36]

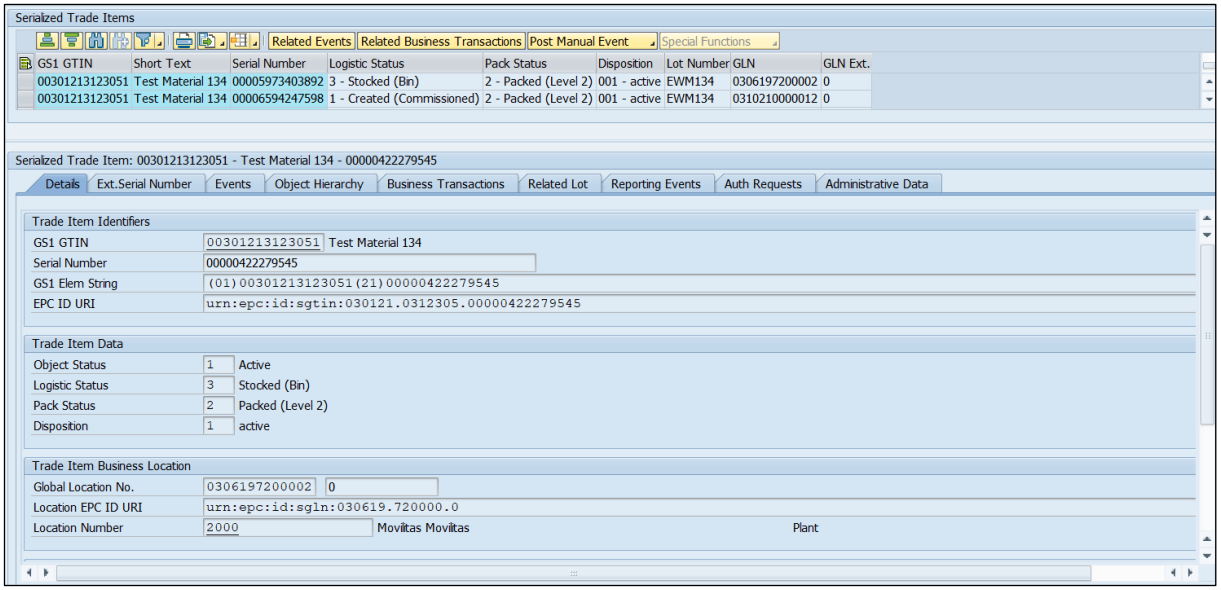


Figure 17: SAP ATTP – Data Cockpit – Serialized Trade Item (SGTIN) details [36]

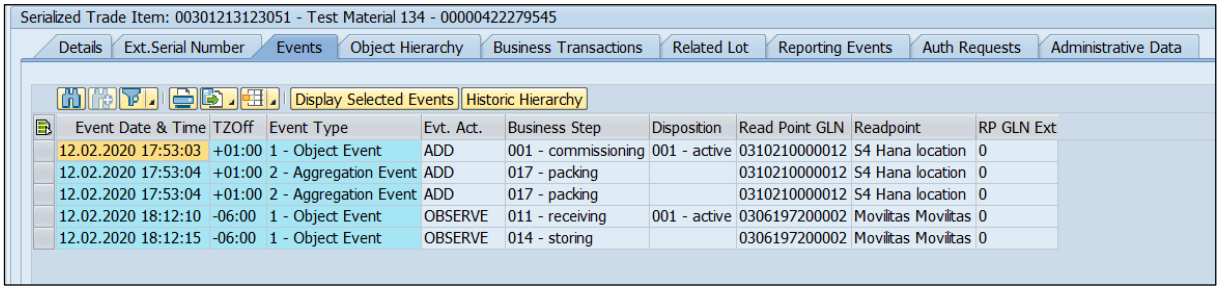


Figure 18: SAP ATTP – Data Cockpit – Events that occurred to the Serialized Trade Item from figure 17 [36]

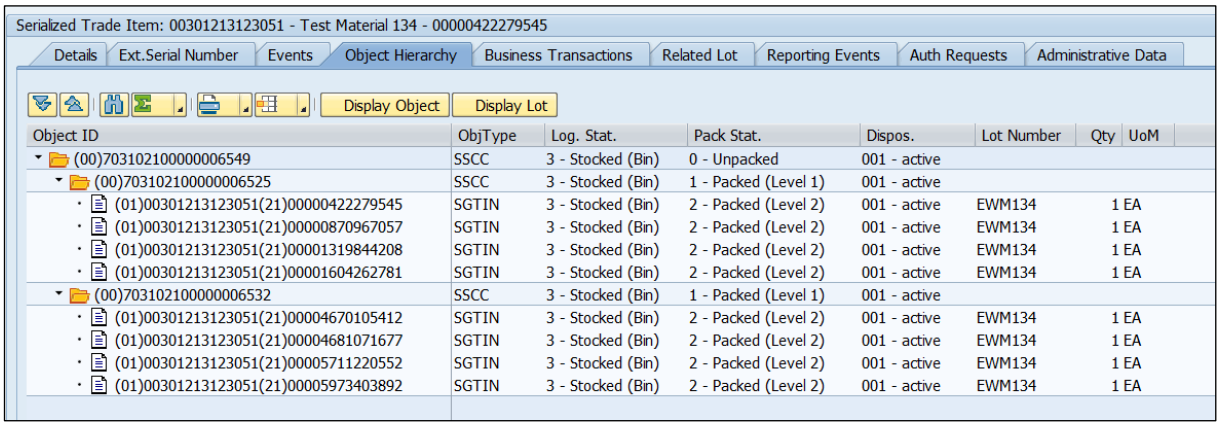


Figure 19: SAP ATTP – Data Cockpit – Levels of packaging hierarchy (SGTIN packed into SSCC) [36]

Recently, many Middle Eastern countries (like Egypt, Qatar and the United Arab Emirates) are considering introducing Track and Trace system as a regulation to fight drug counterfeiting, therefore SAP has created a test version of ATTP in Arabic, which is not yet officially released.

This screenshot (figure 20) was also taken from internal system therefore it is referenced as Movilitas official website [36].

Figure 20: Arabic version of SAP ATTP – Data Cockpit – Batch details [36]

Figure 21 shows an example of an authentication mobile application taken from internal Movilitas system. The data presented in the screenshots is test data for the purpose of illustrating how a drug verification request looks like after scanning the 2D Data Matrix Code printed on a pharmaceutical product or by entering the code manually. This is a standard mobile application, however, there are other different mobile applications with different functionalities depending on the customer's requirements [36].

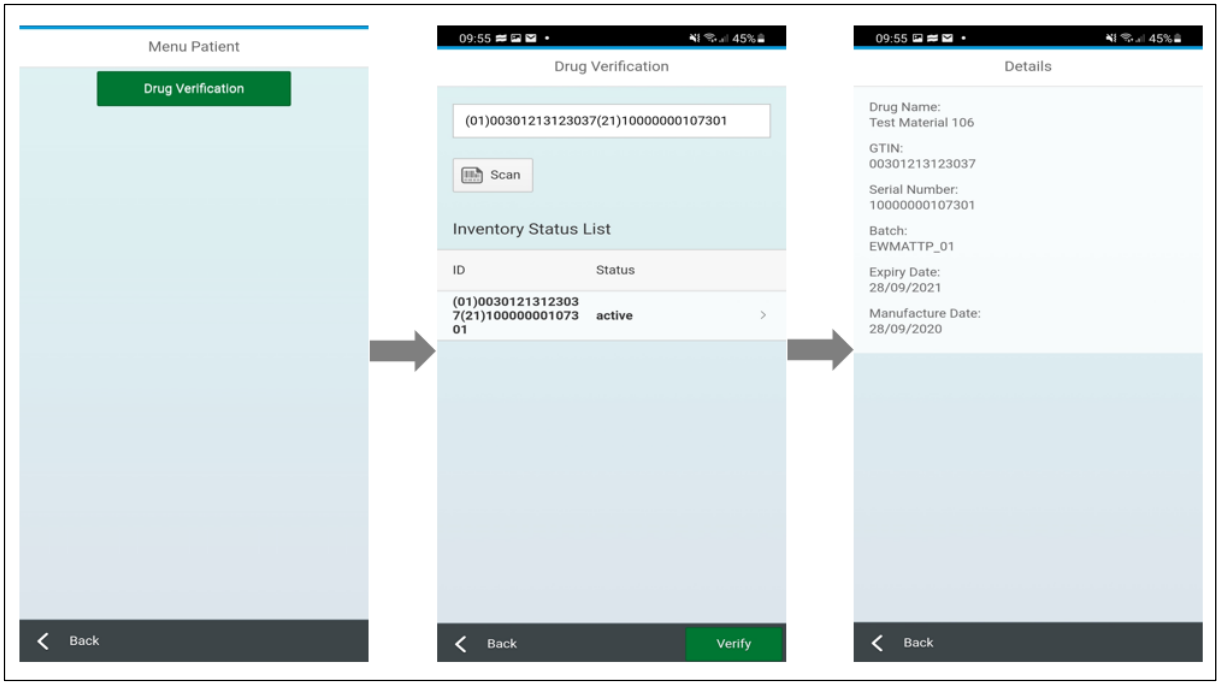


Figure 21: Screenshots from a mobile application after scanning the code of a pharmaceutical product.

Note: The middle screen shows that the scanned drug is in status "active" and the screen on the right side gives more details about that specific drug product (like drug name, GTIN, serial number, batch number, expiry date and manufacturing date) [36]

2.2.2.4 Summary

In summary, whether it's SAP ATTP or a different system, implementing a Track and Trace system allows supply chain partners, pharmacies, hospitals, the government and even the patient to verify whether a medicinal product is genuine or not, by scanning the 2D Data Matrix code printed on the package, thus ensuring patient safety and protecting the supply chain from counterfeit medicines.

2.2.3 Global Regulations for Pharmaceutical Serialization

In recent times, more countries are taking action towards fighting illicit trade of counterfeit medicaments. Many governments all around the world already launched or are in the progress of launching Track and Trace programs and setting deadlines for implementation.

Considering how quickly technology is developing and how smart counterfeiters might be, it is crucial for governments and health authorities to keep up to date with the latest technological innovations and set suitable requirements to prevent these counterfeiters from finding their way to introduce fake medicines into the market. More than 40 countries across the globe have guidelines for item level pharmaceutical serialization and traceability, yet no two countries have the exact same requirements. This section will describe different regulations in 9 different countries. The selection of the 9 countries was done in a way to present different versions of Track and Trace regulations with different timelines and different approaches. The countries are listed in a chronological order starting with Turkey, which was the first country to implement a Track and Trace system and ending with Lebanon and Egypt, which are in the progress of launching a Track and Trace system. Section 2.2.3.10 mentions briefly the status of implementing a Track and Trace system in other different countries.

2.2.3.1 Turkey

For many years, the social healthcare system in Turkey was facing corruption and witnessing numerous incidents of fraud activities and drug counterfeiting, which cost the Turkish government approximately $150 million yearly. One of the main known fraud activities which the Turkish health system suffered from was the “repeat reimbursement” scams. There was no controlled system for distributing prescription drugs therefore the government did know when, what and to whom it was paying, and it would end up paying twice or even more for the same drug without even knowing. There were several types of repeat reimbursement scams. One of them was when the same pack of prescription drug would be reused or recycled and then the drug would be reimbursed. Another one, is when a doctor or a pharmacist makes up fictitious patients and claims the cost of a non-existing drug from the government. Apart from the repeat reimbursement issue, obtaining prescription drugs without prescription was considered another significant drawback of the Turkish health system [1].

In October 2007, the Turkish government decided to tackle all those fraud activities by launching a Track and Trace / Serialization program, which was initially planned to be implemented by 2009 but was eventually postponed till July 2010. The main objectives of this new regulation and system are:

1. To combat the reimbursement fraud issues thus control and save unnecessary money which the government was spending every year on reimbursed pharmaceutical products.
2. To prevent drug counterfeiting, smuggling and illegal sale of pharmaceutical products thus protect public health and patient safety.
3. To help direct inspections by providing information on medicines usage.
4. To support rational drug use and control the distribution system of prescription drugs.
5. To make product recalls more efficient by having all steps of the drug product within the supply chain saved and stored in a live data source [1][37].

Additionally, the Turkish T&T system has a mobile application available for the use of the general public, which allows them to scan the 2D Data Matrix Code printed on a drug product or enter the barcode and serial number manually and check the product's status whether it is counterfeit, recalled and/or expired or not. It also facilitates reporting of adverse events. The answers that a consumer gets in the mobile application when scanning a drug's 2D Matrix Code or by entering it manually are:

- "Your medication is registered in the system"
- "The expiration date of this medicine has passed, and you should inform the pharmacist you received the medicine"
- "The medicine is not registered in the system, please report the situation" → When this message appears, the "Notify" button appears on the screen so that the user can report this incident to the control centre.

- "The medicine has been recalled from the market and its use is discouraged. Inform the pharmacist you received the medicine" [37]

Turkey in fact was the first country worldwide to successfully implement an end-to-end Track and Trace system of this type, which covers the whole pharmaceutical industry and supply chain. The system was given the name İlaç Takip Sistemi (ITS) which means “Drug Tracking System” [4].

The scope of ITS in terms of products includes all prescription drugs, over the counter (OTC) medicines, and dietary supplements (also known as Medical Nutrition Products). In terms of stakeholders, it involves all stakeholders within a pharmaceutical supply chain: manufacturers, wholesalers, importers, physicians, hospitals, pharmacies and reimbursement institutions [4].

ITS was introduced in two phases:

- Phase 1 was implemented in July 2010 and included serialization of secondary packaging.
- Phase 2 was implemented in January 2012 and included aggregation as well [4].

Serialization and printing requirements:

Machine readable and human readable 2D Data matrix code which includes:

- GTIN
- Serial number
- Expiry date
- Batch number [4]

ITS Concept:

The concept of the ITS is to track each and every drug package (unit packs, cases and pallets) in every single step throughout the supply chain. The ITS provides an additional system called

Package Transfer Service (PTS) system, which allows supply chain stakeholders to share and exchange data related to transfer of pack either by uploading data to PTS or downloading data from PTS. Figure 22 describes the workflow across the supply chain using ITS and PTS [38].

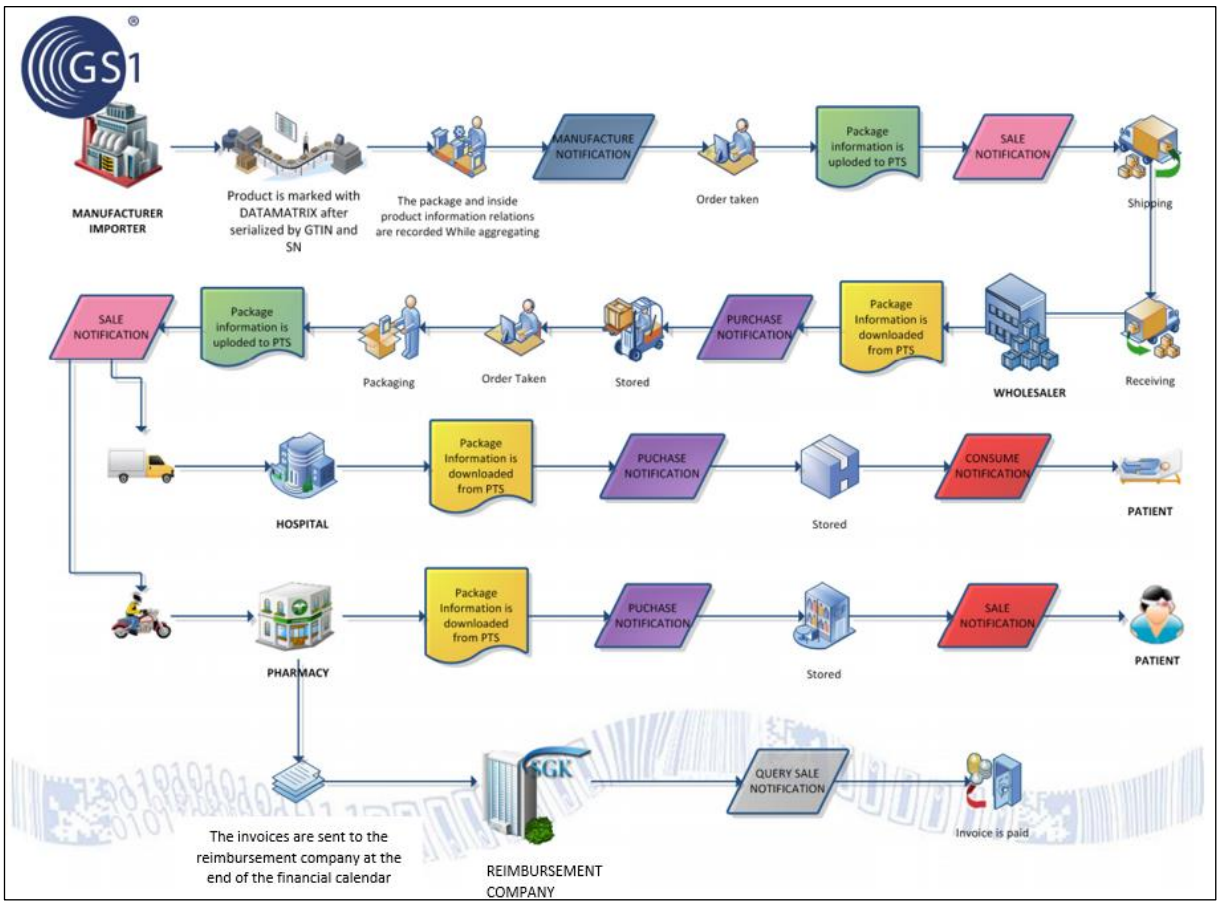


Figure 22: ITS Workflow through the pharmaceutical supply chain [38]

The tracking of each and every drug package is therefore accomplished by:

- Placing a unique serial number encoded in a 2D Data Matrix Code on every package.
- Recording every transaction through the supply chain by sharing data between supply chain stakeholders using PTS.
- Reporting, by supply chain stakeholders, of the following events to ITS:
    - Production / Manufacture Notification
    - Sale Notification
    - Sale Cancellation Notification

- Product Purchase Notification
- Consumption Notification
- Receiving Provision
- Product Return Notification
- Product Transfer Notification
- Product Transfer Cancellation
- Export Notification
- Export Cancellation Notification
- Deactivation Notification [38]

As seen in figure 23, the blue arrows show the interaction between different supply chain stakeholders and the data exchange about product transfer via the PTS system. While the green arrows show the interactions between each and every stakeholder with the ITS, where the above-mentioned transaction reports / notifications are sent directly from the system of each supply chain stakeholder to the ITS system [37].

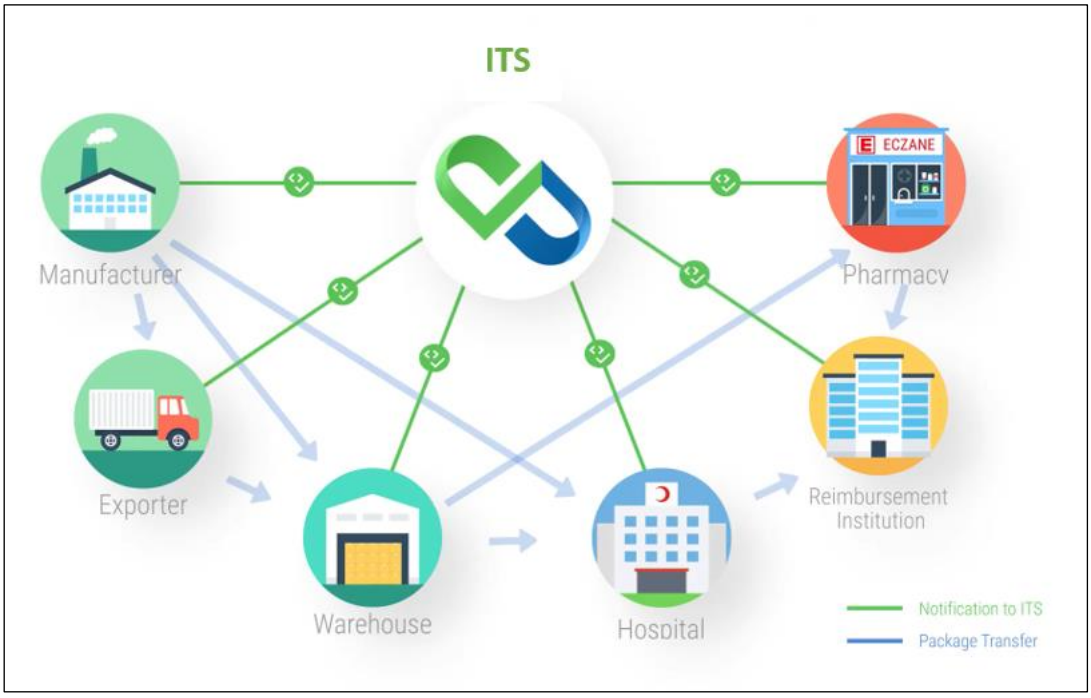


Figure 23: Overview of the interaction between different supply chain stakeholders with PTS and ITS [37]

On the 31st of August 2019, a new amendment has been enforced, which states that if a stakeholder misses reporting any step of the notifications (production, import, sale, return, purchase, disposal, withdrawal etc.) to the ITS then the Turkish Ministry of Health (MoH) will suspend their product's licence [36].

Benefits of the ITS:

- ✓ Combats corruption
- ✓ Tracks the drug from the point of manufacturing until it is dispensed to the patient
- ✓ Prevents the sale of counterfeit drugs
- ✓ Prevents the sale of smuggled drugs
- ✓ Prevents illegal sale of drugs
- ✓ Prevents barcode scams
- ✓ Prevents drug theft
- ✓ Prevents the resale of the drugs, which have already been sold to the reimbursement institutions
- ✓ Provides safe and genuine drugs to the patients
- ✓ Supports rational use of medicines
- ✓ Supports the fight against narcotics
- ✓ Prevents black market that arise especially during any period of epidemics (e.g., during our times now with the covid-19 pandemic)
- ✓ Takes instant and precise actions on recalls
- ✓ Does more effective and accurate market surveillance and inspection
- ✓ Makes faster decisions and does more consistent estimations by using instantly updated data
- ✓ Prepares effective administrative reports to manage the pharmaceutical industry
- ✓ Prevents tax fraud by reports created using the stock and sale data of the participants

- ✓ Regulates participants such as wholesalers, public and private hospitals and pharmacies by certain standards and supports their workflow by software applications
- ✓ Creates reports for market control, public health and managerial aspects from the collected data by using data mining [37][38][36]

According to the ITS official website, the pharmaceutical T&T system is used by more than 42,000 stakeholders in Turkey up until the time of writing, as shown in figure 24 [37].

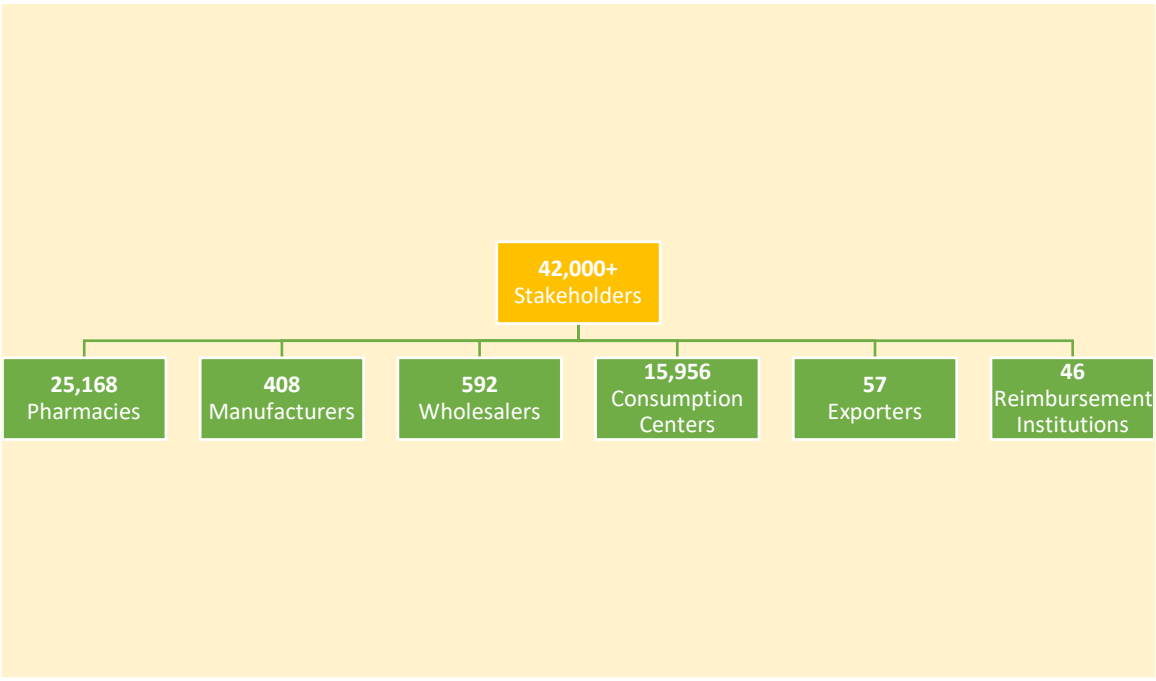


Figure 24: Number of stakeholders using T&T system in Turkey [37]

Table 3: Summary of T&T requirements and deadlines in Turkey.

Country	**Turkey**
Authority	Turkish Ministry of Health
System Name / Regulatory Act	İlaç Takip Sistemi (ITS)
Scope	Combat reimbursement fraud and drug counterfeiting
Stakeholders / Participants	- Manufacturers - Wholesalers - Importers - Physicians - Hospitals

Country	Turkey
	- Pharmacies and their warehouse - Reimbursement institutions
Serialization & Printing Requirements	2D Data Matrix Code encoded with GTIN, serial number, batch number and expiry date
Regulatory Reporting	Yes, to the ITS
Timelines	July 2010 → serialization January 2012 → aggregation

2.2.3.2 China

There are 2 sides of the story when it comes to China. From one side, China is known to be one of the main origins of counterfeit pharmaceutical products, as already mentioned in section 1.2, thus posing risk to the public health of people all around the world. From the other side, people of China are also suffering and are dramatically affected by the counterfeiting criminal activities within China itself. Drug counterfeiting in China is causing poisoning and death of hundreds of thousands of its own nation. In 2007, the Chinese government executed the former head of the State Food and Drug Administration after finding out about the corruption which he was causing and his utterly ugly crimes, where he approved drugs by accepting bribes with a total of $850,000. As a result of this incident, China requested to review about 170,000 medical licenses that were approved during the occupancy of the former head of the State FDA [1].

Additionally, the Chinese government decided to take action and combat drug counterfeiting in order to protect its nation from fake medicines by introducing the track and trace regulation in phases. In 2008, the Chinese FDA (CFDA) made serialization mandatory for over 275 therapeutic classes of individual saleable product units by December 2015. Some therapeutic classes had to be serialized by 2013 while others had to be serialized by 2014. However, by the 31st of December 2015, all pharmaceutical products had to comply with the track and trace / serialization regulation as well as government reporting. The track and trace regulation applies for manufacturers, distributers and pharmacies.

Unlike the regulation of other countries where the pharmaceutical companies or manufacturers are responsible for generating their own unique serial numbers according to GS1 standards, the CFDA decided to be the one controlling and responsible for providing these serial numbers to pharmaceutical companies.

The CFDA owns a track and trace system called Product Identification, Authentication and Tracking System (PIATS) to track drugs' regulatory, manufacturing, composition and expiration data. This system is developed and maintained by Alibaba Health Information Technology Ltd. in China [36][39].

How does the serialization and government reporting in China work?

Figure 25 gives an overview of the Track and Trace system in China.

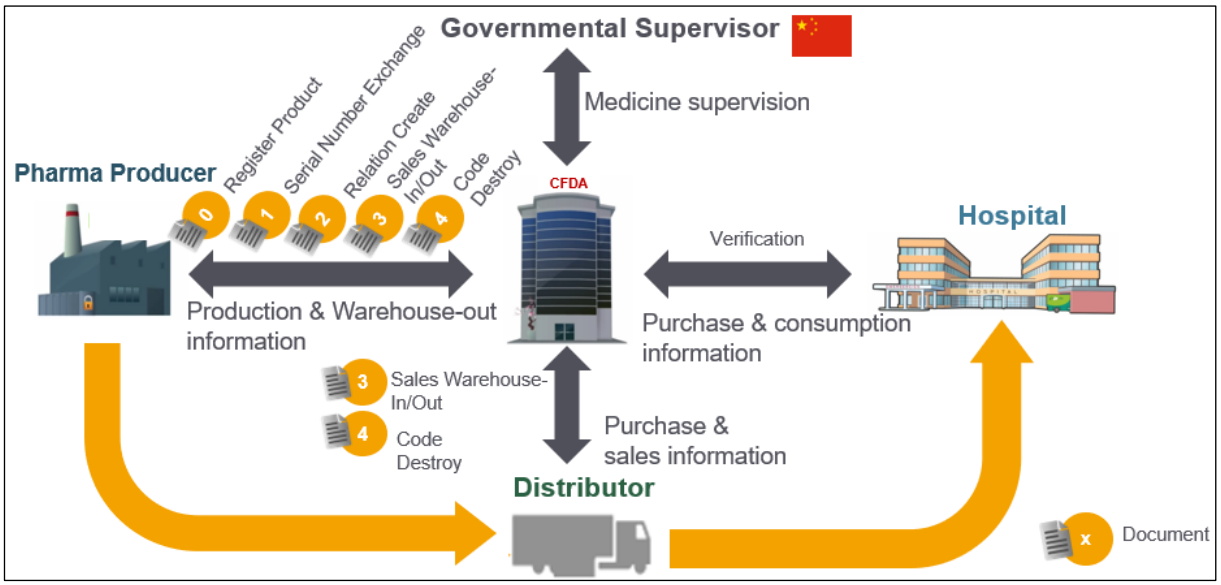


Figure 25: T&T Process Overview in China [36][39]

- First, pharmaceutical companies must register themselves in PIATS platform. They must also implement a quality control system with an electronic drug-monitoring system, a standardized documentation system, and barcodes to ensure pharmaceutical traceability.

- Once registration is done and connection is established between the two systems, serial number exchange can be executed. The PIATS provides the pharmaceutical companies with non-GS1 serial numbers in a specifically designed text-file.
- This text-file is then imported into the systems of the pharmaceutical companies so that serial numbers are available during production.
- Once production is done, the items / packs need to be aggregated, scanned and verified.
- Before any product is shipped and released into the Chinese market, pharmaceutical companies must report all serial numbers of all packaging levels (unit, bundle, case and pallet) to the CFDA's system, i.e., PIATS. There are 3 types of reporting:
    - "Relation Create" report, which is a batch related report containing all serial numbers and the level of hierarchy.
    - "Sales Warehouse-in/out" report, which is a report generated as part of the delivery process and indicates sales to 3rd parties.
    - "Code Destroy" report, which is a report including damages and returned products thus the reported serial numbers become invalid.
- All the above-mentioned reports are Extensible Markup Language (XML) files which are reported by manually uploading them into the CFDAs' system. There is a restriction from the governments' system that the size of the uploaded XML file should not exceed 5 megabytes (MB), which could be very challenging especially for large batches [36][39].

Companies importing drugs into China must designate a local pharmaceutical company or wholesaler as their electronic monitoring agent in the country.

Printing requirements of the Chinese government:

Printing requirements include a 20-digit Electronic Drug Monitoring Code (EDMC), which is a linear barcode and does not follow GS1 standards or any other international standards, as shown in figure 26.

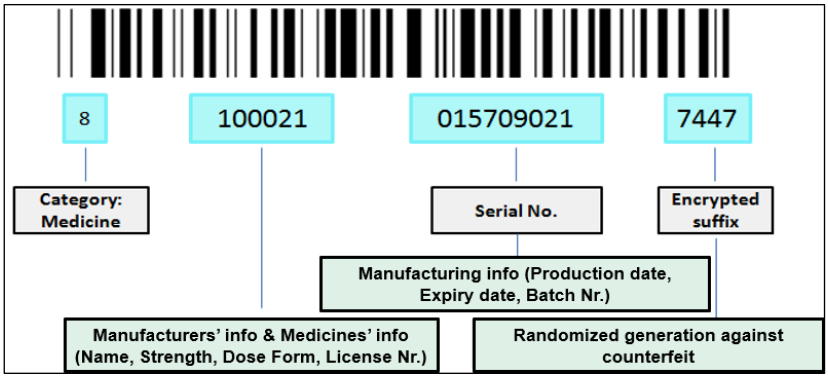


Figure 26: Printing requirements for China [36][39]

On the 20th of February 2016, CFDA announced the suspension of the implementation of the track and trace regulation due to a large number of complications, while drafting new changes and adjustments to the regulations. However, Alibaba Health confirmed that they will continue providing technical support and maintenance services to the PIATS platform until receiving an official notice from the CFDA. At the time of writing, the PIATS system was still functioning, and manufacturers were still able to request and receive serial numbers from the system [40].

On the 28th of April 2019, the National Medical Products Administration (NMPA), which was formerly known as CFDA, published 2 documents. These 2 documents are meant to clarify the new traceability requirements.:

- ✓ Encoding requirements for drug traceability code
- ✓ Guidelines for drug traceability information system construction

On the 13th of October 2020, the NMPA announced new updates confirming the use of GS1 standards. The new regulation is to be implemented by 2022. According to current available information, the new regulation allows:

- ✓ The use of GS1 standards.
- ✓ Manufacturers to choose between linear code or a 2D Data Matrix Code following GS1 standards.
- ✓ Manufacturers to choose their software provider of serial numbers, as they do not need to request the serial numbers from CFDA anymore [41]

The new Track and Trace in China is expected to make the system more international standardized thus more robust against drug counterfeiting. Additionally, using international standards like GS1 makes it easier for pharmaceutical companies (whether importers or exporters) to comply with the regulations and it also facilitates in enhancing the process of product recall.

Table 4: Summary of T&T requirements and deadlines in China.

Country	**China**
Authority	NMPA
System Name / Regulatory Act	PIATS
Scope	Combat drug counterfeiting
Stakeholders / Participants	- Manufacturers - Distributers - Pharmacies
Serialization & Printing Requirements	Current available information: 2D Data Matrix Code
Regulatory Reporting	Yes
Timelines	December 2015 → Serialization was implemented not according to GS1 standards. By 2022 → Serialization must be implemented following GS1 standards.

2.2.3.3 USA

The combat against drug counterfeit started as early as 1906 when the Food and Drug Administration (FDA) was enacted. Congress tried to fight drug counterfeiting and protect US consumers by enforcing regulations about specific pharmaceutical labelling. Unfortunately, this did not prevent or reduce drug counterfeiting, therefore Congress enacted Prescription Drug Marketing Act (PDMA) in 1987, which introduced the use of paper pedigrees [42]. According to the FDA, "the PDMA was enacted (1) to ensure that drug products purchased by consumers are safe and effective, and (2) to avoid the unacceptable risk to American consumers from counterfeit, adulterated, misbranded, subpotent, or expired drugs. The legislation was necessary to increase safeguards in the drug distribution system to prevent the introduction and retail sale of substandard, ineffective, or counterfeit drugs." [43]

Even though the PDMA was enacted but the FDA did not enforce it as a legislation. Since a Federal legislation was missing, it has been left to each State to decide on its own national legislation [44].

Florida was the first State to enact a legislation on prescription drug pedigrees followed by California. In July 2005, Florida State enacted a legislation on prescription drug pedigrees (2005-R-0580). According to Florida's legislation "Pedigree paper refers to a document, either in paper or electronic form, that contains information that records each distribution of any given prescription drug, from sale by a manufacturer, through acquisition and sale by any wholesaler or repackager, until final sale to a pharmacy or other person administering or dispensing the drug" [45].

Dr. Scott Gottlieb, Deputy Commissioner for Medical and Scientific Affairs, US Food and Drug Administration, said in his speech on 20th of September 2005, "In 2000, the FDA opened six counterfeit drug cases, in 2003, we opened 30, and last year, we opened 58... Just this past month, on 31 August, we busted up a Lipitor counterfeiting and smuggling operation that was

trafficking almost $50 million worth of the drug". On 2nd January 2007, California's Law took effect, followed by 14 other States [44].

In 2012, the U.S. Centers for Disease Control and Prevention (CDC), together with state health departments and the FDA traced the outbreak of fungal contamination in three batches of preservative-free Methylprednisolone Acetate (MPA) steroid injections. This multistate outbreak of fungal meningitis was responsible for killing 64 people and sickening 687 others (figure 27) who received contaminated steroid injections from the New England Compounding Center (NECC) in Framingham, Massachusetts, across 20 states (figure 28) [46]. According to local news, the owner of NECC, Barry Cadden was arrested, charged with second-degree murder and sentenced to 9 years in prison. Barry was also accused for faking cleaning logs, using expired ingredients with false labels, not recalling drugs when microbes were found, and compounding drugs in clean rooms that failed to comply with the most basic health standards [47][48].

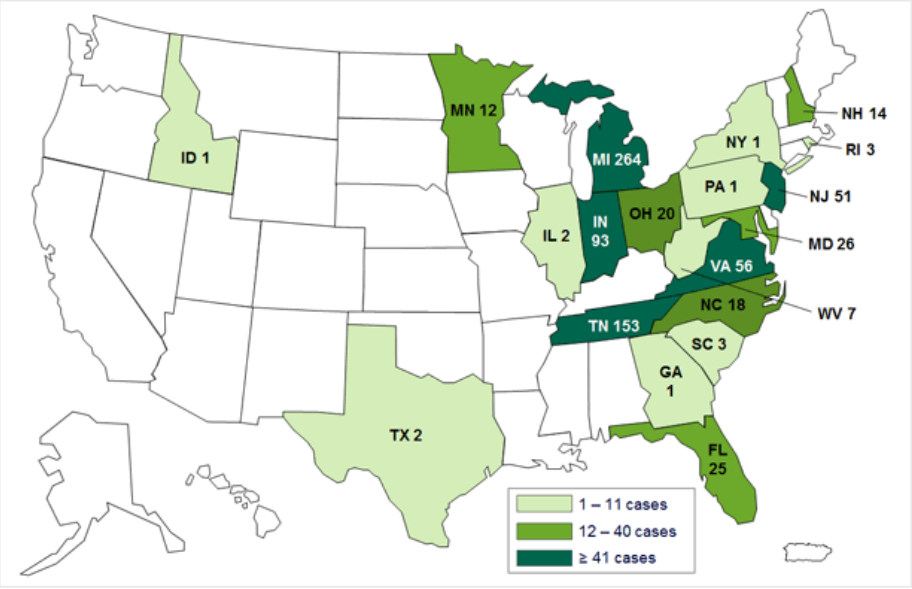


Figure 27: Number of people with fungal infections linked to steroid injections, by State [46]

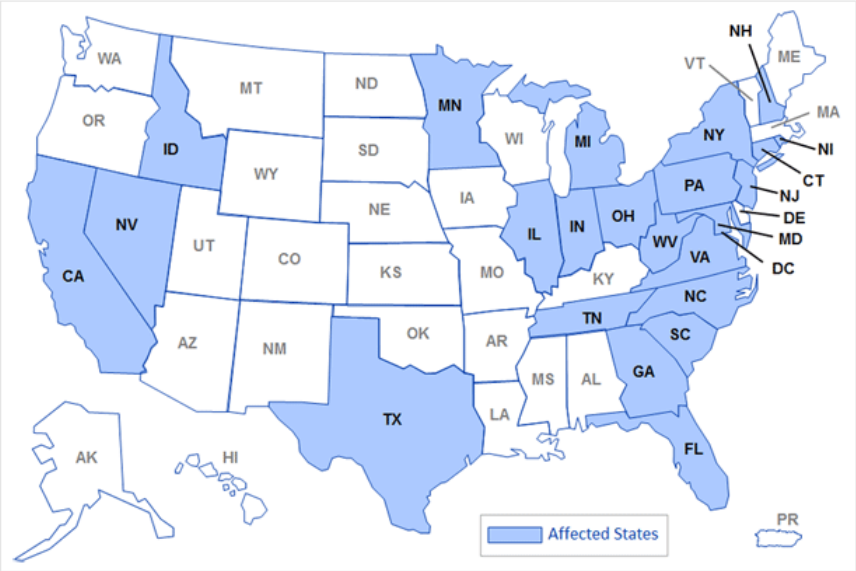


Figure 28: Map of Healthcare Facilities that received contaminated steroid injections from NECC [46]

Following this outbreak, the Drug Quality and Security Act (DQSA) was signed into law by President Barack Obama on the 27th of November 2013. As shown in figure 29, the DQSA includes 2 independent titles (laws): Title I and Title II. Title I is related to drug compounding (i.e., approval of the drug by FDA before marketing, correct labelling and compliance with current Good Manufacturing Practices (cGMP). Title II is related to the security of the drug supply chain and includes the Drug Supply Chain Security Act (DSCSA), which describes steps for building an electronic, interoperable system to track and trace prescription drugs that are sold in the United States. Implementing such a system will help the FDA to protect US consumers from counterfeited drugs. Implementation of the track and trace system started in the USA on 27th November 2017 [49][50].

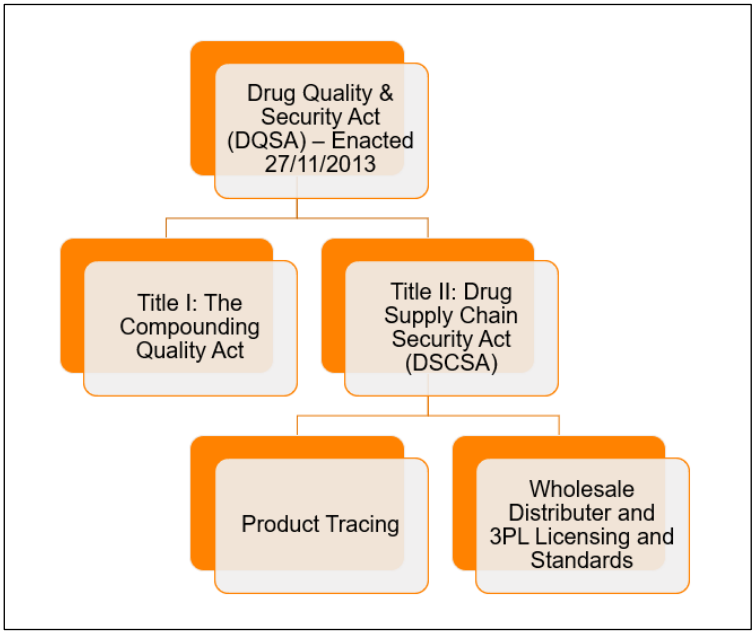


Figure 29: Overview of the DQSA [51]

According to the FDA, tracking of pharmaceutical products via serialization was found to be as the best method for improving supply chain security and fighting drug counterfeiting. As mentioned above, the DSCSA was signed on the 27th of November 2013 and the track and trace system was planned to be fully implemented in phases by November 2023. By 27th of November 2023, there will be an enhanced, interoperable T&T system, which must allow electronic tracing of pharmaceutical products on package level i.e., smallest saleable unit, within a legal supply chain [49].

Serialization requirements:

2D Data Matrix Code and human readable Product Identifier which include:

- ✓ Standardized Numerical Identifier (figure 30):
  - National Drug Code (NDC)
  - Serial Number
- ✓ Lot Number
- ✓ Expiration Date [49]

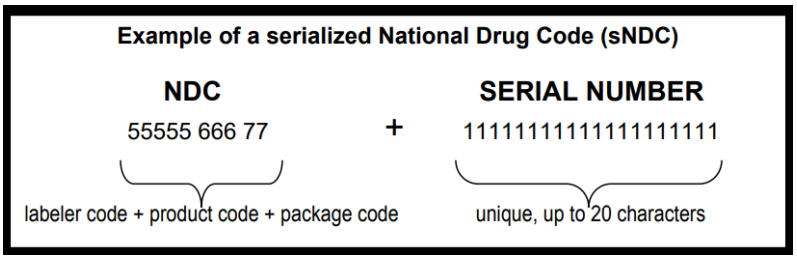


Figure 30: Example of a serialized NDC [52]

Below are some important terms as defined in title II of the DQSA, which help to understand regulations requirements. Considering that these definitions are part of a fixed law, they have been copied as is:

"Transaction: Transfer of product where a change of ownership occurs.

Product Tracing Information: consists of the following;

- **Transaction Information (TI):** Drugs' name, strength, dosage form, NDC, container size, number of containers, lot number, date of the transaction, date of the shipment (if more than 24 hours after the date of the transaction) and business name and address of the person from whom and to whom ownership is being transferred.
- **Transaction History (TH):** A statement in paper or electronic form, including the transaction information for each prior transaction going back to the manufacturer of the product.
- **Transaction Statement (TS):** A statement, in paper or electronic form, that the entity transferring ownership in a transaction:
    - Is authorized as required under DSCSA;
    - Received the product from a person that is authorized as required under DSCSA;
    - Received transaction information and a transaction statement from the prior owner of the product, as required under the law;
    - Did not knowingly ship a suspect or illegitimate product;

- Had systems and processes in place to comply with verification requirements under the law;
- Did not knowingly provide false transaction information;
- Did not knowingly alter the transaction history" [53]

The exact details of the regulation's requirements and expected timelines in the USA are explained in table 5.

Table 5: Summary of the timelines and regulations expected for each participant within the pharmaceutical supply chain [51].

Year	DSCSA Regulation
2013	27.11.2013 ✓ The DQSA (including Title II: DSCSA) was signed into law by President Barack Obama.
2015	01.01.2015 ✓ *Trade Partner Authorization:* Manufacturers, repackagers, wholesale distributers 3PLs and dispensers must be authorized as defined by the Food, Drug and Cosmetic Act (FD&C) i.e., valid registration with the FDA and valid State or Federal license. ✓ *Product Tracing (on a lot-level):* Manufacturers, repackagers and wholesale distributers must exchange transactions (TI, TH, TS), in paper or electronic or other agreed format, about a drug and who handled it each time a drug is sold in the U.S. market. ✓ *Product Verification (on a lot-level):* Manufacturers, repackagers, wholesale distributers and dispensers (primarily pharmacies) must establish systems and

Year	DSCSA Regulation
	processes to comply with the following verification requirements for the handling of suspect or illegitimate product: o Must be able to respond to verification requests from FDA or other appropriate Federal or State official in the event of a product recall or for the purpose of investigating a suspect or illegitimate product. The response must include applicable TI, TH and TS and shall be provided no later than 2 business days after receiving the request. o Quarantine and investigate suspect product to determine if illegitimate product (includes validating applicable TI and TH). o Notify trading partners and FDA of illegitimate product (within 24 hours of determination). o Respond to notifications of illegitimate product. o Recordkeeping (maintain transactions for not less than 6 years after the date of the transaction). 01.07.2015 ✓ The same above-mentioned regulations apply on dispensers (primarily pharmacies) as well.
2017	27.11.2017 – Beginning of Serialization for Manufacturers ✓ *Product Identification (serialization):* Manufacturers must place a unique product identifier on each package and homogenous case of a product. ✓ Manufacturers must provide transactions (TI, TH, TS) in electronic format to trading partners for all sales. ✓ *Product Verification (on a package-level):* Manufacturers must respond to verification requests from trading partners not later than 24 hours after

Year	DSCSA Regulation
	receiving the request. They must verify the product identifier at the package level, including the standardized numerical identifier, for any product they suspect is counterfeit. They must also verify product identifiers of products that are intended for resale.
2018	27.11.2018 – Beginning of Serialization for Repackagers ✓ *Product Identification (serialization):* Repackagers must place a unique product identifier on prescription drug packages and are only allowed to buy or sell products encoded with unique product identifiers. ✓ *Product Verification (on a package-level):* Repackagers must respond to verification requests from trading partners not later than 24 hours after receiving the request. They must verify the product identifier at the package level, including the standardized numerical identifier, for any product they suspect is counterfeit. They must also verify product identifiers of products that are intended for resale.
2019	27.11.2019 – Beginning of Serialization for Wholesale Distributors ✓ *Product Identification (serialization):* Wholesale distributors are only allowed to buy or sell products encoded with unique product identifiers. ✓ *Product Verification (on a package-level):* Wholesale distributors must respond to verification requests from trading partners not later than 24 hours after receiving the request. They must verify the product identifier at the package level, including the standardized numerical identifier, for any product they suspect is counterfeit. They must also verify product identifiers of products that are intended for resale.
2020	27.11.2020 – Beginning of Serialization for Dispensers

Year	DSCSA Regulation
	✓ *Product Identification (serialization):* Dispensers are only allowed to buy or sell products encoded with unique product identifiers. ✓ *Product Verification (on a package-level):* Dispensers must respond to verification requests from trading partners not later than 24 hours after receiving the request. They must verify the product identifier at the package level, including the standardized numerical identifier, for any product they suspect is counterfeit.
2023	27.11.2023 – Full Enhanced Track and Trace System on a Package-level ✓ Manufacturers, repackagers, wholesale distributors and dispensers must all participate in the end – end package level traceability system. ✓ Electronic exchange of transaction information for each sale of certain prescription drugs ✓ Verification of Product Identifiers at the package level ✓ Prompt response to suspect and illegitimate products when found ✓ Improved efficiency of recalls [51]

Table 6: Summary of T&T requirements and deadlines in USA.

Country	**USA**
Authority	US FDA
System Name / Regulation Act	DSCSA
Scope	Traceability and combat counterfeiting
Stakeholders / Participants	- Manufacturer - Wholesaler / Distributor - Third party logistics provider - Repackager - Dispenser (hospitals and pharmacies)

Country	**USA**
	- International Regulatory Counterparts - FDA - State Officials
Serialization Requirements	2D Data Matrix code encoded with NDC, serial number, lot number, expiry date
Regulatory Reporting	FDA
Timelines	2017 → Serialization was implemented by manufacturers. 2018 → Serialization was implemented by repackagers. 2019 → Serialization was implemented by wholesale distributors. 2020 → Serialization was implemented by dispensers. 2023 → Full Track and Trace must be in place

2.2.3.4 European Union

Compared to the rest of the world, EU has less seizures and less importation of counterfeit medicines. According to existing studies, 47% of the total value of fake medicines being shipped to the EU and seized by EU customs authorities are originating from India (figure 31).

In terms of transit points, the 3 main countries taking the lead are Iran, Switzerland and the United States, where counterfeit medicines are being shipped through these regions to Europe [5].

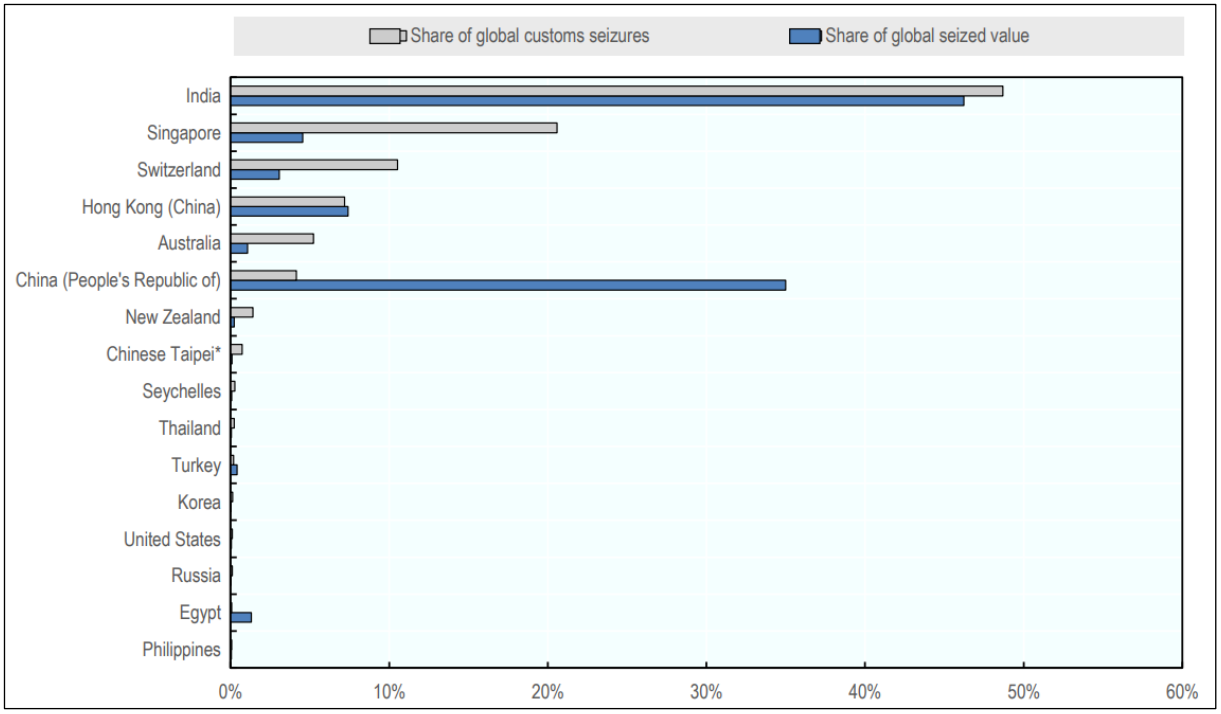


Figure 31: Top provenance economies of counterfeit pharmaceuticals imported into the EU, 2014- 2016 [5]

In order to protect public health and legal pharmaceutical supply chain from drug falsification, the European Council and European Parliament published the Falsified Medicines Directive (FMD) 2011/62/EU on the 1st of July 2011. This Directive introduced mandatory safety features on prescription medicines, strengthened the requirements of Good Distribution Practice (GDP), reinforced the rules on importing, inspecting and controlling of active substances and their manufacturers. In addition to that, it has set an EU-wide logo for online pharmacies to allow the identification of legal online distributers of medicines [54]. In 2016, Commission Delegated Regulation (EU) 2016/161 was published, which provided more technical details about the mandatory safety features (i.e., serialization requirements) as well as the deadline for complying with these mandatory safety features [55]. These mandatory safety features included printing a unique identifier, which is a unique serial number carried by a 2D data matrix code on every single pack and adding a tamper evident device. Both rules on the safety features have been implemented on all prescription drugs sold in the European Union starting from 9th February 2019. Greece and Italy however, have the option to postpone the implementation to an

additional six years [26]. In addition to implementing the safety features, some EU countries like Hungary, have made some changes to the penalties that are related to falsification of medicines, active substances and excipients [54].

Not only prescription drugs but also Pandemic–influenza vaccines like the COVID-19 vaccine for example, which is authorised via the mock-up procedure, should also include the safety features in accordance with the FMD regulation.

Free samples of medicinal products must also comply with the FMD safety obligations and MAH's need to ensure that these samples are clearly indicated in their system as free samples and that they are decommissioned before providing them to the people that are qualified to prescribe them (Article 41 of Commission Delegated Regulation (EU) 2016/161) [55].

As a result of the serialization requirement and in order to help combat drug counterfeiting, some European stakeholders took the initiative to create the European Medicines Verification Organisation (EMVO), which is a Belgian non-profit organization representing manufacturers, wholesalers and community pharmacists. EMVO has taken the initiative and responsibility to build a system which complies with FMD's regulations, provides a secure, interoperable and cost-effective system across Europe and guarantees medicines authenticity by an end-to-end verification. This system is called European Medicines Verification System (EMVS) and it is comprised of:

- EU Hub, which stores and transmits product data to the relevant national system. The EU Hub is under the responsibility of the EMVO, as shown in figure 32.
- National Medicines Verification Organisation (NMVO) which runs national repositories, National Medicines Verification System (NMVS), as shown in figure 32.

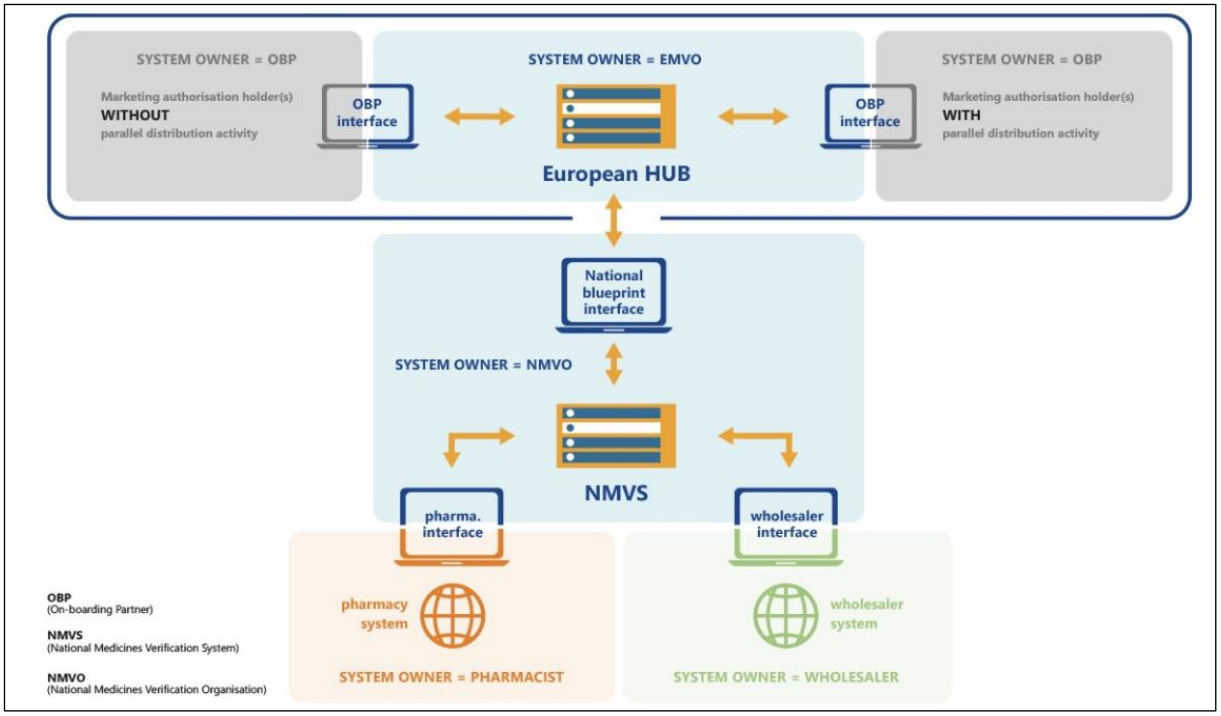


Figure 32: EU System Landscape and connections via EMVO [56]

Figure 33 shows all EU countries connected to EMVO. Every individual EU country has its own NMVO and NMVS. The main objective of the NMVS is to act as a verification platform for drug products that are being scanned by pharmacists or other authorized and registered parties such as wholesalers, doctors or hospital pharmacies in order to determine whether these products are authenticated or not [56].

Figure 33: EU countries, EMVO [56]

Concept of the FMD

The concept of the EU serialization regulation is a “Point of Dispense Verification” concept; The point of printing a unique serial number on the package of a drug product is to be able eventually to identify whether the product is genuine or not. Each medicines’ package will be scanned at the point of dispense, checked and verified for authenticity against a national (or supranational) repository. When the data matrix code is scanned, the serial number is verified against the database system of the pharmaceutical industry. If the serial number is verified and identified by the system, the pharmacist or the authorized registered party receives a notification in the system that the product is authenticated, as a result the pack is decommissioned and dispensed to the patient.

If the serial number is not verified and is unknown to the system, then the pharmacist or the authorized registered party receives a warning and subsequently the drug product will not be dispensed to the patient. However, not every warning means that the drug is counterfeited therefore it's important to carry out an investigation and check whether there is drug falsification involved or whether there's a different reason for this warning [56].

As shown in figure 34, responsibilities of the Supply Chain Partners within the legal trade of pharmaceutical products include:

- ✓ Serialization by MAH
- ✓ Risk based verification by wholesalers
- ✓ Verification and check-out at point of dispense

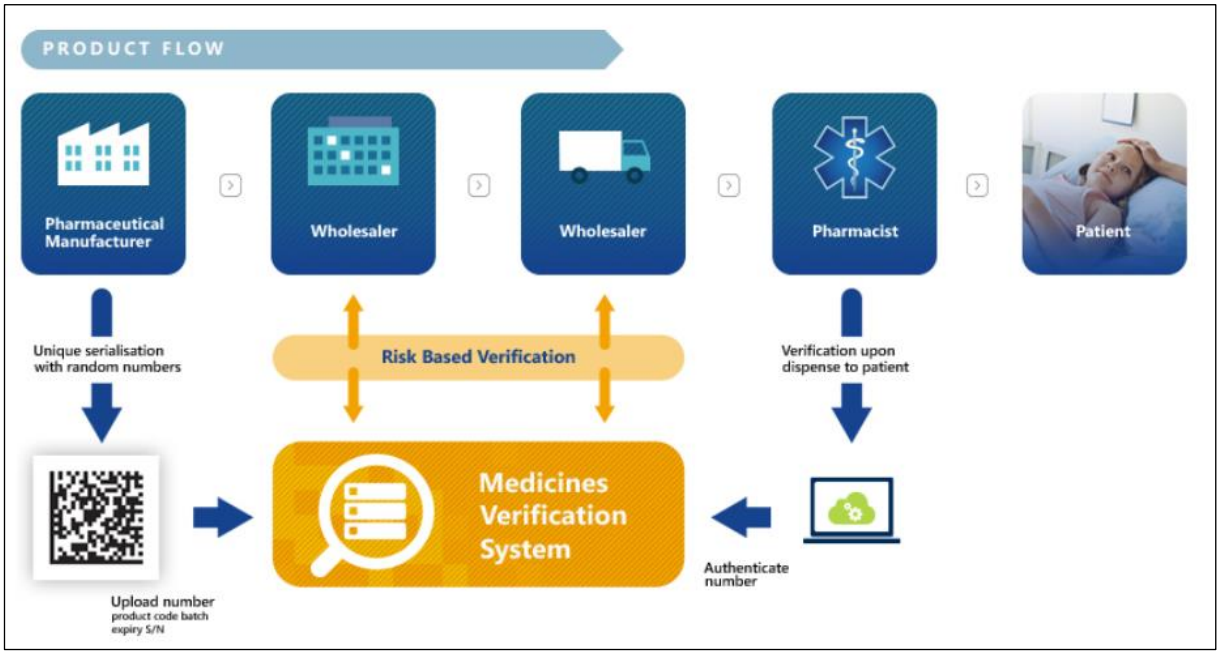


Figure 34: Pharmaceutical product flow through the supply chain [56]

As shown in figure 35, each European country is responsible for its own national system which should be reporting to the EMVO / European Hub. In Germany for example, some stakeholders from the German pharmaceutical market have founded an organization called "securPharm

e.V.", which established a system called securPharm system that complies with the FMD's regulations [57].

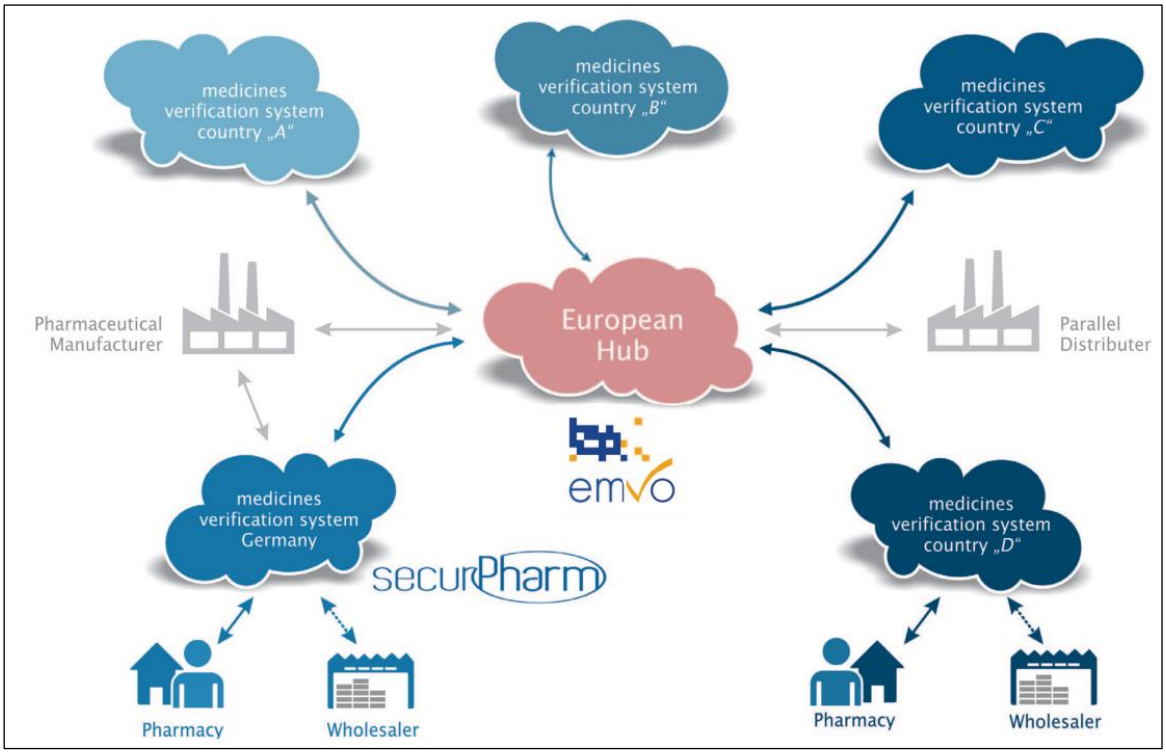


Figure 35: The European network for protection from drug falsification [57]

Table 7: Summary of T&T requirements and deadlines in Europe.

Country	**EU**
Authority / Regulatory Act	FMD
System Name	EMVO
Scope	Combat drug counterfeiting
Stakeholders / Participants	- Manufacturers - Wholesaler / Distributors - Importers
Serialization & Printing Requirements	- 2D Data Matrix code encoded with GTIN, serial number, lot number, expiry date - Tamper evident device
Regulatory Reporting	EU Hub
Timelines	09.02.2019

2.2.3.5 Saudi Arabia

Saudi Food and Drug Authority (SFDA) was established in 2003 with the mission to protect public health by ensuring safety, quality, efficacy and accessibility of human and veterinary drugs, biological products and cosmetics [58].

In 2012, SFDA started drafting a Drug Track and Trace regulation as part of their contribution to the National Transformation Program 2020. This program aims to achieve the kingdom's Vision 2030 by adopting a new technology for tracking all human registered drugs manufactured in Saudi Arabia or imported from abroad [58] [25].

The Track and Trace System of Saudi Arabia was given the name RSD "رصد", which in Arabic means "to monitor". In English, it was given the official name Drug Track and Trace System (DTTS) and it was introduced in Saudi Arabi in the following 3 phases:

- Phase 1 was implemented in March 2015, where manufacturers were obliged to print on each drug package (secondary package i.e., smallest saleable unit) 2D Data Matrix Code encoded with a GTIN, batch number and expiry date.
- Phase 2 was implemented on the 12th of March 2017, where global manufacturers supplying pharmaceutical products to Saudi Arabia were obliged to print a unique serial number as well.
- Phase 3 was initially planned in 1st of October 2019 but was postponed until 20th of August 2020, where aggregation and reporting was required for global manufacturers supplying pharmaceutical products to Saudi Arabia, were obliged to serialize cases and pallets as well and not only secondary packages [25]

Serialization and printing requirements:

For the secondary packaging, it is required to print a GS1 Data Matrix Code encoded with:

- GTIN (14 digits)

- Expiry date
- Batch number
- Unique serial number

For the case and pallet, it is required to print either a linear barcode (GS1-128) or a GS1 Data Matrix code encoded with SSCC or GTIN + Serial number. If the case or the pallet are homogenous then it is optional to include beside the SSCC, a GS1 Data Matrix encoded with:

- GTIN
- Expiry date
- Batch number

Note: GTIN+SN will be used only with homogenous case or pallet [25]

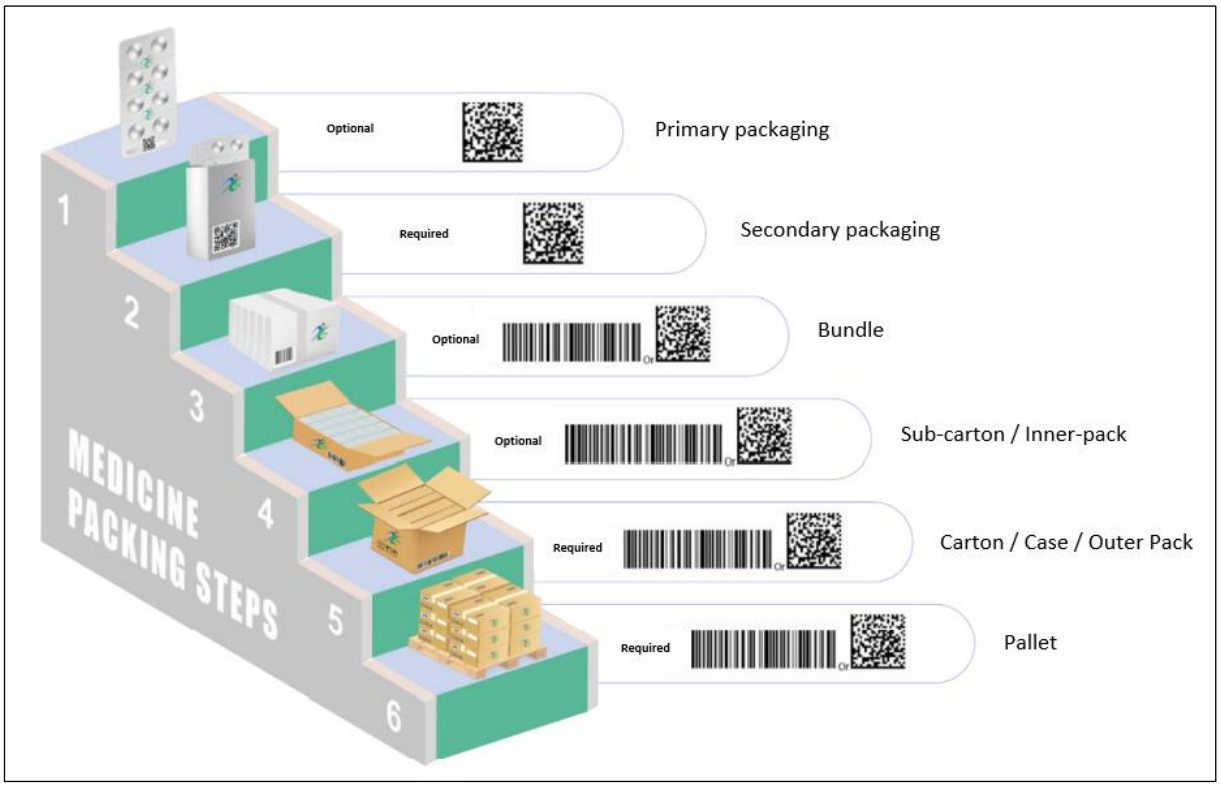


Figure 36: SFDA printing requirements according to level of aggregation [25]

Concept of DTTS:

The concept of DTTS is very similar to the concept of the ITS Turkish system, which tracks each and every drug package (unit packs, cases and pallets) in every single step throughout the supply chain, shown in figure 37. The supply chain stakeholders must share and exchange data related to transfer of pack either by uploading data to PTS or downloading data from PTS. Additionally, each supply chain partner must report certain notifications directly to the DTTS. Table 8 shows the notifications that need to be reported by each stakeholder [59].

Table 8: Notifications that need to be reported by each stakeholder [59].

Notification	Manufacturers	Warehouses	Consumption Centers	Pharmacies
Supply Product	✓			
Supply Cancel Product	✓			
Import Product	✓	✓		
Import Cancel Product	✓	✓		
Dispatch Product	✓	✓		
Dispatch Cancel Product	✓	✓		
Accept Product	✓	✓	✓	✓
Accept Dispatch Service	✓	✓	✓	✓
Deactivate Product	✓	✓	✓	✓
Deactivate Cancel Product	✓	✓	✓	✓
Pharmacy Sale Product				✓
Pharmacy Sale Cancel Product				✓
Consume Product			✓	

Notification	Manufacturers	Warehouses	Consumption Centers	Pharmacies
Consume Cancel Product			✓	
Export Product	✓	✓		
Export Cancel Product	✓	✓		
Return Product	✓	✓	✓	✓
Transfer Product			✓	✓
Transfer Cancel Product			✓	✓
PTS Upload	✓			✓
PTS Download	✓			✓
PTS Query	✓			✓

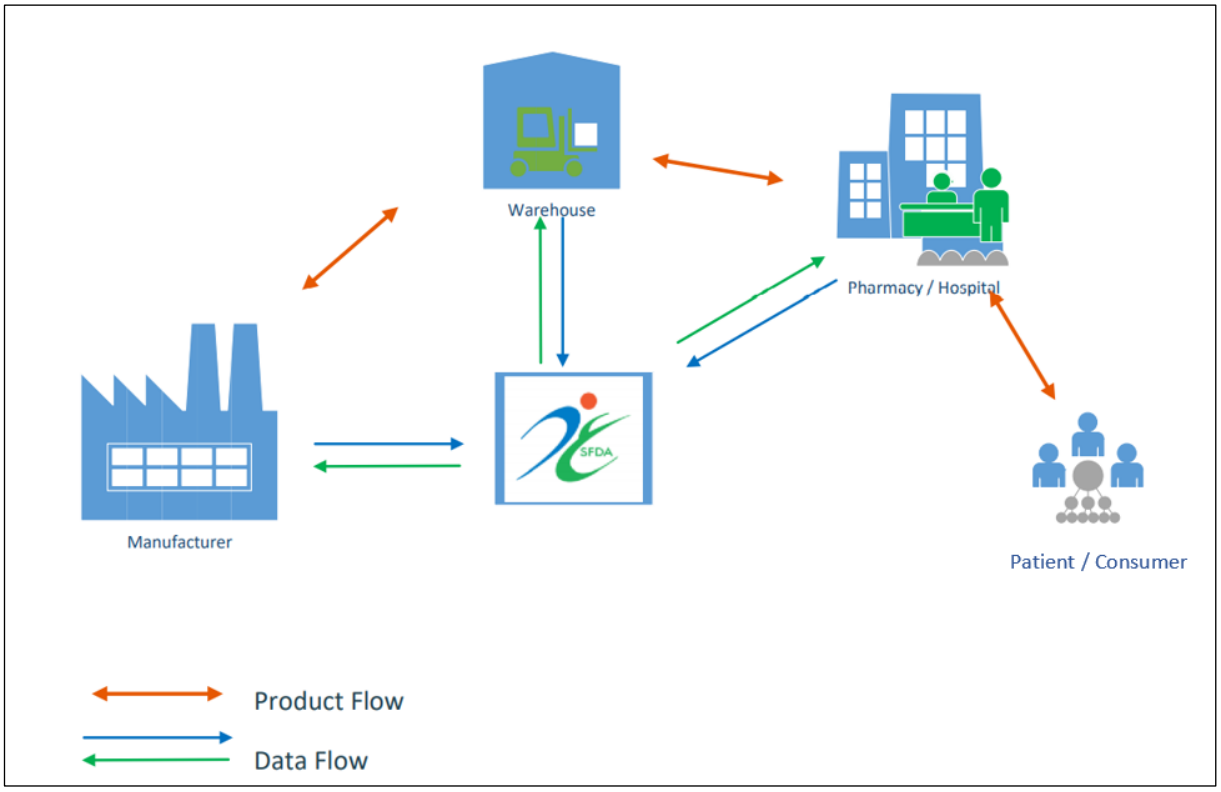


Figure 37: Overview of the product and data flows within the DTTS [59]

Objectives and Benefits of DTTS:

The main objectives and benefits of the Saudi Track and Trace system are:

- Prevent drug counterfeiting
- Monitor all operations within a pharmaceutical supply chain
- Track a drug product within the supply chain, from the point of manufacturing until the point of dispensing the drug to the patient
- Provide safe and genuine medicines to the patients
- Obtain reliable statistics about both; targeted pharmaceutical products for counterfeiting and the origin of the counterfeit products being sold
- Support the optimal use of drugs
- Ensure accurate, real-time information flow among stakeholders within the supply chain
- Provide a mobile application for the consumers where they can easily obtain information about medications, check the safety and authenticity of a dug, and report adverse events
- Recall and withdraw products in a fast manner [58] [25]

Table 9: Summary of T&T requirements and deadlines in Saudi Arabia.

Country	**Saudi Arabia**
Authority	Saudi FDA
System Name / Regulatory Act	RSD / DTTS
Scope	Combat drug counterfeiting
Stakeholders / Participants	- Manufacturers - Wholesalers/Distributors - Importer
Serialization & Printing Requirements	GS1 2D Data Matrix Code encoded with a 14-digit GTIN, serial number, expiry date and lot number
Regulatory Reporting	Yes, to SFDA

Country	Saudi Arabia
Timelines	March 2017 → Serialization August 2020 → Aggregation

2.2.3.6 Kingdom of Bahrain

The Kingdom of Bahrain is another Middle Eastern country that understands the importance of patient safety and the need to protect public health from any kind of drug counterfeiting. In 2009, the National Health Regulatory Authority (NHRA) was founded with a vision to have a safe and high quality in the delivery of health care in the kingdom of Bahrain. As part of fulfilling this vision, Bahrain has introduced the Track and Trace regulation [60].

On the 30th of November 2017, decree no. 41 was released with the announcement that by 31.12.2019, all pharmaceutical products, whether locally produced or imported from abroad or repackaged within the Kingdom, must have a 2D Data Matrix Code encoded with a GTIN, serial number, expiry date and lot number. Additionally, all supply chain stakeholders must upload their Master Data into Brandsync (GS1 portal of UAE, which is used for Bahrain as well) by end of April 2018. This is to ensure accurate synchronization of data between supply chain stakeholders.

By 1st of September 2021, aggregation of shipper cases and pallets must be implemented for all medicinal products.

Objectives of the Track and Trace system in Bahrain:

- Increase patient safety
- Reduce medication errors
- Fight drug counterfeiting
- Provide full track and trace of pharmaceutical products
- Enhance the process of product recalls and withdrawals and make it faster
- Allow real-time data exchanging and sharing between supply chain stakeholders [61]

According to latest updates received from internal Movilitas resources, implementation of serialization has been postponed until 01.10.2021 and implementation of aggregation has been postponed until 01.05.2022 [36].

Table 10: Summary of T&T requirements and deadlines in the Kingdom of Bahrain.

Country	**Kingdom of Bahrain**
Authority	NHRA
System Name / Regulatory Act	NHRA Track and Trace
Scope	Combat drug counterfeiting
Stakeholders / Participants	- Manufacturers - Wholesalers/Distributors - Importers
Serialization & Printing Requirements	GS1 2D Data Matrix Code encoded with a GTIN, serial number, expiry date and lot number
Regulatory Reporting	No
Timelines	01.10.2021 → Serialization 01.05.2022 → Aggregation

2.2.3.7 Jordan

In 2003, Jordan Food and Drug Administration (JFDA) has been founded to ensure food and drug safety, efficacy and quality [62]

In 2007, following many drug counterfeit incidents, the FDA has closed down 56 pharmacies for periods not more than one month, compared to 10 pharmacies in 2006 and only one pharmacy in 2004. The counterfeit drugs seized that year had an approximate value of 10 million JD according to JFDA [63].

In order to control drug counterfeiting, JFDA has released a decree on the 9th of November 2015 announcing that starting from 1st of July 2018, pharmaceutical companies must print on each secondary packaging material, a GS1 2D Data Matrix Code encoded with GTIN, lot

number and expiry date. By 2020, serialization must be implemented by adding a serial number in the GS1 2D Data Matrix Code [64].

On the 9th of September 2018, JFDA postponed the printing of a 2D Data Matrix Code until the 31st of December 2019. On the 31st of January 2021, JFDA postponed serialization until the 30th of June 2021, however this deadline might be postponed again [65].

Table 11: Summary of T&T requirements and deadlines in Jordan.

Country	**Jordan**
Authority	JFDA
System Name / Regulatory Act	Not available yet
Scope	Combat drug counterfeiting
Stakeholders / Participants	Manufacturers
Serialization & Printing Requirements	2D Data Matrix Code encoded with GTIN, serial number, batch number and expiry date
Regulatory Reporting	Not available yet
Timelines	These deadlines are subject to change: 31.12.2019 → GS1 2D Data Matrix Code 30.06.2021 → Serialization of secondary packaging

2.2.3.8 Lebanon

Background

Lebanon is another country in the world which realized the importance of protecting its nation against drug counterfeiting and started acting by planning for a future Track and Trace System.

On the 4th of March 2013, the Lebanese Ministry of Public Health (MoPH) released Decree No. 227/1 for the establishment of the National E-Health Program, which targets to ensure safe drug delivery to the patient and control smuggled and counterfeit drugs [66]. As part of the National E-Health Program, a Track and Trace System called MediTrack was developed with the support of the WHO [67].

On the 14th of December 2020, Dr. Hamad Hassan, the Minister of Public Health in Lebanon, launched the MediTrack system together with the WHO. Minister Hassan said in his speech (please note that all the following quotes are translated from Arabic to English): “We have suffered over the past period from more than one dilemma in the medicine market, but the effort made, and the field visits led to the identification of the defect, whether in importing or keeping quantities of medicines in warehouses or at the agent, or through non equitable distribution and seizure of medicines in pharmacies, and the people's rush to accumulate them”. He expressed his satisfaction that "these problems have been solved by seventy or eighty percent, as the hype in the subject of medicine has subsided by a large percentage, with the exception of some problems in speeding up the transactions of importing a number of medicines." He stressed "the continuation of the field methodology in tracking medication," noting that "the MediTrack system will achieve more in this context," and said: "This project comes from among several projects that reflect our commitment to completing the development process and transforming the difficult circumstances we are going through into an opportunity."

In turn, Dr. Al-Shanqeeti, Representative of the WHO in Lebanon, pointed out that "the World Health Organization has been supporting the system of tracking drugs via two-dimensional barcode for more than three years, as part of an integrated project that aims to fully develop the drug system in Lebanon, especially a system for controlling the quality and rationalization of drug use in general." She said, "While medicine constitutes the largest portion of what the Lebanese pay out of their pocket, so that the size of the drug market in Lebanon has exceeded one billion dollars annually, it was necessary to put in place a system that links import to distribution and consumption and confirms the quality of medicines in the Lebanese market and contributes to rationalizing their consumption and use." End of quote [68].

Objectives and functionalities of the MediTrack System:

- Identify: the ability to identify every pharmaceutical product by using GS1 standards and printing a 2D Data Matrix Code, which is encoded with a GTIN, lot number and expiry date.
- Verify: the ability to verify every pharmaceutical product when scanning the 2D Data Matrix Code and ensure its authenticity, safety and quality.
- Track: the ability to track forward the movement of every pharmaceutical product all along the supply chain which facilitates in combating drug counterfeiting thus ensure patient safety.
- Trace: the ability to trace backward product's movement history which makes product recall process faster and easier.
- Report: the ability to upload real time data of the product within the supply chain to the MoPH database thus making it easier for the government to track, monitor and control drug movement within the supply chain and in the market. It also facilitates in fast reimbursement and fraud control at the 3rd party payers [67] [69].

Concept of the MediTrack System:

MediTrack System is similar to most T&T systems where supply chain stakeholders like manufacturers, distributors, wholesalers, 3PLs, hospitals and pharmacies exchange product's data between each other and each one of them is reporting events data to the government's system. However, at the time of writing, the MediTrack system was still in continuous development and is not achieving full Track and Trace yet.

From 2017 up until the time of writing, the Lebanese MoPH constantly released new Decrees and new updates on existing Decrees about the T&T regulation and planned timelines. These updates were mainly resulting from the pilot phase which was conducted during 2018 with

several supply chain stakeholders. The following paragraph summarizes main updates and announcements from the MoPH [66].

On the 2nd of October 2017, MoPH released a Decree No.1817 to establish a committee to study the implementation of the T&T program and the introduction of the 2D Data Matrix Code.

On the 11th of December 2017, MoPH released Decree No.2405/1, which states that:

- All pharmaceutical products produced in Lebanon or imported into Lebanon must have a 2D Data Matrix Code encoded with a GTIN, lot number and expiry date printed on the secondary package. This regulation excludes free samples, injections that have no outer package and vaccines and medicines which are ordered for individual use.
- Starting from 01.01.2019, any pharmaceutical product which does not have a 2D Data Matrix Code printed on it, will not be allowed to be imported into Lebanon.

On the 14th of December 2017, MoPH released memo no. 132, which postpones the deadline from 01.01.2019 until 30.06.2020 but only for some pharmaceutical products which appear in the list within memo 132. Figure 38 shows some of the drugs within the mentioned list.

الجمهورية اللبنانية
وزارة الصحة العامة

لائحة بالأدوية التي تم تمديد الفترة الزمنية لتطبيق الباركود عليها

Importer	Manufacturers/Products	Countries
Abela Freres	GSK **(19 products) ex: Augmentin ES, Flixotide, Relvar Ellipta, Seretide Diskus,Valtrex, Ventolin, Xyzal, Zovirax, Zyrtec**	UK, France, Italy, Switzerland
	Aspen **(4 products) Fraxiparine, Lanoxin**	Ireland
	Erleada 60mg 120tablets	USA
Mersaco	Stada laboratories **14 products: Proxen, Tramal, Zaldiar (all doses)**	Germany, Italy
	Sanofi 5products: **Bi-Rodogyl, Enterogermina 2billions, Enterogermina 6billions, Toplexil, Magnevie B6**	France, Italy
Broadmed	**Kolbet**	Japan
Pharmamedic	**12 products Diclodent, Cefixime Neocef, Olmetec (3), Sevikar (3), Hirudoid (2), D-Cure 25000**	Portugal, Germany, Belgium
	Algocod, Fenosup Lidose, Fenogal, Golaseptine-Lidocaine, Pravafen, Fluoxone divule, D-Cure, Zephirus (120mcg and 240mcg)	Belgium
Medicapharm	**Tobrastill, Zindaclin**	Germany
Spephal	**Cetraxal Otico, Cetraxal plus**	Spain
Cesar Chalhoub	**5 Products (Doxylag, Exomuc, Neo-Codion, Panfurex, Tergynan)**	Switzerland, France
Taba Chemipharm	**Actonorm oral suspension, Histergan cream, Asacol enema, Colpermin capsules, Cardzaar tablets, Lucipral syrup,Histalix syrup**	

Figure 38: List of drugs taken from memo 132 [66]

On the 19th of October 2018, MoPH released Decree No. 2062/1, which states that the deadline for the implementation of 2D Data Matrix Code on all imported pharmaceutical products is postponed until 31.12.2019 and for local manufacturers it is postponed until 31.12.2022.

On the 17th of September 2019, MoPH released Decree No. 1894/1, which states that starting from the 1st of January 2020, all pharmaceutical products imported into Lebanon must have a 2D Data Matrix Code encoded with a GTIN, lot number and expiry date printed on the secondary package. This regulation excludes free samples, injections that have no outer package and vaccines and medicines which are ordered for individual use. This Decree also provided more technical details on the printing requirements of the 2D Data Matrix Code.

On the 17th of July 2020, MoPH released memo no. 107, which is an update of memo no. 132. This memo postpones again the timeline for some pharmaceutical products (same list mentioned in memo 132) from 30.06.2020 until 31.12.2020 the latest. This postponing was due to the COVID-19 pandemic and the challenges which some manufacturers and importers are facing due these difficult times.

On the 18th of September 2020, MoPH released Decree No. 1253/1, which states that starting from 01.01.2021, all vaccines should also have a 2D Data Matrix code encoded with GTIN, lot number and expiry date. This Decree was released as a result of the COVID-19 pandemic and the rising criminal activities related to selling fake COVID-19 vaccines online, making use of people's vulnerability in these difficult times.

On the 3rd of November 2020, MoPH released Decree No. 1476/1, which states that importers and distributors are obliged to start using MediTrack system starting from 01.12.2020 by uploading events data to it only of products with 2D Data Matrix Code. Any product without 2D Data Matrix Code will not be accepted. Importers and distributors need to make sure that data is updated periodically and within no longer than 1 week from every last updated event.

MoPH also announced in this decree that they are the only official responsible party for all the data within MediTrack system.

On the 24th of March 2021, MoPH released 2 memos:

- Memo no. 29, which states that all importers and distributors must comply with the above-mentioned Decree No. 1476/1 and start using MediTrack to register all importing and selling events by 05.04.2021 latest, otherwise they won't be able to import, sell or distribute any products.
- Memo no. 30, which states that all pharmacies are obliged to ensure that registered and imported pharmaceutical products have a 2D Data Matrix Code printed on them and not a QR Code, as shown in figure 39 [66].

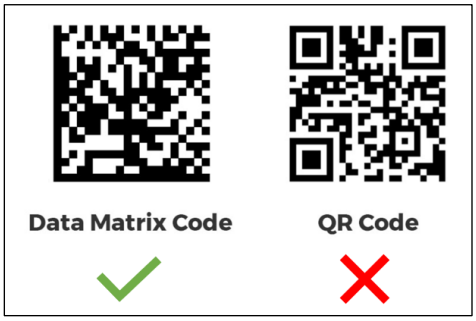


Figure 39: Data Matrix Code versus QR Code [66]

In Quarter 3 (Q3) and Quarter 4 (Q4) of 2020, the MoPH conducted training sessions on MediTrack system for supply chain stakeholders. They published one of these training sessions on their official website, which was conducted for importers. Lina Abou Mrad, Director of the National E-Health Program announced the following during that session:

- A Guideline on the implementation of the 2D Data Matrix Code, edition 2, was published and was available for all supply chain stakeholders.
- A compliance platform was developed to ensure successful integration with pharmacies software.

- MediTrack system was implemented in the following administrative units of the MoPH, and workshops and trainings are being held:
    - The Department of Pharmacy
    - Pharmacist Inspection Department
    - Department of Narcotics
    - Department of Medicines Import
    - Karantina Drug Distribution Center

Figures 40 and 41 were taken as screenshots from the above-mentioned training session, which shows how the MediTrack system looks like [70].

Figure 40: Login screen of MediTrack system [70]

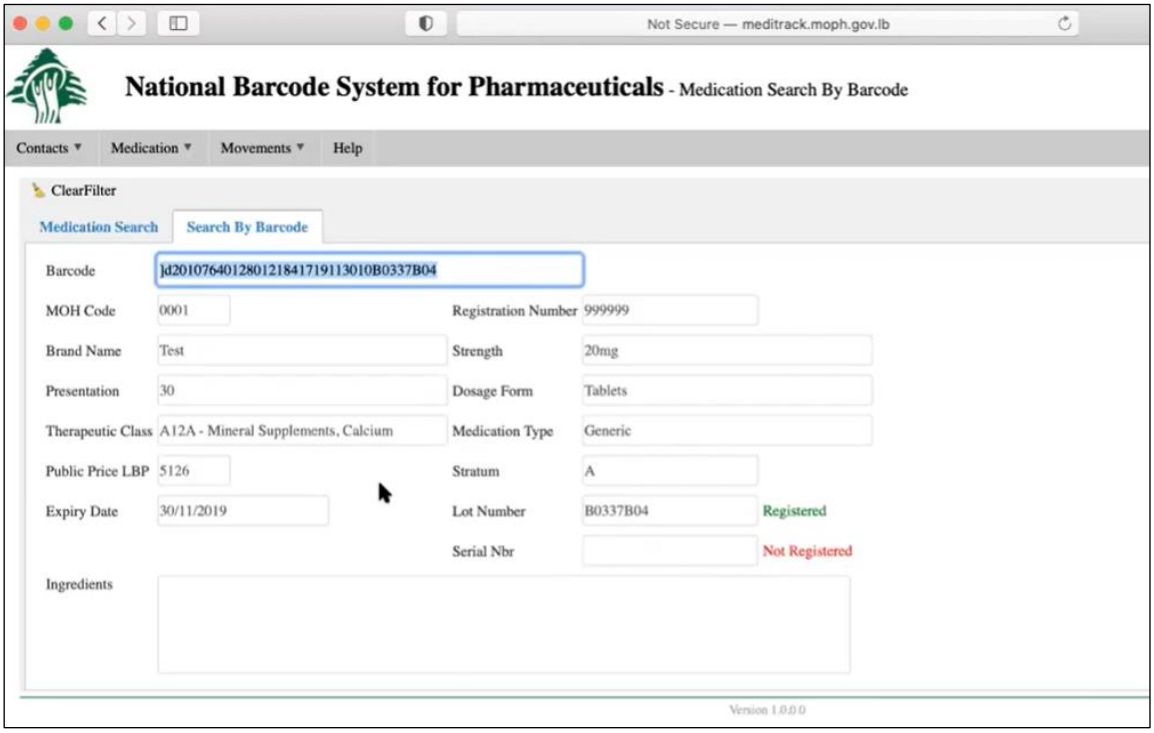


Figure 41: Product search screen of MediTrack system [70]

Next steps for the MediTrack program, as per Lina Abou Mrad, include:

1. Complete training sessions for drug importers and distributors.
2. For importers and distributors to start using MediTrack system.
3. Deployment of the system in the drugs warehouse and dispensing center at Karantina.
4. Integrate with pharmacies software.
5. Integrate with Primary Health Care Centers (PHC).
6. Update the Ministry's mobile application to enable consumers to scan barcodes and check product’s authenticity and to obtain new information about the drug.
7. Run awareness campaigns to increase citizens' awareness of the benefits of the T&T system and the National E-Health Program [70].

Summary

The Lebanese MoPH visualizes a full track and trace system including serialization and aggregation, however it is not in place yet. Serializing pharmaceutical products by printing a

unique serial number on secondary packages and encoding it within the 2D Data Matrix Code is only optional till now.

I would also like to emphasize here that during recent years especially last year (2020), Lebanon and the Lebanese nation have experienced lots of difficulties and challenges due to several reasons such as demonstrations, corruption, economic and political problems, 4th of August Beirut explosion, COVID-19 pandemic and much more. However, despite all of these hindrances, they were able to understand and recognize the importance of such a regulation and system on public's health and therefore are continuously working on developing it and making it happen by 2022.

Table 12: Summary of T&T requirements and deadlines in Lebanon.

Country	**Lebanon**
Authority	MoPH
System Name / Regulatory Act	MediTrack
Scope	Combat drug countefeiting
Stakeholders / Participants	Manufacturers, importers, distributors, wholesalers
Serialization & Printing Requirements	2D Data Matrix code encoded with GTIN, expiry date and lot number
Regulatory Reporting	Yes, MediTrack
Timelines	**31.12.2019** → Importers and distributers to print 2D Data Matrix code with GTIN, expiry date and lot (some products were postponed till 31.12.2020) **01.01.2021** → Vaccines to have 2D Data Matrix code with GTIN, expiry date and lot number **05.04.2021** → Importers and distributers to use MediTrack to upload data

Country	Lebanon
	31.12.2022 → Manufacturers to print 2D Data Matrix code with GTIN, expiry date and lot number

2.2.3.9 Egypt

Background

Egypt is the 3rd largest country in the Middle East with an area of 1.01 million km^2 and a population of 100.4 million (as of 2019 according to the world bank). With such an enormous population, controlling the healthcare system and monitoring pharmaceutical trade becomes an extremely vital mission of the Egyptian government as it directly affects the lives and health of millions of people. Figure 42 illustrates the number of stakeholders including patients involved within a pharmaceutical supply chain [71][72].

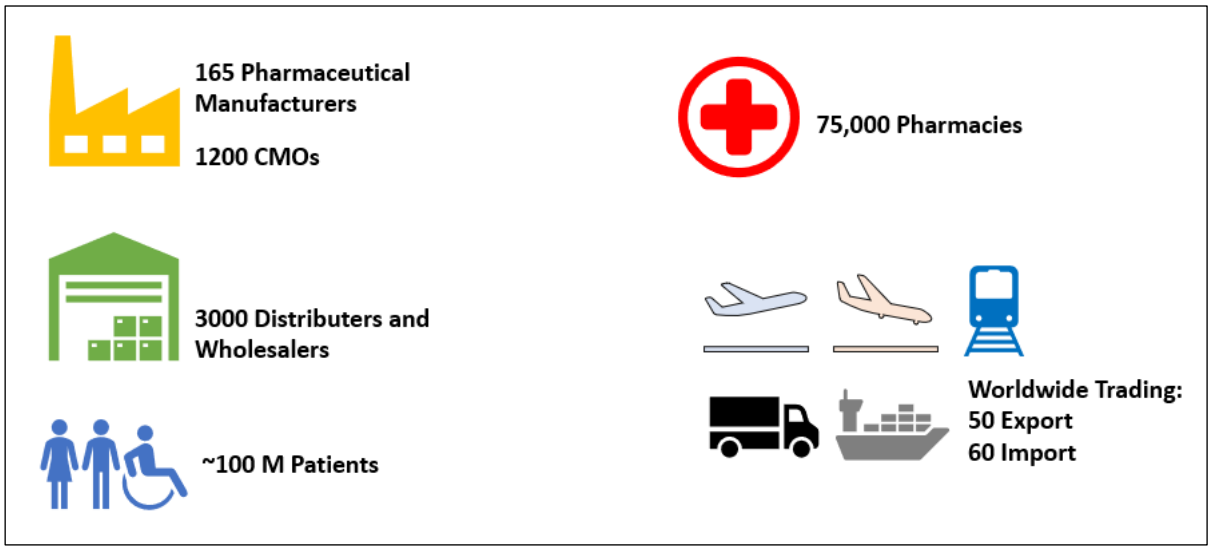


Figure 42: Number of stakeholders within a pharmaceutical supply chain [71]

On the 18th of April 2016, the Egyptian Ministry of Health (MOH) released decree no. 29/2016 as a step forward to establish a Track and Trace system called Egyptian Track and Trace System (EPTTS), which mandates all stakeholders within a pharmaceutical supply chain i.e.,

manufacturers, distributors, wholesalers, hospitals and pharmacy retailers, to use GS1 standards i.e., GLN, GTIN and Data Matrix Code [71][72].

On the 25th of August 2019, the Egyptian Drug Authority (EDA) was established in accordance with Law No. 151 of 2019. Then on the 29th of March 2020, the Prime Minister issued Decree No. 777 of 2020 issuing the executive regulations for the law establishing the authority. EDA is an independent pharmaceutical regulatory body of the Egyptian MOH and it has a number of responsibilities. Some of these major responsibilities are:

- Protect public health by regulating and controlling the quality and safety of pharmaceutical products.
- Regulate and legislate pharmaceutical related topics including drug registration.
- Control drug pricing and ensuring the availability of high-quality pharmaceutical products at affordable prices.
- Set standards of pharmaceutical services for both hospitals and consumers.
- Control the market and the ability to detect drug shortages and act accordingly.
- Enhance and raise public awareness of possible adverse events of pharmaceutical products, the danger of misusing them and warnings against counterfeited medicines.
- Cooperate with international organizations such as the WHO in order to improve standards of pharmaceutical products and practices [73].

Additionally, EDA has several goals and one of them is to establish binding systems that guarantee the quality, efficacy and safety of medical preparations and supplies subject to the provisions of the law. As well as tracking and following them through all stages of circulation and applying these systems to all entities participating in the process from manufacturers, importers and distributors of pharmaceutical products. Taking the necessary procedures for withdrawing pharmaceutical products from circulation is another objective. This is where the responsibility of EPTTS lies in [74].

Objectives of the EPTTS:

The objective of the EPTTS is to achieve improved tracking, tracing, management, monitoring, controlling and evaluation of pharmaceutical products throughout different phases in the supply chain and thus making the supply chain more efficient and reducing drug counterfeiting. This will ultimately lead to the following:

- Protect public health and enhance patient safety.
- Provide transparency within the supply chain and protect it from the entry of counterfeit products thus prevent distribution and dispensation of fake, expired, recalled or illegitimate drug products.
- Enhance the process of product recall and make it faster, more effective and more efficient.
- Enable verification and validation before any reimbursement claim is carried out [73].

Figure 43 gives an overview of the pharmaceutical product flow within the supply chain in Egypt using EPTTS system.

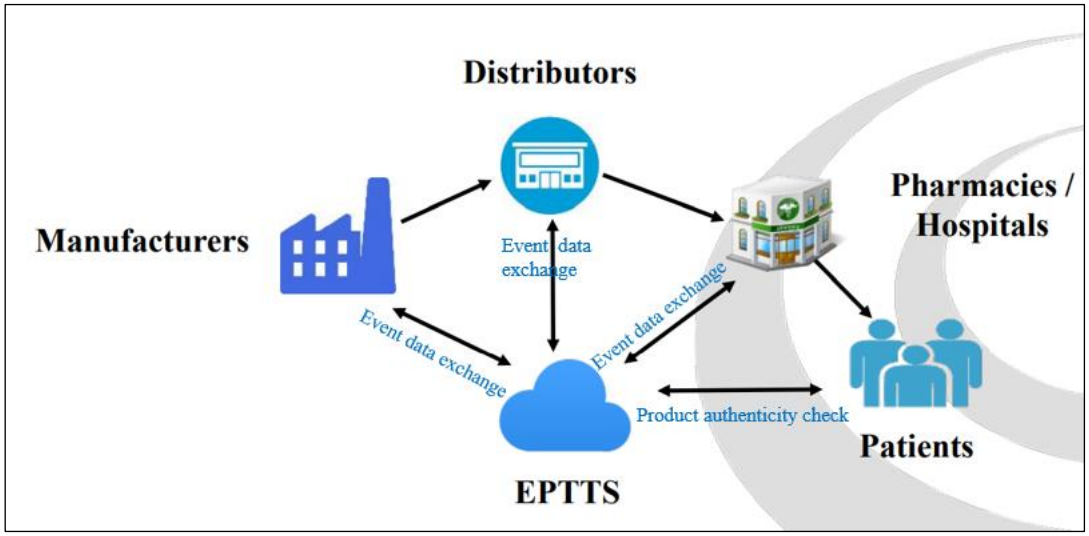


Figure 43: Overview of the product and data flows within EPTTS [71]

The implementation of the EPTTS was planned to be introduced in the following phases:

- **Phase 1:**
    - On the 1st of September 2017, supply chain stakeholders (manufacturers, importers, distributors and warehouses) were obliged to have a registered GTIN for every product entering the supply chain and a registered GLN for every location involved in production or shipment of products within and outside of Egypt.
    - On the 1st of December 2017, pharmacies were obliged to register in GS1 and obtain a GLN for every pharmacy location.
- **Phase 2**: in December 2018, supply chain stakeholders were obliged to enter their registered GTINs and GLNs into Central Administration of Pharmaceutical Affairs Data Base (CAPA DB).
- **Phase 3:** in December 2018, supply chain stakeholders were obliged to print a 2D Data Matrix Code encoded with a unique serial number, GTIN, lot number and expiry date on every product unit (secondary package). Additionally, they were obliged to upload event data to the MOH track and trace system.
- **Phase 4:**
    - In March 2019, first trial pilot project was launched with several supply chain stakeholders that included 11 manufacturers and 3 pharmacies.
    - In October 2019, second trial pilot project was conducted.
    - In July 2020, third trial pilot project was conducted.
- **Phase 5:** Full Track and Trace to be implemented depending on the results from the pilot project. However, the guidelines and deadlines for implementing a Track and Trace system were not published. According to EDA, they are expected to be published

during this year (2021) and by next year (2022), they are expecting to have full Track and Trace system in place [36][72][73][75].

On the 20th of March 2021, EDA announced the seizure of large quantities of unregistered, expired, and smuggled medicines in several pharmacies and drug stores, some of which are licensed and others are not. This seizure resulted from unexpected inspection campaigns carried out by the authority's inspectors during the period of November 2020 to March 2021. Dr. Yass Rajaei, Head of the Central Department of Operations at the Drug Authority estimated that the quantity of seizures reached approximately 6 million violating drug pills through 12,000 violating seizures, and that the total financial value of the seizures reached approximately 52 million Egyptian pounds [76].

This basically strengthens the urge and importance of having a full Track and Trace system in place so that such violations can be prevented in advance and at an earlier stage, before smuggled/expired/counterfeit/substandard drugs reach pharmacies and most importantly before they reach patients.

Table 13: Summary of T&T requirements and deadlines in Egypt.

Country	**Egypt**
Authority	EDA
System Name / Regulatory Act	EPTTS
Scope	Combat drug counterfeiting, track and trace and make the supply chain more efficient
Stakeholders / Participants	Manufacturers, wholesalers, distributors, pharmacies and hospitals
Serialization & Printing Requirements	Not clear yet
Regulatory Reporting	Not clear yet
Timelines	Expected in 2022 but not officially announced yet

2.2.3.10 Other Markets

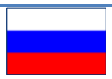
Apart from countries mentioned in previous sections, many other countries around the world introduced already T&T regulation or are in the progress of doing it. Table 14 provides a summary about the status of other countries worldwide in terms of T&T implementation and planned timelines.

Table 14: Track and Trace implementation status in different countries worldwide [36]

Country	Track & Trace Status and Timeline
Algeria 	Regulation is still under development. Item level Serialization and 2D Data Matrix Code have been discussed but not confirmed as of 2016.
Angola 	Regulation is still under development. No defined timeline.
Argentina 	T&T implemented in 2011, 2012, 2013, 2015 and 2016 depending on drug classes.
Armenia 	Regulation is still under development. No defined timeline.
Australia 	Serialization of certain blood products was implemented in 2017 and 2018. As of 01.09.2020, pharmaceutical products must have a machine-readable code, which: (a) encodes GTIN for the medicine as allocated under the GS1 System; and (b) identifies different product variants and differentiates between different strengths, pack sizes and dose forms. Type and implementation of full T&T is being discussed.

Country	Track & Trace Status and Timeline
Azerbaijan 	Currently, no plans or regulation
Belarus 	Regulation is still under development. No defined timeline.
Brazil 	October 2020 → serialization was implemented for 25% of pharmaceutical products. April 2022 → serialization must be implemented for 100% of pharmaceutical products and reporting to the Brazilian authority must be achieved as well
Chile 	Identification and traceability implemented in 2013 (not including yet serial number).
Colombia 	Regulation is still under development. No defined timeline.
Ethiopia 	T&T plan is in progress. By 05.07.2021, pharmaceutical products must have a GS1 barcode (GTIN). By 2026, serialization is expected to be implemented.
India 	**Export Market** January 2011 → Serialization of tertiary level packaging January 2013 → Serialization of secondary level packaging Initially 2015 but postponed till 2020 → Aggregation and data reporting **Domestic market and import:** Regulation is still under development. No defined timeline.

Country	Track & Trace Status and Timeline
Indonesia 	T&T implementation is in progress. 2023 → Identification for all pharmaceutical products 2025 → Authentication for all pharmaceutical products
Iran 	Serialization implemented in January 2015
Japan 	T&T implementation is in progress. August 2021 → E-labelling (e.g., electronic leaflet) must be implemented. December 2022 → Serialization must be implemented for drugs and medical devices.
Kazakhstan 	Regulation is still under development. No defined timeline.
Kenya 	Regulation is still under development. No defined timeline.
Malaysia 	T&T implementation is in progress. By 2023, full T&T is expected to be implemented.
Malawi 	Regulation is still under development. No defined timeline.
Mexico 	Regulation is still under development. No defined timeline.
Nigeria 	Mobile authentication service implemented for anti-malaria drugs and antibiotics in 2013. Full T&T system for all pharmaceutical products is under development and is expected to be implemented by December 2024.

Country	Track & Trace Status and Timeline
Oman 	Serialization was initially planned in March 2019, however it has been postponed. The new date is not defined yet
Pakistan 	T&T regulation is under development. By 2024, full T&T is expected to be implemented.
Palestine 	Currently, no plans or regulation
Qatar 	By 2025 → Full Track and Trace including primary package
Russia 	Track and Trace implemented since July 2020
Singapore 	A draft regulation was published in 2019 about e-labelling and printing of QR code. However, requirements are not finalized and there are no defined timelines.
South Africa 	Regulation is still under development. No defined timeline.
South Korea 	Serialization implemented since January 2016
Tunisia 	Serialization was planned to be implemented by January 2019, however, it is currently on hold. No defined timeline
United Arab Emirates 	Regulation is still under development. No defined timeline.
Uzbekistan 	Regulation is still under development. No defined timeline.

2.2.4 Track and Trace/Serialization Project Management Approach and Challenges

It might seem simple to implement serialization as many people tend to think of it as just printing a code on the package or just changing the artwork design. Others might consider it as an Information Technology (IT) related project only which does not really interest them. In fact, it is much more than that, it involves and affects almost every department within a pharmaceutical organization. Organizations need to understand that having a Track and Trace system in place is more than just changing the artwork or complying with the regulation. This section will provide a brief overview of an overall approach to manage a serialization project including what an organization needs, at which cost and which challenges it might face [29].

2.2.4.1 How to start with implementing a serialization project?

First, an organization needs to understand the following:

- What is required from a legislative point of view to fulfil T&T regulation?
- What is the scope of the project?
- How can it be achieved?
- Which impact does it have on current business processes and on the organization?
- Who are the involved stakeholders and supply chain partners?
- Which departments and personnel are involved?
- What are the anticipated benefits and what are the desired benefits?
- Which risks does it have on an organization and how can these risks be mitigated?
- Who will own this project?
- How will this project be managed?

A good and recommended approach here in order to answer all these questions is to consider this regulatory change as an opportunity to enhance business processes and to think of long-term benefits rather than just considering it as a burden and wanting to fulfil as minimum

requirements as possible. A program roadmap needs to be defined and understood including prioritization, critical timelines and initial budgeting.

2.2.4.2 Who is usually involved in a serialization project?

This kind of project requires full synchronization and teamwork internally between different departments within an organization and externally with external resources and parties. Figure 44 shows internal departments that are required in a serialization project.

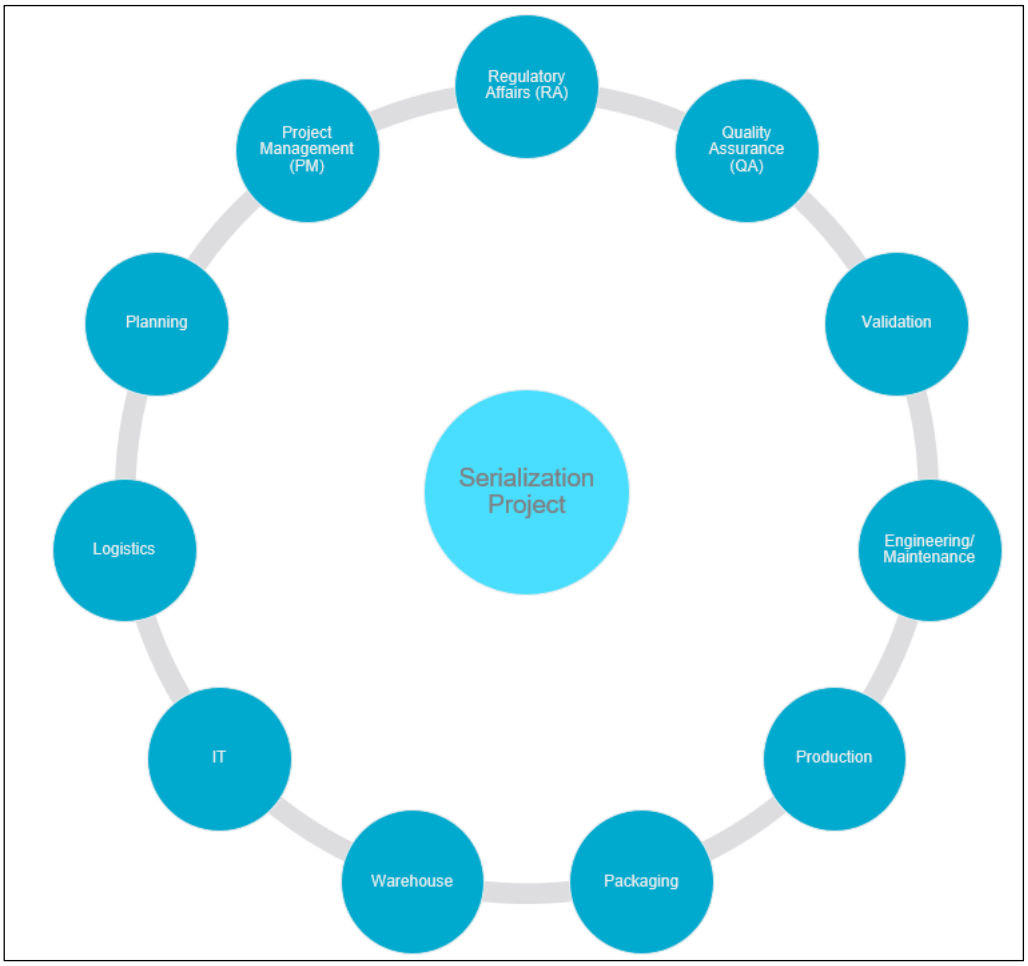


Figure 44: Internal resources involved in a serialization project [29]

In addition to all internal resources, in most cases, external resources are required as well. External resources could be 3PLs, CMOs, distributors, wholesalers, external warehouse operators, consumers, IT service providers, IT suppliers, repackaging companies, devices suppliers (e.g., new packaging line, new scanners, printers etc.) and consulting companies.

2.2.4.3 Common issues found in serialization projects:

- Lack of understanding of the project scope, importance, benefits, deadlines, impact.
- Lack of understanding of general Track and Trace / Serialization terms and definitions.
- Lack of understaing of GS1 Standards (if they are not already in use).
- Underestimation of the efforts, time and budget that are needed to implement such a project.
- Underestimation of the time and effort needed to introduce new packaging lines.
- In terms of IT, lack of a clear URS (User Requirements Specification) for the line systems, which makes it difficult to implement the required system with the required functionalities.
- Involvement of different systems and line suppliers, which makes it challenging to link deliverables with timelines and meet the deadline. If not aligned properly, it might lead to failure in hitting the deadline and quality goals.
- Underestimation of the impact on daily operations and involvement of team members for the serialization project, which might eventually cause burnout, stress and not meeting quality goals.
- Companies usually consider meeting minimum regulatory requirements only and do not make use of this new regulation/change to enhance their business. They tend to miss what is beyond those regulatory requirements.

2.2.4.4 How to avoid some of these issues?

The top management of an organization needs to make sure that:

- A full dediacated team is available and assigned to the serialization project.
- Internal and external departments are aligned and have full understanding of the project scope and of the critical deadlines.

- A program manager is assigend to monitor the progress of the overall project, manage different teams, identify any risks or issues and escalate to the top management accordingly to find a mitigation plan or a solution.
- A training is conducted to internal team members to have full understanding of serialization related topics, therefore involvement of an external company (like Track and Trace consulting companies) might be useful.

2.2.4.5 What are the important aspects to successfully manage a serialization project?

Here are 6 aspects of successful program management:

1. **Collaboration:** make sure that benefits of all members and departments are identified and communicated. In fact, communication is very important for the success of a project.
2. **Planning:** understanding of the overall project, scope, activities, dependencies between departments and with external entities. Often tasks are underestimated, which subsequently affects productivity of team members. It could also significantly affect project timelines and budget.
3. **Resource pool:** availability of resources especially in critical phases/activities. Make sure to have several available resources with knowledge and avoid keeping knowledge with one person only. Conduct knowledge transfer sessions and trainings if necessary.
4. **Management commitment:** top level management might underestimate the efforts and budget needed for such a project, thinking only of regulatory aspects and not thinking about long run benefits for the company. Management should be engaged with the project, support decisions, be aware of the importance of the project and raise that awareness to team members accordingly.

5. **Expertise:** hire experts from different areas. It is not expected to have experts within the organization as Track and Trace is relatively a new topic in the pharmaceutical industry and usually it's a one-time project. It is also not expected to have a dedicated department or team or experts only for serialization related topics (unless they have implemented such a project already). Therefore, it would be important to hire the right expertise whether it's in the regulation field, IT, line suppliers, T&T external consultants etc.

6. **Risk management:** risk management needs to be conducted at the beginning to identify risks and mitigation plans, especially that it's a project which involves internal and external team members, specific budget and critical timelines [29].

It is important to keep in mind that a successful implementation of a Track and Trace system means success in protecting public health. If the project fails or if the implementation timelines are poorly planned, then this might affect the overall target of implementing such a system, which is to protect public health from counterfeited medicines. Additionally, failure in implementing a T&T system on time might lead to drug shortages [77].

2.2.4.6 What are the estimated timelines to implement a Track and Trace system?

Track and Trace implementation timelines could vary significantly depending on the party that is implementing it, the size of the organization, regulation requirements, complexity of the requirements, infrastructure of the organization, number of supply chain partners involved, availability of internal and external resources, budget, planning, etc., therefore it is difficult to give an exact estimation of timelines. It could be a 3-month project (if the implementing party is a small-sized wholesaler for example) and it could also be a 10-year program divided into phases (if it is the government for example). For an averaged size pharmaceutical company, Track and Trace implementation project might vary between 1 to 2 years approximately.

Some examples of timelines to take into consideration:

- Artwork approval (e.g., it might take up to 6 months, could be more or less).
- Time from the moment a new packaging line is ordered until it is physically received and installed in the packaging department of a pharmaceutical company (e.g., it might take up to 8 months, could be more or less).
- All kinds of validation activities required for a new packaging line, scanner, printer, serialization system, etc. A great amount of validation activities (e.g., Site Acceptance Test-SAT, Factory Acceptance Test-FAT, Design Qualification-DQ, Installation Qualification-IQ, Operational Qualification-OQ, Performance Qualification-PQ) need to be performed for the involved packaging lines and systems in the manufacturing area in order to ensure that all lines and systems will work as intended all the time.
- Possible line shutdown when performing tests.
- Writing and approving SOPs (Standard Operating Procedures) [17] [29].

According to GS1, figure 45 illustrates an example of an achievable timeframe to implement a Track and Trace system from a governmental perspective:

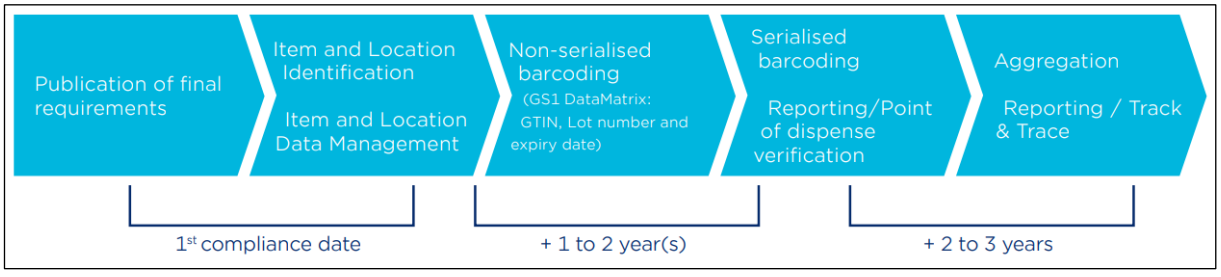


Figure 45: Example of an achievable timeframe for Track and Trace implementation [17]

2.2.4.7 What are the estimated costs of a serialization project?

Costs can vary significantly depending on the size and complexity of the serialization project, size of the company, availability of resources and expertise, type of the supply chain partner

that is implementing the serialization project (e.g., manufacturer, distributor, pharmacy, government, etc.), purchase of suitable packaging lines and systems, etc.

Typical costs in a serialization project include costs of the packaging lines and other devices such as printers, scanners and mobile devices, validation activities, recruitment of new employees if necessary, training, IT related costs (purchase and implementation of serialization system like ATTP, purchase of serial numbers, purchase of licenses, hiring external consultants and vendors), any other related external suppliers or consultants and operational costs [17].

In 2008, it was estimated that a single supply chain requires an investment of €400 million to implement a track and trace system, which was translated at that time into an investment of €10 billion for the EU as a whole [4].

According to GS1, figure 46 illustrates an example of implementation costs of a Track and Trace system. Please note that this is just a rough estimation and example and does not necessarily represent costs of any company implementing a Track and Trace system [17].

		Typical Track and Trace Solution in Emerging Markets		
		Item	Qty	Cost ($)
Capital				
Equipment	New Packaging line	New Packaging line	1	$ 100,000-400,000
	Serialisation print & verify	Serialisation print & verify equipment	1	$ 13,000-70,000
	Tamper evidence	Tamper evidence module	1	$ 28,000-50,000
	Warehouse station	Rework station	1	$ 7,000-17,000
	Quality assessment station	Rework station	1	$ 7,000-17,000
Serialisation software	Plant software	License	1	$ 15,000-50,000
	Line software	Included in equipment prices		$ 0
	Integration to internal communication system of the company	If necessary	1	$ 6,000-25,000

Figure 46: Example of implementation costs of a Track and Trace system [17]

2.2.4.8 Summary

In summary, organizations need to have a thorough understanding of the regulation requirements, project scope, impact on their business and also take advantage of this change to enhance their business processes. Planning, communication, resources, budget and time are all required for the sake of successfully implementing such a project. Furthermore, serialization will be soon enough implemented in almost all countries, therefore better to be ready in advance and plan correctly rather than ending up stressed and tight in time, which might eventually lead to project failure, extra costs and most importantly might affect public health and cause drug shortages [77].

2.2.5 Advantages and Benefits of a Track & Trace System

1. Provides high security in the supply chain and protects it from the entrance of counterfeit drugs.
2. Helps in combating drug counterfeiting due to the fact that each single pack of a pharmaceutical product has a randomized serial number, which is difficult to guess. Also having a sophisticated system, makes it even more difficult and more complex for criminals to fake medicinal products.
3. Allows easy verification of product authenticity via scanning the 2D data matrix code printed on the package.
4. Provides full visibility and transparency of data between different supply chain partners and with the government / health authorities.
5. Improves supply chain efficiency.
6. Allows exchange of real-time data between different supply chain partners and with the government / health authorities.

7. Makes the process of product or batch recall easier by having the ability to trace historical events.
8. Allows tracking of the drug product from the manufacturer till the point of dispensing.
9. Benefits manufacturers in terms of regulation, financial and reputational risk protection. By having the ability to identify and recall counterfeit products within a supply chain, the reputation of manufacturers can be saved, which simultaneously helps in reducing costs of dealing with such legal situations. This helps to protect the manufacturers brand products.
10. Facilitates in detecting that a crime has happened before it reaches the patient.
11. Allows the government and health authorities to manage stock on a national level thus provides them the ability to identify which product is missing at which location, which is crucial especially in our current critical times with the COVID-19 pandemic and the urgent need for vaccination.
12. Contributes to protecting our environment by reducing the use of paper and making it digital instead. For example, EPCIS files are being exchanged digitally between supply chain partners instead of using paper. Japan plans to get rid of paper leaflets use only electronic leaflets, which could be accessed by scanning a 2D Data Matrix Code. Other countries as well are looking into such digital transformation [4][1][7].

Eventually, implementing such a high secure system leads to the most important point which is to protect patients and public health as much as possible from criminals and from counterfeit medicaments [7].

2.2.6 Disadvantages and Challenges of Track &Trace System

1. It is a complicated system, time-consuming, requires lots of efforts and investments.

2. Involves lots of parties (different internal departments, external suppliers, supply chain partners, health authorities etc.), which makes the project more complicated and urges the need to have good planning, constant alignments and continuous communication.
3. Involves a huge amount of validation activities, which increases the costs.
4. In many cases, requires production line shut down when installing a new machine or when doing all kinds of validations, which might affect sales.
5. If the system is not set up correctly with high levels of security, then it might end up being not that effective against the entrance of counterfeit medicines in a supply chain.
6. For manufacturers that produce and export to several countries worldwide, they must keep adapting their systems or even implementing new ones to comply with different regulatory requirements.
7. Relies on the association of the product with a unique set of pre-defined information and does not rely on any physical properties/visual check of the package itself, which might be in some cases considered as a disadvantage.
8. In some countries or in some locations such as seaports, wireless access to database might be challenging or even not be possible.
9. Implementing a Track and Trace system facilitates in fighting drug counterfeiting but does not completely prevent it from happening.
10. As any other technological system, it might be hacked. Even though, it’s not that easy to hack it but it is still a possible option.
11. In poor countries, they cannot afford buying a whole pack of a drug product. They can only afford buying single pills or tablets, which makes challenging to identify whether those pills or tablets are coming from a genuine product or not.

12. Serialization is a requirement on the secondary packages whereas it is optional on the primary packages.
13. Even though it is not that easy, however, there is a possibility that codes and serial numbers are duplicated or mimicked by criminals [4][1][7].

2.3 COVID-19 Pandemic and Track & Trace

It has been over a year now since the first COVID-19 incident was publicly announced in China and yet we are still struggling to produce, distribute and supply vaccines to people all around the globe. Even though it might sound obvious how valuable our health is but in reality, we were underestimating it and we started to realize its importance and value only after the COVID-19 pandemic with its tremendous effects on our lives in almost every single aspect of life. This pandemic made us also understand the need of having global standards and the need for a visible and transparent supply chain that is capable of supplying a genuine vaccine at the right time, to the right location and to the right patient.

Counterfeiters did not wait long until they started making use of this pandemic, especially of people's vulnerability and weakness, to produce fake vaccines. Their criminal activities are not restricted to faking vaccines only, but they expanded to faking vaccine passports, stealing people's data by sending suspicious links and e-mails related to COVID-19 and much more. The International Institute of Research Against Counterfeit Medicines (IRACM) has already recorded a large number of counterfeiting events of COVID-19 vaccines in Africa and in Asia [23]. In late 2020, the International Criminal Police Organization (INTERPOL) disrupted criminal networks in China and South Africa and had their first international arrests and seizures connected to fake COVID-19 vaccines. On the 24th of March 2021, the INTERPOL together with the United States' Homeland Security Investigations (HSI) issued a public warning to warn public health from online vaccine scams as seen in figure 47 [78].

Figure 47: INTERPOL public warning about fake COVID-19 vaccines [78]

One of the solutions and technologies to protect public health from the purchase and consumption of counterfeited vaccines is by securing the supply chain and implementing a Track and Trace system, which will allow to identify each vaccine and track it from the manufacturer until it is given to the patient. The Developing Countries Vaccine Manufacturers Network (DCVMN), which is a voluntary public-health driven alliance of 41 vaccine manufacturers from 14 different countries globally, has set Track and Trace as one of its priorities to achieve supply chain efficiency and safety. By implementing a full and appropriate Track and Trace system and allowing data sharing between supply chain partners, governments and patients, not only tracking of vaccines would be possible, but also monitoring the safety of vaccines via pharmacovigilance and adverse event reporting would be achievable. Additionally, governments will have full visibility of vaccines stock and will be able to do balance between demand and shortage and therefore supply vaccines to different locations as per need. This increases the demand and importance of enforcing Track and Trace as a regulation in all countries.

Considering the fact that vaccines are usually produced in vials and then several vials are packed into a secondary package, it is difficult to identify and track each single vial if the serialization is done only on the secondary packaging. As a result, this requires manufacturers

to implement serialization on the primary package itself i.e., the vial. This introduces a new and additional challenge and possibly an increased cost on the manufacturer in order to allow printing a 2D Data Matrix code (encoded with a GTIN, serial number, expiry date and lot number) on a very small vial, where an upgraded packaging line and an updated system would be required as well as additional piloting and testing to make this happen.

Bio Farma, a state-owned vaccine manufacturer, launched in 2018 a piloting project on implementing a full Track and Trace system within the supply chain of vaccines including serializing primary packages and not only outer packages like in all other typical Track and Trace regulations. A 2D Data Matrix code encoded with a GTIN, serial number, expiry date and lot number were printed on the label of the vaccine vial allowing the tracking and tracing of each single dose, as shown in figure 48. Additionally, a mobile application was developed for the patients so that they can authenticate any vaccine before it is being administered to them. In 2020, Bio Farma published an article about their piloting project which took 2 years and they also mentioned that they still do not have detailed plans regarding Track and Trace implementation deadline for Indonesia. From the pilot phase, they concluded that serialization on the primary package is possible and comes with a moderate investment [23]

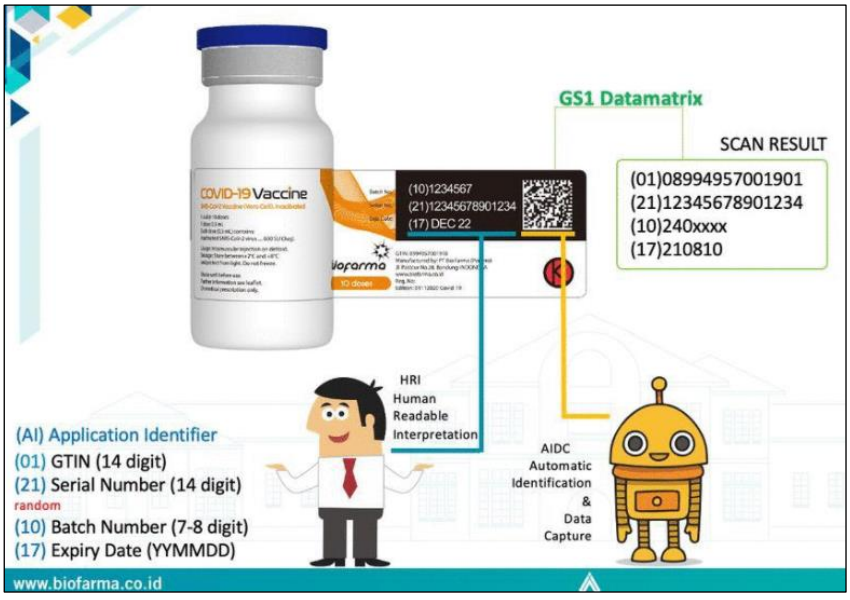


Figure 48: Serialization on primary package of COVID-19 vaccines [73]

In summary, implementing a Track and Trace system on vials is feasible and recommended. It has benefits far more than just printing a serial number on a package to track it; it allows stock management of vaccines, monitoring safety of vaccines via pharmacovigilance and reporting adverse events, it enables patients to authenticate any vaccine before use and it facilitates in tracking the administration of each vaccine dose into each person. Since Track and Trace was successfully achieved on vaccine vials, it should also be feasible and achievable on other primary packaging materials (e.g., blisters). Therefore, governments and manufacturers should look into implementing serialization on primary packages of other pharmaceutical products and not only vaccines [23].

3. Chapter Three – Methodology

In order to be able to understand the importance of Track and Trace and what challenges lie behind the implementation of such a system, a survey has been distributed to supply chain stakeholders. To be more specific, six surveys were distributed as follows:

- Three surveys in Palestine:
  - One for pharmaceutical manufacturers (Appendix 1)
  - One for wholesalers (Appendix 2)
  - One for pharmacies (Appendix 3)
- Three surveys in Europe:
  - One for pharmaceutical manufacturers (Appendix 4)
  - One for wholesalers (Appendix 5)
  - One for pharmacies (Appendix 6)
- One survey for a wholesaler in Saudi Arabia (Appendix 5)

The surveys were distributed in the following method:

- A face-to-face interview together with a survey was held with four Palestinian pharmaceutical companies: Jerusalem Pharmaceuticals, Birzeit Pharmaceuticals, Bet Jala Pharmaceuticals and Pharmacare.
- The surveys for Palestinian wholesalers, Palestinian pharmacies, European pharmaceutical companies and Saudi Arabian wholesaler, were distributed via e-mail.
- The surveys for wholesalers and pharmacies in Europe were partially distributed via e-mail and partially filled together in an interview. Three interviews with three pharmacies in Germany were held face-to-face. One interview with one wholesaler in Germany was held virtually using Microsoft Teams.

The interaction and communication with different participants in Palestine were restricted and limited due to COVID-19 pandemic. As a result, the number of participants was relatively small (3 wholesalers and 9 pharmacies) and all communications had to be done virtually (via e-mail).

As for the surveys in Europe and Saudi Arabia, the communication had to be only virtual since the participants were spread in different countries across Europe, which made it impossible to have personal interviews with each one of them, it also limited the number of participants (9 pharmaceutical companies, 3 wholesalers and 8 pharmacies). Therefore, all communications were held via e-mail and Microsoft Teams (except for 3 interviews, where I had the opportunity to do it face-to-face in pharmacies in Germany).

Notes:

1. The surveys were prepared and written differently to fit each country and each stakeholder. Given the fact that serialization was already implemented in Europe and in Saudi Arabia since February and October 2019, respectively (as explained in sections 2.2.3.4 and 2.2.3.5), the type of questions and objectives of the surveys for Palestine (Appendix 1 – Appendix 3) were different than that of Europe and Saudi Arabia (Appendix 4 – Appendix 6). Additionally, the results from the surveys of Europe and Saudi Arabia are revealed discussed together under section 4.2.
2. Two surveys (Appendix 4 and Appendix 5) were prepared and written based on an existing survey with some modifications [79].

4. Chapter Four – Results and Discussion

In this section, results from six different surveys (Appendix 1 – Appendix 6) are revealed and discussed. It is divided into three sub-sections: first sub-section for results and discussion of surveys in Palestine, second sub-section for results and discussion of surveys in Europe and Saudi Arabia and third sub-section for comparison and discussion of the first two sub-sections.

4.1 Palestine

This section is divided into three sub-sections to reveal results from the three different surveys of pharmaceutical companies (Appendix 1), wholesalers (Appendix 2) and pharmacies (Appendix 3) in Palestine and discuss in depth accordingly.

4.1.1 Pharmaceutical Manufacturers (MAHs / CMOs)

Awareness about serialization

Table 15 reveals results about awareness of pharmaceutical companies with regards to serialization and whether they received any notification from the Palestinian MoH.

Table 15: Awareness of pharmaceutical companies about serialization

Manufacturer's Name	Jerusalem Pharmaceuticals	Birzeit Pharmaceuticals	Beit Jala Pharmaceuticals	Pharmacare
Awareness of serialization	Aware	Not aware	Aware	Aware
Received notification from Palestinian MoH about serialization regulation	No	No	No	No

As per table 15 and as per the interview held, three out of four companies were aware of serialization, while one company was not aware at all of serialization and did not hear about it.

We can see also that none of the four companies received any kind of notification or regulation from the Palestinian MoH, which enforces them to implement serialization. There were also no expected timelines for serialization.

Export market of pharmaceutical companies

Table 16 reveals results about the export market of pharmaceutical companies, whether serialization is required in those specific countries and whether there are any plans to implement it.

Table 16: Export market of pharmaceutical companies and serialization plans

Manufacturer's Name	Export Market(s)	Requires Serialization?	Any plans to implement serialization?
Jerusalem Pharmaceuticals	Jordan	Yes	Yes
Birzeit Pharmaceuticals	Armenia, Belarus, Azerbaijan, Kazakhstan	No (for none of the mentioned countries)	No
Beit Jala Pharmaceuticals	Algeria, Yemen, Jordan, Tunisia, Morocco	Yes, but only for Jordan	Yes
Pharmacare	Azerbaijan	No	Yes

As per the results from table 16, all of the four pharmaceutical companies export some of their products outside of Palestine and only two of them export their products to a country where serialization is an enforced regulation. This country is Jordan. As mentioned in section 2.2.3.7, JFDA initially announced that serialization must be implemented by 2018, which is why

Jerusalem Pharmaceuticals and Beit Jala Pharmaceuticals had plans in 2018 to start implementing serialization and to comply with JFDA's regulation. However, JFDA has postponed the serialization deadline until June 2021, which is subject to change and might be postponed again. This is also the reason why Jerusalem Pharmaceuticals and Beit Jala Pharmaceuticals postponed their plans and did not implement serialization up until now. Additionally, Jerusalem Pharmaceuticals has confirmed recently that they did not implement serialization yet.

Birzeit Pharmaceuticals export their products to countries (Armenia, Belarus, Azerbaijan and Kazakhstan) that do not have the serialization regulation in place (please refer to section 2.2.3.10 for serialization status of these countries), therefore they were not aware of serialization and did not have any plans to implement it. As for Pharmacare, they currently export their products to Azerbaijan, which does not have serialization regulation in place, therefore there were no plans in Pharmacare Palestine to implement serialization. Nevertheless, they have a sister company in Malta (Qualified Person – QP release site), which does the QP release for products that have been manufactured in Palestine and exports them to Europe (Italy, Spain and Germany). Therefore, the implementation plan was for Malta company and not Palestine.

Readiness for serialization and estimated efforts needed to implement such a system

Table 17 shows how many packaging lines pharmaceutical companies have and whether they need any upgrade or new lines for the purpose of fulfilling serialization requirements.

Table 17: Number of packaging lines in each pharmaceutical company

Manufacturer's Name	Number of packaging lines	Requires packaging line upgrade or a new one
Jerusalem Pharmaceuticals	5	New packaging line will be required
Birzeit Pharmaceuticals	8	Both, line upgrade and a new packaging line
Beit Jala Pharmaceuticals	3	3 lines will require an upgrade
Pharmacare	1	New packaging line will be required

Based on the interviews held with the four pharmaceutical companies, three out of four will require a new packaging line and four out of four will require packaging line upgrade if they plan to implement serialization due to the serialization regulation, whether it's from Palestine or any of their export market countries (like Jordan). The decision whether a new line is required or only a line upgrade is required was taken based on the existing packaging lines that these pharmaceutical companies had. From what I have seen in the four pharmaceutical companies is that most of the packaging is done manually therefore a new packaging line would be required in order to fulfil serialization requirements. While some of them have semi-automatic lines, therefore, an upgrade for the line would be sufficient. The number of new packaging lines required was decided based on what the manufacturer confirmed that they need.

As mentioned in section 2.2.4.6, implementing serialization could be a complicated project and time-consuming depending on the serialization requirements, timelines, size of the company etc. It might take them 1 – 3 years to implement this kind of project. Therefore, Palestinian companies must plan well in advance in order to be able to meet critical timelines. Additionally,

employees must be informed in advance about the serialization regulation, requirements, basic understanding and definitions to ensure more efficient work and better productivity. This also allows the alignment and understand between different departments as mentioned in section 2.2.4.2.

Another factor that Palestinian companies should be taking into consideration is the budget. As mentioned in section 2.2.4.7, there are lots of costs involved in a serialization project such as new packaging lines, devices, training, validation, external vendors if needed, etc.

Conclusion

The main market of the above-mentioned 4 companies is the local market, therefore their focus and interest lie in the local market and local regulations. Since the Palestinian MoH did not enforce any serialization regulation, these companies do not consider serialization as a high priority or as a necessity. The main driver for making two of these companies (Jerusalem Pharmaceuticals and Beit Jala Pharmaceuticals) plan to implement serialization was the regulatory requirements coming from their export market countries i.e., Jordan.

4.1.2 Wholesalers

Awareness and status of serialization

Table 18 shows results of wholesaler's awareness about serialization and whether they were requested to implement it either from the Palestinian MoH or from their supply chain partners.

Table 18: Awareness of wholesalers about serialization and its status

Question	Wholesaler A	Wholesaler B	Wholesaler C
Have you heard about serialization?	Yes	Yes	Yes
If yes, did you already introduce serialization?	No	No	No
Did the Palestinian Ministry of Health contact you regarding the Serialization regulation?	No	No	No
Are there any requirements from your partners/customers/suppliers to implement serialization?	No	No	No
Do your partners/customers/suppliers do serialization on their products?	Not all of them	Yes	Yes

All three wholesalers were familiar with serialization, but none of them implemented it as they did not receive any regulation from the Palestinian MoH, nor did they receive any request from their suppliers / partners.

The wholesalers were asked about their suppliers and where do they buy their pharmaceutical products from. All of them answered names of global pharmaceutical companies such as Novonordisk, Sanofi, Boehringer Ingelheim, MSD, Pfizer, J&J, etc., therefore they do receive serialized products, however, they are not obliged to have systems or devices that are capable of storing, reading or sharing serialized related data.

Existing processes/systems of warehouse activities

Table 19 shows whether wholesalers have any automated systems in place, which could be used as a basis for serialization or whether their activities are performed mostly manually.

Table 19: Means of performing warehouse activities within a wholesaler

Question	Wholesaler A	Wholesaler B	Wholesaler C
When preparing a delivery for a customer, do you use a mobile device/scanner to scan products into a system before picking and packing them into pallets or do you perform the pick and pack process manually?	We perform manual pick and pack process	We perform manual pick and pack process	We perform manual pick and pack process

All three wholesalers perform warehouse activities manually, which means that implementing serialization would require extensive efforts and upgrades. New devices, new systems and new processes will be required in order to be able to fulfil serialization requirements. The process of implementing serialization might not be as complicated or as costly or as time-consuming as pharmaceutical manufacturers, nevertheless, wholesalers must also plan in advance all activities and budget needed for implementing serialization.

Counterfeiting incidents and personal opinions

Table 20 reveals whether wholesalers experienced any incidents of having their shipments either stolen or counterfeited. Additionally, they were asked about their personal opinion about drug counterfeiting and serialization.

Table 20: Results of incidents of counterfeit/stolen products and personal opinions of wholesalers about serialization.

Question	Wholesaler A	Wholesaler B	Wholesaler C
Did you ever have an incident where the shipment of drug products was stolen?	No	No	No
Did you ever have an incident where the drug products which you bought or distributed were fake/counterfeit?	No	No	No
On a personal level, do you have any concerns about consuming, buying or selling a counterfeit product?	Yes	No	Yes
If yes, will having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell?	No	No answer	Yes

All three wholesalers answered that they did not experience any incident where a certain shipment of drug products was stolen, and they also did not experience any incident where the drug products that they bought or distributed were fake.

Two out of three wholesalers had concerns on a personal level about consuming, buying or selling a counterfeit product and only one of them believes that having serialization in place makes them feel more secure about the authenticity of pharmaceutical products which they consume, buy or sell.

Conclusion

Wholesalers did not receive any request from the Palestinian MoH or from their suppliers / partners about implementing serialization, therefore they have no plans at the moment to implement it. Additionally, they did not experience any incident of drug counterfeiting, therefore one of them did not see the necessity of implementing it, while another one did see the necessity.

4.1.3 Pharmacies

Awareness about serialization

Table 21 reveals results about awareness of pharmacies with regards to serialization and whether any notification has been received from the Palestinian MoH.

Table 21: Awareness of pharmacies about serialization

Question	Ph. 1	Ph. 2	Ph. 3	Ph. 4	Ph. 5	Ph. 6	Ph. 7	Ph. 8	Ph. 9
Have you heard before about the new regulatory requirement “Track and Trace” / “Serialization”?	No	Yes	No	Yes	Yes	No	Yes	No	No
Did the Palestinian Health Authority contact you regarding the Serialization regulation?	No	No	No	No	No	No	No	No	No

Ph. = Pharmacy

Four out of nine pharmacists answered that they heard about Track and Trace regulation and nine out of nine answered that they did not receive any notification from the Palestinian MoH about serialization regulation.

Existing processes/systems when dispensing a product to patients

Table 22 reveals whether pharmacies have at the moment any system which enables them to scan the product and check in the system whether it's authenticated or not, before dispensing it to the patient.

Table 22: Exisitng system in pharmacies

Question	Ph. 1	Ph. 2	Ph. 3	Ph. 4	Ph. 5	Ph. 6	Ph. 7	Ph. 8	Ph. 9
When scanning and dispensing a pharmaceutical product to a patient, do you get a notification on your system whether the product is authenticated/verified or not?	No	No	No	No	No	No	No	No	No

Ph. = Pharmacy

All nine pharmacists answered that when scanning and dispensing a pharmaceutical product to a patient, they do not get a notification on their system whether the product is authenticated/verified or not. Which was the expected answer since serialization is not implemented yet in Palestine. To clarify, the scanning process mentioned here is not the regular scanning of a barcode, it's rather scanning of a 2D Data Matrix Code using a device which is connected to a serialization system (e.g., ATTP), which upon scanning gives a response back whether the product is authenticated (e.g., active, recalled, expired) or not.

When serialization becomes a regulation in Palestine, pharmacies will have to consider adjusting their devices and systems to be able to comply with the regulation and integrate their system with the chosen serialization system (e.g., SAP ATTP). As mentioned in section 2.2.2, Track and Trace system allows connecting between all supply chain partners including pharmacies so that at the end of the supply chain process and before pharmacists dispense medicines to patients, they can scan the 2D Data Matrix Code (which automatically connects

to the serialization system) and get an immediate response whether the product is authenticated or not. Based on that, pharmacists can decide whether a certain product can be given out to a patient or not. This is basically the most important part of Track and Trace, which ensures patient safety by providing the patient with verified genuine products only.

Counterfeiting incidents and personal opinions

Table 23 reveals whether pharmacies experienced any incidents of having their products stolen or if they encountered any incident, where they purchased or sold counterfeit medicines. Additionally, their personal opinion was asked about drug counterfeiting and serialization.

Table 23: Results of incidents of counterfeited/stolen/recalled products and personal opinions of pharmacists about serialization.

Question	Ph. 1	Ph. 2	Ph. 3	Ph. 4	Ph. 5	Ph. 6	Ph. 7	Ph. 8	Ph. 9
Did you ever have an incident where the drug products were stolen from your pharmacy or warehouse?	No	No	No	Yes	Yes	No	No	No	No
Did you ever have an incident where the drug products which you bought from a supplier or sold to a patient were later on discovered to be fake/counterfeit products?	No	No	No	No	Yes	No	-	No	Yes
Did you ever have an incident where a complete batch of a drug product had to be recalled and taken out of the pharmacy?	Yes	No	No	Yes	No	No	No	No	No
On a personal level, do you have any concerns about consuming or selling a counterfeit product?	Yes	No	No	No	No	No	Yes	No	No

Question	Ph. 1	Ph. 2	Ph. 3	Ph. 4	Ph. 5	Ph. 6	Ph. 7	Ph. 8	Ph. 9
If yes, will having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell?	Yes	No	No	No	-	-	Yes	-	-

Ph. = Pharmacy

- Two out of nine pharmacists answered that they had an incident where the drug products were stolen from their pharmacy or warehouse. When asked what did they do when this incident happened, one of them did not answer and the other one just answered that they called the police. Usually, when a drug product shipment / container is stolen, its destiny is known, which is the black market. There are several possible scenarios of what might have happened to those stolen drugs:
    1. Drug product's contents and drug's packages have not been touched or changed and have been sold as is in the black market (in terms of content not in terms of price).
    2. Primary packages of the drug product (e.g., blisters) have been taken out of their original secondary packages and have been sold to the black market, while filling the original secondary packages with fake products and selling them either in the black market or to distributors, which would then be possibly sold to pharmacies. This would subsequently have two effects:
        a. Puts patient's health at risk as fake medicinal products packed into original manufacturer's packages (secondary packages) are being sold to pharmacies or patients, in which case, they won't be able or they won't have the means to differentiate whether the medicine that they are buying is genuine or not.
        b. Puts manufacturer's reputation at risk as fake medicinal products are being sold under their name and intellectual property.

If a serialization system was in place, it would have helped to:

1. Identify the GTIN, serial numbers and batch number of the shipment / container that has been stolen and identify at which point the shipment diverted from the supply chain.
2. Deactivate all serial numbers of the stolen drug product. There is a functionality in SAP ATTP which allows to mark all serial numbers as “lost”. This will mainly help the manufacturer to protect its reputation.
3. Notify supply chain stakeholders about the stolen product, especially pharmacies and hospitals so that they are aware of the incident and of the stolen product’s details, which helps them to take necessary precautions and be more careful when getting a shipment of that same drug product. This will basically facilitate in protecting patients from the consumption of fake medicines and will protect the reputation of the manufacturer (of the stolen product) as well.

What I would like to clarify here is that having a serialization system in place does not mean that it will completely stop such incidents from happening, but it certainly helps in reducing the number of instances of such incidents and it also facilitates in detecting or discovering the crime at an early stage before it actually happens and before the counterfeit drug reaches the patient.

- Two out of nine answered that they had an incident where the drug products which they bought from a supplier or sold to a patient were later on discovered to be counterfeit. One decided not to answer this question. Having a serialization system in place, would have allowed pharmacists to scan and verify the authenticity of the product before dispensing it to patients, which could have prevented the harm and damage caused to people who utilized these counterfeit medicines.
- Two out of nine answered that they had an incident where a complete batch of a drug product had to be recalled and taken out of the pharmacy. However, they did not answer or

give details about the recalling process. Having a serialization system in place helps to make the recalling process easier, faster and more efficient since real time data is available for supply chain stakeholders and can be checked and shared at any time, as explained in section 2.2.2.

- Two out of nine answered that on a personal level, they have concerns about consuming or selling a counterfeit product and two out of nine answered that having a serialization system makes them feel more secure about the authenticity of pharmaceutical products which they consume, buy or sell. Four did not answer the latter question.

Conclusion

Pharmacies in Palestine do not have a serialization system in place and none of them received any notification from the Palestinian MoH about serialization related requirements and regulations. The results clearly show that drug stealing and counterfeiting incidents do exist in Palestine. Even if we are talking about a small percentage of 22.2%, that does not mean that such incidents do not happen or that we can ignore them. On the contrary, now it's the time to take action and fight these incidents before it's too late and before we find ourselves having a higher percentage of drug stealing or counterfeiting. Implementing a Track and Trace system could facilitate in combating drug counterfeiting.

4.2 Europe

This section is divided into three sub-sections to reveal results from the three different surveys of pharmaceutical companies (Appendix 4), wholesalers (Appendix 5) and pharmacies (Appendix 6) in Europe (and Saudi Arabia) and discuss in depth accordingly.

Note: Both Europe and Saudi Arabia have already implemented serialization in February and October 2019, respectively.

4.2.1 Pharmaceutical Manufacturers (MAHs / CMOs)

Export market and types of serialization systems depending on country's regulations

As seen from figure 49, the three main countries to which the nine pharmaceutical manufacturers export their products to are Russia, EU and China. All nine manufacturers (100%) export their products to Russia, 88.9% export to EU and 66.7% export to China. In the 4th place comes Saudi Arabia, Turkey and other countries (which are comprised of Australia, UAE, South Africa, Japan and Jordan) with 55.6% of manufacturers exporting to these countries. In the 5th place, South Korea and USA with 44.4% and in the last place Brazil and Egypt with 22.2% of manufacturers exporting their products to these 2 countries.

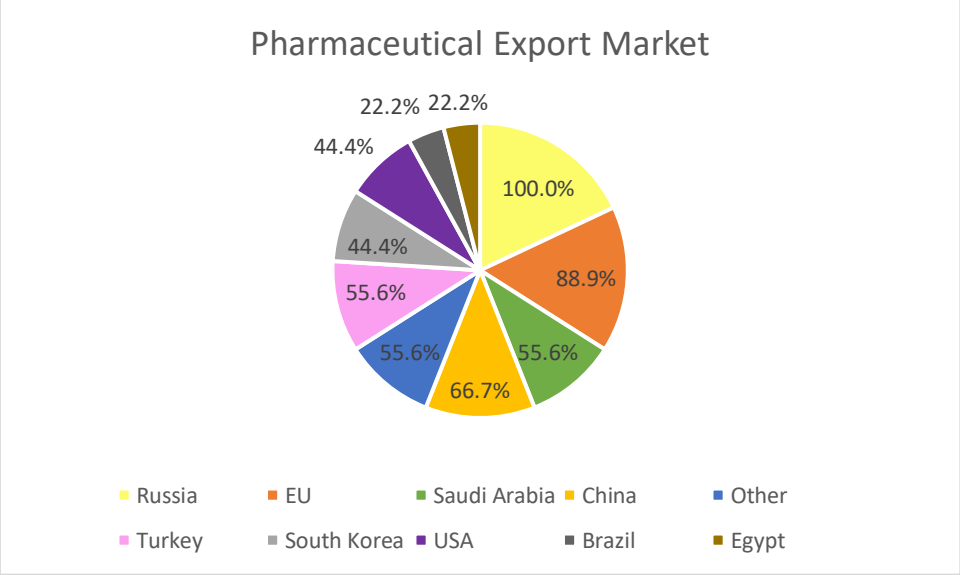


Figure 49: Export market of the 9 participating pharmaceutical companies

Table 24 reveals the status of serialization in the countries which the 9 pharmaceutical manufacturers export their products to, including timelines.

Table 24: Status of serialization in different countries of the export market

Country	Serialization Status
Russia	Serialization was implemented since July 2020

Country	Serialization Status
EU	Serialization was implemented since 09.02.2019
China	December 2015 → Serialization was implemented not according to GS1 standards. By 2022 → Serialization must be implemented following GS1 standards.
Saudi Arabia	March 2017 → Serialization was implemented. August 2020 → Aggregation was implemented.
Turkey	July 2010 → Serialization was implemented. January 2012 → Aggregation was implemented.
Australia	Serialization of certain blood products was implemented in 2017 and 2018. As of 01.09.2020, pharmaceutical products must have a machine-readable code, which: (a) encodes GTIN for the medicine as allocated under the GS1 System; and (b) identifies different product variants and differentiates between different strengths, pack sizes and dose forms. Type and implementation of full T&T is being discussed.
UAE	Regulation is still under development. No defined timeline.
South Africa	Regulation is still under development. No defined timeline.
Japan	T&T implementation is in progress. August 2021 → E-labelling (e.g., electronic leaflet) must be implemented. December 2022 → Serialization must be implemented for drugs and medical devices.
Jordan	30.06.2021 (date is subject to change) → Serialization must be implemented.
South Korea	Serialization was implemented since January 2016
USA	2017 → Serialization was implemented by manufacturers. 2018 → Serialization was implemented by repackagers.

Country	Serialization Status
	2019 → Serialization was implemented by wholesale distributors. 2020 → Serialization was implemented by dispensers. 2023 → Full Track and Trace must be in place
Brazil	October 2020 → Serialization was implemented for 25% of pharmaceutical products. April 2022 → Serialization must be implemented for 100% of pharmaceutical products and reporting to the Brazilian authority must be achieved as well.
Egypt	Full Track and Trace is expected to be implemented in 2022, however, the latest guidelines and timelines were not published yet.

All pharmaceutical companies had at least one serialization system in place, which is the Russian Track and Trace system. Russia is following GS1 standards in its Track and Trace system, so do all the above-mentioned countries that have their Track and Trace system already in place (like USA and Turkey for example). The fact that GS1 standards exist already in all 9 manufacturers, this makes it easier for them to adapt their systems to upcoming/new regulatory requirements (like for Australia, Japan, Jordan, Brazil, Egypt, UAE and South Africa), because it acts as a basis for implementing any Track and Trace system that is following GS1 standards, as explained in section 2.2.1. This is one big step towards having a global business language and understanding between different systems and regulations in different countries worldwide. However, each country has different printing requirements, different reporting requirements, different levels of serialization/aggregation etc., which makes it challenging for pharmaceutical companies to upgrade their systems every time there is a new regulation for a new country. What makes it even more challenging is that each country has a different timeline, therefore, pharmaceutical companies cannot treat it as one big project and implement everything together.

They have to wait for the regulation and requirements of each single country to be able to implement them accordingly.

Internal Challenges faced during the implementation of a T&T system

Figure 50 illustrates the internal challenges that the nine participants faced during Track and Trace implementation. It is obvious from the figure, that defining a system architecture was the most significant challenge for six out of nine participants. Two participants found it as a medium challenge while one participant found it as a slight challenge. As explained in section 2.2, the Track and Trace system landscape could be very complex depending on the company size, the regulatory requirements and the number of supply chain stakeholders involved.

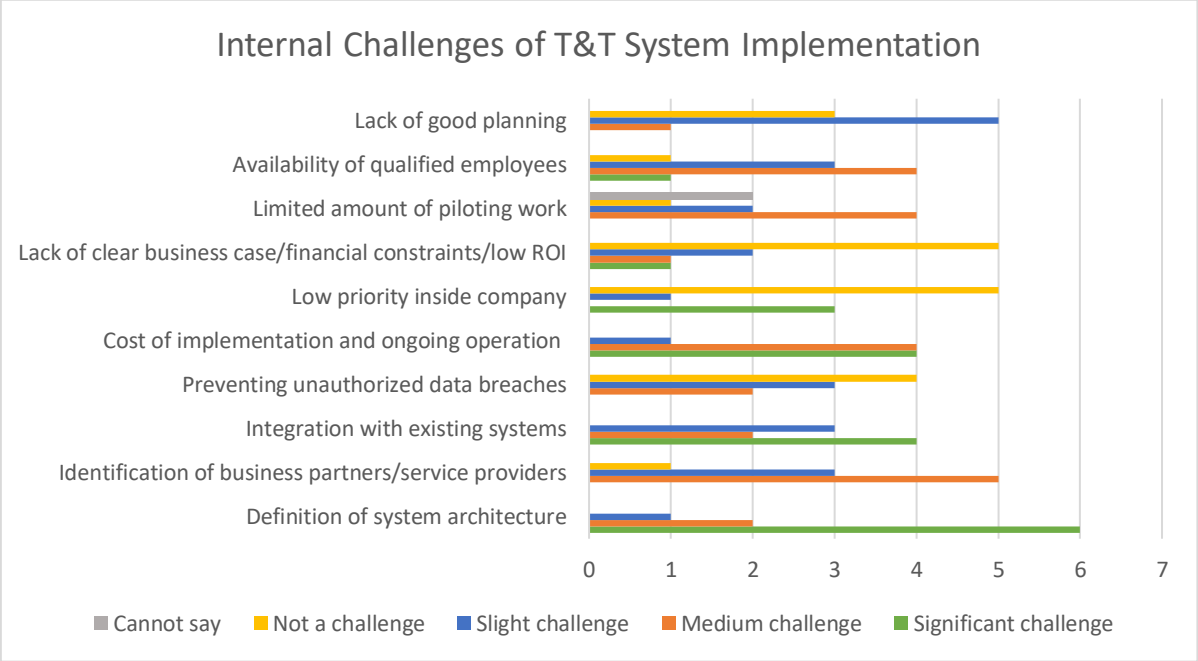


Figure 50: Internal challenges faced during T&T implementation

The next significant challenge faced by four out of nine participants, was the integration process with existing systems. Two considered it as a medium challenge and three considered it as a slight challenge. The integration with existing systems is related to the complexity of the system landscape and architecture, which should be achieved as per ISA-95 model as mentioned in section 2.2.2.3. As mentioned in section 2.2.4.3, one of the common issues found in a

serialization project is lack of a clear URS for the line systems, which makes it difficult to implement the required system with the required functionalities. This subsequently leads also to facing a challenge in integration with existing systems as reported by 44.4% of participants. Cost of Track and Trace implementation and ongoing operations was another significant challenge faced by four out of nine participants. Four considered it as a medium challenge and one considered it as a slight challenge. This challenge is related to the large investments that manufacturers must make in packaging lines and other devices such as printers, scanners and mobile devices, validation activities, recruitment of new employees if necessary, training, IT related costs (purchase and implementation of serialization system like SAP ATTP, purchase of serial numbers, purchase of licenses, hiring external consultants and vendors), any other related external suppliers or consultants and operational costs, as mentioned in section 2.2.4.7.

All nine manufacturers that participated in the survey were large companies with more than 500 employees, which explains why defining a system architecture, integrating with existing systems, costs of implementation and operational costs, were found to be a significant challenge for many of them.

Three out of nine participants answered that they faced a significant challenge in terms of the priority given to the Track and Trace implementation, where three companies considered it as a low priority. The fact that three participants considered this as a significant challenge proves that one of the common issues found in a serialization project is underestimation of efforts and time needed to implement such a project as well as underestimation of the impact on daily operations and involvement of team members for the serialization project, which might eventually cause burnout, stress and not meeting quality goals, as mentioned in section 2.2.4.3. On the other side, five out of nine participants did not consider “Low priority inside company” as a challenge, which indicates that these companies were well aware of the importance and significance of implementing such a system and were acting accordingly.

One participant considered “Lack of clear business case/financial constraints/low Return on Investment (ROI)” as a significant challnege, while 5 out of 9 did not consider it as a challenge.

“Identification of business parnter / service providers” was found to be a medium challenge for five out of nine participants, a slight challenge for three out of nine participants and not a challenge for one participant. This challenge falls under the same category of defining and understanding the system landscape, understanging which system is connected with what and based on that deciding which service providers or suppliers need to be provided in order to fulfil the requirements.

Four out of nine participants faced a medium challenge due to limited amount of piloting work, two faced a slight challenge, two weren’t able to answer and one did not find it as a challenge. The opportunity of piloting work allows manufacturers to test how the serialization system works and test their capabilities before the system is enforced as a regulation. This gives them more time to understand the system functionalities and adapt to it accordingly. Many governments did some pilot work with a number of supply chain stakeholders before enforcing the Track and Trace regulation. Egypt and Lebanon for example are currenlty in the piloting phase before finally announcing T&T regulation.

“Lack of good planning” was also considered as a challenge which manufacturers faced during the implementation of T&T system. One out of nine participants considered it as a medium challenge, five considered it as a slight challenge and three did not consider it as a challenge. Good planning is one of the most important aspects for the successful implementation of a T&T system as mentioned in section 2.2.4.5.

Another challenge asked about was “Preventing unauthorized data breaches” which was considered as a medium challenge for two participants, slight challenge for three participants and was not considered as a challenge for four participants out of nine. If implemented correctly and if the IT-system landscape and infrastrcutre are mature enough, a Track and Trace system

can be highly secure where preventing unauthorized data breaches should not be a significant issue or challenge.

One participant considered “Availability of qualified employees” as a significant challenge, four considered it as a medium challenge, three considered it as a slight challenge and one did not consider it as a challenge. To sum it up, eight out of nine considered “Availability of qualified employees” as some kind of a challenge, which is why training employees or hiring external experts is a very crucial step when implementing a T&T project, as explained in section 2.2.4.5. In regards with this challenge, participants were asked three additional questions:

First question was whether they hired external consultancy in order to cope with this challenge. Eight out of nine answered that they did indeed hire consulting companies to get the required support and expertise.

Second question, they were asked whether serialization related trainings were provided to their employees. Six out of nine answered that they conducted trainings to the employees, whereas two participants answered that they had no trainings and one participant decided not to answer this question.

Third question, they were asked whether they had a dedicated team for serialization and what was the reason for establishing such a team. The results are show in table 25 (copied as is):

Table 25: Reasons for having a dedicated team for serialization.

Manufacturer	Do you have a team?	Reasons for the need of a dedicated serialization team
Manufacturer nr.1	Yes	Dedicated and clear responsibility including know-how development / dedicated counterparts within the company for specific T&T topics / faster reaction times whenever new requirements are arriving / organized and structured

Manufacturer	Do you have a team?	Reasons for the need of a dedicated serialization team
		way of executing projects / clear responsibility on support.
Manufacturer nr.2	No	1.Complexity of the whole requirements. 2.Quantity of involved departments (production, regulatory, sales and distribution, marketing, warehouse, IT etc.). 3.Quantity of involved personal (which have to be trained for the new processes for example). 4.Complexity of master data management. Serialization requirements are a running process worldwide.
Manufacturer nr.3	Yes	Project team was needed to implement all required changes in HW (hardware), SW (software), processes, procedures, documentation, training, etc.
Manufacturer nr.4	Yes	There is a permanent established team for serialization topics, but some of the team members have also non serialization related tasks. Anyway, the reasons for this serialization team are: To build up and sustain knowledge / know-how, to efficiently resolve issues, to have central points of contact, to be well-prepared for future changes and projects in the Track & Trace area.
Manufacturer nr.5	Yes	No answer

Manufacturer	Do you have a team?	Reasons for the need of a dedicated serialization team
Manufacturer nr.6	Yes	Reasons for establishment: Creation of a central organization as single point of contact and interface to stakeholders, creation of new roles in form of company administrators for serialization software, centralized rights management, bundling of internal knowledge, operational troubleshooting, monitoring of international legislative changes.
Manufacturer nr.7	Yes	The serialization is an ongoing almost never-ending project (new markets are coming with serialization requirements) and it is easier to solve any issues if you have dedicated team.
Manufacturer nr.8	Yes	Additional systems and processes have been implemented that required additional control and management.
Manufacturer nr.9	Yes	To follow up on serialization requirements development in each market and collaborate across the company to make sure we are in compliance.

External Challenges faced during the implementation of a T&T system

Figure 51 illustrates the external challenges that the nine participants faced during Track and Trace implementation. As seen in the figure, lack of clear regulatory requirements was considered as a significant challenge for eight out of nine participants and a medium challenge for one participant. This challenge can be clearly observed in section 2.2.3, where different regulations of different countries were detailed, showing how the implementation timelines and requirements were being changed and postponed several times by some governments like

Jordan and Lebanon for example. This makes it more challenging and difficult for manufacturers to understand, plan and implement a Track and Trace system accordingly.

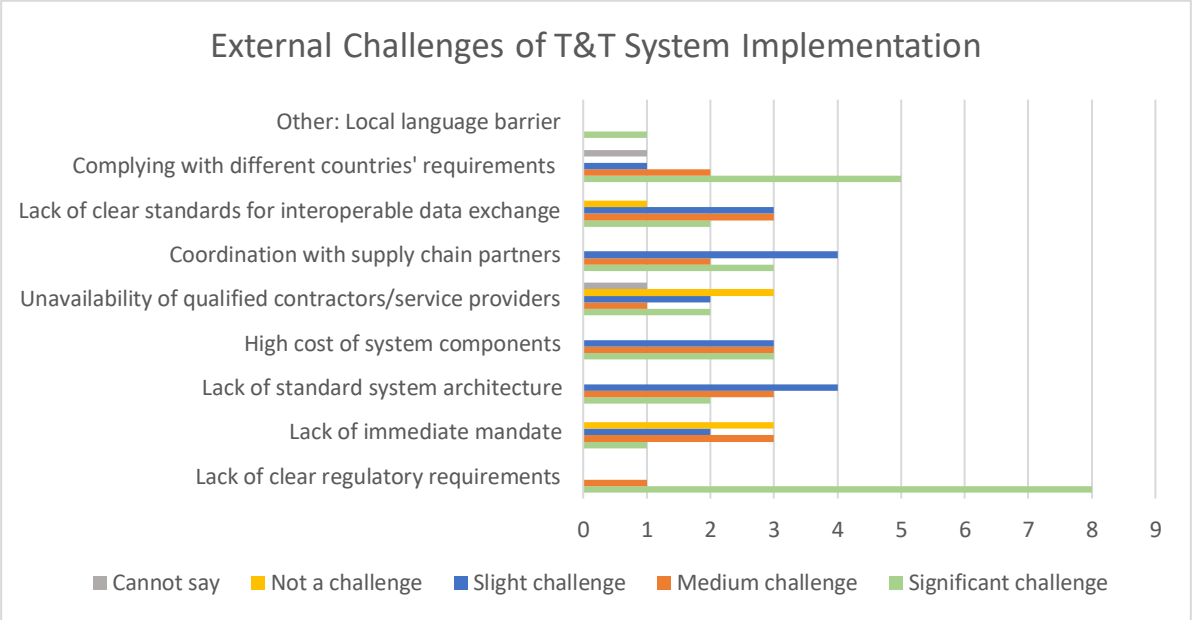


Figure 51: External challenges faced during T&T implementation

Next challenge is complying with different countries' requirements and regulations, where five out of nine participants considered it as a significant challenge, two considered it as a medium challenge and one was not able to answer. Having to comply with different Track and Trace regulations for different countries at the same time could be significantly challenging due to different system landscapes and different requirements for each country as seen in section 2.2.3. Therefore, it is very important to plan correctly and wisely when implementing a Track and Trace system taking into consideration the long run benefits rather than just complying with minimum requirements of a specific country regulation, as mentioned in section 2.2.4. Implementing GS1 Standards is one step closer to having a standard system which could possibly talk and connect to any other system using GS1 Standards as well.

Three out of nine participants faced a significant challenge in coordination with supply chain partners, two faced a medium challenge and four faced a slight challenge. This was mentioned as one of the challenges of a Track and Trace system, in section 2.2.6. It involves many supply

chain partners, which makes the project more complicated and urges the need to have good planning, constant alignments and continuous communication, as explained in section 2.2.4.

“High cost of system components” is another known challenge faced by all manufacturers. Three found it to be as a significant challenge, three found it to be as a medium challenge and three found it to be as a slight challenge. As mentioned in section 2.2.4.7, packaging lines, systems and devices could be of a high cost on the manufacturer, which need to be taken into account when planning for such a project.

“Lack of standard system architecture” is another challenge faced by all manufacturers, which is connected to the fact that different regulations exist for different countries as already previously mentioned. There isn’t one single regulation or one single set of requirements which is standard for all countries. Two participants found this challenge to be significant, three found it as medium and four found it as slight.

Two participants faced a significant challenge in finding qualified contractors/service providers. One participant faced a medium challenge, two participants faced a slight challenge, three participants did not find it as a challenge and one participant was not able to answer.

“Lack of clear standards for interoperable data exchange” was found to be another challenge faced by manufacturers, where two participants considered it as a significant challenge, three participants considered it as a medium challenge, three participants considered it as a slight challenge and one participant did not consider it as a challenge. GS1 standards made it possible to have clear standards for interoperable data exchange by using EPCIS messages for example, which can be easily used between supply chain stakeholders to share required product information. The challenge here, however, is lack of understanding of GS1 standards, which is a common issue found within a serialization project as mentioned in section 2.2.4.3.

“Lack of immediate mandate” was found to be a significant challenge for one participant, a medium challenge for three participants, a slight challenge for two participants and not a challenge for three participants.

One participant added a new challenge, which is local language barrier and considered it as a significant challenge. This is related to regulations being published in own’s country language rather than English, making it difficult for manufacturers to understand full requirements needed for the implementation of country’s specific Track and Trace regulation. Russia is an example, which I personally experienced throughout my work at Movilitas. The Russian government first published its regulations and requirements in Russian language only, which caused a significant challenge for manufacturers that export their products to Russia to understand the Russian Track and Trace requirements and to implement them on time. It took some time until English documents were available and due to this challenge, the Russian government decided to postpone the T&T implementation from 01.01.2020 until 01.07.2020.

Further Challenges faced during the implementation of a T&T system

The nine participants were asked to describe in detail the top three challenges (regardless whether internal or external) that they faced during the implementation of a Track and Trace system. The results from eight participants were copied as is and revealed in tables 26 – 33 (manufacturer number 7 decided not to answer the question).

Table 26: Top three challenges faced by manufacturer nr.1 during T&T implementation.

Challenge	Root Cause
Lack of awareness within the management level for the need of implementation considering very high costs.	-

Challenge	Root Cause
Lack of clear legislative or regulatory requirements (e.g., Russia).	Would have to ask the Russian government. The constant changes / (back and forth) caused many process iterations / adjustments and resulted in higher implementation costs than expected.
Availability of the qualified employees with a needed experience.	At least at the beginning (3-4 years back) the topics and the needed system architecture were completely new.

Table 27: Top three challenges faced by manufacturer nr.2 during T&T implementation.

Challenge	Root Cause
Timely definition of clear legislative or regulatory requirements.	Clear legislative and regulatory requirements (e.g., EU) were published too late for an optimal implementation project.
High cost of system components such as software, hardware, service, licences.	Extreme high additional costs for changing of packaging lines, implementation of an IT solution, licences for all national systems and changes of all involved processes without any chance of a good ROI.
Unavailability of qualified personal on contractor side for implementation of requirements on our packaging line.	The vendor/service contractor for our packaging line was not a bit prepared for this great challenge. No project management, no qualified personal for

Challenge	Root Cause
	projects, no availability of service technician was given.

Table 28: Top three challenges faced by manufacturer nr.3 during T&T implementation.

Challenge	Root Cause
Lack of clear legislative or regulatory requirements.	Late finalization/publication of requirements, constant changes.
Lack of standard system architecture.	SW (software) and HW (hardware) needed to be built almost from scratch, a lot of changes, prototyping, testing, needed to be done.
Adoption of serialization in existing landscape/organization/processes.	Introduction of serialization had a huge impact on company processes (production, supply, QA, regulatory, warehouse and logistics), all these needed to be adjusted and people needed to be trained.

Table 29: Top three challenges faced by manufacturer nr.4 during T&T implementation.

Challenge	Root Cause
Changing requirements.	Lack of clear legislative or regulatory requirements.
A degree of uncertainty about the right way to go.	Less experience and know-how in the field of serialization/Track & Trace in the organisation.

Challenge	Root Cause
Scope of the implementation.	New processes, new production lines, new production line equipment, introduction of several solutions at once (L1/L2, L3, L4). (Note: L1/L2, L3, L4 are the levels according to ISA-95 model as mentioned in section 2.2.2.3).

Table 30: Top three challenges faced by manufacturer nr.5 during T&T implementation.

Challenge	Root Cause
In-time data collection and training of key users worldwide.	Design, Implementation delays and global availability of users.
Strategy alignment in a shared global system environment.	Internal processes.
Workload and knowledge transfer.	Less internal staff.

Table 31: Top three challenges faced by manufacturer nr.6 during T&T implementation.

Challenge	Root Cause
Importance of serialization projects is not known within the company.	Lack of top management commitment and communication due to lack of information.
Availability of all necessary compliance reports from the serialization solution provider.	Lack of preparation of the serialization software provider and changing legal requirements.
(Changing) Requirements and timely internal adjustment of the ERP system.	Changing legal requirements and priority conflicts with other projects.

Table 32: Top three challenges faced by manufacturer nr.8 during T&T implementation.

Challenge	Root Cause
Adjusting the processes for Russian serialization and aggregation in time.	Lack of reliable and detailed regulation.
On-board all of partners on time.	Different systems used by partners.
Financial investments needed.	Installation of new equipment and implementation of adequate systems.

Table 33: Top two challenges faced by manufacturer nr.9 during T&T implementation.

Challenge	Root Cause
Acquire knowledge of specific local serialization requirements internally.	Lack of experts of serialization across all markets.
Collaboration with supply chain partner during implementation.	Language and cultural barrier.

Figure 52 shows which software solution is used by pharmaceutical manufacturers for the serialization system. Most of the manufacturers (7 out of 9) use SAP ATTP, four use TracLink, two use both SAP ATTP and TraceLink and two use some other systems. Having different systems between different supply chain partners adds a challenge in system integration and connection. As mentioned in section 2.2.2, SAP ATTP and TraceLink are the two most common software for serialization.

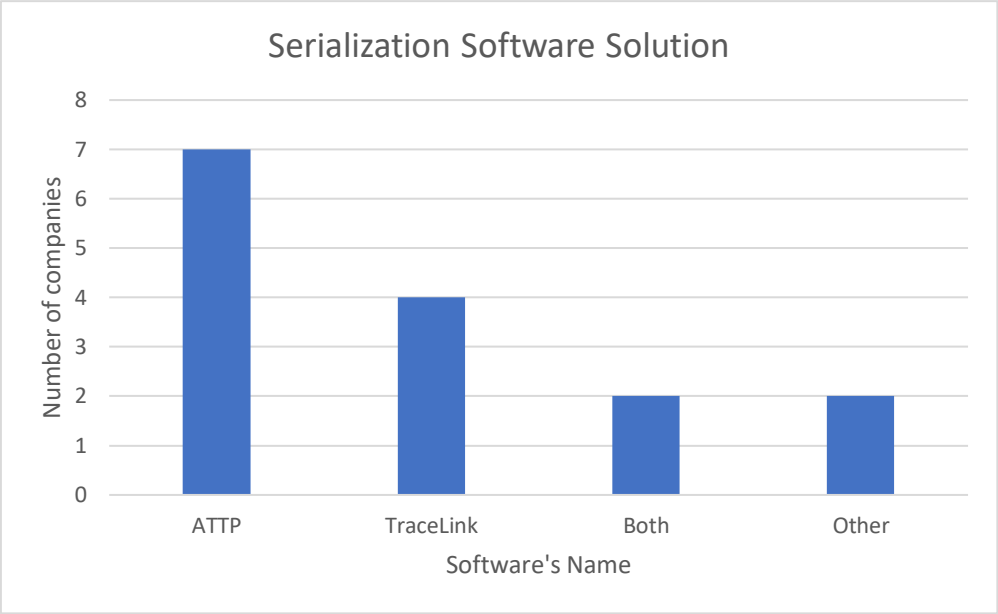


Figure 52: Software solution for the serialization system

Lifesaving medicines

As shown in figure 53, 44.44% of manufacturers produce lifesaving medicines and 44.44% produce specific medicines for specific patients. 44.44% is considered a relatively high percentage, which supports the importance and significance of implementing a Track and Trace system in order to be able to protect patients from counterfeit medicines in general and to protect them from counterfeit lifesaving medicines in specific. People that are in need for lifesaving medicines are already in a very critical healthy situation, where their lives are dependent on a specific medicine in order to stay alive. Imagine if on top of that, they are given fake lifesaving medicines! The chances for them to live will then most probably be ZERO.

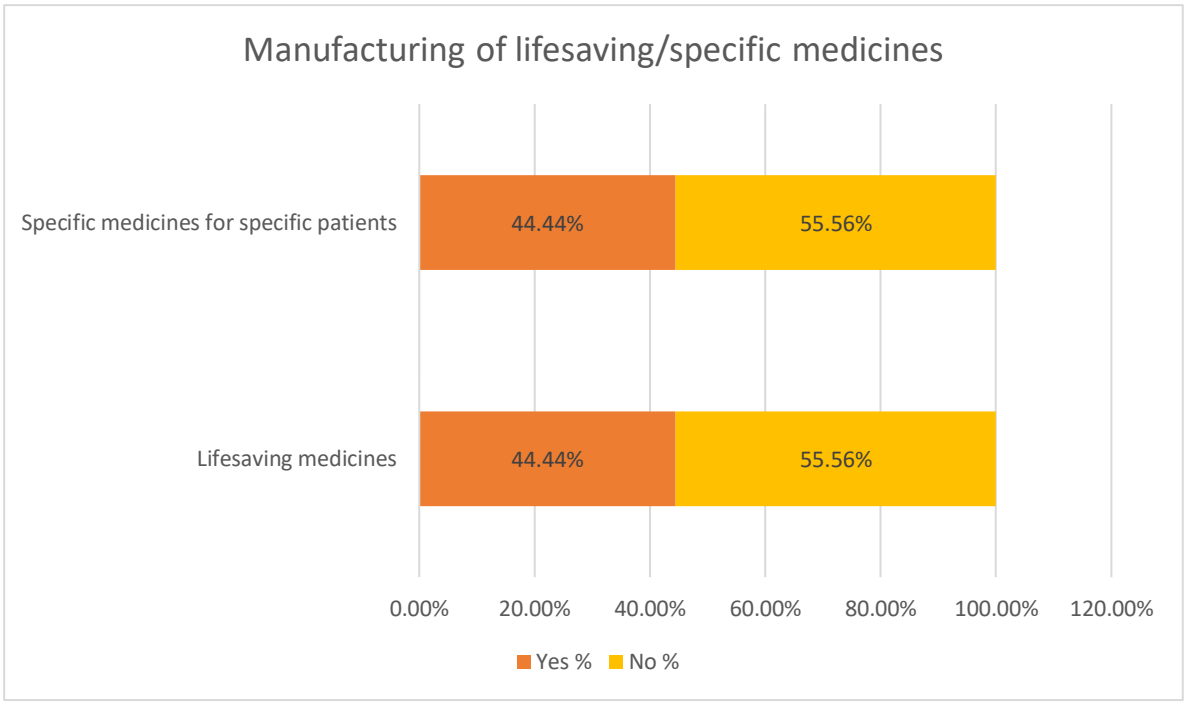


Figure 53: Percentages of manufacturing lifesaving and specific medicines for specific patients

Main driver for implementing a T&T system

As seen from figure 54, regulatory requirements were the main driver for all nine manufacturers to implement a Track and Trace system. 55.6% of participants implemented Track and Trace in order to protect their business and brand on the long run. 22.2% of participants implemented Track and Trace as a proactive approach to prevent potential infiltration of counterfeit, stolen or diverted products and 22.2% of participants implemented it for the purpose of gaining greater supply chain information and transparency. As it is in human nature, people usually tend to get things done only when they are obliged to or when they have a specific deadline. A pupil for example, does his/her homework only if forced and only if there is a consequence for not doing it. However, a pupil who wants to benefit and learn more would do his/her homework even if not forced to. Same concept applies here. There were some manufacturers that decided to do their homework and implemented Track and Trace in advance, not only because they were forced to, but in order to benefit from it as well. While other manufacturers implemented it only because they were forced to and because the consequence of not implementing it meant that

they won't be able to sell their products anymore and therefore won't be able to profit and gain money anymore. The difference between a pupil and a manufacturer in this case is that failing in reducing or preventing drug counterfeiting means failing in protecting patient's health and failing in ensuring patient safety.

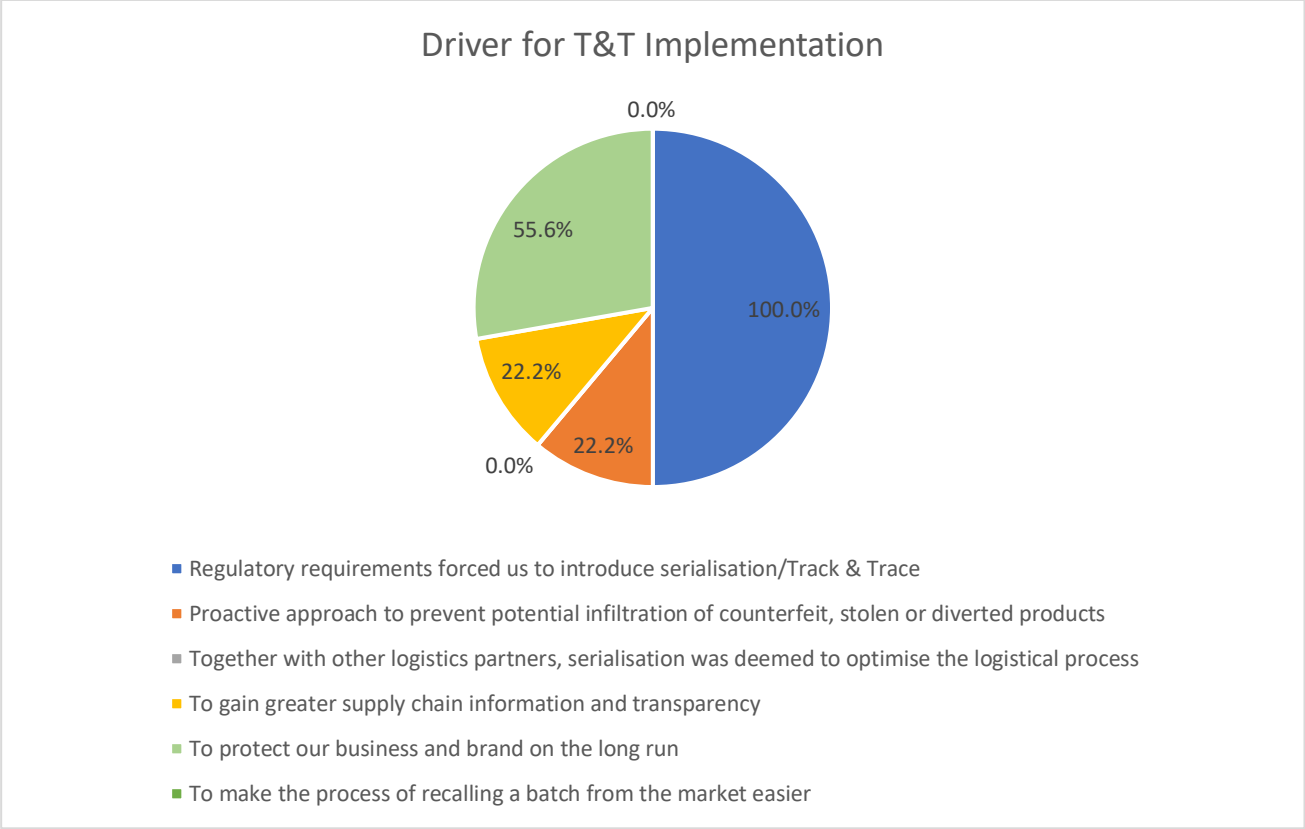


Figure 54: Driver for Track and Trace implementation

The nine participants were also asked whether they had any experience with any counterfeited, stolen or diverted products and surprisingly, five out of nine answered "yes", three answered "no" and one did not know the answer to this question. This means that 55.56% of the pharmaceutical manufacturers experienced such incidents, which supports the importance of implementing a Track and Trace system not only because the regulation says so but also to prevent drug counterfeiting, stealing or diversion and eventually ensure patient safety.

Effects and benefits of implementing a T&T system on the manufacturer

As figure 55 illustrates, all nine participants agreed on two effects as a result of introducing T&T system in their companies:

1. More IT intervention is needed since dealing with serial numbers.
2. Serialization has brought in increased complexity for the manufacturers and for their supply chain partners.

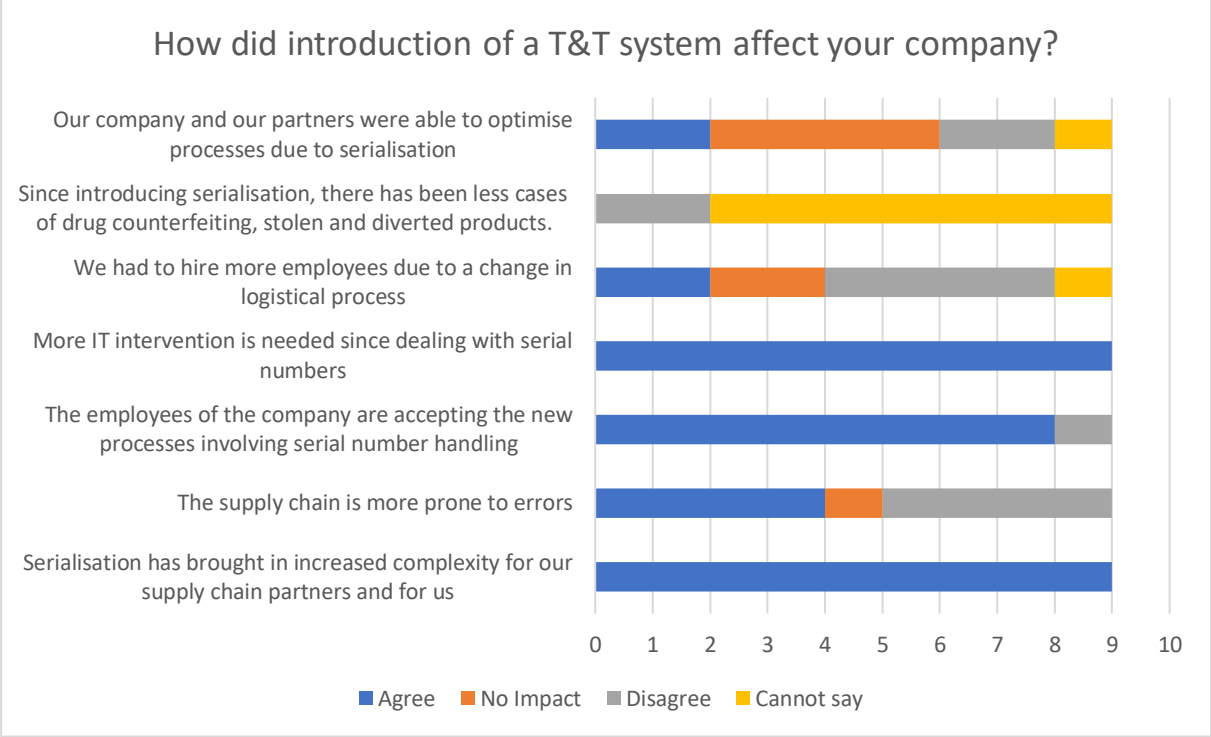


Figure 55: How did the introduction of a T&T system affect manufacturers

With regards to serial numbers and in order to understand the complexity it brings to a company as mentioned above, the manufacturers were asked about the number of serial numbers that they issue per year. The results are shown in table 34.

Table 34: Number of serial numbers issued per year by each manufacturer.

How many serial numbers do you issue per year?	Number of manufacturers
1 - 5 million	1
20 - 80 million	4
5 - 20 million	1
Less than 1 million	1
More than 80 million	2

Four out of nine issue 20 – 80 million serial numbers per year and two of them issue more than 80 million serial numbers per year. This is a huge amount of data that needs to be handled and managed properly, which is one of the reasons why participants answered that serialization increased complexity for them and for their supply chain partners.

Eight out of nine participants agreed that the employees of the company are accepting the new processes involving serial number handling. While one participant disagreed.

Regarding this impact "Since introducing serialization, there has been less cases of drug counterfeiting, stolen and diverted products", seven out of nine could not answer this question and two disagreed about this impact. In order to get a proper and accurate answer to this question, it needs to be asked to the governments or to the health authorities because they would have the required information. Additionally, since Track and Trace has been only recently introduced into the pharmaceutical industry, it might take some more time until they can do proper research and statistics about the impact of T&T on reducing drug counterfeiting.

Figure 56 shows that the one benefit that all manufacturers agreed on from implementing a T&T system, was "Improve supply chain visibility", where five participants considered it as a significant benefit and four considered it as a minor benefit. This is basically the concept of Track and Trace as explained in section 2.2, that it is able to track a pharmaceutical product

along the supply chain and know at any point what is that product, where is it, where did it come from, what event happened to it (e.g., packing, shipping, recalling) and when did that event happen. This is achieved by having a barcode on the product for identification, which captures and carries specific information about the product such as serial number, GTIN, expiry date and lot number. The specific product related information and events are shared and exchanged between supply chain partners and with the government, allowing full visibility and transparency of the drug movement within the supply chain until it reaches the patient.

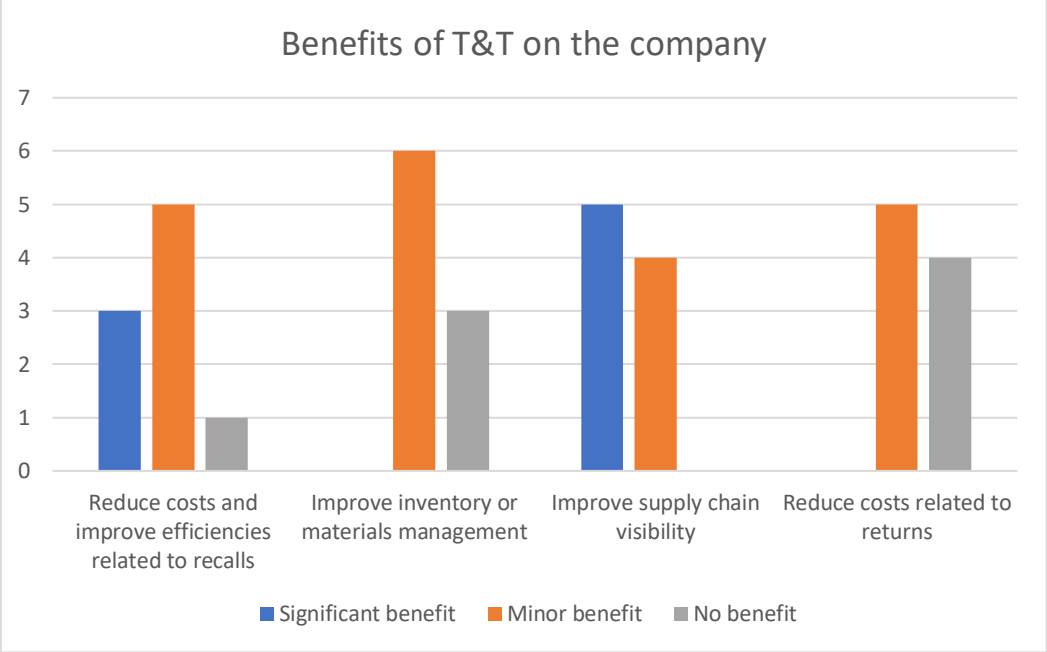


Figure 56: Benefits of T&T on the company

Three out of nine participants found that Track and Trace had a significant benefit on reducing costs and improving efficiencies related to the recall process, which is one of the advantages of the T&T system as mentioned in section 2.2.5. Five participants answered that it had minor benefit and one participant answered that it had no benefit.

Another 2 benefits asked about were “Improve inventory or materials management” and “Reduce costs related to returns”, where some participants had a minor benefit from both, and some had no benefit from either of them.

When asked about the effect of T&T implementation on daily operations, eight out of nine participants answered that it did indeed affect their internal operations, production, distribution activities and interaction with wholesalers, as seen in figure 57. This supports what has been explained in section 2.2.4 how a serialization project involves interaction between different departments and supply chain stakeholders and affects daily operations. Whether it's having new SOPs or new team structure and teamwork, or additional check-ups and testing, all of these activities affect normal daily operations.

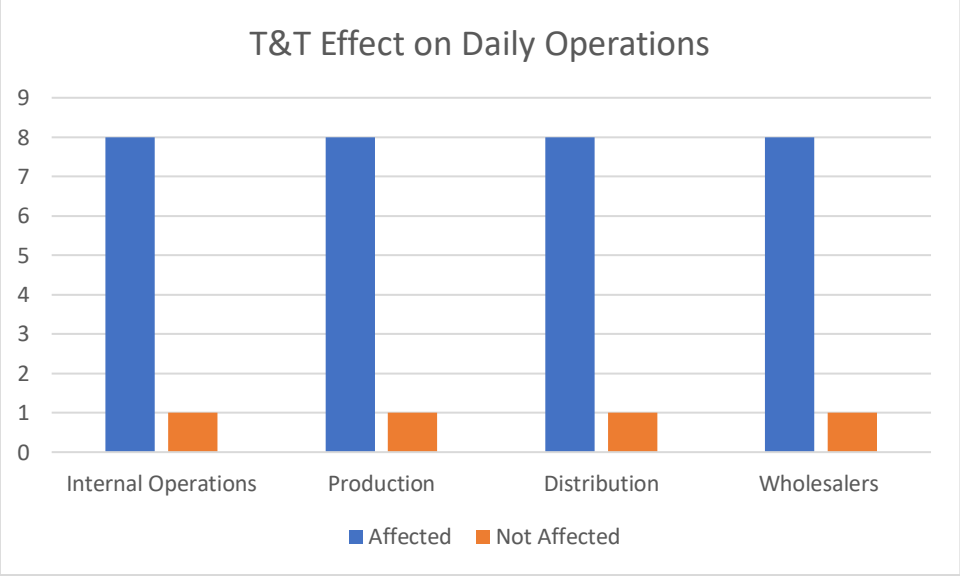


Figure 57: Benefits of T&T on the company

Satisfaction of manufacturers with implementing a T&T system and their opinions about it

As seen in figure 58, all participants agreed that they received helpful support in a timely manner when they needed it.

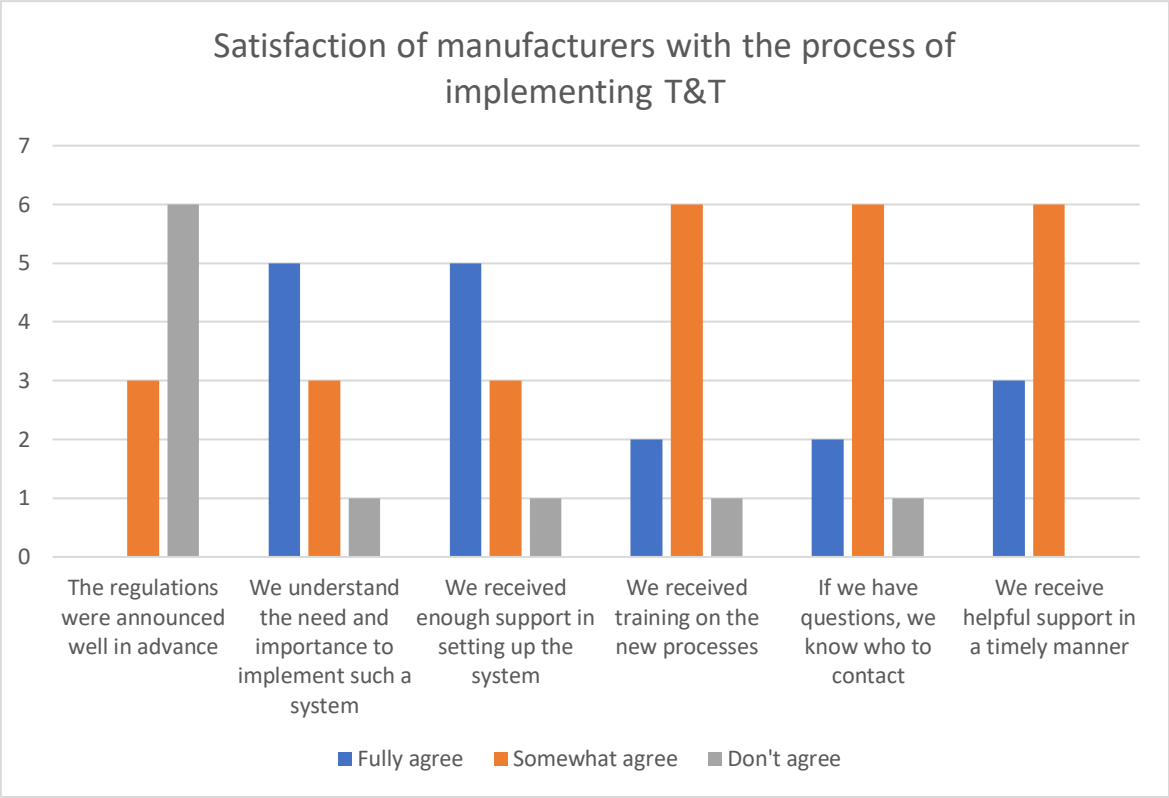


Figure 58: Satisfaction of manufacturers with the process of implementing T&T

Many participants (6 out of 9) disagreed about having the regulations announced well in advance, three out of nine somewhat agreed. This goes back to the same issue previously discussed about governments not publishing clear regulations or clear timelines which poses a challenge on manufacturers in the implementation of such a system.

Eight participants agreed that they understand the need and importance of implementing a Track and Trace system, while one of them disagreed.

Most of the participants agreed that they received enough support and trainings throughout the implementation phase.

Figure 59 illustrates the opinions of the nine participants about what would be affected by having a T&T system in place. One thing that all participants agreed about is that T&T improves increased data sharing across the supply chain. Most participants also agreed that T&T improves the following:

1. Prevent insertion of counterfeit drugs into the legitimate supply chain.
2. Prevent reintroduction of stolen drugs into the legitimate supply chain.
3. Prevent reintroduction of diverted drugs into the legitimate supply chain.
4. Improve public health by strengthening the distribution system's ability to safeguard medicines.

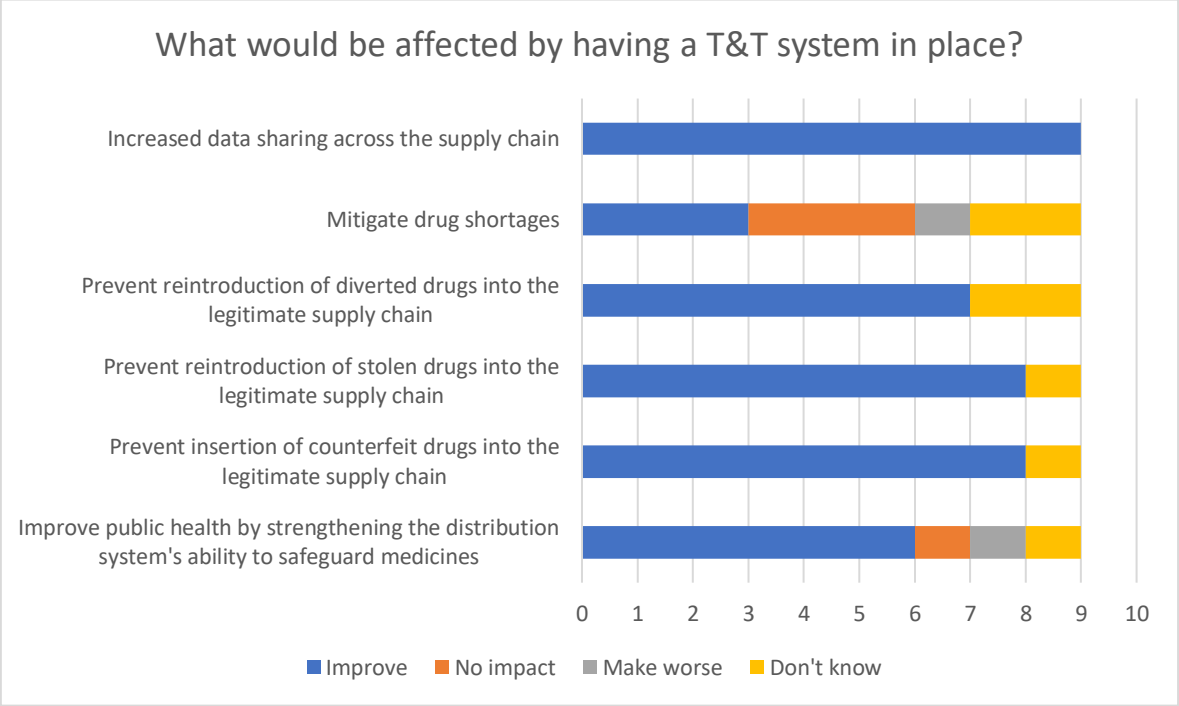


Figure 59: What would be affected by having a T&T system in place, according to participant's opinions

In terms of mitigating drug shortages, opinions were split between three that answered "improve", three answered "no impact", one answered "make worse", two answered "don't know". It would be more correct and accurate to ask this kind of question to the government's health authorities as they would have a better overview and understanding in this area.

When asked the following question: "On a personal level, do you have any concerns about consuming, buying or selling a counterfeit product?", seven of them answered that yes, they do have concerns, while 2 answered that they do not have such concerns.

For those who answered yes, the following additional question was asked: “If yes, does having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell?”. There were four interesting answers which are presented below (copied as is):

Answer 1: “Personally, YES. However, the majority of the patients across the world are not even aware of the T&T regulations and their impact on the authenticity of pharmaceutical products – therefore this question can only by answered (in a proper way) probably by a very small group of people.”

Answer 2: “Yes, but even before serialization, official supply chain within EU was quite well protected.”

Answer 3: “In a certain way, YES. There is always not the fully 100% trusted process, but with clear rules for Serialization with Aggregation of data along the Supply Chain it will be much safer for the patients. In hospital I’m always checking the products and I’m happy to find our products or other pharmaceutical companies with a Data Matrix Code.”

Answer 4: “In short, yes. The idea and philosophy behind a serialization system is right. But its implementation and monitoring are hard work.”

4.2.2 Wholesalers

Export market and types of serialization systems depending on country’s regulations

Figure 60 illustrates the export market of the three wholesalers, where it shows that the three main export markets of the three wholesalers were Russia, EU and Saudi Arabia.

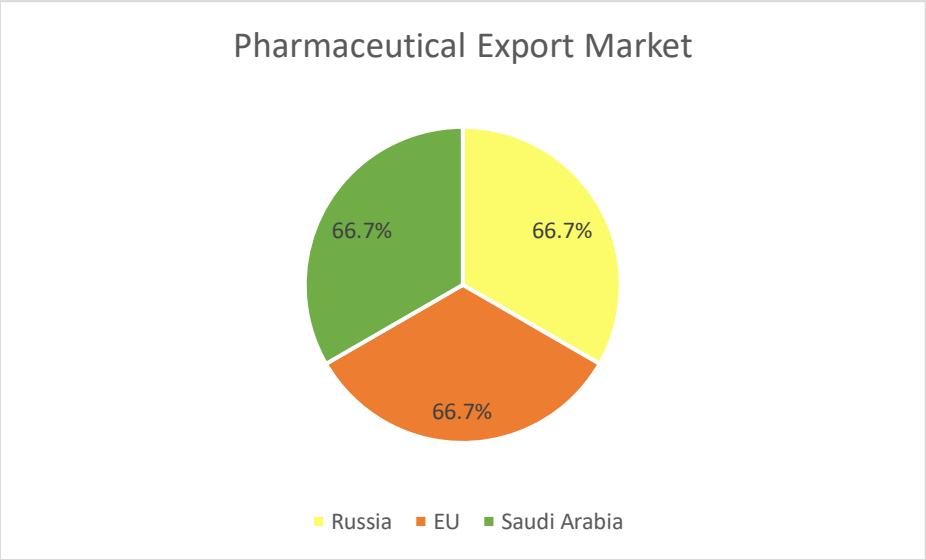


Figure 60: Export market of the 3 participating wholesalers

As seen from table 35, all three countries already have T&T system in place, therefore the three wholesalers were obliged to implement T&T system according to mentioned timelines to be able to proceed exporting products to these countries. As mentioned in section 2.2.3, each country has different regulations and requirements, which means that the three wholesalers had to implement three different requirements to comply with the different regulations of Russia, EU and Saudi Arabia separately.

Table 35: Status of serialization in different countries of the wholesalers' export market.

Country	Serialization Status
Russia	Serialization was implemented since July 2020
EU	Serialization was implemented since 09.02.2019
Saudi Arabia	March 2017 → Serialization was implemented. August 2020 → Aggregation was implemented.

Internal Challenges faced during the implementation of a T&T system

As seen in figure 61, all three wholesalers agreed that definition of system architecture and integration with existing systems is considered as a medium challenge. Also, all three

wholesalers agreed that they did not face a challenge of having T&T as a low priority in their companies, meaning that they were well aware of the importance and priority of having a T&T system in place.

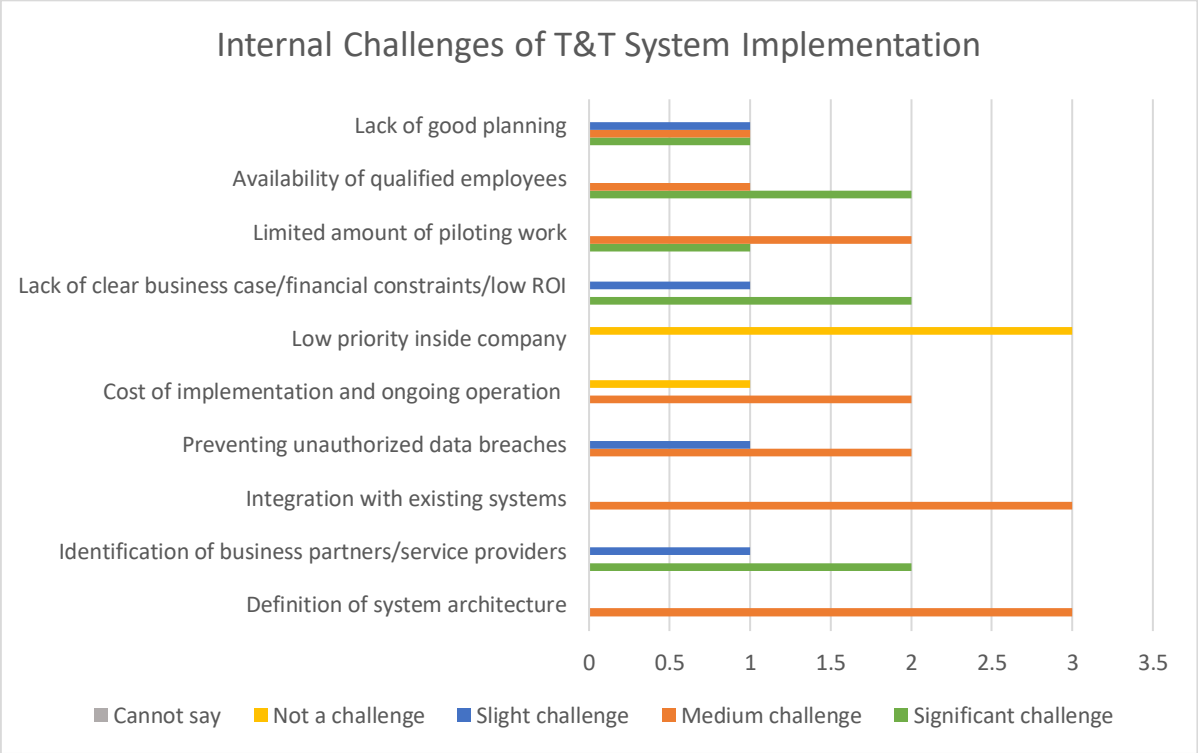


Figure 61: Internal challenges faced during T&T implementation

The following three challenges were considered as significant challenges for two wholesalers:

1. Identification of business partners/service providers.
2. Lack of clear business case/financial constraints/low ROI.
3. Availability of qualified employees.

Two wholesalers faced a significant challenge due to limited amount of piloting work and lack of good planning.

As part of studying the internal challenges, wholesalers were asked whether they had a dedicated team for serialization and the reason for having/not having a dedicated team. Additionally, they were asked whether they hired any external companies or consultants to help them with the T&T implementation. The results are shown in tables 36 and 37 (copied as is).

Table 36: Results about having a dedicated team for serialization.

Question	Wholesaler 1	Wholesaler 2	Wholesaler 3
Did you have a dedicated serialization team?	No	No	Yes
Please specify your reasons for establishing/not establishing a dedicated serialisation team?	The management did not want to spend further money on serialisation. This led to the fact that the project management got sucked in to Hypercare way too long and effectively could not leave the project due to issues popping up daily.	The resources are not available.	For master data maintenance and working with EPICS files for our suppliers.

Table 37: Results about hiring externals to support in T&T implementation.

Question	Wholesaler 1	Wholesaler 2	Wholesaler 3
Did you hire any externals to support you with the implementation?	No	No	No

Question	Wholesaler 1	Wholesaler 2	Wholesaler 3
If no, would hiring an external company have been useful to you?	Yes	Yes	No
Comments	We clearly lacked people who have implemented such a solution in a 3PL environment before, which caused time delays and cost explosion as all of us had to teach ourselves on how to implement serialization. In hindsight there would have been many things to improve on and a guiding hand from an external would have helped.	Our sister companies are CMOs therefore we got very useful insights as well as some shared resources during the project. Otherwise, we probably would have gotten external assistance.	-

In order to evaluate how much time did it take for wholesalers to implement serialization, they were asked to give time estimations. Table 38 reveals the results.

Table 38: Time estimation for serialization implementation.

How long did it take to implement serialization?	Wholesaler 1	Wholesaler 2	Wholesaler 3
EU	12 - 18 months	6 months or less	-
Russia	6 - 12 months	6 months or less	-
Saudi Arabia	6 - 12 months	NA	6 months or less

As seen from table 38, the time needed to implement a T&T system varies significantly depending on the regulations, requirements, company's size, availability of expertise, availability of budget etc., as explained in section 2.2.4.6.

External Challenges faced during the implementation of a T&T system

As seen in figure 62, two wholesalers faced a significant challenge in coordination with supply chain partners and complying with different countries' requirements.

Two wholesalers agreed that the following five challenges were considered as a medium challenge:

1. Lack of clear regulatory requirements
2. Lack of immediate mandate
3. Lack of standard system architecture
4. High cost of system components
5. Lack of clear standards for interoperable data exchange

One wholesaler faced a significant challenge due to unavailability of qualified contractors/service providers.

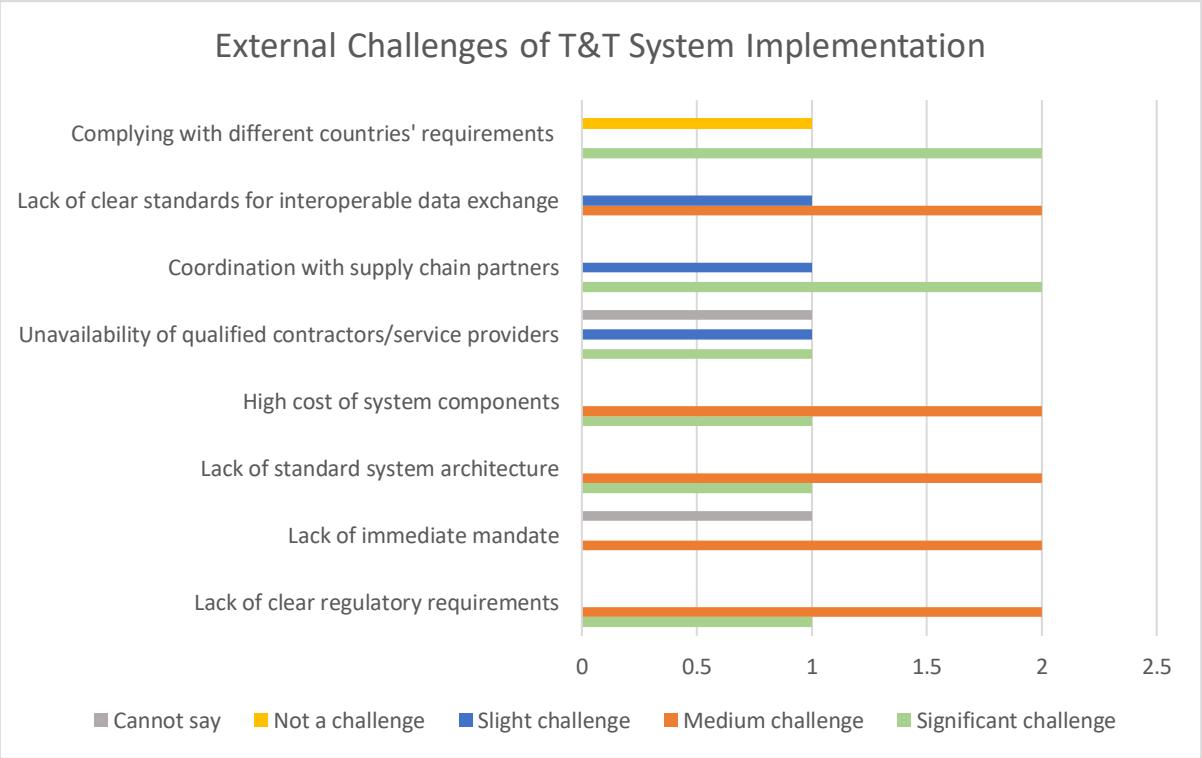


Figure 62: External challenges faced during T&T implementation

Further Challenges

The three wholesalers were asked to describe in detail the top three challenges (regardless whether internal or external) that they faced during the implementation of a Track and Trace system. The results were copied as is and revealed in tables 39, 40 and 41.

Table 39: Top three challenges faced by wholesaler nr.1 during T&T implementation.

Challenge	Root Cause
A standard solution could not be rolled out across to all customers	Every client is set-up differently in its SAP structure which does not allow to install a standard solution
Lack of interest from senior management led to little understanding of challenges and	Serialisation was seen as a burden which only brings cost to the organisation but no extra value

Challenge	Root Cause
frustration within the project team as they did not feel recognised enough	
Different country requirements came in one by one rather than all by one. We designed the system in a certain way which was then difficult to add another country requirement to the existing logistical process	We first adapted only to EU and then the Russian and Saudi Arabian system was a bit different in terms of requirements (no verification, aggregation needed). We struggled to integrate that into one system

Table 40: Top three challenges faced by wholesaler nr.2 during T&T implementation.

Challenge	Root Cause
Availability of qualified employees	In a Subject Matter Expert (SME), the resources available are always small, as the overhead costs need to be as small as possible. The then get people that have the capacity to dig into a topic such as serialization without constant interruptions from daily business is nearly impossible
Limited amount of piloting work	Internal as well as external uncertainty created a moment in which everyone was waiting for instructions. Therefore, it was not able to properly test together with clients. Also, CMOs are contracted to our clients, not to us. Their willingness to give us data for testing purposes was very limited.
Integration with existing systems	Integration in the system was a black box for us. In the end, everything worked out but with a delay of some weeks

Table 41: Top three challenges faced by wholesaler nr.3 during T&T implementation.

Challenge	Root Cause
Partner's onboarding (our suppliers and customers)	NA
Regulatory reporting	NA
Finding an implementation partner	NA

Figure 63 shows which software solution is used by wholesalers for the serialization system. The results were split equally between SAP ATTP (1 wholesaler), TraceLink (one wholesaler) and other system (one wholesaler). As mentioned previously, having different systems between different supply chain partners adds a challenge in system integration and connection.

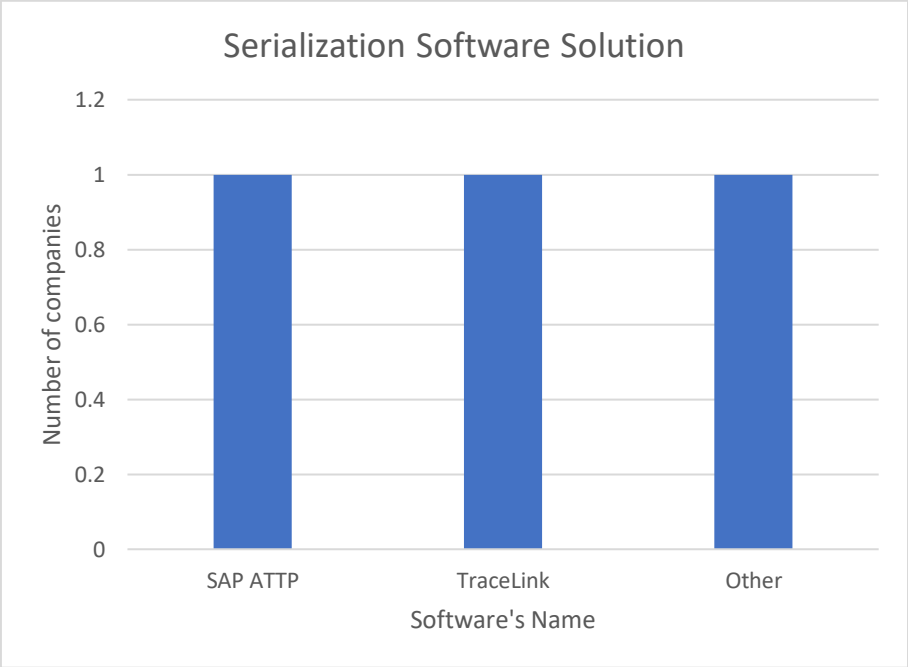


Figure 63: Software used for the serialization system

Main driver for implementing a T&T system

When asked about the reason for implementing a Track and Trace system, all three wholesalers answered that they had to implement it due to regulatory requirements.

Effects and benefits of implementing a T&T system on the manufacturer

As shown in figure 64, all three wholesalers agreed that the impact of T&T was that the logistics process became more complex as a result of the serialization requirements.

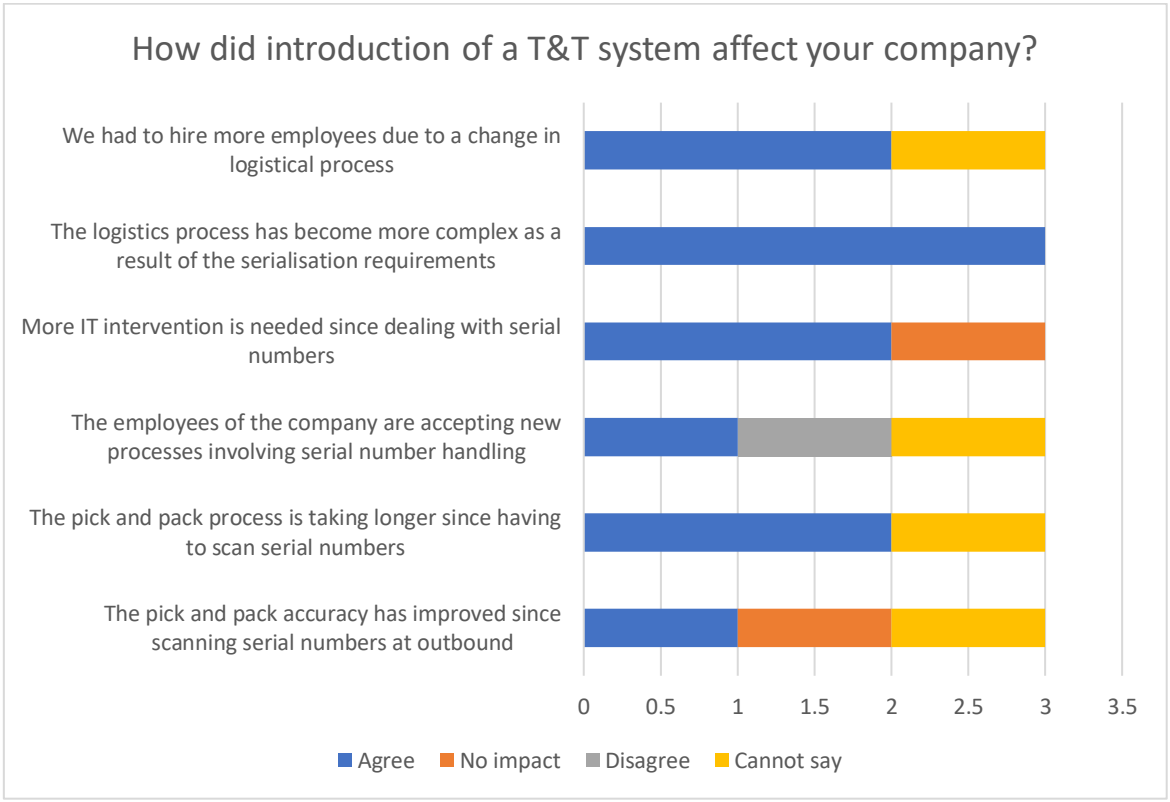


Figure 64: How did the introduction of a T&T system affect wholesalers

At least one of the three wholesalers agreed that T&T had the following impacts:

1. The pick and pack accuracy has improved since scanning serial numbers at outbound.
2. The pick and pack process are taking longer since having to scan serial numbers.
3. The employees of the company are accepting new processes involving serial number handling.
4. More IT intervention is needed since dealing with serial numbers.
5. More employees were hired due to a change in logistical process.

Satisfaction of manufacturers with implementing a T&T system and their opinions about it

Table 42 reveals the opinions of wholesalers when asked whether they were satisfied with the T&T system or not.

Table 42: Satisfaction of wholesalers with T&T system

Question	Wholesaler 1	Wholesaler 2	Wholesaler 3
In general, are you happy that a T&T system was introduced?	No	Yes	No
Could you please clarify in simple words why yes or why not?	Although we understand the necessity for us this system has brought cost and additional efforts and reduced our productivity	As counterfeits are increasing in all fields of consumer products, it totally makes sense to introduce a security net to make a potential counterfeit more difficult and higher the burden to enter the black market with officially scrapped products. So yes – I think it was a good idea	-

4.2.3 Pharmacies

Awareness about serialization

When pharmacists were asked if they were familiar with Track and Trace / serialization, all 8 pharmacists answered that yes, they were familiar with it. This was the expected response considering that serialization was implemented in EU since 09.02.2019 and considering that the concept of the EU serialization is “Point of Dispense Verification” as explained in section 2.2.3.4. This means that the pharmacist needs to scan the 2D Data Matrix Code to verify the authenticity of the medicine before dispensing it to the patient. If the received response is a positive verification, meaning that the medicine is genuine and not expired or recalled etc., then the pharmacist dispenses the medicine to the patient. If the received response is a negative response, meaning that the product is either fake or expired or recalled, etc., then the pharmacist will not dispense the medicine to the patient and will have to investigate further before making any decision regarding that specific medicine.

Serialization implementation

When pharmacists were asked about the way that they were informed about serialization, some answered that they were informed about the serialization regulation from an association (e.g., Austrian Chamber of Pharmacists), while others answered that they were informed from a regulatory body. In both cases, pharmacies were informed in advance about the introduction of the serialization regulation and system.

When asked about the responsible party for serialization implementation and costs, most of the pharmacists answered that the pharmacy was responsible for the implementation and the costs. Some of them, however, were not able to answer this question.

Affect of serialization on daily operations

Pharmacists were asked whether they have been given instructions on how to handle special cases such as negative verifications, non-readable barcodes, etc. Table 43 reveals the results for this question showing also comments that were provided by the pharmacists (comments were copied as is).

Table 43: Instructions for pharmacies on how to handle exception cases.

	Given instructions?	If yes, provide more information
Pharmacy 1	No	We never had that.
Pharmacy 2	Yes	The most frequent case is that we do not have a connection to the database. We then hand out the product anyway.
Pharmacy 3	Yes	We hardly have exception cases and most of the times it is the system being offline. In case of exceptional cases, we just take a different unit. Especially as we verified it previously it can only be down to an offline system.
Pharmacy 4	No	Not really – still not sure what has to be done if the QR code is not readable or negative.
Pharmacy 5	Yes	Negative verification has to be checked if damaged or already used.
Pharmacy 6	Yes	Check why negative verification, often errors when reading the QR code, i.e., use another computer and thus another scanner. Or the pack was inadvertently booked out too early in another work step in your

	Given instructions?	If yes, provide more information
		own pharmacy. If the verification is really negative, sort out the package, check it again in the next few days, if remains negative, report pack.
Pharmacy 7	Yes	-
Pharmacy 8	Yes	-

As seen in table 43, six out of eight pharmacies received instructions on how to handle exception cases, whereas two pharmacies did not receive any instructions. Three pharmacies answered that they hardly had any exceptional cases and if they did then it's mostly related to an issue with the system rather than a real issue with the medicine itself. Additionally, if and when a product has a negative verification upon scanning, pharmacists need to check first the reason for this negative verification before reporting the product to the health authorities.

Pharmacy number 2 answered that they hand out the product anyway even if they received a negative verification. Upon more clarification during the interview, the pharmacist explained that the products are scanned upon receiving them from the distributor, and then they are scanned again before dispensing them to the patient. The pharmacist also mentioned that the issues that they had so far were always with the system, sometimes the connection to the database would be disrupted for a couple of minutes or even seconds. If they have any suspicions then they do not dispense the medicine to the patient, however, so far, they did not have any issues with any fake medicines.

Figure 65 shows the frequency of getting a negative verification in daily operations. Four pharmacies never had negative verifications. One pharmacy has negative verifications every week, two pharmacies have negative verifications once or twice a month and one pharmacy has

it once or twice a year. The negative verifications were mainly related either to a non-readable barcode or to an issue with the system.

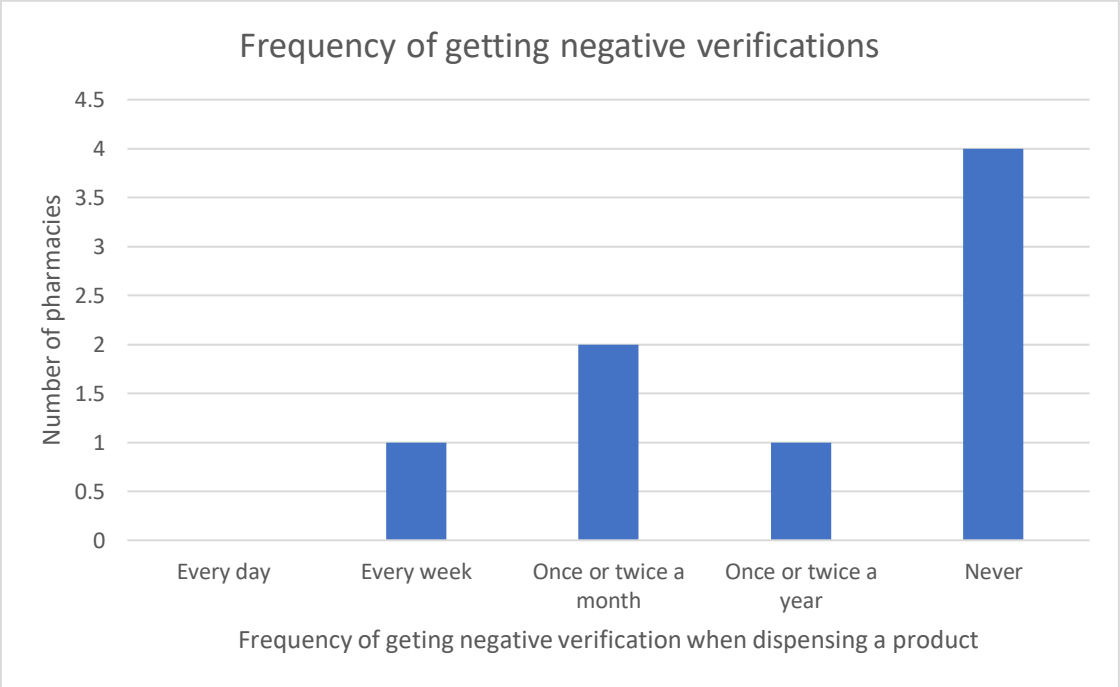


Figure 65: Frequency of getting negative verification upon scanning a product

In general, all eight pharmacies did not experience any negative verification, which was caused from a fake product.

The next question asked to the pharmacies was, who do they notify when they get a negative verification. The results are shown in table 44.

Table 44: Who do pharmacists notify when they get negative verifications.

	Who do you notify when you receive negative verifications?
Pharmacy 1	-
Pharmacy 2	If we receive negative verifications, it will be stored by the system automatically.
Pharmacy 3	This case has never happened, so I do not really know.

	Who do you notify when you receive negative verifications?
Pharmacy 4	If a negative verification occurs, we ask the Austrian chamber of pharmacists what has to be done correctly.
Pharmacy 5	-
Pharmacy 6	As far as I know, an automatic message is triggered in the Securpharm system. Notification to the competent authority.
Pharmacy 7	This case has never happened, so I do not really know.
Pharmacy 8	-

As seen from table 44, three pharmacies were not able to answer the question. Two pharmacies did not experience a negative verification, so they did not know what needs to be done in case it happens. Two pharmacies answered that it will be stored in the system automatically and one pharmacy answered they contact the Austrian Chamber of Pharmacists to get instructions on what to do.

In general, the impression that I got from the pharmacies, especially from the three interviews which I was able to have face-to-face, is that pharmacists did not seem to have experience with fake products and therefore did not know really know what needs to be done in case they face such an issue. Additionally, I got the impression that they do not really care what needs to be done since they are convinced that they won't have fake products. The scanning and verification step was more of a burden to them, especially that they have more steps and processes in place and more investigations need to be done in case of any negative verification. They cannot simply decide to dispense products with negative verifications, they have to investigate first, check and only then decide whether the product can be dispensed or not. The issues that they had were more related to having an issue with the system (e.g., system is offline) rather than having an issue with a fake product.

Satisfaction of pharmacies with implementing a T&T system and their opinions about it

Figure 66 reveals the satisfaction of pharmacies with having a Track and Trace system in place. Six out of eight pharmacies fully agreed that the regulations were announced well in advance. Five pharmacies agreed that they do understand the need for having a T&T system in place (1 fully agrees and 4 somewhat agree), whereas three pharmacies did not agree and do not understand the need for having such a system. Most pharmacies agreed that they received the help and support needed to implement the system and that they know who to contact in case they need any help or support.

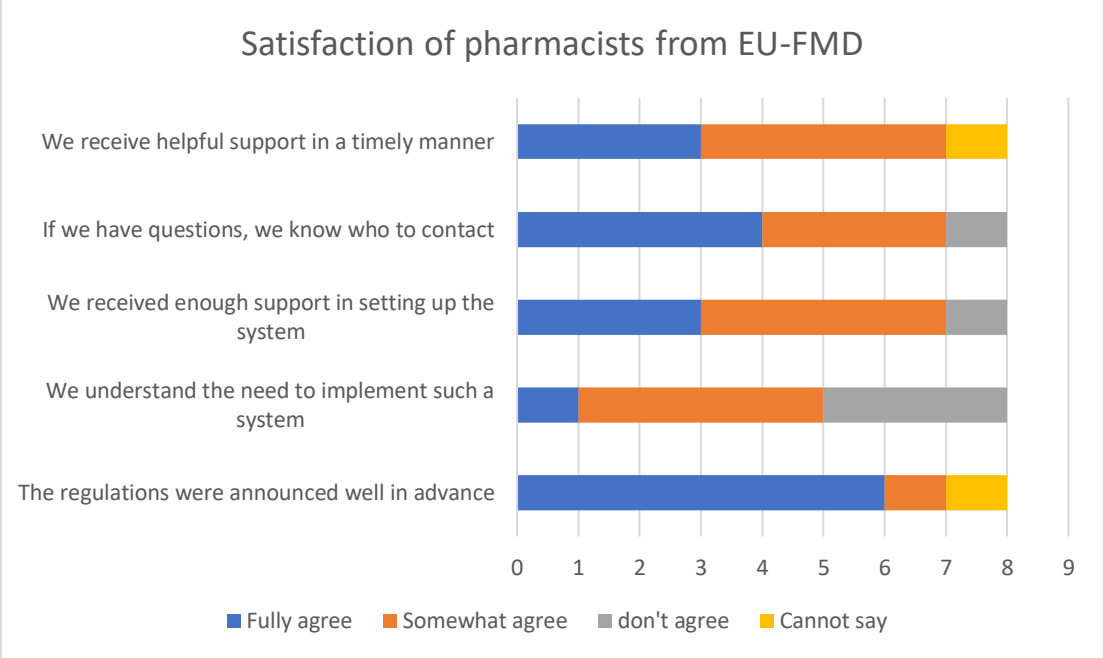


Figure 66: Satisfaction of pharmacies from EU-FMD

Pharmacies were asked, what things they found successful about serialization. I was able to get the following two answers:

1. It can be recorded if someone brings in falsified medicine.
2. Idea is important but realization is not optimal.

Pharmacies were then asked, what are the things that they think need to be improved. Below are their answers (copied as is):

1. We face a problem when we hand out and decommission the medicament to the patient and the patient then says it is the wrong one or he does not want to buy it. The product is then decommissioned and hence cannot be sold again and is thrown away.
2. At weekends when supplying care homes or homely patients we often break down a big pack of a medicament as they often need little quantities (e.g., only 20 of 100 blisters). This is now not possible anymore as the units are now sealed with a temper-evident seal.
3. Scanning and feedback takes too long.
4. Verification of the authenticity of the medicaments should be done a couple of steps before reaching the pharmacy or the pharmacist – pharmacists should double check, but the system should be optimized regarding the time-consuming method – it should be enough to be checked by the pharmacy assistants on arrival!!!
5. To get response from the Securpharm system also on Saturdays.
6. Use the system only for expensive drugs.
7. Every product should be serialized.
8. It is very tiring that each product needs to be scanned 3 times.

In summary, as mentioned before, serialization is considered more of a burden on pharmacists rather than an improvement. They need to scan the product several times (when arrived and when dispensed) and they seem to face some issues with the system, which causes delays to their daily work. Some of them complained that when the system is offline or not working, patients have to wait until the system is back and not all patients have patience, which causes them stress at work.

4.3 Comparison between Palestine and Europe

It's a bit difficult to compare between Palestine and Europe since Track and Trace is not enforced as a regulation in Palestine yet, whereas in Europe, it has been already implemented since 09.02.2019.

Most Palestinian pharmaceutical companies did hear about serialization or did have initial plans to implement it but according to the interviews held with them, they were still lacking knowledge about it and they also had little interest in it. They were not aware yet of the magnitude of such a project, its challenges and effects. Additionally, the Track and Trace regulations keep postponing, like in Jordan for example, therefore they did not have the chance yet to dig deep into Track and Trace and learn more about it. I'm hoping that this research might help Palestinian pharmaceutical companies to learn more about Track and Trace and be able to plan its implementation accordingly.

As for pharmacies and wholesalers in Palestine, almost all of them did not have any idea about serialization and did not even hear of it, which makes it more challenging. Proper awareness and knowledge need to be provided for all supply chain stakeholders when the time comes for Palestine to have a Track and Trace system in place.

The situation in Europe was different, all supply chain stakeholders were already aware of serialization and were working with the system on a daily basis. However, not all of them were convinced that having such a system in place will help in fighting drug counterfeiting. To some extent, I agree, as Track and Trace on its own is not expected to completely prevent drug counterfeiting, it is just a tool that helps in reducing drug counterfeiting. Nevertheless, since there is such an advanced technological tool that might facilitate in reducing drug counterfeiting and might save patients from consuming fake medicines, then why not take the advantage of it and use it? Anything that helps in ensuring patient safety is worth the try, especially if it works

properly and has good effect. Additionally, this strengthens the urge to educate people about counterfeit medicines and their impact on our lives.

5. Chapter Five – Conclusion

We have seen that almost all types of drugs in so many different countries worldwide are being counterfeited even lifesaving ones, which is putting people's health at risk. Therefore, it is very crucial for governments to develop and enforce an anti-counterfeiting regulation such as Track and Trace / serialization, which helps in reducing drug counterfeiting and ensures patient safety. A Track and Trace system is a highly secure system which protects the pharmaceutical supply chain from the entrance of any fake medicine by allowing the tracking of the movement of a medicinal product all along the supply chain from the manufacturer until it is dispensed to the patient, by using GS1 standards to identify, capture and share important product information. However, the implementation of such a system is usually complicated, challenging and involves lots of efforts, resources, time and money.

Track and Trace regulations and requirements might differ from one country to another, however, the main concept stays the same. Many countries worldwide have already implemented serialization such as Turkey and EU, while others are in the progress of implementing it such as Egypt and Lebanon. Other countries such as Palestine and Azerbaijan, still do not have any regulations or any plans to implement serialization.

The challenges related to the implementation of a Track and Trace system are usually underestimated. In this study, different regulations of different countries have been explained and the challenges related to implementing such a system have been discussed. It was seen from the results of the surveys of the pharmaceutical companies, wholesalers and pharmacies in Europe, how implementing a T&T system is indeed challenging from different perspectives and at the same time brings benefits for the company and for the patient.

The impression that I got from the results of the surveys of pharmaceutical companies, wholesalers and pharmacies in Palestine, is that the topic of drug counterfeiting is not given much attention, even though, it was seen from the results that pharmacies for example did

experience incidents of drug counterfeiting. Additionally, the implementation of a Track and Trace system and the challenges related to it were completely underestimated.

Track and Trace is a completely new topic in Palestine and my aim from this research is to emphasize the importance of fighting drug counterfeiting, to introduce Track and Trace into Palestine, explain it, clarify its advantages and disadvantages and to reveal all challenges related to it. In critical times such as the pandemic that we are currently facing, protecting the supply chain from the entrance of fake vaccines is extremely crucial. This urges the need for having an anti-counterfeiting technology in place to protect people from the consumption of fake vaccines and fake medicines.

Another impact of the pandemic is that the world is moving towards digitization and digitalization, which makes Track and Trace the perfect solution in a pharmaceutical industry. Instead of using a paper leaflet for example, e-leaflets could be used, which is the approach that Japan is taking.

To conclude, Track and Trace is the future of fighting drug counterfeiting and the future of obtaining all information that a patient needs about a specific medicine simply by scanning a 2D Data Matrix Code. Both companies and patients will benefit from this technology. Other countries in the world have already implemented serialization and are acting towards ensuring patient safety, why can’t we do the same?

6. Chapter Six – Recommendations and Future Work

Based on the outcome of this study, I would recommend the following for future work:

1. **Educate people about drug counterfeiting and raise awareness:** since the most important element of this whole topic is the patient or human health and since the main purpose of implementing a Track and Trace solution is to ensure patient safety, it is very vital to educate people and raise their awareness about the fact that counterfeit medicines exist. Unfortunately, many people worldwide are not aware of drug counterfeiting or are convinced that counterfeiting does not exist in their countries, like in Palestine for example. Others might not have the right means or knowledge to be able to differentiate between a genuine product and a fake one.

   A survey could be first conducted to study how aware / not aware people are about drug counterfeiting and based on the results, specific conferences, workshops, webinars, education courses or mobile applications could be provided to help people understand the importance of this topic and the risk of using falsified medicines. For example, there is a campaign called “Fight the Fakes”, which targets to raise awareness about the dangerous impacts of falsified medicines on our health, supporting those who have been personally affected and those working to stop this crime. The campaign seeks to build a global movement of organizations and individuals who will spotlight the complex, worldwide threat of falsified medicines and strive to reduce its negative consequences. A similar campaign could be launched in Palestine to shed light on the drug counterfeiting crime and its effects [80].
2. **Evaluate the situation from the government’s perspective in terms of efforts, investment and budget needed to launch and implement a Track and Trace program:** the needs of a pharmaceutical company differ from the needs of a government when it comes to implementing a Track and Trace system. It is complex

for both sides, however, it is even more complex for a government since it all starts with the government.

A survey could be conducted for different governments and health organizations worldwide to evaluate the efforts, investments, time, planning, etc. needed to implement a Track and Trace system. The results from this kind of survey and challenges faced in such a project, on a government level, could be then studied and shared with the Palestinian government and MoH to learn from other's governments experiences. It can be considered as "lessons learnt" so that the Palestinian government together with Palestinian supply chain stakeholders can join forces and together come up with a solution that fits the Palestinian health system and allows the protection of Palestinians from fake medicines.

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Appendices

Appendix 1 – Palestinian Pharmaceutical Manufacturer's Survey

Survey on Track and Trace / Serialization – Palestinian Pharmaceutical Companies

Company name:

Name of participant and department:

1. Are there any plans for serialization?
2. Did your Regulatory Affairs (RA) department receive any regulations about serialization from the Palestinian Ministry of Health (MoH)?
3. Do you have an export market? If yes, did you receive any requirements for serialization on products that are exported?
4. How many packaging lines do you have?
5. How many products do you have?

Appendix 2 – Palestinian Wholesaler's Survey

Survey on how Track and Trace / Serialization impacts 3PLs (3rd Party Logistics) and Wholesalers

Dear Participant,

As part of my master's thesis on "Pharmaceutical Serialization", I am conducting a survey to analyse how does the Track and Trace solution impact patient's health, pharmaceutical industries, business and related stakeholders. There will be 3 different surveys upon different types of participants (3PLs/wholesalers, MAHs/CMOs and pharmacies).

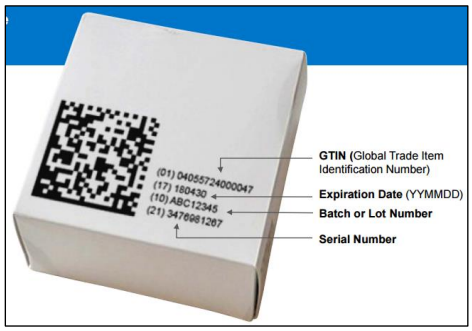
Your participation is voluntary, valuable and appreciated. The survey completion should not take more than 5-7 minutes. If you do not feel comfortable in answering certain questions, please just mark them and skip them. All answers collected from this survey will be exclusively used for my master's thesis only. Personal and company information will not be used without prior approval.

Please fill in the following information about yourself. This information will be used only to get some more clarifications or approvals if needed, it will not be collected as part of the thesis data.

Name	
Title/position	
Organization	
(Telephone)	
E-mail address	

Before starting with the survey, here's a short definition of serialization:

Serialization requires a comprehensive system to track and trace the passage of prescription drugs through the entire supply chain (from the manufacturer until the patient). This is accomplished by printing on each unit (of secondary packaging material) a 2D GS1 data matrix code incorporating GTIN (Global Trade Item Number), batch number, expiry date and serial number (unique identifier) as can be seen in the following figure:



1. Have you heard before about the new regulatory requirement "Track and Trace" / "Serialization"?

   ☐Yes ☐No

   If yes, did you already introduce serialization into your logistical process?

   ☐Yes ☐No

   If no, could you please say in a few words why not?

2. Did the Palestinian Health Authority contact you regarding the Serialization regulation?

   ☐Yes ☐No

3. From which pharmaceutical companies do you buy your drug products?

   ☐ Novartis

   ☐ Novonordisk

   ☐ Pfizer

☐ Hikma

☐ Birzeit Pharmaceuticals

☐ Jerusalem Pharmaceuticals

☐ Other, please specify below which other companies:

4. Are there any requirements from your partners/customers to do serialization?

☐Yes ☐No

5. Do your partners/customers do serialization on their products?

☐Yes ☐No

6. When preparing a delivery for a customer, do you use a mobile device/scanner to scan products into a system before picking and packing them into pallets or do you perform the pick and pack process manually? (please select what is applicable for you)

☐ We use a mobile device/scanner to scan products into a system before picking and packing them into pallets

☐ We perform manual pick and pack process

☐ Other, please specify:

7. If you are using a mobile device/scanner, could you please specify which device and which system are you using?

8. Did you ever have an incident where the shipment of drug products was stolen?

☐Yes ☐No

If yes, what did you do and how did you handle it?

9. Did you ever have an incident where the drug products which you bought or distributed were fake/counterfeit?

☐Yes ☐No

If yes, what did you do and how did you handle it?

10. On a personal level, do you have any concerns about consuming, buying or selling a counterfeit product?

    ☐Yes ☐No

    If yes, will having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell?

Appendix 3 – Palestinian Pharmacies Survey

Survey on how Track and Trace / Serialization impacts pharmacies

Dear Participant,

As part of my master's thesis on "Pharmaceutical Serialization", I am conducting a survey to analyse how does the Track and Trace solution impact patient's health, pharmaceutical industries, business and related stakeholders. There will be 3 different surveys upon different types of participants (3PLs/wholesalers, MAHs/CMOs and pharmacies).

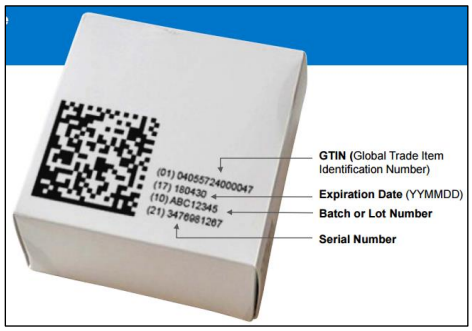
Your participation is voluntary, valuable and appreciated. The survey completion should not take more than 5-7 minutes. If you do not feel comfortable in answering certain questions, please just mark them and skip them. All answers collected from this survey will be exclusively used for my master's thesis only. Personal and company information will not be used without prior approval.

Please fill in the following information about yourself. This information will be used only to get some more clarifications or approvals if needed, it will not be collected as part of the thesis data.

Name	
Title/position	
Organization	
(Telephone)	
E-mail address	

Before starting with the survey, here's a short definition of serialization:

Serialization requires a comprehensive system to track and trace the passage of prescription drugs through the entire supply chain (from the manufacturer until the patient). This is accomplished by printing on each unit (of secondary packaging material) a 2D GS1 data matrix code incorporating GTIN (Global Trade Item Number), batch number, expiry date and serial number (unique identifier) as can be seen in the following figure:



1. Have you heard before about the new regulatory requirement "Track and Trace" / "Serialization"?

   ☐Yes ☐No

   If yes, did you already introduce serialization into your system?

   ☐Yes ☐No

   If no, could you please say in a few words why not?

2. Did the Palestinian Health Authority contact you regarding the Serialization regulation?

   ☐Yes ☐No

3. Who is the main supplier of your pharmaceutical products? Please write as many as possible.

Nr.	**Supplier**
1	

Nr.	Supplier
2	
3	
4	
5	

4. When scanning and dispensing a pharmaceutical product to a patient, do you get a notification on your system whether the product is authenticated/verified or not?

☐Yes ☐No

5. Did you ever have an incident where the drug products were stolen from your pharmacy or warehouse?

☐Yes ☐No

If yes, what did you do and how did you handle it?

6. Did you ever have an incident where the drug products which you bought from a supplier or sold to a patient were later on discovered to be fake/counterfeit products?

☐Yes ☐No

If yes, what did you do and how did you handle it?

7. Did you ever have an incident where a complete batch of a drug product had to be recalled and taken out of the pharmacy?

☐Yes ☐No

If yes, what did you do and how did you handle it?

8. On a personal level, do you have any concerns about consuming or selling a counterfeit product?

☐Yes ☐No

If yes, will introducing the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume or sell?

Appendix 4 – European Pharmaceutical Manufacturer's Survey

Survey on how Track and Trace / Serialization impacts MAHs (Marketing Authorization Holders) / CMOs (Contract Manufacturing Organizations)

Dear Participant,

As part of my master's thesis on "Pharmaceutical Serialization", I am conducting a survey to analyse how does the Track and Trace solution impact patient's health, pharmaceutical industries, business and related stakeholders. There will be 3 different surveys upon different types of participants (3PLs/wholesalers, MAHs/CMOs and pharmacies).

Your participation is voluntary, valuable and appreciated. The survey completion should not take more than 20-25 minutes. If you do not feel comfortable in answering certain questions, please just mark them and skip them. All answers collected from this survey will be exclusively used for my master's thesis only. Personal and company information will not be used without prior approval.

If you have questions or need further clarifications about this survey, please do not hesitate to contact me, Marlen Asbih (marlen.asbih@movilitas.com). Please fill in the following information about yourself. This information will be used only to get some more clarifications or approvals if needed, it will not be collected as part of the thesis data.

Name	
Title/position	
Organization	
(Telephone)	
E-mail address	

1. General

1.1 To which serialization/Track & Trace relevant countries do you produce/market your pharmaceutical products?

☐ Saudi Arabia

☐ Russia

☐ EU

☐ Turkey

☐ South Korea

☐ China

☐ USA

☐ Other (please specify)

1.2 What is the size of your company?

☐ Small, less than 100 employees

☐ Medium, 100 – 500 employees

☐ Large, more than 500 employees

1.3 Name 3 of your main pharmaceutical products:

Nr.	**Product's name**
1	
2	
3	

1.4 Do you manufacture or market lifesaving products?

☐Yes ☐No

If yes, name those products?

1.5 Do you have products which you manufacture or market in small quantities for specific patients with specific health conditions?

☐Yes ☐No

If yes, name those products?

2. Motivation/Background

2.1 Why did you introduce serialization into your supply chain? (multiple answers possible)

Reason	Applicable	Comment
Regulatory requirements forced us to introduce serialization/Track & Trace	☐Yes ☐No	
Proactive approach to prevent potential infiltration of counterfeit, stolen or diverted products	☐Yes ☐No	
Together with other logistics partners, serialization was deemed to optimise the logistical process	☐Yes ☐No	
To gain greater supply chain information and transparency	☐Yes ☐No	
To protect our business and brand on the long run	☐Yes ☐No	

Reason	Applicable	Comment
To make the process of recalling a batch from the market easier	☐Yes ☐No	
Other (please specify)		

2.2 Apart from drug counterfeiting, which additional benefits does your organization believe would result from implementing such a system?

	Significant benefit	**Minor benefit**	**No benefit**
Reduce costs and improve efficiencies related to recalls	☐	☐	☐
Improve inventory or materials management	☐	☐	☐
Improve supply chain visibility	☐	☐	☐
Reduce costs related to returns	☐	☐	☐
Other (please specify)			

2.3 Did your organisation have any experience with any counterfeited, stolen or diverted products?

☐Yes ☐No

If yes, please provide more information.

2.4 How important is implementing an item level serialization and traceability system to your organization?

☐ High priority

☐ Medium priority

☐ Low priority

☐ Not a priority

2.5 What system capability do you prefer for drug authentication and why?

☐ Drug authentication by retail/dispensing sectors only (entities that purchase drugs to sell or dispense to patients)

☐ Drug authentication at all points in the supply chain (from the manufacturer until the patient)

☐ None

☐ Other (please specify)

2.6 Please select from the following list any concerns your company has regarding traceability data storage and communication. Check all that apply.

	Very Concerned	**Somewhat concerned**	**Not concerned**
Data security and the potential for illegal breaches of information	☐	☐	☐
The ability to prevent other supply partners from accessing our proprietary information	☐	☐	☐
The number of data connections we may need to establish with our trading partners	☐	☐	☐

	Very Concerned	Somewhat concerned	Not concerned
Quality/accuracy of the aggregation data we will produce/receive	☐	☐	☐
Operations will be slowed due to late or inaccessible data that will be needed	☐	☐	☐
The possibility of drug shortages caused by poor- quality traceability, late or inaccessible data	☐	☐	☐
We may not have our systems ready in time for current mandates	☐	☐	☐
Trading partners may not have their systems ready in time for current mandates	☐	☐	☐
Ability of our systems to interoperate with those of our trading partners	☐	☐	☐
Providing full chain of custody for returned products	☐	☐	☐
Liability for data errors made by our trading partners	☐	☐	☐
Managing errors and exceptions	☐	☐	☐
Other (please specify)			

3. Implementation

3.1 Did you hire any external consultants to support you with implementation?

☐Yes ☐No

If yes, was this useful?

☐Yes ☐No

If no, do you believe that hiring an external resource would have been easier or better for you?

☐Yes ☐No

3.2 Which software solution(s) are you using to depict serialization requirements?

☐ SAP ATTP

☐ TraceLink

☐ Other (please specify)

Were there any additional system developments needed (compared to the standard solution)?

☐Yes ☐No

Comments:

3.3 What internal challenges did/does your organization face regarding implementing a pharmaceutical serialization and traceability system?

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Definition of system architecture	☐	☐	☐	☐	☐
Identification of business partners/service providers	☐	☐	☐	☐	☐

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Integration with existing systems	☐	☐	☐	☐	☐
Preventing unauthorized data breaches	☐	☐	☐	☐	☐
Cost of implementation and ongoing operation (internal system and development costs)	☐	☐	☐	☐	☐
Low priority inside company	☐	☐	☐	☐	☐
Lack of clear business case/financial constraints/low ROI	☐	☐	☐	☐	☐
Limited amount of piloting work	☐	☐	☐	☐	☐
Availability of qualified employees	☐	☐	☐	☐	☐
Lack of good planning	☐	☐	☐	☐	☐
Other (please specify)					

3.4 What external challenges or factors have delayed or would delay your organization's implementation of a pharmaceutical serialization system?

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Lack of clear legislative or regulatory requirements	☐	☐	☐	☐	☐

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Lack of immediate mandate	☐	☐	☐	☐	☐
Lack of standard system architecture	☐	☐	☐	☐	☐
High cost of system components such as software, hardware, service	☐	☐	☐	☐	☐
Unavailability of qualified contractors/service providers	☐	☐	☐	☐	☐
Coordination with supply chain partners	☐	☐	☐	☐	☐
Lack of clear standards for interoperable data exchange	☐	☐	☐	☐	☐
Complying with different countries' requirements	☐	☐	☐	☐	☐
Other (please specify)					

3.5 Did the preparation of the serialization requirements affect the daily operations of your company or your supply chain partners?

	Affected	Not Affected	Cannot say
Internal (MAH)	☐	☐	☐
Production	☐	☐	☐
Distribution	☐	☐	☐

	Affected	Not Affected	Cannot say
Wholesalers	☐	☐	☐
Hospitals	☐	☐	☐
Pharmacies	☐	☐	☐
Other (please specify)			

3.6 How did you or your partners cope with those challenges?

	Applicable	Comment
External consultancy input	☐Yes ☐No	
Stopping operations	☐Yes ☐No	
Pre-emptive training of staff to improve decision making and planning	☐Yes ☐No	
Working outside of normal working hours	☐Yes ☐No	
Stopping operations to make required changes	☐Yes ☐No	
Other (please specify)		

3.7 Based on the above, can you describe in greater detail the three top challenges you faced during the implementation?

Challenge	Root Cause

3.8 Did your company or your supply chain partners experience any challenges once you had gone live with serialization?

☐Yes ☐No

If yes, please specify the challenges below and what severity they had.

Challenge	Applicable	Severity	Mitigation Action
Employees were overwhelmed with the new process and potentially made mistakes.	☐Yes ☐No	☐High ☐Medium ☐Low	
Process(es) was/were not tested appropriately and hence caused problems within the production environment.	☐Yes ☐No	☐High ☐Medium ☐Low	
Issue which caused the shutdown of a production line	☐Yes ☐No	☐High ☐Medium ☐Low	

Challenge	Applicable	Severity	Mitigation Action
Regulatory Reporting events were missed	☐Yes ☐No	☐High ☐Medium ☐Low	
Infrastructure (scanner, warehouse layout etc.) of your company or your supply chain partners was not ready for the new processes.	☐Yes ☐No	☐High ☐Medium ☐Low	
Other non-serialization relevant processes were unexpectedly affected by the Go-Live.	☐Yes ☐No	☐High ☐Medium ☐Low	
Connection issue between the systems of the supply chain partners	☐Yes ☐No	☐High ☐Medium ☐Low	
Wrong or incomplete serialization data provided by your supply chain partners	☐Yes ☐No	☐High ☐Medium ☐Low	
Other (please specify)			

4. Costs

4.1 Were you charged for any implementation costs by your supply chain partners for the serialization implementation?

☐Yes ☐No

Comment:

4.2 Do you get charged for any increased running costs due to the introduction of serialization into your supply chain?

☐Yes ☐No

Comment:

4.3 Have you changed your pricing of pharmaceutical products in order to cover the additional expenses caused by serialization?

☐Yes ☐No

Comment:

5. Organization/Daily Operations

5.1 Do you have a dedicated serialization team?

☐Yes ☐No

5.2 Please specify your reasons for establishing/not establishing a dedicated serialization team?

5.3 What are the responsibilities of serialization involved personnel? (multiple selection is possible)

Responsibility	Applicable
Central point of contact in case of any production issues concerning serialization	☐Yes ☐No
Daily Monitoring of production system	☐Yes ☐No
Supporting any form of testing involving serialization	☐Yes ☐No

Responsibility	Applicable
Raising/assessing change requests involving serialization	☐Yes ☐No
Keeping up to date with new serialization regulatory requirements	☐Yes ☐No
Training of other employees in the company	☐Yes ☐No
Other (please specify)	

Comments:

5.4 How do you keep up to date with new or enhanced serialization requirements?

5.5 How did the introduction of serialization affect your company?

	Agree	No impact	Disagree	Cannot say
Serialization has brought in increased complexity for our supply chain partners and for us	☐	☐	☐	☐
The supply chain is more prone to errors	☐	☐	☐	☐
The employees of the company are accepting the new processes involving serial number handling	☐	☐	☐	☐
More IT intervention is needed since dealing with serial numbers	☐	☐	☐	☐

	Agree	No impact	Disagree	Cannot say
We had to hire more employees due to a change in logistical process	☐	☐	☐	☐
Since introducing serialization, there has been less cases of drug counterfeiting, stolen and diverted products.	☐	☐	☐	☐
Our company and our partners were able to optimise processes due to serialization	☐	☐	☐	☐
Other (please specify)				

5.6 How many serial numbers do you issue per year?

☐ Less than 1 million

☐ 1 – 5 million

☐ 5 – 20 million

☐ 20 – 80 million

☐ More than 80 million

5.7 On a daily operational level, how satisfied have you been with the whole process of implementing and introducing a serialization system? Please answer in the following table.

	Fully agree	Somewhat agree	Don't agree	Cannot Say
The regulations were announced well in advance	☐	☐	☐	☐
We understand the need and importance to implement such a system	☐	☐	☐	☐
We received enough support in setting up the system	☐	☐	☐	☐
We received training on the new processes	☐	☐	☐	☐
If we have questions, we know who to contact	☐	☐	☐	☐
We receive helpful support in a timely manner	☐	☐	☐	☐

5.8 Which of the below would be affected by serialization and traceability system? Select all that apply.

	Improve	No impact	Make worse	Don't Know
Improve public health by strengthening the distribution system's ability to safeguard medicines	☐	☐	☐	☐
Prevent insertion of counterfeit drugs into the legitimate supply chain	☐	☐	☐	☐
Prevent reintroduction of stolen drugs into the legitimate supply chain	☐	☐	☐	☐

	Improve	No impact	Make worse	Don't Know
Prevent reintroduction of diverted drugs into the legitimate supply chain	☐	☐	☐	☐
Mitigate drug shortages	☐	☐	☐	☐
Increased data sharing across the supply chain	☐	☐	☐	☐
Other (please specify)				

5.9 On a personal level, do you have any concerns about consuming, buying or selling a counterfeit product?

☐ Yes ☐ No

If yes, does having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell? [79]

Appendix 5 – European and non-European Wholesaler's Survey

Survey on how Track and Trace / Serialization impacts 3PLs (3rd Party Logistics) and Wholesalers

Dear Participant,

As part of my master's thesis on "Pharmaceutical Serialization", I am conducting a survey to analyse how the Track and Trace solution impacts patient's health, pharmaceutical industries, business and related stakeholders. There will be 3 different surveys upon different types of participants (3PLs/wholesalers, MAHs (Marketing Authorization Holders)/CMOs (Contract Manufacturing Organizations) and pharmacies).

Your participation is voluntary, valuable and appreciated. The survey completion should not take more than 15-20 minutes. If you do not feel comfortable in answering certain questions, please just mark them and skip them. All answers collected from this survey will be exclusively used for my master's thesis only. Personal and company information will not be used without prior approval.

If you have any further questions about this survey, please contact me, Marlen Asbih (marlen.asbih@movilitas.com). Please fill in the following information about yourself. This information will be used only to get some more clarifications or approvals if needed, it will not be collected as part of the thesis data.

Name	
Title/position	
Organization	
(Telephone)	
E-mail address	

1. General

1.1 Did you introduce serialization into your logistical process?

☐Yes ☐No

If yes, please answer the following questions.

If no, why not?

1.2 To which serialization/Track & Trace relevant countries do you ship/distribute your pharmaceutical products?

☐ Saudi Arabia

☐ Russia

☐ EU

☐ Turkey

☐ South Korea

☐ China

☐ USA

☐ Other (please specify):

1.3 Which ERP (Enterprise Resource Planning) System are you using?

☐ SAP

☐ Oracle

☐ Microsoft Dynamics

☐ Infor

☐ Deltra

☐ Other (please specify):

1.4 When did you first start to handle serial numbers in your logistics?

1.5 How long did it take you to implement serialization (from conception into the Go-Live) into your logistical system?

Country 1:	Country 2:	Country 3:	Country 4:
☐ 6 months or less ☐ 6 to 12 months ☐ 12 to 18 months ☐ 18 or longer ☐ Other (please specify):	☐ 6 months or less ☐ 6 to 12 months ☐ 12 to 18 months ☐ 18 or longer ☐ Other (please specify):	☐ 6 months or less ☐ 6 to 12 months ☐ 12 to 18 months ☐ 18 or longer ☐ Other (please specify):	☐ 6 months or less ☐ 6 to 12 months ☐ 12 to 18 months ☐ 18 or longer ☐ Other (please specify):

Comment:

2. Implementation

2.1 Why did you introduce serialization into your logistical process? (multiple answers possible)

Reason	Applicable	Comment
Regulatory requirements forced us to introduce serialisation/Track & Trace	☐Yes ☐No	
MAHs required us to capture serial numbers for greater	☐Yes ☐No	

Reason	Applicable	Comment
data transparency within the supply chain		
For optimisation of the logistical process	☐Yes ☐No	
For better data measurement of internal processes	☐Yes ☐No	
Other (please specify)	☐Yes ☐No	

Comments:

2.2 Did you hire any externals to support you with the implementation?

☐Yes ☐No

If yes, was this useful?

☐Yes ☐No

If no, do you believe that hiring an external resource would have been easier or better for you?

☐Yes ☐No

2.3 Which software solution(s) are you using to depict the serialization requirements?

☐ SAP ATTP

☐ TraceLink

☐ Other (please specify)

Were there any additional system developments needed (compared to the standard solution)?

☐Yes ☐No

Comments:

2.4 What internal challenges did/does your organization face regarding implementing a pharmaceutical serialization and traceability system?

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Definition of system architecture	☐	☐	☐	☐	☐
Identification of business partners/service providers	☐	☐	☐	☐	☐
Integration with existing systems	☐	☐	☐	☐	☐
Preventing unauthorized data breaches	☐	☐	☐	☐	☐
Cost of implementation and ongoing operation (internal system and development costs)	☐	☐	☐	☐	☐
Low priority inside my company	☐	☐	☐	☐	☐
Lack of clear business case/financial constraints/low ROI	☐	☐	☐	☐	☐
Limited amount of piloting work	☐	☐	☐	☐	☐
Availability of qualified employees	☐	☐	☐	☐	☐
Lack of good planning	☐	☐	☐	☐	☐
Other (please specify)					

2.5 What external challenges or factors have delayed or would delay your organization's implementation of a pharmaceutical serialization system?

	Not a challenge	Slight challenge	Medium challenge	Significant challenge	Cannot say
Lack of clear legislative or regulatory requirements	☐	☐	☐	☐	☐
Lack of immediate mandate	☐	☐	☐	☐	☐
Lack of standard system architecture	☐	☐	☐	☐	☐
High cost of system components such as software, hardware, service	☐	☐	☐	☐	☐
Unavailability of qualified contractors/service providers	☐	☐	☐	☐	☐
Coordination with supply chain partners	☐	☐	☐	☐	☐
Lack of clear standards for interoperable data exchange	☐	☐	☐	☐	☐
Complying with different countries' requirements	☐	☐	☐	☐	☐
Others (please specify)					

2.6 Based on the above, can you describe in greater detail the three top challenges you faced during the implementation?

Challenge	Root Cause

2.7 Did you experience any challenges once you had gone live with serialization?

☐Yes ☐No

If yes, please specify the challenges below and what severity they had.

Challenge	Occurred	Severity	Mitigation Action
Employees were overwhelmed with the new process and potentially made mistakes.	☐Yes ☐No	☐High ☐Medium ☐Low	
Process(es) was/were not tested appropriately and hence caused problems within the production environment.	☐Yes ☐No	☐High ☐Medium ☐Low	
Infrastructure (scanner, warehouse layout etc.) was not ready for new processes	☐Yes ☐No	☐High ☐Medium ☐Low	
Other non-serialisation relevant processes were unexpectedly affected by the Go-Live.	☐Yes ☐No	☐High ☐Medium ☐Low	

Challenge	Occurred	Severity	Mitigation Action
Connection issue between your systems and other supply chain partners	☐Yes ☐No	☐High ☐Medium ☐Low	
Transport of developments from development environment into the production environment was (partially) forgotten.	☐Yes ☐No	☐High ☐Medium ☐Low	
Regulatory Reporting Events were missing	☐Yes ☐No	☐High ☐Medium ☐Low	
Other (please specify)			

Comments:

3. Costs

3.1 Did you charge the incurring implementation cost to your MAH (Marketing Authorization Holder)?

☐Yes ☐No

Comment:

3.2 Do you charge a scanning price within the pick and pack/returns and scrapping process for serialized products to the MAH? (this relates to whether you capture the number of serial numbers and SSCCs you scan during your processes which is then billed to the MAH).

☐Yes ☐No

Comment:

4. Organization/Daily Operations

4.1 Do you have a dedicated serialization team?

☐Yes ☐No

4.2 Please specify your reasons for establishing/not establishing a dedicated serialization team?

4.3 What are the responsibilities of serialization involved personnel? (multiple choice is possible)

Responsibility	Applicable
Central point of contact in case of any production issues concerning serialisation	☐Yes ☐No
Daily Monitoring of production system	☐Yes ☐No
Supporting any form of testing involving serialisation	☐Yes ☐No
Raising/assessing change requests involving serialisation	☐Yes ☐No
Keeping up to date with new serialisation regulatory requirements	☐Yes ☐No
Training of other employees in the company	☐Yes ☐No
Other (please specify)	

Comments:

4.4 How do you keep up to date with new or enhanced serialization requirements?

4.5 Do you have the same processes across different clients/serialization requirements?

☐Yes ☐No

If no, why not, and how is it affecting your organisation?

4.6 How has the introduction of serialization affected your company/processes?

	Agree	No impact	Disagree	Cannot say
The pick and pack accuracy has improved since scanning serial numbers at outbound	☐	☐	☐	☐
The pick and pack process is taking longer since having to scan serial numbers	☐	☐	☐	☐
The employees of the company are accepting new processes involving serial number handling	☐	☐	☐	☐
More IT intervention is needed since dealing with serial numbers	☐	☐	☐	☐
The logistics process has become more complex as a result of the serialisation requirements	☐	☐	☐	☐
We had to hire more employees due to a change in logistical process	☐	☐	☐	☐
Other (please specify)				

Comments:

4.7 On a daily operational level, how satisfied have you been with the whole process of implementing and introducing a serialization system? Please answer in the following table.

	Fully agree	Somewhat agree	Don't agree	Cannot Say
The regulations were announced well in advance	☐	☐	☐	☐
We understand the need and importance to implement such a system	☐	☐	☐	☐
We received enough support in setting up the system	☐	☐	☐	☐
We received training on the new processes	☐	☐	☐	☐
If we have questions, we know who to contact	☐	☐	☐	☐
We receive helpful support in a timely manner	☐	☐	☐	☐

4.8 On a personal level, do you have any concerns about consuming, buying or selling a counterfeit product?

☐ Yes ☐ No

If yes, does having the serialization system make you feel more secure about the authenticity of pharmaceutical products which you consume, buy or sell? [79]

Appendix 6 – European Pharmacies Survey

Survey on how Track and Trace/ Serialization impacts pharmacies

Dear Participant,

As part of my master's thesis on "Pharmaceutical Serialization", I am conducting a survey to analyse how does the Track and Trace solution impact patient's health, pharmaceutical industries, business and related stakeholders. There will be 3 different surveys upon different types of participants (3PLs/wholesalers, MAHs/CMOs and pharmacies).

Your participation is voluntary, valuable and appreciated. The survey completion should not take more than 10-20 minutes. If you do not feel comfortable in answering certain questions, please just mark them and skip them. All answers collected from this survey will be exclusively used for my master's thesis only. Personal and company information will not be used without prior approval.

If you have questions or need further clarifications about this survey, please do not hesitate to contact me, Marlen Asbih (marlen.asbih@movilitas.com).

Please fill in the following information about yourself. This information will be used only to get some more clarifications or approvals if needed, it will not be collected as part of the thesis data.

Name	
Title/position	
Organization	
(Telephone)	
E-mail address	

1. General

1.1 How many branches do you have for your pharmacy within Germany?

☐ 1

☐ 2

☐ 3

☐ More than 3

1.2 Are you familiar with Track & Trace / Serialization?

☐Yes ☐No

If yes, how did you initially find out about it?

Reason	Applicable	Comment
The MAH (Marketing Authorization Holder) contacted us with all the important information	☐Yes ☐No	
We got notified by a regulatory authority (health department, state)	☐Yes ☐No	
We got informed through an association	☐Yes ☐No	
We informed ourselves	☐Yes ☐No	
Other (please specify)		

1.3 What did you have to do to acquire the infrastructure and connection to the NMVS (National Medicines Verification System)?

1.4 Who covered the costs of the infrastructure and system implementation?

2. Daily Business

2.1 How did you handle the transition period when both non-serialized products (produced before 9 Feb 2019) and serialized products (produced after 9 Feb 2019) were in circulation?

2.2 Have you been given instructions on how to behave in exceptional cases? (e.g., negative verifications, non-readable 2D matrix codes)

☐Yes ☐No

If yes, please provide more information.

2.3 How often do you get negative verifications when dispensing a product?

	Applicable	Comment
Every day	☐	
Every week	☐	
Once or twice a month	☐	
Once or twice a year	☐	
Never	☐	

2.4 How do you handle negative verifications?

	Applicable	Comment
We do not issue the product and store it within a separated area	☐Yes ☐No	
There are scenarios where we still give the customer the product	☐Yes ☐No	
Other (please specify)		

2.5 Who do you notify when you receive negative verifications?

	Applicable	Comment
We contact the MAH to ask to return the product	☐Yes ☐No	
We contact the NMVO (National Medicines Verification Organization) and wait for further instructions	☐Yes ☐No	
We do nothing	☐Yes ☐No	
Other (please specify)		

2.6 Do you have any experiences of the NMVS system being offline?

	Applicable	Comment
Every day	☐	
Every week	☐	
Once or twice a month	☐	
Once or twice a year	☐	
Never	☐	

2.7 What do/would you do in the scenario of having the NMVS system offline?

	Applicable	Comment
We would still give the medicine out to the customer and decommission it later	☐Yes ☐No	
We would not hand out any medicine until the system is back online	☐Yes ☐No	
Other (please specify)		

2.8 Is the response time to receive feedback from the NMVO delaying your daily business or making it more complicated?

☐Yes ☐No

If yes, please provide more information.

2.9 How often do you have cases of non-readable 2D matrix code?

	Applicable	Comment
Every day	☐	
Every week	☐	
Once or twice a month	☐	
Once or twice a year	☐	
Never	☐	

2.10 What would you do in the scenario of a 2D matrix code not being readable?

	Applicable	Comment
We would decommission the serial numbers manually by entering the human readable identifiers into the system	☐Yes ☐No	
We would not issue the product	☐Yes ☐No	
We would send the product back to the distributor/MAH	☐Yes ☐No	
Other (please specify)		

2.11 What would you do if a patient returns a product to the pharmacy?

	Applicable	Comment
We take back the product and throw it away/destroy it	☐Yes ☐No	
We take back the product and reactivate it in the system so that it can be resold	☐Yes ☐No	
We do not accept to take back any product	☐Yes ☐No	
Other (please specify)		

3. Feedback

3.1 On a daily operational level, how satisfied have you been with the whole process of implementing and introducing a serialization system? Please answer in the following table.

	Fully agree	**Somewhat agree**	**Don't agree**	**Cannot Say**
The regulations were announced well in advance	☐	☐	☐	☐
We, as pharmacists, understand the need and importance to implement such a system	☐	☐	☐	☐

	Fully agree	Somewhat agree	Don't agree	Cannot Say
We received enough support in setting up the system	☐	☐	☐	☐
We received training on how to handle the new dispensing process/system	☐	☐	☐	☐
If we have questions, we know who to contact	☐	☐	☐	☐
We receive helpful support in a timely manner	☐	☐	☐	☐

3.2 With regards to serialization, what things do you think have been particularly successful or could be improved?

Successful	Could be improved