Is serialization for drug traceability a cost or an investment? A study on its implementation in Brazil

Is serialization for drug traceability a cost or an investment? A study on its implementation in Brazil

ERIKA DIAGO RUFINO
UNIVERSIDADE DE SÃO PAULO

GLENDA BORGES MADEIRA DE SOUZA

JEFFERSON TEIXEIRA BUENO

JAIRO CARDOSO DE OLIVEIRA
UNINOVE – UNIVERSIDADE NOVE DE JULHO

Nota de esclarecimento:
O X SINGEP e a 10ª Conferência Internacional do CIK (CYRUS Institute of Knowledge) foram realizados de forma remota, nos dias 26, 27 e 28 de outubro de 2022.

Is serialization for drug traceability a cost or an investment? A study on its implementation in Brazil

Objetivo do estudo
Este estudo visa contribuir para o debate sobre a rastreabilidade de medicamentos, apresentando uma resposta à questão se a serialização seria um investimento ou um custo, a partir de um modelo de business case desenvolvido especialmente para isso.

Relevância/originalidade
A serialização de medicamentos seria uma medida para evitar produtos médicos falsificados, fora do padrão ou roubados, que podem causar mortalidade e diversos prejuízos. Além de sua importância, ainda há dúvidas sobre a viabilidade financeira de sua implantação.

Metodologia/abordagem
A pesquisa foi realizada em duas partes. Primeiro, pesquisa sobre parâmetros específicos usados ??para analisar casos de negócios, e em seguida, um modelo de negócios foi construído e aplicado a 32 empresas farmacêuticas com diversos tamanhos de investimento e linhas de produção.

Principais resultados
Com os resultados da análise, é possível concluir que a implantação da rastreabilidade pode ser considerada um investimento para a saúde em geral, pois tem potencial para inibir medicamentos falsificados, roubados, extraviados e fora do padrão.

Contribuições teóricas/metodológicas
O business case elaborado nesta pesquisa pode ser utilizado/adaptado para outros contextos, pois envolve conceitos universais do mercado farmacêutico.

Contribuições sociais/para a gestão
Este trabalho propõe uma discussão sobre tecnologias de saúde pública que podem melhorar a qualidade de vida da população e os investimentos necessários para alcançá-la.

Palavras-chave: Medicamentos falsificados, Rastreabilidade, Serialização, Data Matrix, Cadeia de Suprimentos Farmacêuticos

Is serialization for drug traceability a cost or an investment? A study on its implementation in Brazil

Study purpose
This study aims to contribute to the debate about drug traceability, presenting an answer to the question of whether serialization would be an investment or a cost, based on a business case model specially developed to attend to this.

Relevance / originality
Medicines serialization would be a measure to avoid counterfeit, non-standard, or stolen medical products, which can cause mortality and several losses. Besides its importance, there are still questions about the financial viability of implementing it.

Methodology / approach
The research was conducted in two parts First, research on specific parameters used to analyze business cases, and then a business model was built and applied to 32 pharma companies with several different sizes of investment and production lines.

Main results
With the results of the analysis, it makes it possible to conclude that the implementation of traceability can be considered an investment for health in general, as it has the potential to inhibit counterfeit, stolen, misplaced, and non-standard medicines.

Theoretical / methodological contributions
The elaborated business case in this research can be used/adapted to other contexts since it involves universal concepts of the pharmaceutical market.

Social / management contributions
This paper proposes a discussion of public health technologies that can improve the quality of life for the population and the necessary investments to achieve it.

Keywords: Counterfeit Drugs, Track and Trace, Serialization, Data Matrix, Pharmaceutical Supply Chain

1 Introduction

The pharmaceutical supply chain is one of the most complex considering all the industries. According to the World Health Organization (WHO, 2021), it is not difficult to find a product being consumed in a country other than where it was produced, which in turn differs from the country of origin of the raw material. This context causes the supply chain to be fragmented, and without adequate supervision, it can be weakened in several of its links, causing severe effects on public health. The weakening of the logistics chain and its complexity makes it vulnerable to corruption and product diversion, facilitating the entry of counterfeit and non-standard products (Pisa & McCurdy, 2019). This industry is also characterized by the fact that it is highly regulated, and the quality of its products needs to be guaranteed during production and throughout the drug distribution cycle (Chiacchio et al., 2020).

According to World Health Organization, the implementation of traceability in the pharmaceutical supply chain is essential to ensure quality, integrity and even improve distribution efficiency (WHO, 2021). Although many advanced techniques are being studied, with some of them suggesting individual tagging (Ludasi et al., 2018) or molecular identification (Altamimi et al., 2019), serialization proves to be a non-invasive technology as it does not interfere with the work of carriers and, once installed on the production line, it does not interfere with the production flow (Rotunno et al., 2014).

In the view of the health authority of the United States (FDA - Food and Drug Administration), traceability must ensure the surveillance and diligence of supply chain systems, acting on all links in this chain, including its stakeholders. Also, according to this entity, traceability should support compliance and enforcement efforts in the chain, adapting to be interoperable with the health system and its global market (Rodgers, 2017).

In turn, the International Coalition of Medicines Regulatory Authorities (ICMRA) also includes some benefits for regulatory agencies, such as real-time notifications of counterfeit or inappropriate products, tracking of product recalls, and alerts for substandard products. This entity, which is made up of the world's leading health authorities, points out that traceability acts in the aspects of supply chain management, product commissioning, equivalence identification, exchange of information on those responsible, products, and supply chain facilities (ICMRA, 2021).

Despite the various benefits, there is no consolidated movement of implementation processes, especially in developing countries (Pisa & McCurdy, 2019). In the case of Brazil, the necessity to change production lines and logistics control processes, among others, is considered the main limiting factor for the adoption of drug traceability. However, discussions on the amount needed for this implementation can be understood as an investment, while others consider it just a cost. Specifically, in the health area, studies carried out by Leatherman et al.(2003) indicate that the business case must be understood from the perspective of its stakeholders in terms of financial return and also a list of collateral benefits. Among the side benefits, authors point to improved marketing positioning, reduced regulation and supervision; improved reputation; better patient retention and reduced enrollment, marketing, and acquisition costs; better recruitment and retention of critical staff; and the emergence of better health outcomes.

In the case of drug traceability, although it is known that authentication technologies are essential enablers in fighting against counterfeiters (Lima et al., 2018), this discussion, however, is still carried out without presenting evidence, such as a business case study that demonstrates, in a decisive manner, whether serialization is configured as an investment or a

cost. Uncertainty about a real potential return on the investment required for serialization generates stagnation in the evolution of traceability in the pharmaceutical supply chain, especially in countries with low resources to invest.

This study aims to contribute to the discussion on drug traceability, presenting a business case model for the implementation of serialization by the pharmaceutical industry and providing an answer to the following research question: is serialization for drug traceability a cost or an investment? The business case model from this study was applied in 32 companies' scenarios in the pharmaceutical sector. The results of this application showed that the cost value for each cartridge unit could vary according to the production line speed, however, with a minimal variation.

The result then characterizes serialization as an investment and not just a cost. Another contribution of the article is the business case model, which can be used and adapted to the reality of each company.

In section 2, this article presents a general description of serialization, traceability, and its economic and health system impacts. Section 3 is dedicated to the method for constructing this survey's business case. In contrast, section 4 demonstrates results obtained from the analysis of 32 patients studied and proposes the discussion in light of the results found. Finally, section 5 presents the authors' conclusion.

2 Theoretical Framework

Traceability and serialization are often treated as synonyms. However, serialization can be considered the initial step that allows drugs to be traced. Traceability encompasses, in addition to serialization, logistical and data transmission processes that allow the identification of all stages the drug has undergone, from its production to its arrival at the dispensing point.

Thus, in this theoretical framework, concepts of serialization, traceability, and economic impacts on the health system will be addressed.

2.1. Serialization

In the pharmaceutical industry, serialization is a technological solution that allows automation of the traceability process. According to Chiacchio et al.(2020), a serialization system is a set of cyber-physical systems that, cooperating at the various levels of the drug production process, allow for the automation of packaging lines.

This solution's effectiveness has been demonstrated by Loncar and Civjanovic (2013) in a study that interviewed professionals from the pharmaceutical industry. Authors report that 84.2% of respondents claim that the introduction of the serialization system allows for complete drug traceability. However, the survey also showed that only 22.2% of industries had introduced this system for their drug lines.

Industries that adopted serialization have opted for the 2D encoding standard, also known as two-dimensional. The chosen model is owned by the GS1 company, which acts as a global collaboration platform, bringing together industry, governments, regulators, and other links in the pharmaceutical supply chain (GS1, 2021). The code chosen and printed on the packaging is named "Data Matrix" and can be a square or rectangular symbol made up of individual dots or squares. This representation is an ordered grid of dark and light dots bounded by a location pattern whose data is encoded using a series of dark or light dots based on a predetermined size (GS1, 2018). This technology and authentication technologies support the

integrity of medical and pharmaceutical products. Thus, it is possible to infer that this control enables the increase in export/import processes between countries, ensuring their quality and safety (Krynytskyi et al., 2019; WHO, 2017a).

In order to implement reliable traceability processes in the pharmaceutical industry, a fundamental step is that each drug package contains a unique identifier. Within the scope of the National Drug Control System (SNCM – Brazilian drug control system), every drug transport package must have its own identifier code that allows for the relationship with the Unique Drug Identifier (UDI) contained therein (ANVISA, 2017, 2019).

On the production line, the serialization process must be monitored by a real-time vision system. This system uses OCR (Optical Character Recognition) technology to recognize characters from high-resolution photographs. The information collected digitally from each serialized unit allows interaction with the software used in the productive packaging line, such as ERP (Enterprise Resource Planning). After encoding the individual information in the serialization system, the cartridges (smallest marketable unit of a drug) are added inside shipping boxes, and information such as batch, origin, and storage is added. The centralization of vertical communication data is carried out by servers controlled by the health authority. This vertical communication flow comes from three sources: register holders, responsible for serialization and activation, distributors, responsible for storing the drugs, and dispensers, responsible for supplying the drug to the patient or consumer (Silva & Mattos, 2019).

2.2. Traceability

A traceability process allows knowing the history and exact location of a product in the supply chain by storing a defined set of information (Rotunno et al., 2014). To be considered an effective system, some functionalities must be implemented, such as identifying products in a unitary form and data capture by reading this identifier. This data must be shared with supply chain partners, to benefit the logistic process (Pisa & McCurdy, 2019).

Specifically for the pharmaceutical industry, traceability brings benefits such as the guarantee that only authorized products will circulate in the legalized supply chain and the correct distribution or dispensing of counterfeit, expired, banned, or recalled products. Also among the benefits is the ease and efficiency of a product recall, reducing the risk of incorrect sales and loss of confidence in the manufacturer by the consumer. Other benefits are reflected internally in companies, such as efficient inventory management, identification of shortages, and monitoring of stock shortages (Rotunno et al., 2014; WHO, 2021).

Drug traceability systems are being used more and more. Worldwide, 2001 was a milestone for traceability in the pharmaceutical industry, as the first law regulating the subject was drawn up in Italy. After that, other European Union countries, in addition to China, Korea, India, the United States, and Brazil, also mobilized in this regard (Rotunno et al., 2014).

In Brazil, in January 2009, Law 11,903/2009 was enacted (Brazil, 2009), which instituted the National Drug Control System (SNCM), established deadlines for implementation, and determined the law application scope to drug types. In 2016, Law 13,410/2016 was enacted (Brazil, 2016), changing the application scope determined in the previous law and attributing to ANVISA (Brazilian Health Surveillance Agency – *Agência Nacional de Vigilância Sanitária*) the responsibility for regulating the SNCM operational aspects.

2.3. Economic and health system impact

According to the World Health Organization (2017a), as drug manufacturing is spread out and distribution systems become their complexity increases, the problem of counterfeit and non-standard drugs increases. Non-standard drugs are authorized products that have not met quality standards, specification standards, or a combination of both. Counterfeit and substandard drugs worldwide represent more than 30 billion US dollars annually (Pascu et al., 2020; Trenfield et al., 2019). Counterfeit and non-standard drugs, in addition to health impacts themselves, generate economic and social impacts as they increase the cost of patients to health systems. Patients and governments spend money on ineffective drugs.

The growing demand for drugs, vaccines, and other medical products in almost every country, in addition to mismanagement of the supply chain and the growth of e-commerce, also creates opportunities for counterfeit drugs to be introduced into the supply chain. Unfortunately, reliable information on the actual socioeconomic and public health impacts of unsafe and counterfeit medical products is scarce. A more robust evidence base is needed to help prevent, detect and respond to unsafe and counterfeit medical products and the public health threat they represent (WHO, 2017a).

Technologies have a significant impact on combating drug counterfeiting. Counterfeit drugs can lead to drug recalls and lawsuits. Furthermore, brand loyalty is compromised as consumers perceive additional risks when using a company's products. An effective anti-counterfeiting strategy prevents this and ensures patient safety. The main ways to combat counterfeiting include lawsuits against illicit traders, countermeasures using technologies, consumer education and information, private investigations, and cooperation with enforcement agencies. Implementing anti-counterfeiting technologies is a preeminent and influential preventive measure (Bansal et al., 2013).

After the Coronavirus outbreak (COVID-19), there was an increase in counterfeit drugs, showing a new global trend in this sector. During just one week in 2020, authorities from Interpol inspected more than 326,000 packages, of which more than 48,000 (14.7%) were seized by customs and regulatory authorities in the quality of counterfeit drugs. Overall, authorities have seized about 4.4 million units of illicit pharmaceuticals worldwide (Interpol, 2020).

The social, economic, and health impacts of low-quality, unregistered or unlicensed counterfeit drugs and medical products are presented in Table 1.

Table 1. Impact of poor quality, unregistered or unlicensed, counterfeit and stolen medical products.

Impact on Health	Social Impact	Economic Impact
Loss of confidence in the treatment	Loss of family income	Loss of tax collection
Increased mortality	Loss of productivity	Wasted resources
Antimicrobial resistance progression	Loss of social mobility	Increased family expenses
High disease prevalence	Increasing poverty and leave period	Industry invoicing losses

Source: Adapted from World Health Organization (2017a) and SETRM 2020 Final Report(INOVA HC, 2020).

Non-standard or counterfeit drugs tend not to act in the body as expected, which can have different impacts. Among the impacts, one of the most harmful is disease prolongation, which can lead to a loss of work and, therefore, a reduction in family income. Not having the expected response to treatment, doctors who do not know that the drug used is not the authentic one, look for alternative paths for a treatment that could be effective. This scenario can lead to wasted time and resources, worsening disease, and drug resistance.

As drug resistance increases and it becomes more difficult to treat certain diseases, it is necessary to increase investment in research and discoveries of new ones (Buckle & Gostin, 2013; WHO, 2017b). Furthermore, this resistance can make diseases impossible to treat today or in the future. In the worst case, people die either from the disease prolongation or from the impact generated on the body by ingesting the false or non-standard drug.

3 Methodology

In order to determine whether an investment will obtain the return desired by asset owners, it is necessary to prepare, evaluate and choose projects, analyzed with a medium and long-term perspective. Business decisions, which usually have profit as the ultimate goal, involve, for example, replacement of assets, expansion of production capacity, and launch of new products (Assaf Neto, 2020). The evaluation of project selection can be carried out in different ways, with financial analysis being one of them, usually through business case studies. According to Kurucz et al.(2008, p.1), the business case is a "pitch for investment in a project or initiative that promises to yield a suitably significant return to justify the expenditure." Authors point out that, in business cases where there is a contribution of corporate social responsibility (CSR), the company can obtain better financial performance not only in its operations, but also to creat a better society. In the health area, according to Leatherman et al.(2003, p.18), the business case can be defined as:

> A business case for a health care improvement intervention exists if the entity that invests in the intervention realizes a financial return on its investment in a reasonable time frame, using a reasonable rate of discounting. This may be realized as "bankable dollars" (profit), a reduction in losses for a given program or population or avoided costs. In addition, a business case may exist if the investing entity believes that a positive indirect effect on organizational function and sustainability will accrue within a reasonable timeframe.

According to Bonem (2018), the development of a business case model has the function of preparing companies for investment needs, whose term used in industries is "CAPpital EXpenditure" (CAPEX). Parameters must be defined to adjust mathematical formulas, which indicate the project's feasibility in financial terms.

A set of parameters that should be considered for this application was researched in developing a drug serialization business case with a view to its traceability. These parameters included the impact on each packaging line, issues related to the speed of each production line in the manufacturing plant (cartridges per minute), the financial value of the asset investment, and the total annual production volume. In order to validate these parameters, the authors asked professionals from three companies in the pharmaceutical sector to indicate the ones that would be more representative. The selected companies are holders of medicine registers of different billing sizes. The responsible for this validation are specialists in industrial engineering, automation, and production, with expertise in the technical area and more than ten years of

experience in the pharmaceutical industry. The characterization of these companies can be seen in Table 2.

Table 2. Details of companies interviewed for the Questionnaire validation

Company	Origin	Product Type	Size	Expert 1 profile	Expert 2 profile
1	Multinational	Several categories	Large	Industrial Engineering Manager, with 29 years of experience	Senior Maintenance Manager, with 21 years of experience
2	Brazilian	Generic Drugs	Medium	Senior Operations Manager, with 16 years of experience	Manufacturing Manager, with 13 years of experience
3	Multinational	Oncological Drugs	Small	Senior Technology System Specialist, with 12 years of experience	Senior Production Engineer, with 10 years of experience

Source: Original survey results

After this phase, a survey was prepared with the validated parameters and sent to representatives of 230 pharmaceutical industries manufacturing drugs in Brazil. They were requested to fill out, anonymously, company-specific data for each parameter. Answers were obtained from 12 Brazilian and 20 international industries, 26 considered large, five medium, and one small. In the case of more than one respondent per company, any differences were clarified through an interview. Positions of companies' representatives that responded to the questionnaire varied among supply chain, regulatory affairs, engineering, and production managers, as shown in Table 3.

The average values of investments made, depending on the quantity and speed of production lines, as reported in the questionnaire are shown in table 3. The field "minimum and maximum value range" shows, respectively, the lowest and highest value cited in the data collection.

Table 3. Serialization investment data (values in thousands of Brazilian Reais)

Line Speed (cartridge per minute)	Number of Lines	Average value of investment	Minimum and Maximum Value Range
Up to 100	29	R$ 452	From R$ 350 to R$ 500
100 to 200	18	R$ 650	From R$ 500 to R$ 800
200 to 300	12	R$ 1.000	From R$ 800 to R$ 1.000
Above 300	9	R$ 1.500	Above R$ 1.000

Source: Original survey results

An essential item in the business case analysis is related to the production capacity, and Table 4 presents the companies' annual production volume in cartridges. In this table, the concentration of companies is in the range of up to 100 million cartridges per year. The higher incidence at the bottom of the table is a consequence of several responding register holders that import drugs already serialized in their countries of origin.

Table 4. Annual production volume, in cartridges, of the 32 companies

Annual volume in cartridges	Number of companies
Over 400 million units	4
Up to 400 million units	2
Up to 200 million units	2
Up to 150 million units	1
Up to 100 million units	3
Up to 50 million units	5
Up to 20 million units	15

Source: Data collected in the survey by authors.

No individual data were presented in this study to maintain the confidentiality of each company participating. According to the case study by Zimmerman et al. (2017), anonymity did not affect or compromise the reliability or validity of the survey satisfaction rates and results presented. Anonymous data from pharmaceutical companies that contributed to the study do not impact the quality of the data presented and do not impact the reproducibility of the methodology used, as well as the verification of conclusions and analyses carried out by the authors.

The method for defining the business case used an average Overall Equipment Effectiveness (OEE) of 55%, as reported by industries. According to Teresa Pereira et al. (2022), the OEE is a measure used to track productivity in an industry's packaging line and compare it through its efficiency in different Stock Keeping Units (SKU). The OEE analysis is essential since inserting new activities and equipment for serialization in a production line has a trend to reduce its efficiency. In this study, a learning period of 90 days was considered, during which the loss of OEE was reduced. Initially, the measured efficiency loss was about 17%. The reported value of lost productivity, which remained stable after this period, was 2%.

Another relevant indicator for calculating the model is the cost of preventive maintenance (fixed cost) and corrective maintenance (variable cost), which were considered an annual average of 5% of the amount invested in Capex. This average value was also obtained through the survey responses.

Depreciation is the financial indicator used for investing in assets that do not affect cash flow. According to Ross et al. (2015), depreciation reflects the accounting estimate of the cost of equipment worn out in the production process. For assets with a long wear time and which maintain the process quality and robustness, the estimate used is 120 months (Ross et al., 2015).

For calculating the business case, it was considered that the individual cost of each ink cartridge for printing Data Matrixes is around R$500,00, and each cartridge can print 80,000 secondary drug packages with qualitative efficiency. According to most interviewed companies' responses, working days in 2 shifts was also considered. Each shift comprises eight hours of work and, on average, 22 days a month.

According to the survey responses, industries do not consider increasing the workforce in serialized production lines. The verification of experience of those who have already carried out the implementation identified that the new processes do not require an increase in the Full-Time Equivalent (FTE) existing in the current lines. Table 5 presents the data compiled from all indicators obtained in the survey with the 32 companies used to validate the business case final result.

Table 5. Indicators used to propose a business case model

Indicator	Amount
Ink cartridge cost (BRL)	500
Cartridge yield	80,000
Hours per shift	8
Number of shifts	2
Working days in the month	22
Maintenance per year (%)	5
OEE (%)	55
OEE drop (%)	2
Depreciation Time (months)	120
Depreciation start date	01/Dec/2020
Depreciation end date	01/Dec/2030
Total Amount of Days	3,652
Monthly Interest Rate (%) referring to Dec/2020	0.42
Daily Interest Rate (%) referring to Dec/2020	0.0140

Source: Data collected in the survey by authors.

To support the discussions regarding results obtained in the business case and to conclude the survey question, secondary data related to theft and loss, counterfeiting, invoicing, and sector taxes, among others, were used. These secondary data are shown in Table 6.

Table 6. Secondary data used in the study

Source	Date	Topic covered	Reference
Seminar on Engineering and Technology for Traceability of Drugs and Strategic Inputs (SETRM)	2020 Edition	Socioeconomic impact of drug counterfeiting	(INOVA HC, 2020)
ANVISA	2020	Official data on theft and loss of medicines	(ANVISA, 2020)
ANVISA	2018	Statistical Yearbook - Billing and Tax Scenario	(ANVISA, 2018)
Websites of companies that participated in the survey	2020	Annual Reports - Financial Information	
World Health Organization	2017	Reports on global impacts due to drug counterfeiting	(WHO, 2017a)
World Health Organization	2021	Report on risk and benefit analysis for traceability	(WHO, 2021)
International Criminal Police Organization (INTERPOL)	2020	Global operation report on counterfeiting medical devices	(Interpol, 2020)

4 Results and Discussions

In order to answer this article's survey question (is serialization for drug traceability a cost or an investment?), the business case was built from mathematical formulas which considered the respondents' inputs and indications by Ross et al.(2015). For better visualization, Figure 1 presents the formulas, and their details are in Appendix 1.

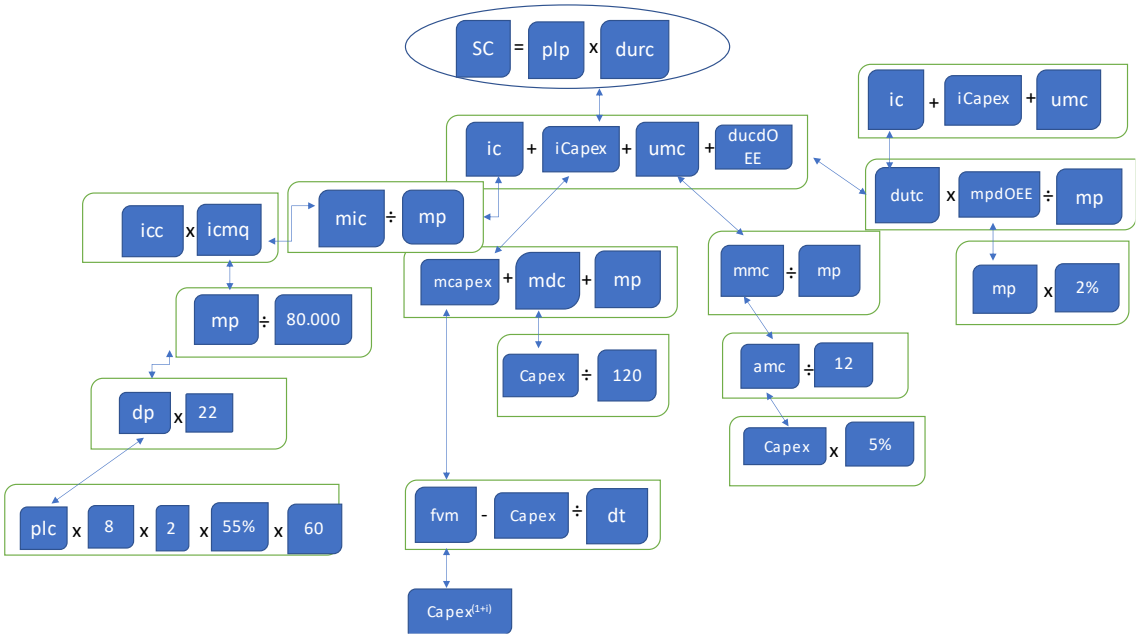

Figure 1. Details of the formulas for calculating the Serialization cost

Four different scenarios were defined for the application of data in Table 5 to the business case mathematical formulas, as seen in Table 7. These scenarios were defined according to cartridges' productive capacity per minute to meet the variations verified with the data obtained through the survey.

Results of a survey carried out with the 32 companies, presented in Table 7, indicate that the introduction of serialization in a drug cartridge would have a slightly higher cost of R$0,01, regardless of the production line speed measured in the cartridge per minute.

However, even the value of a little more than R$0,01 must be analyzed considering the drug sale price in such a way that it can be evaluated as significant or not. For this, an analysis was carried out that considering the worst case of production speed (below 100 cartridges per minute) and an average sale price of the ten most sold drugs in Brazil in 2020, according to the pharmacy guide website (Guia da Farmácia, 2020). The price research was carried out through an online consultation on www.drogariasaopaulo.com.br. In order to standardize the analysis, individual units of cartridges and the discounts informed were considered. The survey was carried out on 10/Dec/2021, and its results can be verified in Table 8.

Table 7. Results of mathematical calculations used to calculate the cost value of serialization/Business Case

Cartridges per Minute (ppm)	Average OEE (%)	Monthly Productivity	Monthly ink cost (R$)	Direct Input Cost per unit	Investment	Monthly Depreciation Cost (R$)	Monthly Capital Cost (R$)	Capital Cost per Unit (R$)	Monthly Maintenance Cost (R$)	Cost per unit Maintenance (R$)	Total cost (per cartridge) (R$)
Above 300	55	4,646,400	29,040	0.0063	1,500,000	12,500	8,342	0.0045	6,250	0.0013	0.0121
200 to 300	55	2,904,000	18,150	0.0063	1,000,000	8,333	5,561	0.0048	4,166	0.0014	0.0125
100 to 200	55	1,742,400	10,890	0.0063	650,000	5,416	3,614	0.0052	2,708	0.0016	0.0130
Up to 100	55	1,161,600	7,260	0.0063	452,000	3,766	2,513	0.0054	1,883	0.0016	0.0133

Source: Data collected in the survey by authors.

Table 8. Calculation of additional cost per cartridge unit

Drug	Register Holder	Price (BRL)	Percentage of serialization cost over drug price
Xarelto 20 mg 28 tablets	Bayer Pharma	241.55	0.006
Dorflex 50 tablets	Sanofi	18.18	0.074
Aradois 25 mg 60 tablets	Biolab-Sanus Farma	53.45	0.025
Glifage XR 500 mg 30 tablets	Merck	7.91	0.171
Saxenda 6 mg/mL	Novo Nordisk	665.27	0.002
Ivermectina 6 mg 4 tablets	Vitamedic	25.99	0.052
Torsilax 30 tablets	Neo Quimica	17.39	0.078
Jardiance 25 mg 30 tablets	Boehringer ing	214.82	0.006
Neosaldina 30 dr	Takeda Pharma	21.90	0.062
Ozempic 0.25 mg	Novo Nordisk	812.89	0.002

Source: Data collected in the survey by authors.

Even for the drug with the lowest sale price, the serialization implementation would incorporate an additional cost of 0.017%. For drugs with a higher sale price, i.e., above R$600,00, serialization would represent a cost of 0.002%. In these percentages, it can be understood that serialization is actually an investment, as the benefits identified with the implementation of this technology tend to avoid the sale of counterfeit and stolen products and the use of these products with doubtful efficacy by the patient.

5 Conclusion

With a focus on local and global needs, this study proves that it is possible to calculate the cost of implementing serialization on each cartridge coming out of a production/import line and that its percentage value can be considered insignificant even for low-cost drugs.

In this sense, the implementation of traceability can be considered an investment for health in general, as it has the potential to inhibit counterfeit, stolen, misplaced, and non-standard medicines. Results found in this study contribute to the Economic, Social, and Health aspects and suggest a business case model for the Serialization Technology implementation.

In future work, it is suggested that the economic feasibility of individualized drug marking be addressed, as techniques and processes are being developed to include identifiers on the tablet surface and primary packaging.

This study does not include the traceability of customized drugs and advanced therapy, which can be considered a limitation. The study involved only the Brazilian market. However, the elaborated business case can be used/adapted to other contexts since it involves universal concepts of the pharmaceutical market.

References

Altamimi, M. J., Greenwood, J. C., Wolff, K., Hogan, M. E., Lakhani, A., Martin, G. P., & Royall, P. G. (2019). Anti-counterfeiting DNA molecular tagging of pharmaceutical excipients: An evaluation of lactose containing tablets. *International Journal of Pharmaceutics*, *571*, 118656.

ANVISA. (2017). *Resolução da Diretoria Colegiada—RDC 157/2017*. Agencia Nacional de Vigilancia Sanitaria. Retrieved 3 November 2021, from: https://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2017/rdc0157_11_05_2017.pdf

ANVISA. (2018). *Anuário Estatístico do Mercado Farmacêutico* (p. 41). Agencia Nacional de Vigilancia Sanitaria. Retrieved 3 November 2021, from: https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/medicamentos/cmed/anuario-estatistico-do-mercado-farmaceutico-2018.pdf/view

ANVISA. (2019). *Resolução da Diretoria Colegiada—RDC 319/2019*. Agencia Nacional de Vigilancia Sanitaria. Retrieved 3 November 2021, from: https://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2020/in0100_23_08_2021.pdf

ANVISA. (2020). *Relatório de Roubo e Extravio—Gerência Geral de Fiscalização* (p. 119). Agencia Nacional de Vigilancia Sanitaria. Retrieved 3 November 2021, from: https://www.gov.br/anvisa/pt-br/assuntos/fiscalizacao-e-monitoramento/roubos-furtos-e-extravios

ANVISA & HC/FMUSP. (2020). *Guia do Sistema Nacional de Controle de Medicamentos*. Agencia Nacional de Vigilancia Sanitaria. Retrieved 11 November 2021, from: https://www.gov.br/anvisa/pt-br/assuntos/fiscalizacao-e-monitoramento/rastreabilidade

Assaf Neto. (2020). *Finanças Corporativas e Valor* (8º ed). São Paulo:Atlas.

Bansal, D., Malla, S., Gudala, K., & Tiwari, P. (2013). Anti-counterfeit technologies: A pharmaceutical industry perspective. *Scientia Pharmaceutica*, *81*(1), 1–143

Bonem, J. M. (2018). 9—Project Evaluation Using CAPEX and OPEX Inputs. In J. M. Bonem (Org.), *Chemical Projects Scale Up* (p. 107–123). Elsevier.

Brazil. (2009). *Lei 11.903 de 14 de Janeiro de 2009.* Presidência da República, Casa Civil. Retrieved 17 November 2021, from: https://legislacao.presidencia.gov.br/atos/?tipo=LEI&numero=11903&ano=2009&ato=027cXVE90dVpWT619

Brazil (2016). *Lei 13.410 de 28 de Dezembro de 2016*. Presidência da República, Secretaria Geral. Retrieved 17 November 2021, from: http://www.planalto.gov.br/ccivil_03/_ato2015-2018/2016/lei/l13410.htm

Buckley, G. J., Gostin, L.O.. (2013). *Countering the problem of falsified and substandard drugs*. Washington, DC: The National Academies Press.

Chiacchio, F., Compagno, L., D'Urso, D., Velardita, L., & Sandner, P. (2020). A decentralized application for the traceability process in the pharma industry. *Procedia Manufacturing*, *42*, 362–369. https://doi.org/10.1016/j.promfg.2020.02.063

Silva, R. B., Mattos, C. A. (2019). Critical Success Factors of a Drug Traceability System for Creating Value in a Pharmaceutical Supply Chain (PSC). *International Journal of Environmental Research and Public Health, 16 (11)*

GS1. (2018). *GS1 DataMatrix Guideline*. Retrived 9 June 2021, from: https://www.gs1.org/docs/barcodes/GS1_DataMatrix_Guideline.pdf

GS1. (2021). *Global Trade Item Number (GTIN)/GS1*. Retrived 9 June 2021, from https://Www.Gs1.Org/Standards/Id-Keys/Gtin. https://www.gs1.org/standards/id-keys/gtin

Guia da Farmácia. (2020, outubro 7). *Consumo de analgésicos e vitaminas cresce durante a pandemia*. Guia da Farmácia. Retrieved 13 December 2021, from: https://guiadafarmacia.com.br/consumo-de-analgesicos-e-vitaminas-cresce-durante-a-pandemia/

ICMRA. (2021). *International Coalition of Medicines Regulatory Authorities: Recommendations on common technical denominators for traceability systems for medicines to allow for interoperability*. Retrieved 13 December 2021, from: https://icmra.info/drupal/en/meetings/2021Brazil

INOVA HC. (2020). *Relatório Final SETRM 2020* (p. 44). Retrieved 9 June 2022, from: https://limhc.fm.usp.br/portal/tag/inovahc/

Buckley, G. J., Gostin, L.O.. (2013). *Countering the problem of falsified and substandard drugs*. Washington, DC: The National Academies Press.

Interpol. (2020). *Global operation sees a rise in fake medical products related to COVID-19*. Retrieved 9 June 2021 form: https://www.interpol.int/News-and-Events/News/2020/Global-operation-sees-a-rise-in-fake-medical-products-related-to-COVID-19

Krynytskyi, I. Y., Noha, P. P., & Sarana, S. V. (2019). Serialization as new quality control system of medicinal products.*Wiadomości Lekarskie*, 2473.

Kurucz, E., Colbert, B., & Wheeler, D. (2008). The Business Case for Corporate Social Responsibility. In *The Oxford Handbook of Corporate Social Responsibility*.

Leatherman, S., Berwick, D., Iles, D., Lewin, L. S., Davidoff, F., Nolan, T., & Bisognano, M. (2003). The business case for quality: Case studies and an analysis. *Health Affairs (Project Hope)*, *22*(2), 17–30.

Lima, F. R. P. de, Da Silva, A. L., Godinho Filho, M., & Dias, E. M. (2018). Systematic review: Resilience enablers to combat counterfeit medicines. *Supply Chain Management: An International Journal*, *12*(3), 117–135.

Lončar, I. M., & Cvijanović, J. M. (2013). Analysis of the importance of drug packaging quality for end users and pharmaceutical industry as a part of the quality management system. *Hemijska Industrija*, *67*(6), 951–959.

Ludasi, K., Sovány, T., Laczkovich, O., Hopp, B., Smausz, T., & Regdon, G. (2018). Unique laser coding technology to fight falsified medicines. *European Journal of Pharmaceutical Sciences*, *123*, 1–9.

Pascu, G. A., Hancu, G., & Rusu, A. (2020). Pharmaceutical Serialization, a Global Effort to Combat Counterfeit Medicines. *Acta Marisiensis - Seria Medica*, *66*(4), 132–139.

Pisa, M., & McCurdy, D. (2019). Improving global health supply chains through traceability. *Center for Global Development*. Retrieved 9 June 2021 from https://www.cgdev.org/sites/default/files/improving-global-health-supply-chains-through-traceability.pdf

Rodgers, D. (2017). FDA DSCSA Public Meeting #1 Exposes Gulf In Goals. Retrieved in 9 June 2022 from: https://www.rxtrace.com/2017/08/fda-dscsa-public-meeting-1-exposes-gulf-goals.html/

Ross, S. A., Westerfield, R. W., Jaffe, J., & Lamb, R. (2015). *Administração Financeira*. 10. ed. Porto Alegre:McGraw Hill

Rotunno, R., Cesarotti, V., Bellman, A., Introna, V., & Benedetti, M. (2014). Impact of track and trace integration on pharmaceutical production systems. *International Journal of Engineering Business Management*, *6*(1), 1–11.

Teresa Pereira, M., Magalhães, H., Ferreira, F. A., & Barreiras, A. (2022). . *Lecture Notes in Mechanical Engineering*, 320–329.

Trenfield, S. J., Tan, H. X., Awad, A., Buanz, A., Gaisford, S., Basit, A. W., & Goyanes, A. (2019). Track-and-trace: Novel anti-counterfeit measures for 3D printedpersonalized drug products using smart material inks. *International Journal of Pharmaceutics*, *International Journal of Pharmaceutics*, 567,118443.

WHO - World Health Organization. (2017a). *A study on the public health and socioeconomic impact of substandard and falsified medical products*. Retrieved 22 November 2021, from: https://apps.who.int/iris/handle/10665/331690.

WHO - World Health organization. (2017b). *WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products.* Retrieved 22 November 2021, from https://apps.who.int/iris/handle/10665/326708

WHO - World Health Organization. (2021).Policy paper on traceability of medical products.World Health Organization. Retrieved 22 November 2021, from https://apps.who.int/iris/handle/10665/340237

Zimmerman, M., Holst, C. G., Mehring, L. B., Moon, S., & Berges, A. (2017). The impact of anonymity on psychiatric patients' ratings of satisfaction with the initial evaluation. *Annals of Clinical Psychiatry: Official Journal of the American Academy of Clinical Psychiatrists*, *29*(4), 220–226.

Appendix 1

Parameter	Description	Definition	Unit
Sc	Serialization Cost	Overall result searched by this paper in money	$
plc	Process Line Capacity	Line Amount in percentage	%
Ic	Individual Ink Cost	Individual ink cost per unit drug product	$
iCapex	Unit Capital Expenditure Cost	Capital invested per finished good	$
umc	Unit Maintenance Cost	Maintenance cost per unit	$
ducOEE	Drug Unit Decreased Cost OEE	Cost of OEE decreased per unit drug product	$
mCapex	Monthly Capital Expenditure Cost	Capital Invested Monthly per Finished Good	$
fv	Future Value	Future Value of Investment	$
Capex	Capital Expenditure	Capital Expenditure Project Investment	$
dt	Depreciation Time	Project Depreciation Time	$
dutc	Drug Unit Total Cost	Total Cost per Unit of Finished Good	$
durc	Drug Unit Real Cost	Real Cost per Unit of Finished Good	$
mpdOEE	Monthly Productivity Decreased OEE	Monthly Productivity after OEE impact	$
mp	Monthly Productivity	Monthly Productive of Packing Lines	UN
mmc	Monthly Maintenance Cost	Monthly Maintenance Cost of Packaging Lines	$
amc	Annual Maintenance Cost	Annual Maintenance Cost of Packaging Lines	UN
tCapex	Total Capital Expenditure	Project Capital Investment Value	$
mdc	Monthly Depreciation Cost	Monthly Depreciation Cost of Equipment	$
mic	Monthly Ink Cost	Monthly Ink Cartoon Cost of Packaging Lines	$
mp	Monthly Productivity	Monthly Productivity of Packaging Lines	$
icmq	Ink Cartridge Monthly Quantity	Number of Ink Cartridges Used Monthly	UN
icc	Ink Cartridge Cost	Ink Cartridge Cost per Unit	$
dp	Daily Productivity	Daily Productivity of Packaging Lines	UN