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Pharmaceutical serialization dynamics to restrain illicit trade and counterfeiting of drugs

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Abstract

Every individual has a fundamental entitlement to healthcare access. It falls upon governments to guarantee the delivery of high-quality healthcare services and infrastructure to their populace.. Over the past few decades, both governments and healthcare industries have been grappling with the challenge of minimizing the adverse effects on public health caused by counterfeit medicines. The World Health Organization has estimated that 40 % medicines in developing and impoverished countries are either counterfeit or potentially adulterated. The global economy suffers billions of dollars in losses due to counterfeit drugs, which also divert funds away from research and development (R&D) initiatives.

In the United States, the Food and Drug Administration (FDA) has devised a 10-year roadmap to implement drug traceability measures. The Healthcare Distribution Alliance (HDA) has been tasked with mandating the printing of multiple barcodes and human-readable data on product packaging. Additionally, the FDA is actively involved in pilot projects with leading pharmaceutical manufacturers and wholesalers to leverage blockchain technology within interoperable digital networks for secure data transfer and traceability among authorized trading partners.

Preventing counterfeit medicines from infiltrating the supply chain remains a significant challenge for governments and regulatory authorities. Consequently, there is a growing emphasis on implementing stringent guidelines to deter criminals and counterfeiters from distributing fake medicines in the market. The healthcare industry requires robust regulations and secure technologies to ensure the delivery of safe and authentic drugs to patients.

Keywords: Pharmaceutical Supply Chain; Drug Traceability; Drug Counterfeit; Pharmaceutical Serialization; Track and Trace System; Enterprise System; Blockchain; IoT

1. Introduction

Pharmaceutical drug serialization stands as a crucial mechanism for digitally tracking and tracing drugs within the supply chain. It operates on the foundational principles of "What, Why, When, and Where," ensuring that all drug-related activities are meticulously recorded digitally for future audits and traceability within the supply chain. However, the implementation of digital drug traceability in the supply chain is rife with complexities. The process involves continuous changes in brand ownership of drugs between manufacturers and buyers. Without stringent regulations and secure technology in place, all stakeholders, including patients, are susceptible to threats to their lives [1,2]. Any errors or adverse events occurring in manufacturing, the supply chain process, material sourcing, ideal storage conditions, or temperature maintenance can compromise the potency of drugs, posing risks to people's health.

The pharmaceutical industry has always been a magnet for criminals and drug traffickers who produce large quantities of counterfeit medicines and distribute them through illicit networks, including online sales via the dark web. The

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COVID-19 pandemic has exacerbated the issue of illicit drug trade, leading to an increase in the production of counterfeit drugs due to disruptions, a lack of skilled resources, low business resilience, and the rapid misuse of technologies [3]. The adverse economic impacts faced by the healthcare sector due to counterfeit and illicit drugs result in significant revenue losses for supply chain partners. This trade also diminishes the profitability of the health sector and its ability to invest in pharmaceutical research and innovation for economic growth [4].

To gauge the size of the counterfeit drug market accurately, four potential scenarios are evaluated, each associated with estimated global counterfeit drug markets of $100 billion, $200 billion, $300 billion, and $431 billion, respectively. Blockchain-based applications, combined with advanced manufacturing technologies, are being deployed to enhance digital drug traceability, with continuous improvements at the forefront of innovation. Critical aspects of traceability, such as material traceability in continuous manufacturing systems, are being systematically tracked and investigated [5].

In the current competitive economic landscape of the pharmaceutical industry, traceability plays a pivotal role as a primary differentiator [6]. It facilitates waste reduction, prevents counterfeiting, and minimizes targeted recalls, thereby improving supply chain processes, synchronization, adaptability, visibility, resilience, and security.

1.1. Online Counterfeit Medicine Market

The issue of illegal and counterfeit pharmaceuticals transcends borders, posing an international challenge. The majority of these falsified pharmaceuticals find their way into developing or underdeveloped nations, such as South Asia and Africa, where the prevalence may soar as high as 70%. Approximately one-third of the world's nations lack robust regulatory bodies for drugs, rendering them vulnerable targets for counterfeiters. In the absence of anti-counterfeiting measures, millions of individuals are exposed to potentially lethal substances, thereby jeopardizing plans for business expansion [7,8].

The proliferation of e-commerce platforms and the globalization of consumer markets have created new pathways for the dissemination of fraudulent medications, including online shopping and delivery. Specifically, the accessibility, anonymity, affordability, and global reach of Internet-based technologies have fueled the rapid growth of online pharmacies, estimated to exceed 35,000 websites [9]. However, the vast majority of these online "pharmacies" operate unlawfully, lacking essential safeguards such as the requirement for a legitimate prescription, valid licensure or certification, and compliance with local, national, or international pharmacy regulations [10, 11].

These illegal or "rogue" online pharmacies pose significant risks to patient safety as they serve as sources and distribution points for medications of questionable quality. They operate outside the regulatory framework of the controlled supply chain and lack clinical oversight from qualified healthcare professionals. Customers who patronize unlicensed online pharmacies contribute to undermining the regulatory mechanisms intended to ensure the quality, safety, and appropriate use of medications. Moreover, they contribute to the expansion of the market for counterfeit pharmaceuticals on a global scale [12, 13].

Consumers also face cybersecurity risks when engaging with these illicit online pharmacies, including financial theft, data phishing, and exposure to computer viruses and malware. This exacerbates existing health-related vulnerabilities [14]. Consequently, the globalization of e-commerce has facilitated the emergence of a "digital" pharmaceutical gray market that operates independently from the legal supply chain, offering convenience but also posing significant risks.

Importantly, persistent challenges in ensuring fair access and affordability to prescription pharmaceuticals remain key drivers behind the continued existence of this alternative demand and sourcing channel [15].

1.2. Drug Serialization challenges and concerns

Enforcing drug traceability is a crucial regulatory requirement aimed at mitigating the risks associated with counterfeit drugs within the supply chain. However, impoverished and developing nations encounter significant hurdles in meeting this mandate. Challenges include inadequate funding for infrastructure improvements, a shortage of skilled personnel, limited access to secure technology, and the inability of local pharmaceutical manufacturers to embrace and invest in drug traceability systems [16, 17]. Small manufacturers face additional critical challenges stemming from geopolitical and economic disparities, civil conflicts, political instability, distrust in government entities, and the impacts of climate change and environmental fragility [18].

The implementation and maintenance of serialization systems for drug traceability necessitate skilled human resources. Any errors—whether human, mechanical, or technical—can have adverse implications for human life. In India, for instance, the Directorate General of Foreign Trade (DGFT) requires manufacturers to upload "dummy" or fake serial numbers for primary packages, which has led to confusion. This requirement poses a potential risk of counterfeiting [19, 20]. To comply with serialization regulations, small manufacturers must invest significantly in computer systems, vision systems, barcode grading systems, and effective quality control measures to ensure compliance with national standards. Processes such as identifying and discarding misprinted drug packages on the packaging line often require AI-based applications to optimize manufacturing processes and minimize human intervention [21].

The implementation of digital pharmaceutical product traceability provisions necessitates additional space within manufacturing facilities for specialized packaging equipment, label grading systems, barcode printers, and vision systems. Such setups require substantial financial investments from manufacturers, potentially exceeding their financial capabilities [22]. Investments in serialization equipment, label software, and digital traceability systems can significantly disrupt the financial status of small pharmaceutical manufacturers. Despite heavy investments in infrastructure to meet serialization compliance, small manufacturers may find themselves forced to explore alternative market segments, resulting in reduced revenue.

As technology evolves rapidly, pharmaceutical industries are leveraging various IT platforms to assist in the planning and execution of clinical trials. However, the adoption of such technologies may pose additional financial burdens and operational complexities for small manufacturers.

1.3. Drug Traceability use to encounter the counterfeiting

Drug serialization and traceability are rapidly becoming global compliance standards as an increasing number of countries adopt and standardize their regulations regarding drug traceability. As we approach 2023, we are entering the final phase of the 10-year implementation period for the Drug Supply Chain Security Act (DSCSA), which was enacted in 2013. Currently, the FDA is conducting a pilot project to explore the feasibility of adopting blockchain technology in an interoperable network.

Under the 2023 DSCSA Act, drug manufacturers will be required to digitally transfer drug traceability data to wholesalers and distributors in the supply chain. Additionally, dispensers and pharmacies will need to receive drug traceability data in the Electronic Product Code Information Services (EPICS) format through a shared and secure interoperable network. Ultimately, all stakeholders in the pharmaceutical supply chain should be seamlessly integrated through a digital interoperable network [23].

The Healthcare Distribution Alliance (HDA) has also issued guidelines for manufacturers to print different levels of barcodes on drug packages to enhance supply chain security and mitigate drug counterfeiting. Noncompliance with these barcode guidelines set by the Healthcare Distribution Alliance can lead to decreased supply chain efficiency, increased costs, product delays, and potential drug shortages [24].

There is a clear need for effective solutions to detect counterfeit medicine in order to improve supply chain visibility and patient safety. Blockchain technology presents an innovative solution for drug traceability. When GS1 compliant barcodes are used on drug packages and unique drug identifiers are digitally stored for traceability, blockchain technology can be highly effective [25]. Serialized data for drugs will be accessible to all stakeholders in the supply chain, including wholesalers, distributors, dispensers, pharmacies, and hospitals, allowing them to digitally verify the authenticity of product identifiers.

Originating from the well-known Bitcoin virtual currency, blockchain technology has now been widely adopted across various industry sectors. It is distinguished from Bitcoin and recognized as one of the most stringent and secure technologies available. Fundamentally, blockchain relies on a complex network of distributed ledger databases maintained by multiple participants. It incorporates technical features such as cryptography, consensus mechanisms, and smart contracts, offering decentralized credibility, immutability, transparent data traceability, and other features. Utilizing this complex network, blockchain can facilitate digital drug traceability throughout the supply chain, particularly when digital data encoding in GS1 compatible barcodes is employed to assign barcodes to all levels of packaging units linked to the digital identity of the product.

1.4. Drug Supply Chain Security Act in United State

In the United States, a notable segment of the population is at risk of potential exposure to counterfeit or stolen medications. This risk disproportionately affects individuals who are Hispanic, have limited educational attainment, live

below the poverty line, are non-citizens, lack health insurance, face high out-of-pocket insurance expenses, and procure counterfeit drugs from illicit dark web or social media platforms. The rollout of serialization compliance in the United States commenced in November 2018, following an initial announcement to enforce serialization regulations in November 2017. However, due to a lack of preparedness among manufacturers, supply chain partners, and wholesalers, compliance was delayed by one year [26].

Under the serialization regulation, all prescribed pharmaceutical medications must feature a unique product identifier for traceability. The Drug Supply Chain Security Act (DSCSA) has delineated an eight-year phased implementation plan spanning from 2015 to 2023. As part of this strategy, obligatory compliance entails the integration of a unique product code with a 2D data matrix on individual medicine packets for electronic traceability. Furthermore, all supply chain partners, encompassing manufacturers, re-packagers, wholesalers, and dispensers, are mandated to electronically transmit data for unit-level traceability. Additionally, the incorporation of packaging hierarchy of aggregated data in Electronic Product Code Information Services (EPCIS) files and electronic transmission to supply chain partners are prerequisites [27,28].

The DSCSA necessitates that stakeholders in the supply chain, such as wholesalers, distributors, dispensers, and pharmacies, authenticate suspected or potentially counterfeit product unique identifiers upon request from trading partners, regulatory agencies, or state entities. Ultimately, the DSCSA 2023 Act supersedes the lot-level requirement with unit-level traceability, compelling all stakeholders in the supply chain to exchange serialized data electronically utilizing interoperable technological means. This provision aims to aid pharmaceutical industries in implementing and harnessing resilient systems [29]. The electronic traceability system must possess the capability to store and process large volumes of data for product traceability. Section 582(a)(9) of the FD&C Act, under the Drug Supply Chain Security Act, stipulates that each product packaging must include a 2-dimensional (2D) data matrix barcode with human-readable data when printing product packaging labels, along with a linear barcode or 2D data matrix barcode when printing labels on homogeneous cases [30].

Transaction information regarding medications, known as T3 information, should be captured and shared with partners to adhere to regulations such as the Drug Supply Chain Security Act (DSCSA). This transaction information encompasses:

1.5. Proprietary or trademarked name(s) or names(s) of the product

- Product strength and dose kind
- The product's national drug code
- Size of Container
- Containers Needed
- Products lot
- The timing of transaction

2. Conclusion

The challenge of counterfeit drugs presents a significant hazard to public health and jeopardizes patient safety. Over recent decades, the World Health Organization (WHO) has spearheaded numerous efforts to reduce the dangers linked with counterfeit medications. It's been noted that the majority of fake and illegal drugs are distributed in developing or economically disadvantaged regions, potentially accounting for up to 70 percent. In the United States, the Drug Supply Chain Security Act (DSCSA) has laid out a 10-year plan for ensuring serialization compliance. The DSCSA 2023 Act mandates that manufacturers and distributor/wholesalers digitally transmit serialized data through interoperable networks. The FDA is also involved in a pilot initiative exploring the integration of blockchain technology into interoperable networks to authenticate "Authorized Trading Partners." Furthermore, the DSCSA 2023 Act requires the electronic transmission of serialization data among all supply chain partners to achieve unit-level traceability. By adopting secure, robust, and innovative technologies and embedding product attributes in barcodes, the risk of counterfeiting in the supply chain can be minimized. The growing acceptance of serialization technologies globally is a promising sign of its efficacy, with many countries expected to soon mandate serialization for prescribed drugs as a regulatory measure.

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