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Review Article

Pharmaceutical Drug Packaging and Traceability: A Comprehensive Review

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Abstract: A Medical devices and pharmaceutical drugs are packaged to maintain their stability and integrity during post-production shipping and storage prior to clinical usage. During delivery and storage, the packaging may come into direct or indirect contact with the drug product or medical device, which may result in chemical interactions between the two. Packaging can be crucial for success, protection, and sale. Like other supermarket items, prescription pharmaceuticals must be packaged in a way that will meet the needs of security and provide speedy packaging, safety, identity, superiority of products, patient safety, and goods superiority. Packaging is a science and an art where many factors are taken into account, starting with the fundamental design and technology used to pack the product without any instability and providing protection, presentation and observance of manufactured goods during transportation, storage, and consumption. In order to keep the drug physiochemical, biological, and chemical stability, packaging professionals create containers that can withstand the pressures that are applied during the supply and shipping processes. Improvements in the analysis of prescription drug development had long been fixated on packaging expertise.

Keywords: Drug Traceability, Drug Counterfeit, Pharmaceutical Serialization, Supply chain, Track and Trace System, Cold Chain, Blockchain, Enterprise System

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1. Introduction

Organizations in the healthcare industry are constantly looking for ways to save costs, boost safety, and keep or improve quality. These tactics comprise locating and enhancing current techniques as well as implementing cutting-edge technologies. The main objective of the research being done is to prevent and reduce the use of spurious and counterfeit drugs, which have emerged as a threat because they undermine the reputation of legitimate drug manufacturers by trying to produce and market placebo medications that resemble the real thing. Due to the misrepresentation of medications in their inventory, also known as loan-licensing arrangements between the drug maker and licensee, many pharmaceutical manufacturers are forced to accept a cost over burn. Such agreements always include a social impact clause to ensure that pharmaceutical companies give low-income nations funding and supply the medical supplies they need to protect their citizens from dangerous diseases. But many businesses are utilizing these shipments to smuggle drugs, transferring the freight to the open market. For conducting complex analytics programs to obtain in-depth insights into consumption patterns, geographic penetration, the effectiveness of sales and marketing spend, etc., unique identification of packaged drugs will be a fantastic enabler. A technique can be devised to instantaneously verify if a medicine is a genuine drug, that is, one that has been made in accordance with the necessary compliance regulations, based on the purchase of drugs by customers. Improved inventory monitoring at different supply chain nodes can help in more correctly estimating demand,

preventing revenue loss due to stock-outs, which will support innovation marketing schema. comprehension the recommendations that have been issued by various compliance authorities from the top producing nations is crucial, and it is necessary to keep in mind that "unique identification" models require at least a basic comprehension of barcoding techniques. The Falsified Medicines Directive, a regulation passed by the European Union Parliament, aims to safeguard patients, improve the safety of the manufacturing and distribution of medicines throughout Europe, and stop the entry of fake drugs into the supply chain. IVEDA, which stands for Integrated Validation of Exports of Drugs from India and its Authentication, was created primarily as a repository database for serialized batch data. It was developed to make the use of secondary and tertiary-level coded data easier, more effective, and more efficient for exporters and manufacturers. The aggregation will take place on a local client server, and once it is finished, the in-process and production reviews have been reviewed and approved, the aggregated data is transferred to a central server. The speed of the aggregation process may increase as a result. Overall, it was decided to add automated equipment that would meet the requirement without compromising the supply chain's pace of packaged goods in order to improve the speed of aggregation of medication packs. Multi-Carton Line, which would make it possible to scan a group of different packs all at once and speed up aggregation. Pallet line that would let the accumulation of the packs in the secured facility where pallet packing is managed. To reduce reliance on the manufacturer's computer network, these packs are locally aggregated on the packaging line. The Track and Trace server instance would be used to manage General Approval activity. In the current study, we assessed the speed of aggregation using automated bulk code reading in the combinations "Child pack to Parent pack" and "Parent pack to Child pack." We discovered that the aggregation of packs was completed more quickly in both of the examples, and we satisfied the needs of our pilot consumers. The Food and Drug Administration (FDA) has not approved pharmaceutical medicines acquired from international internet pharmacies, and they may not adhere to US labelling and packaging requirements.

2. Pharmaceutical drug packaging

Critical success factors for establishing a Safe Pharmaceutical Supply Chain can be attributed to the influence and gradual reduction in drug counterfeits. Labels for pharmaceutical packaging should adhere to safety regulations and pose no toxicological concerns for its extractables, leachable, and indirectly contactable components. It can be difficult to spot extractables or leachable in pharmaceutical packaging materials because their content is often low. It allows for quick screening and qualitative compound analysis in a single step. Pharmacists should use packaging that preserves the integrity of the drug product in addition to correct labelling. The type, quantity, and method of use of the medication that will be prescribed should be taken into consideration when the pharmacist selects the container [1]. The container should maintain a product's identity, strength, quality, and purity as well as prevent contamination. It should be comparable to the packaging that manufacturers use to package drug items. The labelling of the manufacturer's prescription product, which is governed by the US Food and Drug Administration (FDA), specifies the kind of container that should be used by a pharmacist when distributing a prescription drug. Products meant to be used in the manufacturer's original container are exempt from the FDA restriction. The original container or the package insert are typically where you can find the manufacturer's packaging and storage instructions. In other words, "labelling" can relate to pharmaceuticals obtained from a manufacturer, and "label" can describe pharmaceuticals that a pharmacist dispenses in accordance with a prescription order [2]. The prescription container's closing should get special consideration in addition to the packaging specifications for dispensing medication items. The closure must prevent pollutants and moisture from entering that could harm oral dosage forms. Aspirin's con-

version into acetic acid and salicylic acid in the presence of moisture is a well-known example in pharmaceutics. Manufacturers are required to put prescription pharmaceuticals in child-resistant packaging if the original package is meant to be delivered straight from the pharmacist to the patient. Similarly, unless the patient or doctor specifically requests differently, pharmacists must administer prescription medications for oral use to the patient in containers with child-resistant safety closures. A signed release from the patient is required and may be used for all of the patient's administered drugs if the patient requests a safety container that is not child-resistant. The pharmacist is required to keep a copy of the signed waiver request on file. There are few exceptions to these rules, such as the packaging of oral contraceptives due to its practical design and some cardiac medications like nitro-glycerine. Patients might need access to the drug right away in these circumstances. Information about the packaging and labelling of medicinal medicines imported through the Internet is currently scarce. A research was started by the Office of Compliance at the FDA's Centre for Drug Evaluation and Research to evaluate the quality of a selected set of pharmaceutical products bought from overseas via the Internet. Almost all of the Internet purchase samples had a serious packaging issue. Many lacked or had very little instruction on how to use something. In unmarked plastic bags, some medicine samples were supplied in loose condition [3]. While imitation, even if not permitted by the brand owner, may occasionally be acceptable and not violate any copyright laws, imitation is still prohibited. This activity is used to create things that "look like" the original, as evidenced with private label imitation of branded goods [4]. Consumers may be confused by two sorts of similarity to the original brand: literal similarity, where a product name may contain common letters or a similar string of characters, and semantic similarity, where the name is different but the extrinsic characteristics of the product are replicated [5]. Consumers may, however, be misled by product imitation into thinking there is a connection or affiliation between the mimicked product and the imitated brand [6]. Only when there is both a customer demand for the goods and a supply from fraudsters can there be non-deceptive counterfeiting [7]. Non-deceptive counterfeit goods can be identified from the branded products they are intended to imitate both physically and by the kind of sales and distribution channels through which they are sold [8]. False copies are intentionally made to look like they work well, but they malfunction or expose security gaps to give their opponents an advantage [9]. Digital systems are susceptible to malicious counterfeiting, which can result in deliberate hardware failure [10]. Fake hardware might leave firms open to future malware introduction and cyber security issues. As a result, it is crucial to implement efficient mitigating measures [11].

3. Anti-counterfeiting technology in pharmaceutical drug packaging

Logistics traceability and qualitative traceability are two traceability components that are of interest as anti-counterfeiting measures [12]. Tracking, tracing, and logging are the three components of logistics traceability. Tracing is backward traceability from completed product to ingredient; tracking is forward traceability from ingredient to finished product; and logging is the physical movement of the product's information, such as quantity, origin, destination, and delivery date. Qualitative traceability connects extra data to the product, such as pre- and post-harvest methods, storage and distribution circumstances. This data serves as the foundation for the product's brand value. Second, brand owners must educate consumers about the dangers of counterfeit goods, particularly through the use of government- and/or celebrity-backed information campaigns [13]. These government-sponsored media campaigns should promote moral behaviour, emphasizing the dangers of purchasing and using counterfeit items as well as their effects on real businesses [14]. Utilizing demand-side tactics to prevent initial instances of counterfeiting. These consist of taking legal action when necessary, enhancing supplier oversight, cultivating relationships based on trust, and instituting verification procedures. To pre-

vent potential counterfeiters from using "third-shift" techniques, another tactic is to outsource only the production of the component parts and then assemble the final product within the brand owner's own business. Track and trace and/or authentication smart technology integration into databases will also prevent counterfeiting [15]. Anti-counterfeiting obstacles are another component of these protocols. The formal system elements known as hurdles serve as a deterrent or help detect behavior, so reducing the chance for counterfeiting [16]. Therefore, obstacles created as online or offline anti-counterfeiting methods are meant to deter people from purchasing fake goods and instead encourage them to become activists against fakes and imitations [17]. Anti-counterfeiting strategies mentioned in the literature have been divided into groups based on how they work: relates to social value, distribution, management, communication, products, processes, and other associated areas [18].

4. Pharmaceutical drug serialization

Pharmaceutical drug tracking to increase awareness throughout the Track and trace drug units are referred to as serialized in modern usage. This procedure is accomplished by supplementing the initial individual package with an electronic pedigree and a special identification number. The primary objective of pharmaceutical serialization is to assign each unit of medication with a unique and exclusive identity. Public security and policy on a global scale will aid in protecting the populace and the government from fake medications. The 2D barcodes for vaccinations, medical equipment, or medications can aid the responsible organizations by encouraging an effective inventory procedure and by providing crucial information for methods of global distribution. Partners participating in the drug marketing process must cooperate in order for serialization to be successful. About 70% of all currently available medications are anticipated to be covered by drug serialization regulations. There are no universal worldwide standards at the moment. Serialization implementation, coordination, and control demand a large financial investment and a solid grasp of the applicable rules.

5. Pharmaceutical drug traceability

The concept of tracking pharmaceutical products to provide visibility across the pharmaceutical supply chain is not new. In addition to markets like China and South Korea, Turkey adopted serialization rules in 2010. Since the turn of the century, China has mandated that all supply chain participants in the distribution of medicines record data about individual drug units in a traceability system. Many nations around the world have begun to emphasize and even require the significance of drug traceability. To identify and track specific prescription pharmaceuticals as they are distributed in the US, the US regulatory body Drug Supply Chain Security Act (DSCSA) has specified methods to enable interoperable, electronic tracing of products at the package level. A barcode is a pattern of bars and spaces that can be read by an optical equipment and serves as a visual representation of a product's unique identifying number and its maker. The most used symbology for identifying products and facilitating inventory control is still barcodes. Barcodes and quick response (QR) codes are examples of machine-readable media that facilitate improved data sharing and data validation [19]. Compared to barcodes, radio frequency identification (RFID) microchips are a more sophisticated data carrier and have more storage space. RFID is used for product tracing and identification [20]. In order to collect, store, and manage information between the tag, reader, and related software, RFID technology uses radio waves that are close to each other [21]. RFID is adaptable because the tag may be integrated into the packaging, can read through various materials (such paper and plastic), is non-intrusive, and enables traceability along the entire supply chain [22]. Two of the most popular technologies for traceability and tracking are barcodes and RFID. In fact, the use of RFID has gone beyond traceability to include individual unit identification

because there is a risk of counterfeiting by actors in the supply chain, such as importers or transporters [23].

6. Emerging technologies for preventing drug counterfeiting

A barcode is a pattern of bars and spaces that can be read by an optical equipment and serves as a visual representation of a product's unique identifying number and its maker. The most used symbology for identifying products and facilitating inventory control is still barcodes. Barcodes and quick response (QR) codes are examples of machine-readable media that facilitate improved data sharing and data validation [24]. Technologies that combat counterfeiting are used to distinguish between genuine and fake goods. The technology must be challenging to replicate, tough to repurpose, yet simple to use, easy to identify visually, and obvious when tampered with [25]. Anti-counterfeiting packaging systems can be categorized as direct, overt (obviously visible to the consumer), or covert (indirect, not readily apparent to the human eye) technologies [26]. Direct or overt technology, such as the use of holograms, watermarks, barcodes, RFID, and tamper-evident seals, enables end users to visually authenticate the uniqueness of the packaging. Business-to-business (B2B) or business-to-consumer (B2C) anti-counterfeiting systems are both possible. At their most basic, tamper-evident systems can be included into packaging designs using film wrappers, shrink seals and bands, breakable or single-use caps, etc [27]. When a package is held up to a light source, watermarks—images or patterns incorporated into the packaging design—can be seen. Preventing product fraud, watermarks are frequently used on packaging. To authenticate their products, food makers might personalize watermarks by utilizing logos or brand names. Visual watermarks are affordable, but in order to verify the legitimacy of a product, company or consumer end-users must be aware of the watermark and know where to look. A plastic or metal ribbon that is woven into paper fibre during the manufacturing process is known as a security thread. The security thread is a hard to replicate feature that can only be seen in transmitted light [28]. When the temperature changes, thermochromic ink changes colour. It serves as an effective anti-counterfeiting measure as well as a crucial indicator of proper temperature storage and/or cumulative temperature abuse [29]. Heat-activated ink that changes from colourless to a strong colour alert, such as blue, green, black, or red, is used to cover the box. With or if there have been temperature changes that have impacted the product's quality. Thermochromic ink has the benefit of being safe to use on food packaging and giving consumers a powerful visual cue. However, since counterfeiters can have access to colour printing equipment, manufacturers shouldn't rely solely on colour alteration as a counterfeiting tactic [30]. Food goods frequently incorporate anti-counterfeiting technology such intaglio printing, security threads, and fluorescence artifacts. On flexible packaging, intaglio printing employs incredibly fine lines and dots and is one of the printing processes that is hardest to copy. In a concerted attempt to reduce the risk of counterfeiting, these packaging technologies can also be integrated with other forms of verification in an anti-counterfeiting measures approach. Consumers that are knowledgeable and skilled may be able to distinguish between a fake and an authentic goods. Whiskey experts and knowledgeable collectors can evaluate the label, the information it carries, and the cork's condition [31]. Consumers now have a means to spot grocery store fraud, thanks to the usage of digital technologies like predictive computing and Internet of Things (IoT) apps, giving them more personal agency. The majority of today's anti-counterfeiting authentication methods are created for use in industrial and laboratory settings [32]. The development of illicit supply networks or the use of illegally produced and/or subpar alcoholic beverages as a substitute for premium products are examples of process-related misrepresentations. Packaging-related misrepresentations include the use of counterfeit packaging or the illegal recycling of genuine liquor bottles. Data-related misrepresentations can also result in counterfeiting [33].

7. Conclusion

A product misrepresentation, such as the use of illegally produced or inferior alcoholic beverages to replace a premium product, a process misrepresentation, such as the establishment of illegal supply networks, and a third misrepresentation of the packaging, such as the use of counterfeit packaging, can all lead to counterfeiting. Despite the numerous anti-counterfeiting measures in place, counterfeiters continue to develop new strategies for producing items while evading detection. The majority of anti-counterfeit packaging technology are standalone devices. It is crucial to take a more comprehensive strategy, creating physical barriers to lessen the possibility of counterfeiting and then creating artefact-based authentication systems integrated with traceability and tracking systems. Thus, in order to prevent counterfeiting and eventually safeguard food supply chains, individual firms, supply chains, and regulators must take into account the types of integrated anti-counterfeiting systems needed.

References

[1] Philadelphia College of Pharmacy and Science. Remington: The Science and Practice of Pharmacy. 21st Edition. Baltimore,MD: Lippincott Williams & Wilkins; 2006:1829-1833.

[2] Thompson JE, Davidow LW. Chapter 2, Labeling Prescriptions and Medications. In: Davidow LW, editor. A PracticalGuide to Contemporary Pharmacy Practice. Baltimore, MD: Williams & Wilkins, A Waverly Company; 1998:2.1-2.4.

[3] Westenberger BJ, Ellison CD, Fussner AS, Jenney S, Kolinski RE, Lipe TG, et al. Quality assessment of internetpharmaceutical products using traditional and non-traditional analytical techniques. Int J Pharm 2005 Dec 8;306(1-2):56-70.

[4] Kapferer, J. N. (1995). Brand confusion: empirical study of a legal concept. Psychology & Marketing, 12(6), 551-568.

[5] Van Horen, F., & Pieters, R. (2012). Consumer evaluation of copycat brands: The effect of imitation type. International Journal of Research in Marketing, 29(3), 246–255.

[6] Zaichkowsky, J.L. (2006), The Psychology Behind Trademark Infringement and Counterfeiting. Mahwah, NJ: Lawrence Erlbaum Associates.

[7] Cesareo, L., & Stöttinger, B. (2015). United we stand, divided we fall: How firms can engage consumers in their fight against counterfeits. Business Horizons, 58(5), 527-537.

[8] Grossman, G. M., & Shapiro, C. (1988). Foreign counterfeiting of status goods. The Quarterly Journal of Economics, 103(1), 79-100.

[9] Bodner, D. A. (2014). Enterprise modeling framework for counterfeit parts in defense systems. Procedia Computer Science, 36, 425-431.

[10] Takahashi, M., Nagata, M., & Miura, N. (2018). Supply-Chain Security Enhancement by Chaotic Wireless Chip-Package-Board Interactive PUF. In 2018 IEEE 68th Electronic Components and Technology Conference (ECTC), 521-526.

[11] Kumar, G. (2023). Critical Success Factors of Adopting an Enterprise System for Pharmaceutical Drug Traceability. Universal Journal of Pharmacy and Pharmacology, 3-10.

[12] Folinas, D., Manikas, I., & Manos, B. (2006), 'Traceability data management for food chains', British Food Journal, 108(8), 622-633

[13] Ting, M. S., Goh, Y. N., & Isa, S. M. (2016). Determining consumer purchase intentions toward counterfeit luxury goods in Malaysia. Asia Pacific Management Review, 21(4), 219-230.

[14] Thaichon, P., & Quach, S. (2016). Dark motives-counterfeit purchase framework: Internal and external motives behind counterfeit purchase via digital platforms. Journal of Retailing and Consumer Services, 33, 82-91.

[15] Kumar, G. (2023). Blockchain in Enterprise Application for Pharmaceutical Drug Traceability. International Journal of Science and Research, 12(8), 130-134.

[16] Spink, J., Moyer, D.C. Park, H. Wu, Y. Fersht, V. Shao, B., Hong, M., Paek, S.Y., & Edelev, D. (2015), Introduction to Food Fraud including translation and interpretation to Russian, Korean and Chinese languages. Food Chemistry. 189, 102-107.

[17] Cesareo, L., & Stöttinger, B. (2015). United we stand, divided we fall: How firms can engage consumers in their fight against counterfeits. Business Horizons, 58(5), 527-537.

[18] Kumar, G. (2023). Securing pharmaceutical supply chain using digital drug serialization. World Journal of Advanced Engineering Technology and Sciences, 10(01), 015–020.

[19] Dabbene, F., Gay, P., & Tortia, C. (2014). Traceability issues in food supply chain management: A review. Biosystems engineering, 120, 65-80.

[20] Meraviglia, L. (2018). Technology and counterfeiting in the fashion industry: Friends or foes? Business Horizons, 61(3), 467-475.

[21] Kumar, G. (2023). Optimizing pharmaceutical supply chain with digital technologies. International Journal of Science and Research Archive, 09 (02), 727–731.

[22] Bibi, F., Guillaume, C., Gontard, N. & Sorli, B. (2017). A review: RFID technology having sensing aptitudes for food industry and their contribution to tracking and monitoring of food products. Trends in Food Science & Technology, 62, 91-103.

[23] Przyswa, E. (2014). Protecting your wine: Stop counterfeiters from selling cheap imitations of your premium brand. Available at: Wines & Vines, August 2014, 38-42.
[24] Dabbene, F., Gay, P., & Tortia, C. (2014). Traceability issues in food supply chain management: A review. Biosystems engineering, 120, 65-80.
[25] Li, L. (2013). Technology designed to combat fakes in the global supply chain. Business Horizons, 56(2), 167-177.
[26] Meraviglia, L. (2018). Technology and counterfeiting in the fashion industry: Friends or foes? Business Horizons, 61(3), 467-475
[27] Woodward, R. (2017). $10,000 glass of Macallan 'is a fake'. Available at: https://scotchwhisky.com/magazine/latest-news/15511/10-000-glass-of-macallan-is-a-fake/
[28] Baldini, G., Fovino, I. N., Satta, R., Tsois, A. & Checchi, E. (2015). Survey of techniques for the fight 460 against counterfeit goods and IntellectualProperty Rights (IPR) infringement. European Commission 461 JCR Technical Report, Eur 27688.
[29] Thermometer (2018). Color change inks. Available at: https://www.thermometersite.com/color change-inks
[30] Kramer, U. (2006). Counterfeiting in the People's Republic of China. Analysis of Impact, Drivers and Containment Options concerning increased Counterfeiting. Diploma Thesis. Diplomica Verlag, GmbH
[31] Charlebois, S., Schwab. A., Henn, R., & Huck, C.W. (2016). Food fraud: An exploratory study for measuring consumer perception towards mislabelled food products and influence on self authentication intentions. Trends in Food Science & Technology, 50, 211-218.
[32] Urickova, V. & Sadecka, J. (2015). Determination of geographical origin of alcoholic beverages using 701 ultraviolet, visible and infrared spectroscopy: A review. Spectrochimica Acta Part A: Molecular and 702 Biomolecular Spectroscopy, 148, 131-137.
[33] Manning L. (2019), Food defence: refining the taxonomy of food defence threats, Trends in Food Science and Technology, 85, 107-115.