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Review Article

Anti-counterfeit technologies

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Corresponding arrangement that covers and safeguards the unit dose of drug is called packaging .One of main reason of deaths , treatment failure , un cure cases and failure of health care set up is counterfeit drugs. Renowned medicines brands in addition to sky-scraping cost of medicine make pharmaceutical ideal for counterfeit medicines and in top of list include medicine for most commonly use disease and high price like medicine use in dyslipidemia, anticancer antihypertensive and other antidiabetic agents. This review article focus on the perfect ways and features present existing anti counterfeit technologies and various other parameters in upcoming and how to remove draw backs in existing technologies during packaging in pharmaceutical industry.

Keywords: Anti counterfeit technologies, dyslipidemia

1. INTRODUCTION

Packaging is a connection in manufacturing of medicine by means of promotion through which medicine arrive to customers from the manufacturing units in a secure and safe way and state in a lowest possible rate and other expenditure should be in range [Kusum, Burande *et al.* 2007]. Another way to define Packaging is the synchronized scheme which be capable of put in or safeguard the medicines for delivery, store, maintenance, carrying, in sequence, and marketing [soroka fundamentals, 2002]. The medicine and other pharmaceutical products are more susceptible to counterfeit because elevated marketplace share, simplicity of manufacturing operations , and better turnover margins [Sangal and Shukla, 2009]. Counterfeit is a dilemma of manufactured medication safety. Medicines are preoccupied from their appropriate allocation control.

Counterfeit is a dilemma of manufactured medication safety. Medicines are preoccupied from their appropriate allocation control, or sold precedent their termination time, or by alteration of the wrap up are connected by means counterfeiting [Dhar, 2010; Olsmats, 2002].

Counterfeits is a process in which illegal productions of a product which are registered legally, which are very much alike or indistinguishable to real products [Cordell, Wongtada *et al.* 1996; Phau , Min *et al.* 2009].

In the the very first conference on the counterfeit drugs held in Geneva on April 1–3, 1992 at World Health Organization (WHO) approved definition of counterfeit drugs and according to that "Counterfeit drugs is that is deliberately plus incorrectly labeled in agreement to individuality in addition to/or basis. Counterfeiting can be relevant jointly to together recognized in addition to basic medicines consisting of any accurate or inaccurate constituents, missing generic constituents, or by bogus covering" [Ruchir, Prajesh *et al*. 2010]. afterward on, the idea was personalized as a result of the meeting of Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) as " drugs with the similar amount of generic constituents because with the intention of authentic product, inadequate otherwise width out generic constituents, drugs which are after termination time , herbal products so as to poisonous otherwise unproductive plus drugs which do not stand the producer information including name and full address are also included in counterfeit" [Clark, 2003]. Counterfeiting is a technique, which causes the violation of property rights, medicine legislations, and other prospects of criminal law [Ruchir, Prajesh *et al*. 2010]. Counterfeiting and copying are in term the same as they both are the reproduction of similar copies of the original product [Phau, Min *et al.* 2009; Zaichkowsky, 1999]. Most of such counterfeit drugs are called lifestyle drugs in developed industrialized

countries. Consumers usually buy such drugs from internet or unauthorized pharmacies [12]. Such counterfeit drugs mainly caused the morbidity and mortality that may leads to the lack of confidence on healthcare system [Swaminath and Faking, 2009]. In India, counterfeit and copied drugs are being use through refill repair and reuse of products [Business Action to Stop Counterfeiting and Piracy (BASCAP) Research report, 2009]. In Europe and US, repackaging is one of counterfeit source [Zurich, 2007]. It is estimated that almost 500,000-1,000,000 people dies per year by use of such counterfeit products [Cockburn, 2005].

2. Need for anti-counterfeit technologies

Patient safety is the main goal, which can be achieved by adopting approach to anti-counterfeit technologies. This reduces drug recalls of companies from markets and also prevents from legal suits. Moreover, the image of brand is defaced and consumer fears of using products of that company in future.

Main strategies against counterfeiting are: liability suits against illegal traders, use of modern technologies, counseling and awareness of consumers and liaison with law imposing agencies. Among all stands the enforcement of technologies [Clark, 2003]. This helps in production of replica drugs and also enhances its production cost than original ones [Phau, Min *et al.* 2009]. Supply chains can be assured by governments that they should be free from counterfeiting, using these kind of technologies [Ruchir, Prajesh *et al*. 2010].

3. Characteristics of ideal anti-counterfeit technology

These technologies should be able to possess high merits of security which cannot be cloned, should be used against wide range of products, efficient in standards with fast process, and may have quality of mechanically be authenticable, even can be used by consumers themselves. Most important it should be legally accepted by companies [Zaichkowsky, 1999]. But, FDA supports use of more and more technologies with variety of types and authenticity [Business insights, 2005].

4. Anti-counterfeit technologies

There are three main ways to use these technologies which have their own merits and demerits [Swaminath and Faking, 2009; Business Action to Stop Counterfeiting and Piracy (BASCAP) Research report, 2009]. These include:

4.1 Tamper-evident/tamper-resistant packing

Film wrappers, bands, tape seals, breakup caps, blister packs , shrinkable seals and many others technologies which may have visual signs and can be easily interpreted by consumers if any hampering or breaching has been done [Zurich, 2007].

4.2 Product authentication

Signs of authenticity can be, embossed or imprinted or embedded on dosage forms and also on packaging, overt, covert markers as shown [Cockburn, 2005].

Table 1: Comparison of Authentication Characteristics.

Features	Overt features	Covert features	Forensic features
Examples	Holograms, color-shift Inks	Embedded images, digital watermarks, invisible printing	Chemical and biological tags, microtaggants
Advantages	User verifiable, more secure, decorative appeal, low cost	Easily added or modified, need regulatory approval, applied in-house or via component suppliers, low cost	High-tech and secure against copying, provide positive authentication, may be disclosed for overt purposes
Disadvantages	Require user education, easily mimicked, rely on covert features for authentication, may be re-used or refilled, provide false assurance	Need strict secrecy, risk of compromise, more secure options add supply complexity and cost	Licensed technologies, significant cost, difficult to implement and control across many markets, unlikely to be available to authorities or public

4.3 Holograms for Anti-counterfeiting

To eliminate counterfeiting holograms is the best approach which can provide both lines of authentication as overt (first line) and covert

(second line) for basic consumers and forensics respectively. The covert signs or markers include microtext, ultraviolent- sensitive, scrambled images and other specialized inks. Sometimes holograms are also used for effective tracing and combat against counterfeiting [Goldhammer and Scott, 2006; Sanjay and Sanjeev, 2009].

4.4 Track and trace technology

In this, a unique identification number is given to each stock unit in manufacturing process until consumption of product. A secure database contains same code as on the product and, which contains all the record of product, and is kept for traceability of product [Europe BRIDGE consortium Problem-Analysis Report, 2007].

4.5 Mass Serialization

The technique of creating, encoding, and verifying the unique identity of individual physical items called Serialization [International Medical Products]. Without it, the accuracy and validity of the purebred relates only to the lot number consisting of thousands of bottles. However, a specific bottle of a particular drug cannot be authenticated [Pharmaceutical Technology Trends, 2008]. Sterilization facilitates the tracking of a product through the supply chain and allows for targeted identification of products for recall [International Medical Products]. Global Standards one (GS1) develops global standards for the identification of goods and services and these standards are used for the identification of pharmaceutical products in sixty countries throughout the world [Tamper Stop Security Technology].

4.6 Global Trade Item Number (GTIN)

A 14/13/12/8 digitally distinctive credentials number is allot by the manufacturer appropriate to GS1 allocation rules for trade objects or goods and services. It is making from a company prefix assigned by GS1, an item indication number designated by the company, and a check digit [Therapeutic Goods Administration Guideline]. Proceeding to market supplies for item-level serialization and verification, Astrazeneca made it as an internal initiative [Securing Pharma Label combines holograms, 2011].

4.7 Serialized Global Trade Item Number (sGTIN)

A distinctive number that identify a fussy trade item, formed by attach a serial number to the GTIN of the product. In their draft guidance for serialized identifier prescription drugs, the FDA proposed the use of the NDC combined with an eight-digit serial number. [Therapeutic Goods Administration Guideline]. In March 2010, the FDA issued guidance deal with the package level SNI (Serialized Numerical Identifier) to be "applied to a recommendation drug at the manufacture and repackaging of the product to assist its track and trace" [US Food and Drug Administration Prescription Drug Marketing Act].

The key defy of execute serialization are the intricacy of data that is to be tracked, and the need for potentially huge, multi-access databases [Joanne SH].

4.8 Data Carriers

Data carriers are graphical systems used to transmit the product identifiers and associated information in computer/ human comprehensible format. A mark, tag, or label applied at the source represents them. Computer readable formats include linear and two dimensional (2D) bar codes and radio frequency identifier (RFID) tags [Therapeutic Goods Administration Guideline]. These are the most commonly employed nowadays [National Chain Drug Stores].

Table 2: Radio Frequency identifier (RFID) Vs 2 Dimensional (2D) Barcode

Features	2D BARCODE	RFID
Direct line of sight requirement	Yes	No
Difficult to duplicate or alter	No	Yes
Readability robustness (interference with liquids/metals)	No	Yes
Cost of tags	Low	High
Tag data storage	Low	High
Bulk tag reading	No	Yes
Initial technology set up cost	Low	High
Eco-system and/or standards maturity	High	Medium
Tag feature's extendibility (ex. Tag with sensors)	Low	High

5. Multi-level approach

Anti-counterfeiting technological approaches are

Inter-reliant for their efficiency, and incorporate they give up a more hearty system. For this, a combination of evident and concealed procedures may give best security as they help avert counterfeiting and reassure end-users [Joanne SH]. For example, using drug product serialization in combination with electronic pedigree greatly improved the level of protection by the aptitude to verify both the product and the operation reliability [US Food and Drug Administration FDA counterfeit drug task force]. For example, the serialization of holographic labels [Joanne SH]. Some organizations such as Authentix and Nosco have made initiatives to combine the respective limitations and the potential of both Data Matrix and RFID, such that cases and pallets can be tracked with RFID tags, while medicines can be tracked with Data Matrix [National Council for Prescription Drug Programs]. yet, a multi-level approach may also result in further expenditure as the technologies become more complicated and should be execute based on the risk analysis of the drug to be counterfeited.

6. Markets of anti-counterfeiting technologies

BCC Research showed that the global sales of anti-counterfeiting packaging technologies were worth US $64 billion in 2010, and the worth is projected to be $74.2 billion in 2015. Track and trace technologies and authentication technologies made up for sales of US$31.7 and $32.4 billion respectively in 2010. Expected values of these by 2015 are US$36.5 and $37.7 billion respectively [US Food and Drug Administration Anti-Counterfeit Drug Initiative Workshop and Vendor Display].

7. Recent technologies

Use of isotope recipient: A current study illustrates the aptitude of labeled excipients in different ratios to provide in-product, batch-specific identification using existing technology in the pharmaceutical industry [Global Standards one Standards Save Lives:GS1 in Healthcare]. For acceptance in developing countries like India, a system named apothecary was anticipated which is a mobile-based authentication system [GS1 healthcare reference book 2011/2012]. A research study anticipated the application of semiconductor nanostructures called quantum dots as a promising strategy against counterfeiting [US Food and Drug Administration Standards for securing the drug supply chain].

8. Anti-counterfeit measures in the pharmaceutical industry

Numerous anti-counterfeit technologies are being developed by pharmaceutical firms to avoid the counterfeits. A few of the products with the consequent anti-counterfeit measures are mentioned in Table. Beside with the anti-counterfeit technologies, the analytical techniques are in addition applied by pharmaceutical industries for authentication which are explicate in a later section.

Table 2: Anti-counterfeit technologies used in brand pharmaceutical products [Deus DBS, 2006; Elisabeth, Alejandro *et al.* 2011]

Pharmaceutical Company	Product	Active Ingredient	Authentication Mark
Pfizer Inc.	Viagra†	Sildenafil citrate	RFID
Hoffmann-La Roche Ltd	Rocephin†	Ceftrioxone sodium	Logo stamps inside vials
GlaxoSmithKline Pharmaceuticals Ltd	Trizivir†	Abacavir/lamivudine/zidovudine	RFID
Purdue pharma L.P.	Oxycontin†	Oxycodone HCl	RFID

9. Analytical techniques

Verification by means of the variety of anti-counterfeit technologies can be done in the delivery sequence, whereas analytical techniques similar to chromatography, optical spectroscopy, and isotopic description prove the constituents possess by a drug [Business Communications Company]. A number of analytical methods were used by diverse pharmaceutical companies intended to the recognition of counterfeits. They comprise straightforward and uncomplicated methods like colorimetry and thin-layer chromatography, to highly developed techniques for example NMR, mass, and raman spectroscopies [Felton, Shah *et al.* 2011]. Small instruments keeps in hand are getting extra significance in addition to many devices are manufactured. Mostly moveable instruments similar to the handholding raman and IR spectrometers are frequently used due to their durability, fast, in addition to dependable features. An augmented order for these is not happen only by the medicine sector, other than also by health departments and establishment, authorities, agencies. A number of the facts due to such command are that these are fast, durable, moveable, and simple to utilize by ordinary worker [Michael and Chen, 2012].

10. Drawbacks of anti-counterfeit technologies

Anti -Counterfeit-methods should be employed by shifting them frequently as they cannot be reproduce by others, frequently within 12–18 months Patients and pharmacist must have to know how of Varity of features and they must have knowledge of shifting of anti-counterfeit technologies Overt and covert packaging technologies are rendered useless if a drug is repackaged [Mukherjee and Ushasi, 2011].

Conflict of Interests

Authors declared no competitive interests for the presented work.

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