ISSN 0976 – 3333

Available Online at www.ijpba.info

International Journal of Pharmaceutical & Biological Archives 2012; 3(4):706-711

REVIEW ARTICLE

A Review on Anti-Counterfeit Packaging and Use of ICT Tools to Combat the Issue of Counterfeiting

Y.A.Chowdary, Soumya.M*, Rajasekhar.N, Sai.S, Manoj Chowdary.S

Department of Pharmaceutics, NRI College Of Pharmacy, Pothavarappadu, Agiripalli Mandal, Krishna District-521212, (A.P), India

Received 15 Apr 2012; Revised 12 July 2012; Accepted 22 July 2012

ABSTRACT

Counterfeit medical products have been detected in most of WHO's Member States and in all its regions. Cases have involved widely-used medicines such as atorvastatin and paracetamol, limited-use medicines such as growth hormone, paclitaxel, and filgrastim, erectile dysfunction medicines, and medical devices such as contact lenses, condoms, surgical meshes, and diagnostic test strips used by diabetic patients to monitor their blood glucose concentrations. Both expensive products and cheap ones, generic and branded products are being counterfeited, that they emerge in community pharmacies and hospitals, as well as in other less-regulated settings. Counterfeit drugs may lead to death in severe cases such as heart attack, epilepsy, angina pectoris, in such condition anti-counterfeit drugs acts as weapon to avoid tragedy. Many methods have been developed till date to combat the problem. Use of 2-barcodes, holograms, active/covert systems such as RFID and 2D-encryption were adopted but still the counterfeiters were able to replicate and evade them. However, now-a-days this problem can be successfully tackled by leveraging the ubiquitous ICT tools. By making presence of these tools mandatory by all manufacturing units and chemists and by educating people about this universal menace, this hitch can be diminished.

Key words: Anti-counterfieting, 2-D barcodes, holograms, RFID, ICT tools.

INTRODUCTION

According to WHO,counterfeit medicine is defined as [1],"any product that is deliberately and fraudulently mislabeled with respect to identity and /or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with correct ingredients or with wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging".

Counterfeiting mechanisms

There are five different types of counterfeit mechanisms in which drugs are distributed without suitable regulatory endorsement and do not meet the determined standards of safety, eminence and efficiency:

1. No active ingredient (43 %)
2. Low levels of active ingredient (21 %)
3. Poor quality drugs (24 %)
4. Wrong ingredients (2 %)
5. Wrong packaging or source (7 %) [2]

Scope of the problem

The problem of counterfeit drugs is worldwide in nature. One of the leading US research agency 'Centre for Medicine in the Public Interest' has an estimate about $75 billion is the worth of counterfeiting in medicines. Although it is difficult to obtain accurate statistics, estimates put counterfeits at more than 10 percent of the global medicines market. It is known to affect both developed and developing countries. A WHO survey of counterfeit medicines reports from 20 countries between January1999 and October 2000 found that 60 percent of counterfeit medicines cases occurred in poor countries and 40 percent in industrialized countries. The largest numbers of reports are related to antibiotics, antiprotozoals, hormones and steroids [3]. In 2006, the WHO established the "International Medical Products Anti-Counterfeiting Taskforce (IMPACT)". European Commission is an active member of IMPACT and has specifically co-funded and supported WHO in the development of the recommendation "Principles and Elements for National Legislation against Counterfeit Medical Products" [4].When drugs proposed for reduced price but make at a higher market price, with the

***Corresponding Author:** Soumya.M **, Email:** soumyamissula@gmail.com

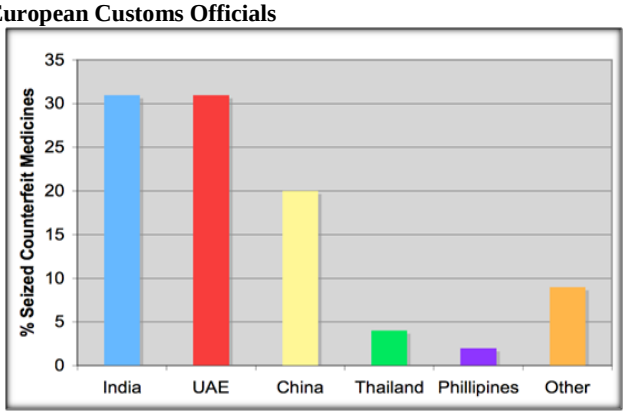
diverter making profits. A rapid growth of internet pharmacies provides counterfeiters with immediate access to clients bypassing the authorized government bodies. The counterfeiting occurs at various stages of production of drugs.

i. Counterfeit active ingredients
ii. Counterfeit finished products
iii. Counterfeit labeling products

Counterfeiting of drugs in India

According to a report by the Organization for Economic Cooperation and Development, "75% of fake drugs supplied world over have origins in India, followed by 7% from Egypt and 6% from China". India is also a leading source of high quality generic and patent drugs in legitimate commerce worldwide. Since drugs made in India are sold around the world, the country's substandard drug trade represents a grave public health threat that extends far beyond the Subcontinent [5].

Fig 1: Breakdown of source of counterfeit drugs seized by European Customs Officials



One of the key problems that counterfeit medicines pose is the damaging national reputation that is emerging for India and its pharmaceutical industry. For this reason the DCGI and other Indian authorities have become engaged in this issue with a stated resolve to combat the courage of counterfeit drug production in India.

Deadly and dangerous examples [6]

One of the most remarkable recent examples is the blood thinner Heparin, which in 2008 was found to have counterfeit active ingredients sourced from Changzhou SPL in China. In this case, the active ingredient in Heparin was substituted with a cheaper counterfeit alternate, causing a range of adverse reactions and a nationwide series of recalls. Ultimately, this resulted in about as many as 81 deaths. Baxter, the company that sold the drug in the U.S., maintains the number far lower. Consequently Baxter faced 740 lawsuits and eventually sold the division that produced the drug.

The Heparin situation is one of the rare examples of counterfeit substances making it into the legitimate U.S. pharmaceuticals system and most cases occur in abroad. In 2005 and 2006, U.K. authorities revealed that thousands of packs of counterfeit Lipitor, a cholesterol drug, has entered the genuine supply chain or had already been consumed by patients. According to the WHO, in 2009, an anti-diabetic medicine that contained six times the normal dose of its active ingredient was found in China and cited in the death of two people. In 2006, the organization also reported that more than 100 patients were killed in Panama by counterfeit glycerin contained in cough medicine. In parts of Africa, where counterfeits account for 70 percent of the market, it is complicated to determine the counterfeit-related deaths, even though some people estimate the number to be in hundreds to thousands per year, typically associated with malaria and tuberculosis drugs.

Table 1: Examples of Counterfeit Medications [7-11]

Counterfeit medicine	Country/Year	Report
Alprazolam (anti-anxiety drug)	Canada/ 2007	Pills found with high levels of aluminum, titanium, arsenic, and other metals (led to Canada's first casualty on fake drugs)
Xenical (obesity medication)	United States/2007	Contained no active ingredient and sold via Internet sites operated outside of the United States
Cavinton (cardiovascular	Russia/2006	Medication included foreign substances. About 600 boxes of false
Zyprexa (biopolar disorder and schizophrenia)	United Kingdom/2006	Detected in the legal supply chain; lacked sufficient active ingredient
Nandrolone (treats osteoperosis and aplastic anaemias)	Spain/2004	Drugs had inadequate amounts of active ingredients. Discovery led to the largest counterfeit drug bust in Spain's history
Cialis (erectile dysfunction)	Singapore/2004	Pills included active ingredients, but also consisted of varying amounts of other medication (sildenafil) to compensate potency.

Elucidations to combat the problem:

Techniques such as infrared Spectroscopy, X-ray powder diffraction, thermal gravimetric analysis, microscopy and various forms of chromatography have been used to check the authenticity of samples. A conclusion cannot be obtained from the packaging and other information; investigation must be done by comparing with the authentic product for which methods are employed which include [12].

a) Chemical characteristics

i)Excipient identity, ii) Impurity profile, iii) Crystal form, iv) Morphology or particle size, v) Thermal behavior.

b) Analytical profiles

i) Major and minor components, ii) Impurities, iii) Isotopic ratios

The introduction of unique coding for each pack of medicine, together with authentication, track and trace systems and physical security in the form of tamper resistant packaging, would dramatically improve the safety of medicines supply.

Anti-counterfeit packing involves following techniques:

1. 2-D Barcodes
2. Holograms
3. RFID

1.2D- Barcodes / Mass Encryption technology

Barcodes are used in the pharmaceutical industry to identify product throughout the supply chain. Different levels of information can be carried in a barcode, including such items as National Drug Code (NDC), Lot Number, and Expiration Date. There are several different types of bar codes, and the standards for what those bar codes should look like and how they are to be used. These are the Uniform Code Council (UCC) and the Health Industry Business Communications Council (HIBCC).

2-D Barcodes are present in following formats

A. Linear format

B. Scripted format

C.2-Ddatamatrixformat

Currently, pharmaceutical labels are regulated by a 2004 FDA rule requiring manufacturers to print a 10-digit linear barcode which encodes the product's National Drug Code (NDC) 8either on the package or on a label.2D data matrix bar codes printed on packaging during manufacture can provide each medicine with a unique identity before it enters the supply chain. Significant quantities of encrypted information can be stored this way to support pharmacists, regulators and government authorities in the authentication and tracing of individual medicines.2D data matrix bar [13] codes help prevent dispensing errors and make counterfeit medicines easily identifiable. Existing scanners found in most pharmacies can read the bar codes and no additional work is required by the pharmacist. Scanned information is transmitted to an independent electronic data hub and a verification message is quickly returned to the dispensing pharmacist.

Fig 2: National Drug Code (NDC) and National Health Related Items Code (NHRIC) for pharmaceutical products

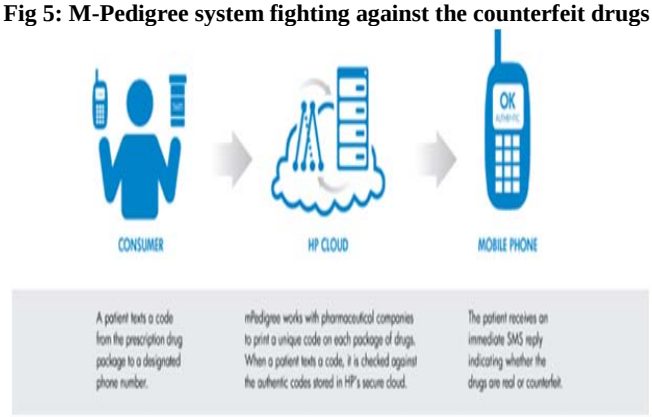
Fig 3: Encrypted codes can be displayed in scripted format(top) or by way of 2D-Data Matrix barcode format (bottom)

In addition to the encryption and decryption of the codes, the software that supports this technology allows brand owners to fully manage their supply chain, i.e., track-and-trace [5]. A major advantage that mass encryption enjoys over all other currently available technologies is that it empowers the consumer to authenticate a drug. Furthermore, it is a software based technology hence cost effective.

In Ghana, a new service called M-Pedigree allows people to send serial numbers (embedded under a scratchpad on drug packets they have bought) by text message. Within seconds they will receive a text message from the manufacturer telling them whether the product is authentic[14].Themis Medicare has become the first Indian healthcare company to sign up with M-Pedigree Network for its text message-based authentication service for medicines [15].

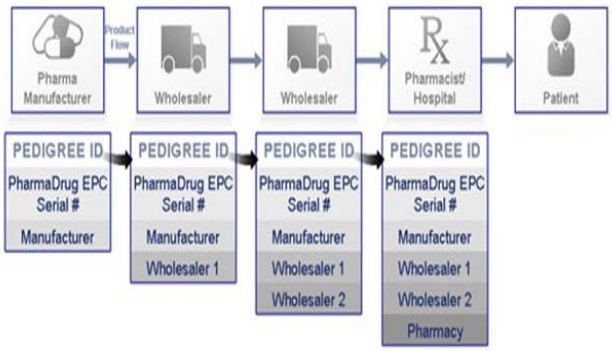
Fig 4: Authentication guaranteed via text message (left); Serial number located under scratchpad on medication (right)

Fig 5: M-Pedigree system fighting against the counterfeit drugs



An ePedigree is another important system for the automatic detection of counterfeit drugs. It is an electronic record containing information regarding each transaction resulting in a change in the ownership of the prescription drug from manufacturer, through acquisition and sale by a wholesaler, until final sale to a pharmacy, or person furnishing, administering or dispensing the prescription drug. States such as California are increasingly requiring pharmaceutical companies to generate and store ePedigrees for each product they handle. On January 5, 2007 EPC globalratified the Pedigree Standards an international standard that specifies an XML description of the life history of a product across an arbitrarily complex supply chain.

Fig 6: The California epedigree approach. Tracks movement through each node in the supply chain



2. Holograms

Holographic technology is the recent emerged technology in pharmaceutical field which provide a simplified means for consumers to deduce the authenticity of a drug. The reasoning is that a blister pack or vial that contains a hologram will be seen to be a genuine product that is resistive to tampering. "Security hologram is ideal 3-in-1 solution as it provides three layers for authentication, overt for identification, overt & covert for authentication and forensic to arrest counterfeits. At each security hologram while overt feature are designed for consumer, high securitycovert and forensic features help enforcement and drug authorities in combating and tracing counterfeits" [16] . The security hologram is used, as they are designed to be easily recognizable to the public and difficult to replicate by counterfeiters [17]. Holograms can cost as much as 10-25paise depending upon their level of sophistication and therefore can add significantly to the MRP of low end medicines that are staple of the indigenous pharmaceutical market [18]. Another problem is that, the holograms themselves can also be eventually duplicated by counterfeiters making the initial investment by the brand owner ineffective when such knock-offs enter the market.

Fig 7: Awell crafted hologram distinguishes authentic from counterfeit

3. RFID

Radio Frequency Identification Technology (RFID) works via a tag that is placed on each product for consequent tracking. The product is then packed into cases, and stacked onto trucks. Scanners track the tag on the product as it moves from place to place. RFID tags do not need to be observable to the scanners (RFID readers) in order to be read. In fact, they can often be read from several feet away. RFID tags contain much more data than a bar code.The tags are all unique, so every single box or product has identifiers, as opposed to bar codes, which only reveal the brand and the type of package. In addition to providing track-and-trace technology, RFID is also an precious tool in detecting counterfeit medicines, since every single product carries a unique tag. RFID tags come under two general categories, active and passive, depending on their source of electrical power. Active RFID tags contain their own power source, usually an on-board battery. Passive tags obtain power from the signal of an external reader. RFID readers also come in active and passive varieties; depending on the type of tag they read [19]. A passive tag reader can constantly broadcast its signal or broadcast it on demand. When a tag comes within the reader's range, it

receives an electromagnetic signal from the reader through the tag's antenna. The tag then stores the energy from the signal in an on-board capacitor; a process called inductive coupling. Counterfeits can also be detected using GENTAG's multi-level authentication process and software using any web-enabled cell phone [20].

Pharmaceutical companies using RFID technology

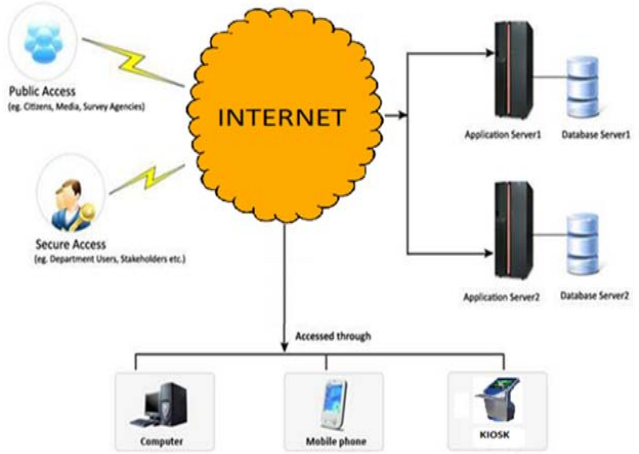
Name of company	Product using RFID technology
GSK	Trizivir
Purdue pharma	OxyContin
Pfizer	Viagra

Fig 8: GENTAG Wireless RFID Button Tags used for Counterfeit Drug Detection

Leveraging Information Technology

With the spread of Information and communication technologies (ICT) such as mobile phones almost throughout the world, benefit can be taken of the same for detection of the products from approved sources. This will give power to the end user to authenticate the product that they are using. In this, all drugs will be allotted by a specific unique code upto individual packet level coupled to Batch No. or date of manufacture. The codes may be stocked up in a central repository preserved by a central regulator with compatible web based software. All retailers be made to maintain authentication kiosks or computers which can be connected to the internet through any of the available modes. The end users shall on entering the Batch/date of manufacture and unique code will get the confirmation of the product that they are going to acquire or people be educated to persist on the authentication from the chemist for their own safety, besides providing required legal framework. Else, authentication can also be received by reply SMS on sending the code to a preselected number.

Fig 9: Supply chain Information and Communication Technology (ICT)



By leveraging the information technology, the drawbacks in the overt and covert systems can be overcome, which is also commercial. Using the technology, the producer will also be able to track and trace his supply chain, thus reducing the chance for counterfeits. The price of setting up the method will by several times offset the loss of income due to counterfeits. Leveraging the extensive mobile usage in the country and cloud computing, the Pharma industry hopes to increase their credibility. Computer companies see a huge business potential in offering technology solutions to the whole industry. Hewlett-Packard is one of the companies offering a solution, a cloud-based platform called Global Authentication Service [21]. Finally, the growth of trafficking networks around the globe has helped bring about a convergence of threats: counterfeit pharmaceuticals, narcotics, human trafficking, dual-use nuclear black markets, small arms and conflict resources including diamonds and timber. Together, these challenges have become so widespread that they threaten to overwhelm the capabilities of even well-intentioned governments to mitigate their destructive effects. Weak legislation is often identified as the single most important factor driving counterfeit trade. . The national security community must be given an explicit mandate to address these challenges in order to ensure the adequate and coordinated resources necessary to ameliorate the threat. In short, like the prevention of drug and human trafficking, counterfeit pharmaceuticals must become a mandate of government security tools.

CONCLUSION

Counterfeiting influences all parts of society, government, brand owners and consumers. While government and brand owners lose the valuable tax and revenue, it is consumer who suffers health problem due to this and sometime leads to death.

Regrettably, drug counterfeiting is rapidly ever-increasing threat to mankind, becoming the world fastest growing industry and the biggest offense in 21st century. The Pharma companies may take benefit of the bang in Information technology and communications network to authorize their supplies through the supply chains by undemanding and cost effective authentication mechanisms. It is in the interest of the Pharma companies to implement the latest technologies as liability issues, consumer confidence and brand erosion costs are motivating them to combat this ever increasing problem.

REFERENCES

1. Discussion paper; Combating Counterfeit Drugs: Building effective International collaboration – International conference – Rome, Italy 16-18 Feb, 2006.
2. Sanjay Modi, "Multiple strategies and technologies to combat counterfeit drugs"; CSC Papers 2009.
3. European Commission Taxation and Customs Union Summary of community customs activities on counterfeit and piracy. Results at the European border; 2006.
4. International Medical Products Anti-Counterfeiting Taskforce, Principles and Elements for National Legislation against Counterfeit Medical Products; IMPACT General Meeting Lisbon; 2007; 1–13.
5. BV Mahalakshmi, "Fake drugs are a growing problem"pharmaceuticals export promotion council (set up by ministry of commerce, govt. of India); 4th October 2010
6. http://www.usatoday.com/money/industries/health/drugs/story/2011-10-09/cnbc-drugs/50690880/1.
7. WHO, Counterfeit medicines: Fact Sheet No. 275, January 2010.
8. National Review of Medicine, "BC woman killed by fake drugs bought online," July 2007.
9. The Partnership for Safe Medicines, Counterfeit Drugs in Europe: Fact Sheet, July 2004.
10. Graham Satchwell, A Sick Business: Counterfeit Medicines and Organized Crime, The Stockholm Network, 2004.
11. The Lancet, "Russia cracks down on counterfeit drugs," October 2006.
12. Mohan RK Nimmagadda, "Impact of counterfeits, parallel trade on global healthcare value chain", Pharmabiz.com, Dec., 2007.
13. Counterfeit Medicines – a New Update on Estimates.Position statement by the International Medical Products Anti-Counterfeiting Taskforce (WHO). November 2006.
14. S.K. Kwok, *et. al*. "An Intelligent RFID-based Electronic Anti-Counterfeit System (IRECS)for the Manufacturing Industry" Proceedings of the 17th World Congress The International Federation of Automatic Control Seoul; Korea; July 6-11; 2008.
15. http://www.securingpharma.com/mpedigree-signs-up-first-indian-client/s40/a979.
16. http://articles.timesofindia.indiatimes.com/2008-05-14/india/27759344_1_fake-drugs-drugcontroller-drug-samples.
17. http://www.pharmaleaders.co.in/Focus-Spuriousdrugs.pdf.
18. MagnarLoken, and AviChaudhuri, "Countering counterfeits", Sept., 2007.
19. Ron Weinstein RFID: A Technical Overview and Its Application to the Enterprise IEEE Computer Society; 1st June 2005.
20. http://electronicsbus.com/counterfeit-drug-detector-system-wireless-pharmaceutical-rfid-tags.
21. Counterfeit drugs targeted by technology in India.source: BBC News.