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COUNTERFEIT MEDICINES: A REAL THREAT TO THE SOCIETY

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ABSTRACT

Counterfeit drug is a pharmaceutical product which is produced and sold with the intent to deceptively represent its origin, authenticity or effectiveness. It may contain inappropriate quantities of active ingredients, may be improperly processed within the body or may contain ingredients that are not on the label, and is often sold with inaccurate, incorrect, or fake packaging and labeling. It is estimated that more than 10% of drugs worldwide are counterfeit, and in some countries more than 50% of the drug supply is counterfeit. In 2003, the WHO estimates that the annual earnings of counterfeit drugs were over US$32 billion. These are inadequate measures to determine the correct prevalence of the problem. There are several technologies that may prove helpful in combating the counterfeit drug problem include radio frequency identification which uses electronic devices to track and identify pharmaceutical items and electronic pedigree (e-Pedigree) system to track drugs throughout its distribution channel.

INTRODUCTION: History of counterfeiting stands long back. It was scaring news when it came in the news papers about the mass poisoning that caused the death of more than 14 children in France. It was a result of counterfeiting. The sweet tasting costly base of syrup, glycerol, the safe one, was replaced by less costly diethylene glycol. A wide range of cases has been reported for counterfeit medications through out the years.

In 2006, lack of sufficient active ingredient has detected in the legal supply of Lipitor, a drug use for lowering cholesterol, at United Kingdom. Xenical, a drug for obesity has sold in United States via internet sites operated outside USA with no active ingredients in 2007.

In 2008, Viagra and Cialis for erectile dysfunction has smuggled into Thailand from an unknown source from an unknown country. One of the most severe one was in 2009, in China an antidiabetic traditional medicine used for lowering the blood sugar, with six times the normal dose of glibenclamide leads to the death of 2 people and the hospitalization of 9.

If not regulated properly counterfeit medications can cause serious harm to the humanity. Apart from that it may lead to the down regulation of the distribution of drugs and can adversely affect the worth of entire healthcare system [1-3].

On the 26th March 2010, FIP was invited to moderate a WHO Open Forum on the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) [2] which brought together 48 WHO Member States and 28 international development agencies, NGOs and private sector organizations from around the world to share information on the work of IMPACT, and review the feed-back from WHO Member States on the use of the term "counterfeit medicines" and/or equivalent in national legislation.

This meeting presented a detailed overview about the works of IMPACT since 2006. In this meeting, it is recognized that the imminent rapid growth of counterfeit medicines will only be stopped through global cooperation among governments, international agencies, legislators, law enforcement units, health care professions, patient groups and industry representatives from all countries of the world. It is also with the social imperative that pharmacists as health care professions need to take in the way we fight against counterfeit medical products in our daily practice. The misnomer of "it will never happen to me" is a dangerous one. FIP continues to work very closely with the WHO Counterfeit Medicines Programme and IMPACT [4, 5].

The World Health Professions Alliance (WHPA) today urged further action against counterfeiting of medical products. Speaking for more than 26 million health professionals in more than 130 countries, WHPA is extremely concerned that the infiltration and sale of counterfeit medical products in the legitimate supply chain can cause death and misery to tens of thousands of patients around the world.

The WHPA announced that it is stepping up its commitment to this issue, with the launch of the 'Be Aware, Take Action' campaign against counterfeiting of medicinal products. This campaign focuses on public health and patient safety issues and enhances the role of health professionals and associations. Through regional workshops dedicated to anti-counterfeiting, the WHPA aims to strengthen advocacy for appropriate investments in the education and capacity of health professionals to detect, report and prevent counterfeit medical products. In addition, the WHPA Be Aware, Take Action toolkit and other campaign resources are provided for health professionals, healthcare advocates and patients. The harm caused by counterfeit medicines is greatest in those communities least able to afford effective regulatory systems and quality health care. WHPA recognizes also that for health professionals to be able to effectively play their role, national authorities must set up effective systems for the collection of information and increase national drug and medical device regulatory capacity to support the enforcement of pharmaceutical guidelines [6, 7].

At December 2010, the Madras High Court upheld the detention of 13 people allegedly involved in selling spurious drugs, some fake and some expired, under the Goondas Act. The Goondas Act allows suspected spurious drug sellers to be detained while being prosecuted, rather than released on bail, to deter them for continued selling until their trial date. The detainees are accused of collecting expired medicine and returning them to the pharmaceutical retail market as valid drugs by altering the batch numbers and expiration dates [8].

The Cambodian Ministry of Health reported a 92% decrease in the number of illegal pharmacies nationwide and a 71% fewer unlicensed health clinics over the past year, on December 22, 2010. The European Union ambassadors approved an agreement to regulate medicines sold over the internet. The agreement approved by the EU ambassadors will create regulation intended to protect legal suppliers of medicine.

New rules will require internet pharmacies to register with authorities in their home country and ensure that the products sold are licensed for sale in the country of purchase reports, the European Voice, on December 24, 2010. A recent EC report claimed that India was the largest source of the 2.7 million counterfeit drugs seized by its custom department in 2006 [9].

Mobile Product Authentication (MPA) (**Fig. 1**) is a technology developed by Sproxil which is a preventive measure for consumers to identify whether the drug is counterfeit or not. By this technology, using a cell phone, customers can text message an item-unique code and get an instant response confirming the brand's genuineness. We can then send highly relevant targeted offers to the consumers right at the point of sale. This is the world-first innovation by Sproxil. The scratch-off technology is proven its trend in the emerging markets. The mobile operator market chose scratch-offs instead of holograms for popular pay-as-you-go subscription schemes [10, 11].

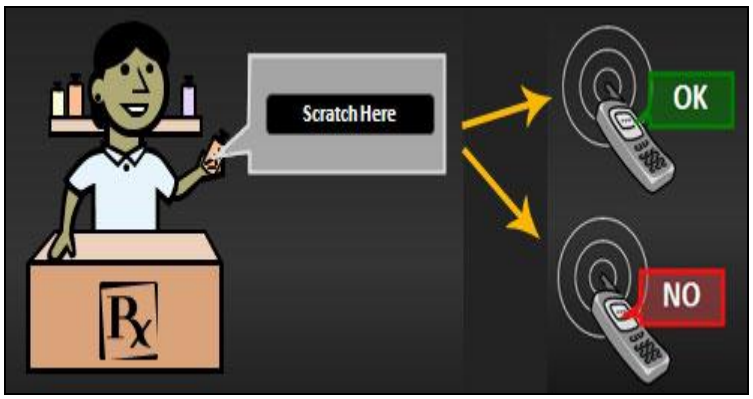

FIG. 1: MOBILE PRODUCT AUTHENTICATION TECHNOLOGY

With Cascading Authentication, we can make sure, only trusted agents handle the products , while each one of the supply chain agents can individually verify the authenticity of products as they disperse through the distribution network (**Fig. 2**).

FIG. 2: TRACKING DRUG DISTRIBUTION THROUGH MOBILE PRODUCT AUTHENTICATION

The use of counterfeit medicine is increasing day by day. So we should be aware of the possible harm these fake ones may cause and should take adequate precautions to get rid of them. A counterfeit medication or a counterfeit drug is a medication or pharmaceutical product which is produced and sold with the intent to deceptively represent its origin, authenticity or effectiveness. WHO defines counterfeit medicine as a medicine which is deliberately and fraudulently mislabeled with respect to identity and/or source.

Now a day these counterfeit medicines are entering into the market through some channels and creates some serious life threatening problems. Counterfeit medicines have been recognized by the WHO as a threat to public health since 1985, but the manufacture of the product appears to be increasing. They mimic the genuine drug in such a way that sometimes they may not be caught by the regulatory authorities also. Counterfeit medicines are found more in the drug markets of developing countries (10-50%) than in developed countries (1%) due to various reasons like poor regulatory control on drug market and economy of the population. That is in developing countries expensive drugs are available at a cheaper rate through black market. So public awareness about the consequences of consuming counterfeit medicine is the main factor in controlling the spread of these medicines in the market [12, 13].

Types of counterfeit drugs and their consequences: Illegal drugs are often produced and sold with the intent to deceptively represent their origin, authenticity or effectiveness. The nature of these fraudulent drugs ranges from those containing no active ingredient (eg. when a bag of powdered lactose claimed to be cocaine), with insufficient active ingredient or with some diluents (e.g., Baking soda or lactose) or sometimes with a wrong active ingredient (e.g., when methamphetamine is sold as cocaine) or with a fake packaging [14, 15]. The various types of counterfeit drugs are

- Counterfeit drugs containing same dose of the active ingredient
- Mislabeled medications

- Counterfeit drugs containing an incorrect dose of the active ingredient
- Counterfeit drugs which do not contain the active ingredient
- Counterfeit drugs containing a potentially harmful substance
- Counterfeit drugs containing an unlisted active ingredient
- Genuine medicines marketed for incorrect or recreational use

Counterfeit drugs containing same dose of the active ingredient: They are close replicas of the genuine drug with the same dose of the active ingredient. They constitute only 5% of the fraudulent medicines. The health risk associated with this type of medicines is very less compared to other types which are different medicines or different dose of same medicine than the originals they claim to replicate. Even though they contain the same active ingredient as the originals they are of poor quality as it is not manufactured according to the rules of good manufacturing practice approved worldwide. They carry the health risk associated with manufacturing process. Since the manufacturing of counterfeit medicines is illegal the base line ingredients cannot be purchased from reliable suppliers and the source of active ingredient remains unknown.

The dissolution profile of the drug may vary, so the amount of drug available for absorption by the body may vary and finally the efficiency of the drug is less. The inactive ingredients in this type of drugs are not documented and they can be detected only by laboratory analysis. Sometimes these inactive ingredients can cause health risks. For example a study of malaria medications sold on the black market in three African countries reported that >50% of the medicines in circulation were counterfeit with the same dose of active ingredient. However the active ingredient was from a different source and had a different dissolution profile to the original [16].

Mislabeled medications: Mislabeled medicines are those which are sold in the package of another brand medicine. The label of counterfeit medicine also contains batch number, manufacturing number and other details which are fraudulent. It may or may not contain the same active or inactive ingredients as the original. These mislabeled medicines are often supplied through e-pharmacies in developed countries. For example in 2006 the US government issued a public warning against buying brand name medicines off the internet. This was after the case of prescription weight loss medication Xenical (orlistat).Upon laboratory investigation; counterfeit medications labeled Xenical were not found to contain orlistat. Some of the counterfeit medicines contain sibutramine another weight loss medication with different action in the body as the active ingredient. They were taken in different doses compared to orlistat. Some contained talcum powder and chalk instead of active ingredient. The packaging appeared authentic but the batch number; (a genuine one) did not matched with the expiry date for the batch by the manufacturer [17].

Counterfeit drugs containing an incorrect dose of the active ingredient: Sometimes counterfeit medicines contain active ingredient in incorrect dose (either too high or too low).This can lead to many health related problems. In case of fatal diseases it can lead to the death of patient due to ineffective dose. In case of antibiotics low dose therapy may not kill the bacteria but may lead to the emergence of resistant strains. In 2000 in Cambodia counterfeit malaria tablets caused death of 30 people [18].

Counterfeit drugs which do not contain the active ingredient: Sometimes Drugs are marketed without any active ingredients. For example instead of cocaine some powdered lactose is marketed. More than 60% of the counterfeit drugs identified by WHO in 2000 was without any active ingredient. Another example is of sibutramine instead of orlistat in Xenical [19].

Counterfeit drugs containing a potentially harmful substance: Sometimes harmful substance may replace the active ingredient in the genuine drug. This can lead to many health problems. For example, in the case of Xenical the genuine drug orlistat is replaced by sibutramine which is a pharmacologically active drug used to reduce weight but by different mechanism. The dosing schedule of orlistat and sibutramine also varies that is orlistat is needed once daily and sibutramine thrice daily. Also the interactions and

contraindication as may vary. Over hundred children died in Nigeria in 1993 due to the harmful substance in the counterfeit cough syrup. Similar cases were reported in China and India in 1990-2007 and in panama due to ethylene glycol in cough syrup instead of glycerol. In 2002 more than 190,000 deaths occurred due to poly ethylene glycol contamination in paracetamol syrup [20].

Counterfeit drugs containing an unlisted active ingredient: This type of counterfeiting is commonly found in recreational drugs which may contain some herbal ingredients. Even though they are natural they may exhibit some pharmacological actions in the body. So it should be taken into consideration and use of such type of drugs should be discussed with the health care provider.

All types of drugs are prone to counterfeiting or fraudulent manufacturing. In developing countries both expensive and inexpensive drugs are available in the black market. According to a report of WHO about one third of counterfeit drugs identified were counterfeit antibiotics. In developed countries counterfeit drugs are often treatments for lifestyle diseases like obesity, erectile dysfunction etc. All these counterfeit drugs are associated with some health risks, if not seeking proper medical advice or treatment.

For example in case of infectious disease the patient condition may get worsen even though he is taking the fraudulent drug .Similarly in chronic conditions like erectile dysfunction, it may be an indicator of some other conditions like diabetes or atherosclerosis which may lost an opportunity to get diagnosed by the use of these drugs from black market [21].

Counterfeit drugs can be purchased from many outlets and in rare cases they get into the legal supply chain. In United Kingdom recently counterfeit drugs for treating high blood cholesterol and bipolar disorder were identified in the legal supply chain. In developing countries they are available in black market and in the unregulated informal sector. In developed countries internet has been exploited by the fraudulent drug manufactures to create market for their product.

Some measures to prevent the use of Counterfeit medicines [17]:

At International level: National and international authorities and pharmaceutical manufactures have put in place measures to curb the spread of counterfeit medicines into the market [8]. Usually the counterfeiters work in borders, i.e. they manufacture the drug in a developing country where regulatory issues are minimum and then transport to a developed country to increase the legitimacy of their appearance on the market and then to the market of either developed or developing country. In order to control the manufacturing of counterfeit drugs in countries with poor regulatory controls international authorities like WHO had established International Medical Products Anti counterfeiting Taskforce in 2006.

At National level: Most developing countries have strict regulatory controls in place to secure their markets from counterfeit drugs. In Australia, the Therapeutic Goods Administration prohibits the manufacture sale, import or exports of counterfeit drugs and has assessment mechanisms like customs inspection to identify those who break the law. It is difficult for the national government to implement legal measures if the counterfeiting or website is based in another country. Government bodies may use public education as a strategy to prevent illegal drugs from entering the market. They may provide public warning against purchase of drugs from internet and notify the public when fake drugs are known to be on the market. Government may also announce product recalls if drugs are suspected or known to be counterfeit. Government may provide advice to the pharmacist and other health care professionals to identify the counterfeit drugs on their shelves and the patients who have consumed it [22].

At the level of pharmaceutical manufactures: Genuine drug manufactures now responded to counterfeiters by introducing physical-chemical indicators. Physical chemical indicators are pharmacologically inactive substances mixed in low concentration with the drug and they can be identified only by specific laboratory tests[9].Using tracking technology we can track the source of any fake drug in the supply chain. Identifying the methods used by counterfeiters in mimicking the

genuine drug is an important step to stop their marketing. But as it is an organized crime the counterfeiters are using such technologies which make it difficult to identify. They can change the method more rapidly that is when one method is detected they can employ another one as yet unidentified to prevent their product being unidentified.

CONCLUSION: Counterfeit medicines represent an enormous public health challenge. It poses a public health risk because their content can be dangerous or they can lack active ingredients. Their use can result in treatment failure and contribute to increased resistance in the case of antimalarials that contain insufficient active ingredient or even death. Unlike substandard medicines where there are problems with the manufacturing process by a known manufacturer, counterfeit medicines are made by people with the intent to mislead. The extreme difficulty in tracing the manufacturing and distribution channels of counterfeit medicines makes their circulation on markets difficult to stop. To fight counterfeit medicines effectively, a range of stakeholders is needed, not just health professionals.

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