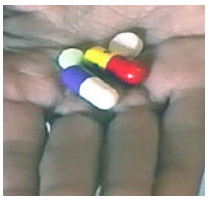

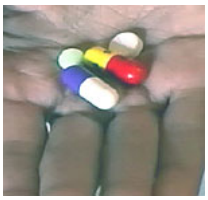

SAFETY OF MEDICINES WITH RESPECT TO DRUG COUNTERFEITING IN DEVELOPING COUNTRIES.

A thesis submitted in accordance with conditions governing candidates for the degree of

DOCTOR OF PHILOSOPHY

In

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Presented by

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ABSTRACT:

Background:

This thesis presents a study of the safety of medicines with respect to drug counterfeiting in developing countries (East Africa and the Middle East). Counterfeit medicines are also present in industrialised countries, but not on the same scale as in developing countries. The aim of the study was to establish the responsiveness of health care professionals at the practice level concerning the counterfeiting of medicinal products in developing countries focusing on six countries in the East African region and seven countries located in the Middle East.

Method:

The method of data acquisition used was by survey questionnaires issued in 13 developing countries (6 in East Africa and 7 in the Middle East). The questionnaires were delivered to the respondents either personally or by e-mail and the questionnaire, responses were returned by the same means. Respondents returned their questionnaire forms direct to the author either on the same day or later by e-mail. The data were analysed with regard to the specific questions.

Results:

The study findings suggested that the poorer the country, the higher the degree of counterfeiting. All the respondents (n: 2180) agreed that there was a fake or counterfeit medicine problem in their own country (71% of respondents in Africa and 63% of respondents in the Middle East considered this a major problem). Both branded and generic drugs were counterfeited and the extent of the problem and several other factors concerning counterfeited drugs differed significantly between industrialised and developing countries. The difference depended on drug regulation control and enforcement and also on the quality and the prices in the legal supply chain. In most industrialised countries like the USA, Japan or the members of the EU, the level

of drug counterfeiting is <1% of the total medicines market value. An exception is the former Soviet Union where up to 20% of the market is occupied by counterfeit drugs. In contrast, within regions of Africa, Asia and parts of Latin America, between 10-30% of the available medicines are fakes (WHO 2006)

Conclusions:

The study showed that healthcare workers were aware of the prevalence of counterfeit medicines and quite a number of them had encountered them in their supply role. There is an indication that the respondents tried to assure themselves of the quality of the drugs they purchased by using several methods. However, no rigorous effort was taken to confirm as well as report suspected counterfeit drugs to regulatory authorities.

In the industrialised world, medicines regulatory authorities have developed strict standards and controls to ensure the safety and effectiveness of drugs. However, as this study has found, in less developed countries a lack of human and financial resources within the health sector as a whole restricted the activity of regulatory agencies, resulting in a sub-optimally regulated environment in which substandard drug production persisted without detection.

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LIST OF ABBREVIATIONS:

API: Active Pharmaceutical Ingredient

CIA: Central Intelligence Agency

CRA: Clinical Research associate

DACAE: Drug Administration and Control Authority of Ethiopia

DRC: Democratic Republic of the Congo

EDA: Egyptian Drug Authority

EU: European Union

FDA: Food Drug Administration

GCC: Gulf Country Cooperation

GDP: Gross Domestic Authority

GSK: GlaxoSmithKline

HIV: Human immunodeficiency virus

IMPACT: International Medical Product Ant Counterfeiting Taskforce

IMS: Institute of Medical Science

INTERPOL: International Criminal Police Organisation

IPF: International Pharmaceutical Federation

IP: intellectual property

KSA: Kingdom of Saudi Arabia

LDC: Less Developed Countries

MHRA: Medicines and Healthcare products Regulatory Agency

MOH: Ministry of Health

MRA: Medicines Regulatory Authority.

NAFDAC: National Agency for Food and Drug Administration

NDA: National Drug Authority

NGO: non-government organisation

OTC: Over the Counter

PPB: Pharmacy and Poisons Board

PSI: Pharmaceutical Security Institute

SFDA: Saudi Food and Drug Authority

TFDA: Tanzania Food and Drugs Authority

VAT: Value Added Tax

UAE: United Arab Emirates

UK: United Kingdom

USA: United State of America

WHO: World Health organization

WPF: World Pharmaceutical Frontiers

YR: Yemen riyal

GLOSSARY OF TERMS

A non-governmental organization NGO: is a legally constituted organisation created by natural or legal persons that operates independently from any government. The term originated from the United Nations (UN), and is normally used to refer to organisations that do not form part of the government and are not conventional for-profit business

Counterfeit Medicine: 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. A counterfeit drug may contain inappropriate quantities of active ingredients, or none, may be improperly processed within the body (e.g. absorption by the body), may contain ingredients that are not on the label (which may or may not be harmful), or may be supplied with inaccurate or fake packaging and labeling.

Developing countries: Also known as, a **less-developed country** is a nation with a low level of material well-being.

Developed countries: is a country has a high level of development according to some criteria. Which criteria, and which countries are classified as being developed, are a contentious issue. According to the International Monetary Fund, advanced economies comprise 65.8% of global nominal GDP and 52.1% of global GDP (PPP) in 2010

Drug Product: A finished formulation, for example a tablet or capsule that contains the active substance, generally in association with one or more other ingredients.

Good Manufacturing Practice (GMP): Are guidance that outline the aspects of production and testing that can impact the quality of a product. Many countries have legislated that pharmaceutical and medical device companies must follow GMP procedures, and have created their own GMP guidelines that correspond with their legislation. Basic concepts of all of these guidelines remain more or less similar to the ultimate goals of safeguarding the health of the patient as well as producing good quality medicine, medical devices or active pharmaceutical products. In the USA, a drug may be deemed adulterated if it passes all of the specifications tests but is found to be manufactured in a condition, which violates current good manufacturing guidelines. Therefore, complying with GMP is a mandatory aspect in pharmaceutical manufacturing

Gross domestic product (GDP): refers to the market value of all final goods and services produced within a country in a given period. GDP per capita is often considered an indicator of a country's standard of living.

HIV: is a lentivirus (slowly replicating retrovirus) that causes *acquired immunodeficiency syndrome* (AIDS) a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive.

Khat: is a flowering plant native to the Horn of Africa and the Arabian Peninsula. Amongst communities from these areas, khat chewing has a long history as social custom dating back thousands of years. Khat contains the alkaloid called cathinone, an amphetamine-like stimulant, which is said to cause excitement, loss of appetite and euphoria.

International Criminal Police Organization – INTERPOL: is an organization facilitating international police cooperation. INTERPOL was established as the International Criminal Police Commission in 1923 and adopted its telegraphic address as its common name in 1956.

International Chamber of Commerce (ICC): is the largest, most representative business organisation in the world. ICC's hundreds of thousands of member companies in over 130 countries have interests spanning every sector of private enterprise

Radio-frequency identification (RFID): is the use of a wireless non-contact radio system to transfer data from a tag attached to an object, for the purposes of automatic identification and tracking. Some tags require no battery and are powered by the radio waves used to read them.

Pearson Product Moment Correlation model: In statistics, the Pearson product-moment correlation coefficient is a measure of the correlation (linear dependence) between two variables *X* and *Y*, giving a value between +1 and −1 inclusive

Substandard medicines: medicines that are genuine medicines produced by legitimate manufacturers that do not meet the quality specifications that the producer says they meet. For example, they may contain less (or more) active ingredient than written on the package.

Viagra: Sildenafil citrate, sold as Viagra, Revatio and under various other trade names, is a drug used to treat erectile dysfunction and pulmonary arterial hypertension

World Intellectual Property Organization (WIPO): is one of the 17 specialised agencies of the United Nations. WIPO was created in 1967 "to encourage creative activity, to promote the protection of intellectual property throughout the world.

World Health Organization: is a specialised agency of the United Nations (UN) that is concerned with international public health. WHO was established on 7 April 1948, with headquarters in Geneva, Switzerland and is a member of the United Nations Development Group. Its predecessor, the Health Organisation, was an agency of the League of Nations.

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1 CHAPTER ONE

1.1 General Introduction:

1.1.1 Introduction:

This thesis presents findings on quality performance at the practice level concerning the safety and use of medicines and counterfeit drugs in developing countries. The study covers 6 East African countries and 7 Middle East countries (see Figure 1.9) and the findings focus on counterfeit medicines.

At the end of 2010, a global effort to combat the distribution and sale of counterfeit and illegal medicines online culminated in "Operation Pangea III," resulting in the seizure of approximately one million illicit and counterfeit medicines valued at approximately $2.6 million. (Mackey and Liang, 2011)

Counterfeit medicines are not confined to specific drug classes, and instead span a broad spectrum ranging from lifestyle to life-saving medicines, as well as generic drug forms. This includes counterfeits in therapeutic classes that extend to antimalarials, antibiotics, birth control, cancer, diabetes, erectile dysfunction, heart disease, schizophrenia, and transplant drugs (WHO. 2010). Surveillance by the Pharmaceutical Security Institute, a non-profit organisation dedicated to the development of anticounterfeiting resources, have shown that close to 1000 counterfeit incidents occurred in 2005 involving some 100 countries, with 687 different pharmaceutical products in a wide array of therapeutic and organ system categories. (Kubic and Mollo, 2006)

Represented by a number of international organisations, approximately 45 countries, and other private and public sectors in a multipronged effort, this operation is the largest

enforcement action in size and scope against criminal internet-based activities involving illegal sales of dangerous counterfeit medicines. (Mackey and Liang, 2011)

Substandard and counterfeit drugs are prevalent throughout the world but developing countries are worst affected. Counterfeiting is generally perceived by society as a victimless crime, with fakes simply constituting a cheap alternative option, and seen by criminals as having a low risk of prosecution with light penalties relative to the large profits to be made. The reality is that the international trade in counterfeit products is estimated to exceed 6% of global trade (Patil et al., 2012).

In today's global environment, it does not matter if you live in the United States of America, Europe, Asia, or Africa—everyone is at risk from unsafe drugs. Counterfeit drugs defraud consumers and deny patients therapies that may alleviate suffering and save lives. Unfortunately, in some cases, these drugs have caused great harm and fatalities especially in developing countries. (Cockburn, 2002)

According to World Health Organization (WHO) estimates, up to 1% of medicines available in the developed world are likely to be counterfeit (WHO 2006 b). This figure rises to 10% globally, although in some developing countries it is estimated that one third of medicines are counterfeit. 36.5 per cent of antibiotics and anti-malarials on WHO essential drug list in Thailand and Nigeria are substandard (Shakoor et al., 1997)

In several developing countries (especial East African Countries like Somalia and Ethiopia) drug quality is a source of concern. There is a general feeling that there is a high incidence of drug preparation, which is not of acceptable quality. Instances, which are quoted, are often

linked with terms such as counterfeit and fake, which carry economic and perhaps political implication. Poor quality drug preparation may lead to adverse clinical results both in terms of low efficacy and encouraging drug resistance (Ten Ham, 1992).

Researchers found that substandard drugs are available in markets across the developed world but the problem is more severe in developing countries. (Charatan, 2001)

Counterfeit medicines are invariably unsafe and ineffective. They result in wasted resources spent on purchasing, inventory, and transport and dispensing, with little or no beneficial effect and they may even cause actual harm to the patient. Counterfeited medicinal products threaten patient safety by at best, producing no improvement or worse, causing an added burden of disease and even death. They endanger public health for instance, by increasing the risk of antimicrobial resistance and by eroding patient trust in health professionals and healthcare systems, which are perceived as providing inadequate treatment. Consequently, public health and patient safety are being put at risk and it is timely to act now. (Cockburn, 2002)

The problem of counterfeiting is difficult to detect, investigate, and quantify. It simply means that it is hard to comprehend or even estimate the true extent of the problem. It is estimated that counterfeit drugs account for nearly 1 % to 50 % of the worldwide trade in pharmaceutical industry (See figure 1.1) (Newton et al: 2006).

The majority of wholesalers are not properly informed on the issue of counterfeit medicines and how to handle such cases. To protect the pharmaceutical product supply chain from

counterfeit medicine intrusion, distributers and wholesalers should be aware and sensitised to countermeasures against counterfeit medicines. (Khan et al., 2011).

1.1.2 Background:

This thesis considers the extent of the counterfeit medicines problem especially in developing countries and provides several examples of drugs which have been counterfeited. Additionally, the effects of counterfeit products on consumers, health care providers, drug manufacturers and the government developing countries are discussed. Counterfeiting is deceptive and immoral in any field but in healthcare, it is criminal and simply unacceptable. (Cockburn, 2002)

It is important to make a distinction between counterfeit medicines and other kinds of substandard medicines. All counterfeit medicines are substandard because they are manufactured and distributed outside of regulatory control and their composition is unpredictable. On the other hand, not substandard medicines are counterfeit because not all of them have been deliberately and fraudulently mislabeled (Cockburn, 2002).

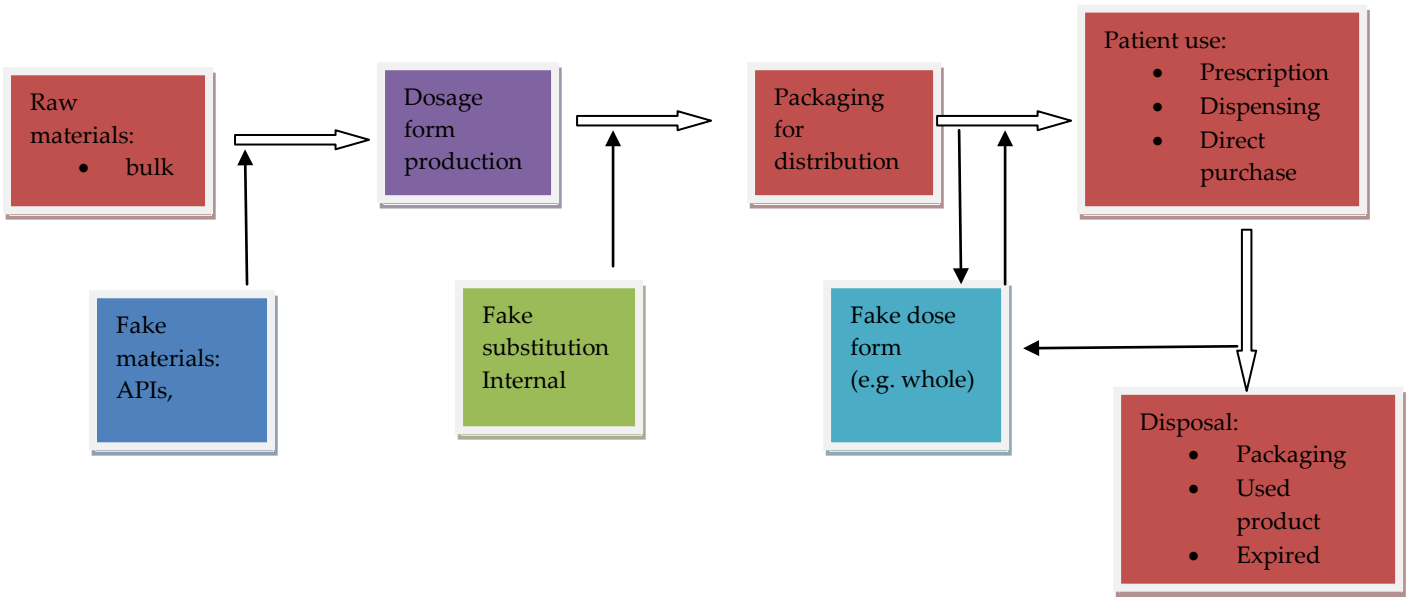
Many cases of counterfeiting have been uncovered while investigating therapeutic failure or adverse events observed in patients. Such cases lead to a serious consequence i.e. the erosion of confidence in health-care systems and counterfeit drugs particularly affect the most disadvantaged people in poor countries.

One of the most worrying implications of counterfeit medicines is the emergence of drug resistant pathogens, bacteria, viruses, and parasites (Newton et al., 2002). Such a situation will often lead to therapeutic failure and a need for the discovery and development of new

drugs. Counterfeit medicines may also cause adverse effects through excessive doses or due to the presence of potentially toxic active ingredients or pathogenic contaminants (Saywell et al., 2002). Loss of confidence and faith in medicines and in the health care system is also another very serious damaging consequence of counterfeit medicines. Not only the patient, but also healthcare professionals, pharmaceutical manufacturers, distributors, suppliers, retailers for example lose confidence in the medicines upon which they rely. In addition, pharmaceutical companies may lose the incentive to invest in research and development as well as future innovation because the counterfeit product may result in a significant loss of revenue.

It is estimated that as many as 20% of the annual deaths from malaria worldwide may be the result of taking ineffective drugs. A study in the Lancet concluded that up to 40% of artusenate products (an effective medicine to combat resistant malaria) contained no active ingredients (Cockburn et al., 2005). Counterfeit Viagra is a worldwide problem and the University of London reported in 2004 that half the men buying Viagra received a counterfeit drug. (Rudolf, 2004)

Fig 1.1: Pharmaceutical production and Counterfeit Drug Distribution Flowchart



Sources: Harper and Gellie, Counterfeit medicines – Survey report, Council of Europe Publishing, 2006, 242 p.

1.1.3 What is Counterfeit Medicine?

A counterfeit medication or drug is a medication or pharmaceutical product, which is produced and sold with the intent to deceptively represent its origin, authenticity or effectiveness. Generic drug products or drug products whose only violation is that of patent laws, are not counterfeit drug products (Cockburn, 2002). A counterfeit drug may contain inappropriate quantities of active ingredients, may be improperly processed within the body (e.g., absorption by the body), or may contain ingredients that are not on the label (which may or may not be harmful), and is often sold with inaccurate, incorrect, or fake packaging and labeling. Medicines, which are deliberately mislabeled in order to deceive consumers, are therefore counterfeit. A drug, which has not received regulatory approval, is not necessarily a counterfeit. Some tested counterfeit medications contain excessive amounts of active ingredients the effect of which may be harmful (Jackson et al., 2010)

Table 1.1: Risk from a patient safety perspective from

Public Risk	**Manufacturer Risk**
Contraindications and other drug, related problems Compliance issues Administration errors Dispensing errors Recalls Expired medical products	The cost of a recall due to counterfeiting can be US$100 million (Euros 64 million) and as high as few billion US$ for future earnings loss and several billions US$ for liability.

(Source: IMS, 2007)

1.1.4 What encourages counterfeiting of medicines?

Table 1.2 provides a breakdown of some of the main reasons for counterfeiting.

Table 1.2. What encourages counterfeiting of medicines?
Medicines attractive for counterfeiting • Lack of political will and commitment to establish a strong national medicines authority • Lack of appropriate medicine legislation • Absence of, or weak national medicines regulatory agency • Weak enforcement including corruption and conflict of interest • Shortage or erratic supply of medicines • Inappropriate use of medicines • Price differentials • Inefficient co-operation between stake holders • Lack of control over export medicines • Trade through several intermediaries • Trade through free-trade zones/free ports

(Source: 3 June 2010: World Health Organisation. Counterfeit medicines)

1.1.5 Global (developed and less developed countries) Perspective of counterfeit medicine:

Countries with advanced regulatory systems are seriously challenged by this deceptive practice. An analysis conducted by International Medical Product Anti-Counterfeiting

Taskforce (IMPACT, 2006) showed that counterfeiting is greater in those areas where regulatory and legal oversight is weaker particularly in developing countries. The extent of the problem and several other factors concerning counterfeited drugs however differ significantly between industrialised and developing countries (Dahiya, 2008).

The most important sources for data on medicine counterfeiting are the WHO and International Medical Products Anti-Counterfeiting Taskforce (IMPACT, 2006) as the WHO's organisation for the fight against counterfeit drugs. For some years the estimation of the global prevalence of counterfeit drugs has been 10 % overall (IMPACT, 2006).

The new estimates differentiate between developed countries, including the EU with the exemption of some of its most eastern parts, the USA, Canada, Australia, New Zealand and Japan, where less than 1 % of the drugs sold are counterfeit and a proportion of over 10 % for some less well developed countries. Indeed, for some countries in parts of Asia and Latin America, the estimations exceed 30 % whilst in several countries of the former Soviet Union, counterfeits reach a prevalence of over 20 % according to the WHO figures (IMPACT / WHO; 2008).

A much higher incidence can be found in drugs bought from illegal Internet pharmacies, where up to 50 % of the medicines sold are found to be fakes even in developed countries. However, occurrence differs between developed and less developed countries or between different world regions, and can also vary significantly within a single country between different cities or cities and rural areas. (IMPACT/WHO, 2008).

Other sources yield similar alarming numbers and between 2000 and 2006 the prevalence of counterfeits are estimated to have grown by 800% expected to grow at an annual rate of 13% up to 2010. This resulted in an estimated market of over $75 billion, an increase of over 90 % in comparison with 2005 figures. This would represent a market share of around 15 % of the legal pharmaceuticals market. (Cheng et al., 2009)

The evidence tends to show that where regulation is less effective, counterfeit products have become more prevalent and less sophisticated. It is clear that the populations of developing countries are at greatest risk. The International Pharmaceutical Federation (IPF) is seriously concerned about the risk to public health represented by counterfeiting, particularly in countries where legislation governing the manufacture and distribution of medicines, or the enforcement of legislation, is ineffective or nonexistent (Alan 2003).

Although more insulated from the dangers of counterfeit medicines introduced into the domestic drug supply chain, reports have emerged from the USA indicating patient safety issues and deaths related to counterfeit medicines. As the world's largest market for pharmaceutical sales, it is natural that counterfeit manufacturers and sellers have targeted the USA as its most lucrative market. (Liang, 2006). In the US, the value of seized fake drugs in 2003 was $200 million while the value of the counterfeits market in the USA was estimated to be $39 billion in total in 2008 (Bate, 2008).

The counterfeit drug cases opened by the US FDA were stable at between 5 to 11 cases per year at the end of the 1990s but this number showed a clearly increasing trend starting in 2000. A maximum was reached in 2010 where 72 cases were reported (See Figure1.2).
(FDA 2011).

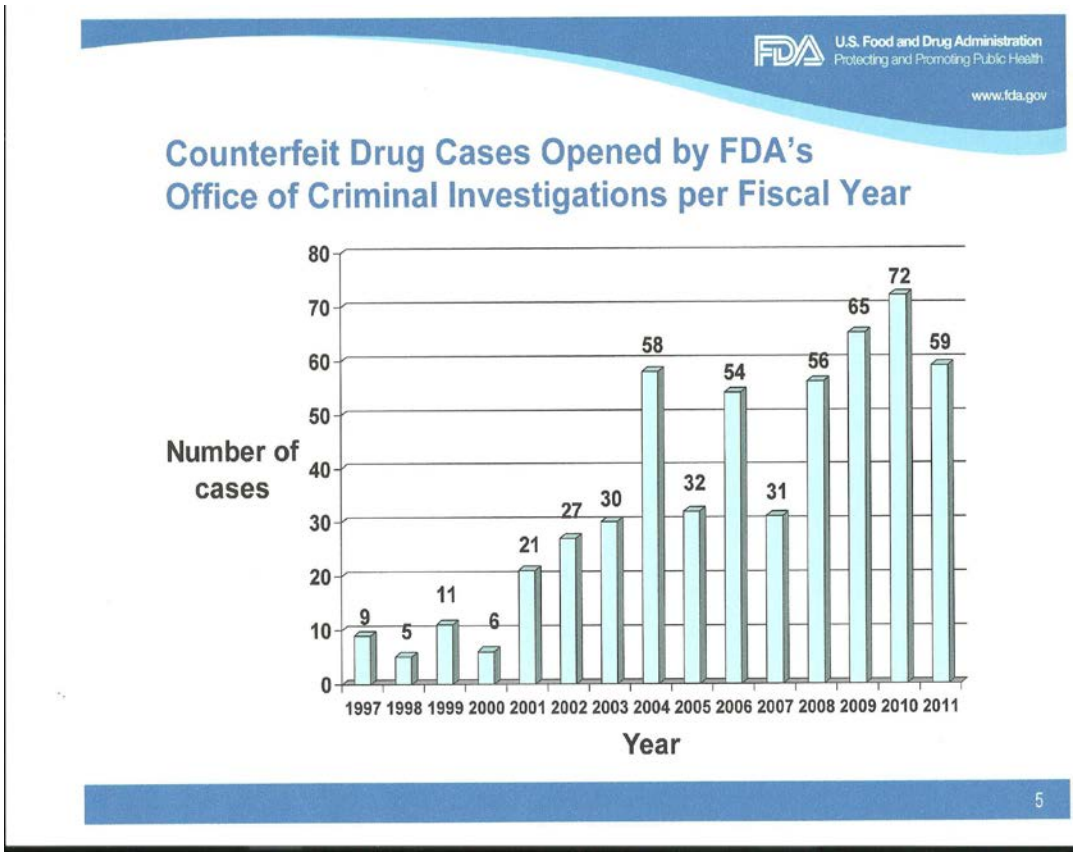


Figure 1.2 showing an ooverview of USA FDA opened counterfeit drug cases from 1997 to 2011. Data obtained from the FDA. FDA Initiative to Combat Counterfeit Drugs (accessed on 02-01-2012) http://www.fda.gov/Drugs/DrugSafety/ucm180899.htm

The European Union (EU) is particularly threatened by an influx of counterfeit medicines, especially those sold on the Internet. Counterfeits have become a serious public health problem in this region with estimates reflecting annual increases in counterfeit sales of 15% per annum and one in five Europeans admitting that they have purchased a prescription drug without a prescription. This increase has also been evidenced by the seizure of 11.4 million counterfeit drugs at EU borders in 2009, representing a 422% increase since 2006 (Tim et al., 2011).

In addition, high-profile discoveries of counterfeiting operations within the EU, such as a counterfeiting operation in the United Kingdom (UK) producing 500,000 counterfeit tablets daily, continue to highlight the risk of both counterfeit production and consumption in middle to high-income countries in Europe (Liang 2006). Similar instances involving counterfeit production and distribution have been discovered in countries such as the Netherlands, Italy, Spain, and France, sold both through EU parallel trade and on the Internet

Of particular concern, is also the rapid spread of counterfeit medicines in resource-poor countries of the developing world, which have low levels of gross national product per capita. These countries are especially vulnerable because they lack sufficient infrastructure and technical expertise to regulate and police criminal activity (Newton et al., 2010).

1.1.6 Dangers of counterfeit medicine:

In this respect, a debate is raging as to whether "counterfeit products are first and foremost a threat to human health and safety or whether provoking anxiety is just a clever way for wealthy nations to create sympathy for increased protection of their intellectual property rights.

Counterfeiting of drugs is a huge industry in Africa; the situation is extremely serious since half of the malaria medications sold may well be ineffective or even harmful. There is currently no good way to identify counterfeit drugs. However, researchers from Lund in Sweden and the UK have now developed a technique that could resolve the situation (Jakobsson, 2010)

1.1.7 Types of Fake Drugs:

Counterfeiters specialising in fake pharmaceuticals invariably try to manufacture a product to resemble any type of drug. Widely used medicines such as atorvastatin and paracetamol are more frequently counterfeited, but so are other, less commonly used products. The most frequently counterfeited medicines are expensive life style medicines such as hormones, steroids and antihistamines (Newton et al., 2001). However, life-saving drugs including antimalarials, anti-HIV/AIDS, anticancer and anti-infectives (antibacterials, antibiotics, antifungals, antiprotozoans and antivirals) are among the most counterfeited drugs found in developing countries (Newton et al., 2001). Other than drugs, the problem extends to medical devices and consumables such as syringes, gauzes and other medical equipment (WHO, 2003). It is clear therefore that counterfeit medicines are not limited to a particular category of pharmaceuticals but can be found amongst many therapeutic categories (See Figs 1.3 and 1.6).

Figure 1.3: A typical collection of counterfeit pharmaceutical drugs seized by the East African Authority.

Figure 1.4: An example of a drug store in Ethiopia taken by one of the agent

Figure 1.5: Location of a typical clinic in Ethiopia taken by one of the agent

1.1.8 The presence of counterfeit medicines globally:

The problem is truly global. Counterfeit medicines are increasingly detected not only in developing countries but also in European and North-American countries (Cockburn, 2002).

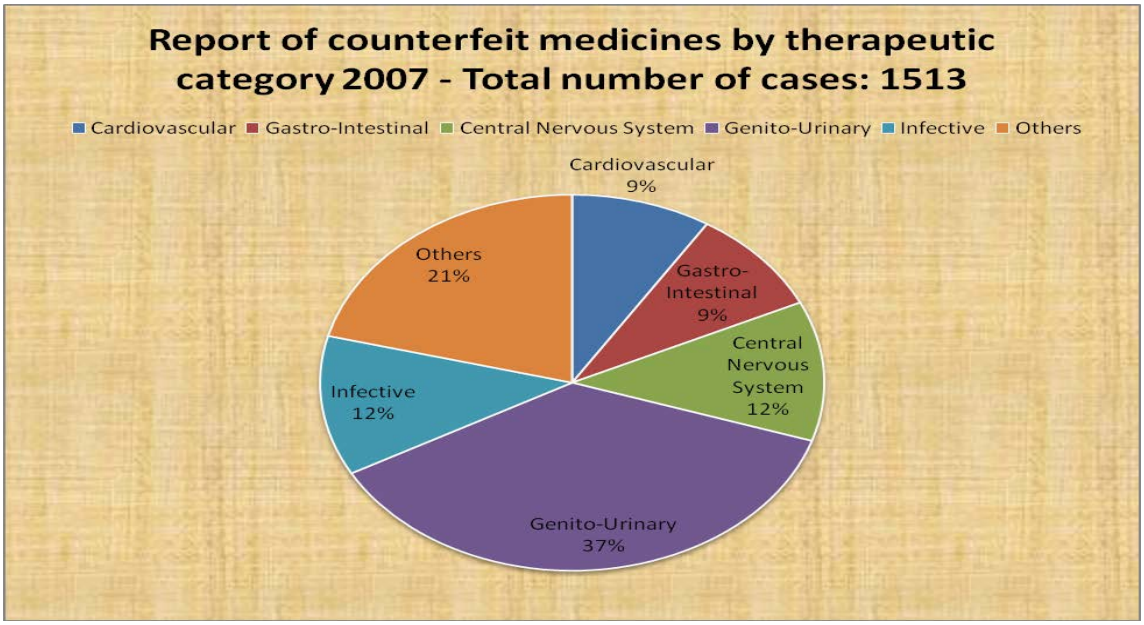


Figure 1.6: Source: PSI - Pharmaceutical Security Institute http://www.psi-inc.org/index.cfm**.**

One case reflects at least one production lot, e.g. thousands of tablets, capsules, or other forms. Several cases included multiple therapeutic categories (See figure 1.6) (PSI). Available data underestimate reality, especially in poorer areas where detection and reporting are extremely weak.

Counterfeit medicines are detected increasingly not only in developing countries but also in Europe and North America. This suggests that even countries with advanced regulatory systems are seriously challenged by this menace (Cockburn, 2002).

In the Mekong countries (Cambodia, Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam), a study undertaken in 2001 indicated that more than one third of products supposedly containing the antimalarial artesunate actually contained no active ingredients at all. A follow-up study in 2004 showed that the situation had worsened, with 99 out of 188 artesunate samples found to be counterfeit (Reggi., 2007). Moreover, in Africa (Gabon, Ghana, Kenya, Mali, Mozambique, Sudan and Zimbabwe), a recent survey of quality of antimalarials concluded that between 20% and 90% of products failed quality testing (Mara, 2010).

In Niger, during the meningitis epidemic of 1995, more than 50, 000 people were vaccinated with fake vaccines, received as a gift from a country, which thought they were safe. The incident resulted in deaths of 2500 people (Newton et al., 2001).

In Haiti the consumption of paracetamol syrup prepared with diethylene glycol (a toxic chemical used in antifreeze) resulted in the deaths of 89 people in 1995 and also 30 infants died in the India in 1998 from an identical adulteration (Newton et al., 2001).

Counterfeit medicines have also been found in Latin American countries with instances in Argentina, Brazil, Colombia, Venezuela, Mexico, Peru, and Guatemala. Mexico is a major source of counterfeit medicines with trade of US $ 650 million per year equal to 10% of total drug sales in Mexico (Bate and Boateng 2007).

1.1.9 The size of the problem:

The extent of counterfeiting is impossible to quantify. Currently, the sources of information available include reports from nongovernmental organizations, pharmaceutical companies, national medicine regulatory and enforcement authorities, ad hoc studies on specific geographical areas or therapeutic groups, and occasional surveys (WHO). These sources of information emphasize the complexity of estimating the problem.

According to the UK's Daily Telegraph report (August 2005), as many as 100,000 people die each year in China as a result of taking counterfeit or fake drugs. These figures indicate that the counterfeit drugs are found in high ratio in china as compared to other neighboring countries (Anon, 2008 c)

Reports from developing countries, especially in East and sub-Saharan Africa, are extremely rare and do not permit a realistic picture of the situation to be drawn. This is generally considered to be highly unsatisfactory because of the weakness of regulatory and enforcement systems and the widespread presence of unregulated distribution and retail facilities.

Counterfeiting is greatest in those regions where the regulatory and legal control is weakest. This situation puts rural and the poorer segments of the population at a particular disadvantage (See figure 1.7).

Fig 1.7: Medicines, including antibiotics and antimalarials on open sale on a market stall in Africa (Caudreon et al 2008).

1.1.10 The limited awareness of the problem:

In general, medical staff tend to be somewhat lacking in awareness of the extent of patient risk posed by substandard products and there is significant underreporting (Moride et al., 1997). Poor reporting in turn reinforces a limited understanding of the problems (usually the concentration of active ingredient).

Up to half of medicines tested in prevalence surveys were substandard (Table1. 3), but these surveys are rare, often limited to a few drug classes and test for a narrow set of

Table 1.3:

Country	Drugs (n = number of different products tested)	% Substandard	Origin of production	Stated issues	References
Kenya	41 different drugs (n = 277)	46%	Kenya	Failure to comply with quality tests	Kibwage et al., (1992)
	37 different drugs (n = 102)	31%	Imported	Failure to comply with quality tests	Roy (1994)
	Antimalarials (sulphadoxine-pyrimethamine and amodiaquine) (n = 116)	41%	Not stated	Under concentration of active ingredient; dissolution failure	Amin et al., (2005)
	Antimalarials	42%	India, China	Over/under concentration of active ingredient	Atemnkeng et al., (2007)
DRC Democratic Republic of the Congo	Antimalarials (artemisinin derivatives) (n = 7)	14%	Belgium	Over/under concentration of active ingredient	Atemnkeng et al., (2007)
Bangladesh	Paracetamol, ampicillin, cotrimoxazole, vitamin B tablets/injectables (n = 137)	27%	Not stated	Under concentration of active ingredient	Roy (1994)
Myanmar	Amoxicillin, chloroquine, metronidazole, paracetamol, tetracycline, ampicillin, chloramphenicol, rifampicin, co-trimoxazole and ranitidine (n = 212)	16%	21 countries (Asia, Europe, US and Australia)	Under concentration of active ingredient; wrong active ingredient	Wondemagegnehu (1999)
Vietnam	Amoxicillin, chloroquine, metronidazole, paracetamol, tetracycline, ampicillin, chloramphenicol. rifampicin. Diazepam, salbutamol (n = 288)	8%	16 countries (Asia, Europe, Canada and Australia)	Over/under concentration of active ingredient	Wondemagegnehu (1999)
Nigeria	21 antimalarials, antibacterials, antihelmitics and antifungals (n = 581)	48%	12 countries, (including Europe, Nigeria, Egypt, Asia)	Over/under concentration of active ingredient	Taylor et al., (2001)

	Chloroquine, amoxicillin, cotrimoxazole, tetracycline, ampiclox (n = 81)	36%	Not stated	Over/under concentration of active ingredient	Shakoor et al., (1997)
Colombia, Estonia, India, Latvia, Russia, Vietnam	Anti-TB drugs (n = 40)	10%	Not stated	Under concentration of active ingredient	Laserson et al., (2001)
Laos	Ampicillin tetracycline, chloroquine, ASA (n = 366)	46%	Laos, Thailand	Over/under concentration of active ingredient	Stenson et al., (1998)
	Ampicillin tetracycline, chloroquine, ASA (n = 300)	22%	Idem (repeat study)	Over/under concentration of active ingredient; over concentration of non-active ingredient; disintegration	Syhakhang et al., (2004)
Thailand	Chloroquine, amoxicillin, cotrimoxazole, tetracycline, ampiclox (n = 15)	40%	Not stated	Over/under concentration of active ingredient	Shakoor et al., (1997)
Tanzania	Antimalarials (n = 33)	36%	Cyprus, Tanzania, India, Kenya	Under concentration of active ingredient; dissolution failure	Minzi et al., (2003)
Cambodia	Antimalarials (n = 451)	27%	16 countries cited	Under concentration of active ingredient; dissolution failure	Lon et al., (2006)
Cameroon, Madagascar, Chad	Antibiotics, analgesics, antiparasitics (n = 429)	18%	Not stated	Over/under concentration of active ingredient; no active ingredient (20%); contamination	ReMeD (1995) “Cited in Caudreon et al 2008”
Gabon, Ghana, Kenya, Mali, Mozambique, Sudan, Zimbabwe	Antimalarials chloroquine and sulphadoxine-pyrimethamine (n = 278)	23% Range: 9% Sudan 41% Mali	Local and Imported	Under concentration	Maponga and Ondari (2003)
Vietnam	Amoxicillin, chloroquine, metronidazole, paracetamol, tetracycline, ampicillin, chloramphenicol.	8%	16 countries (Asia, Europe, Canada and Australia)	Over/under concentration of active ingredient	Wondemagegnehu (1999)

	rifampicin. Diazepam, salbutamol (n = 288)				
Nigeria	21 antimalarials, antibacterials, antihelmitics and antifungals (n = 581)	48%	12 countries, (including Europe, Nigeria, Egypt, Asia)	Over/under concentration of active ingredient	Taylor et al., (2001)
	Chloroquine, amoxicillin, cotrimoxazole, tetracycline, ampiclox (n = 81)	36%	Not stated	Over/under concentration of active ingredient	Shakoor et al., (1997)
Colombia, Estonia, India, Latvia, Russia, Vietnam	Anti-TB drugs (n = 40)	10%	Not stated	Under concentration of active ingredient	Laserson et al., (2001)
Laos	Ampicillin tetracycline, chloroquine, ASA (n = 366)	46%	Laos, Thailand	Over/under concentration of active ingredient	Stenson et al., (1998)
	Ampicillin tetracycline, chloroquine, ASA (n = 300)	22%	Idem (repeat study)	Over/under concentration of active ingredient; over concentration of non-active ingredient; disintegration	Syhakhang et al., (2004)
Thailand	Chloroquine, amoxicillin, cotrimoxazole, tetracycline, ampiclox (n = 15)	40%	Not stated	Over/under concentration of active ingredient	Shakoor et al., (1997)
Tanzania	Antimalarials (n = 33)	36%	Cyprus, Tanzania, India, Kenya	Under concentration of active ingredient; dissolution failure	Minzi et al., (2003)
Cambodia	Antimalarials (n = 451)	27%	16 countries cited	Under concentration of active ingredient; dissolution failure	Lon et al., (2006)
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Gabon, Ghana, Kenya, Mali, Mozambique	Antimalarials chloroquine and sulphadoxine-pyrimethamine	23% Range: 9% Sudan 41% Mali	Local and Imported	Under concentration	Maponga and Ondari (2003)

, Sudan, Zimbabwe	(n = 278)				

Common problems associated with substandard medicines include under or over concentration, contamination, poor quality ingredients, poor stability and packaging problems.

Table 1.4 provides a summary of these problems together with some recent examples.

Issue	Example	Country	Origin of product	Reported
Over concentration	TB drugs	Chad	Europe (6 countries), Kenya, India	ReMeD
	Antimalarials	Kenya, DRC		Atemnkeng et al.,(2007)
Under concentration	TB drugs	Colombia, Estonia, India, Latvia, Russia and Vietnam	Not stated	Laserson et al.(2001)
	Paracetamol, ampicilin, co-trimoxazole	Bangladesh	Not stated	Stenson et al. (1998)
Irregular filling of vials	Over or subdosed Thiopental Sodium vials	Belgium (MSF procurement centre warehouse)	Cyprus	Company alert (1998) "Cited in Caudreon et al 2008"
Contamination	Microbial contamination of distilled water	MFS procurement in Europe	Hungary	MSF (1999). "Cited in Caudreon et al 2008"

	Detergent contamination of i.v. fluids	MSF procurement centres in Europe	UK	AFSSAPS (French DRA) and company alert (2003). "Cited in Caudreon et al 2008"
	Fungal contamination of i.v. fluid bags	MSF procurement centres in Europe)	India	MSF (2004). "Cited in Caudreon et al 2008"
	Black particles in SSG (Pentostam) vials	Sudan UK	Switzerland	MHRA (UK DRA) and company alert (2006, 2007). "Cited in Caudreon et al 2008"
	Ethyl methane sulphonate (EMS) contamination of Nelfinavir API and formulations	EU and Africa		EMEA (2007). "Cited in Caudreon et al 2008"
Mislabelling (not counterfeit)	Paracetamol tablets labelled as co-trimoxazole	Democratic Republic of Congo	India	MSF (2007). "Cited in Caudreon et al 2008"
Problems with active ingredient	Variable solubility and bioavailability of active ingredients of Rifampicin		Not stated	MSF (2006). "Cited in Caudreon et al 2008"
	Morphology of the active ingredient (furosemide) affecting the	France	France, Kyghizstan, Kenya	Cavenaghis(1989),Bauer et al. (2002)

	dissolution			
Problems with excipient	Glycerin contaminated with diethylene glycol used in 15 000 bottles of paracetamol liquid caused death of 88 children	Haiti	Glycerin imported from China viaEurope	O'Brien et al. (1998)
	Diethylene glycol used instead of propylene glycol in a cough syrup killed more than 30 children in India	India	India	Singh et al. (2001)
	Diethylene glycol used in a cough syrup killed 21 persons in Panama	Panama	Panama	FDA (2006). "Cited in Caudreon et al 2008"
Poor stability	Changes in color: amoxicillin and clavulanic acid tablets	Georgia	Cyprus	MSF (2006). "Cited in Caudreon et al 2008"
	Change in smell: erythromycin tablets (two sources)	Armenia	Malta, India	MSF (2004). "Cited in Caudreon et al 2008"

	Change in consistency: crystalization in SSG vials	Sudan	India	MSF (2004). "Cited in Caudreon et al 2008"
	Loss of potency (measles vaccine)	Nigeria	UNICEF	Onoja et al. (1992)
	Loss of active ingredient: ergometrine injections	Zimbabwe	Not stated	Nazerali and Hogerzeil (1998)
Packaging problems	I.v.fluid bottles contaminated	Kenya	India	MSF (2002, 2003)
	Microcracks caused by wrong bottle shape, poor quality plastic or rough transportation	Sudan	India	MSF (2004)
Packaging problems	TB drugs moisture-damaged due to water-permeable blister packs	India	India	Singh and Mohan (2003)
Unsatisfactory dissolution profiles	Higher dissolution rate of active ingredient in antidiabetic drugs (resulting in higher and quicker peak in	France	Cyprus, UK, Kenya	Ba et al. (2005)

	blood and toxicity)			
	Poor dissolution of antimalarials	Kenya	Cyprus, Tanzania, India, Kenya	Amin et al. (2005)
		Tanzania		Minzi et al. (2003)

(Table 1.3 and 1.4 source taken from Caudron, J.-M. Ford, N. Henkens, M. Mace C, Kiddle-Monroe R. and Pinel J. Substandard medicines in resource-poor settings: a problem that can no longer be ignored Tropical Medicine and International Health volume 13 no 8 pp 1062–1072 august 2008)

1.1.11 Counterfeit drug impacts on health and economies:

According to INTERPOL, malaria, tuberculosis, and HIV/AIDS are responsible for the deaths of more than 6 million people each year (Ly et al., 2007). Overall, P. falciparum malaria kills more than 900,000 Africans annually, mostly children under 5 years old (Centers for Disease Control, 2009). It is also estimated that 200,000 children die each year after taking counterfeit anti-malarial medications (INTERPOL 2008b). When the total deaths from malaria and tuberculosis are combined, the estimated number of deaths attributed to counterfeit drugs rises to 700,000 annually (Harris et al., 2009). Although this is an alarming number in itself, some researchers claim it is actually a conservative estimate (Harris et al., 2009). Empirical studies in bacteria and parasite drug resistance and tests of active ingredient levels in counterfeit drugs have been conducted.

The danger of receiving drugs with inadequate levels of active ingredient is two-fold. First, the individuals receive no therapeutic value from the drug, which increases their risk of death, and secondly, the low levels of active ingredient assist the microorganisms in adapting to the drugs making them less effective.

Regarding the drug resistance of the malaria parasite (Plasmodium), malaria expert Dr. Nick White of Oxford University said the following, "Counterfeit medicine is a major reason why malaria has become, over the past 30 years Africa's biggest child killer, from an illness that used to be easily treated with medicines and there is now just one family of drugs left that malaria has not built up resistance to, artemisinins – which are being faked….Resistance to the Artemisinins would be an absolute catastrophe for our current attempts to try to control malaria (Shah, 2007).

Patients are often unaware that they are buying a counterfeit product or of the risks to which they are exposed by purchasing such a medicine. Consumers may bypass the healthcare system to obtain treatment because they do not believe that their condition is serious enough to warrant medical attention (Shabsigh et al., 2004).

Therefore, measuring the true amount of counterfeit product in the market place is notoriously difficult. Popular brands attract brand parasites lookalikes that do not exactly copy the original but trade-off its expensively generated brand recognition and kudos, Pfizer heavily targeted Viagra is a classic example of this (Davison, 2011).

Sustained political will and financial support for coordinated action from the police, customs officials and MRAs is crucial. A recent forensic investigation into the trade in fake artesunate

demonstrated that police, scientists, the pharmaceutical industry, governments and the WHO can work together to combat these problems (Newton et al., 2008).

1.1.12 Challenges:

Because of a lack of regulation and enforcement, the quality, safety and efficacy of both imported and locally manufactured medicines in many developing countries cannot be guaranteed. Subsequently, smuggling and illegal importation of drugs are often common. Substandard and counterfeit drugs are then not only sold in these countries but also exported or re-exported (Bagozzi, 2006).

The situation is worsened by the fact that medicines exported from many industrialized countries are not regulated to the same level as those domestically consumed, while export of drugs to developing countries via free trade zones (i.e. Dubai Free Port) is increasing. Relabeling of products to mask details of their origin is also known to occur (Schofield, 2001).

Pharmaceuticals, however, cannot be considered a standard commodity since consumers and prescribers are unable to assess their quality, safety and efficacy and the results can be harmful to patient health. Growing international and national trade in alternative medicines, including herbal products, is also becoming more complex following rapid increases in demand (WHO 2006 Fact sheet 2003). Significant quantities of herbal products are now imported by countries in Europe, North America and Asia. However, the use and production of herbal products remains largely unregulated and their safety and therapeutic value cannot always be guaranteed (Morris and Stevens, 2006)

In many countries, the official supply chain fails to reach rural areas. Poverty and the lack of an official supply chain are major factors in creating markets for counterfeit products. Also

international shipments are not searched or verified in free trade zones (WHO, 2006 b) making infiltration in the supply chain easier.

Counterfeiting medicines is not properly defined and is dealt with in the same way as all other types of counterfeiting. The absence of deterrent legislation in many countries also encourages counterfeiters since there is no fear of being apprehended and prosecuted. Currently, the penalties do not match the crime and are therefore not acting as a sufficient deterrent. There is also a lack of a dedicated work force to handle the problem, no uniform international obligations and no specific treaty to tackle the problem (Latin America Battles Counterfeit Drug Threat: Daily International Pharmacy Alert: Washington Business Information: 2006: 292).

The conclusion of a conference on counterfeit drugs held in Geneva in 2002, was that there is a glaring lack of political will to tackle the seriously underestimated problem of counterfeit drugs (Pincock, 2003). Combating counterfeit medicines requires collaboration, at national, regional and international levels involving all stakeholders of the public sector and the civil society including health professionals, patients, manufacturers, distributors, as well as communication professionals and the media (WHO, 2006 b).

Players in this important battle are the health professionals. This includes nurses and pharmacists who should be vigilant in detecting and reporting suspicious products. Similarly, physicians should rule out counterfeits as a possible cause of adverse reactions or therapeutic failure. Patients must report to their pharmacists and doctors if they sense any irregularity with their medication, if they experience a side effect or a decrease in beneficial effect.

1.1.13 Factors encouraging counterfeiting of drugs:

The production of counterfeit drugs need not occur in large infrastructures or facilities. The majority of the counterfeiters apprehended so far carried out their activities in ordinary households, small cottage industries, in backyards or under the shade of a tree.

1.1.14 Internet and Counterfeit medicine:

Internet pharmacy is also known as online pharmacy, cyber-pharmacy, e-pharmacy, and virtual pharmacy/drugstores. The Internet is a global distribution channel for these fake medicines, but little is known about the extent to which consumers are able to buy medicines online safely. Hundreds of online pharmacies advertise themselves as cheap, fast alternatives to typical drugstores in developed countries compared to developing countries (Bate et al., 2008). These websites can be an enormous temptation for Americans facing the highest pharmaceutical prices in the world. In some ways, the internet has improved the pharmaceutical market with increased patient access and economic efficiency, but it is also a major source of counterfeit distribution.

The pharmacy internet industry continues to grow as the result of consumer interest in more competitive prices and greater convenience. Estimates of the number of internet pharmacy sites range between 500 and 600 (Newton et al., 2002).The proliferation of online pharmacies has generated considerable controversy, largely due to the variability of sites and professional concerns. Significant variation exists with respect to the quality and level of service provided by internet pharmacies and requires prior approval of a third-party (Crawford, 2003).

Consequently, there has been a significant increase in internet use for the provision of direct patient care services, and these uses range from informal e-mail communications between

physicians and patients, to more formal services involving fees for storing medical records online, physical consultations with diagnoses and formulating treatment plans.

Additionally, the Web hosts countless online forums for support groups, in which patients can become involved in global exchanges of clinical and non-clinical discussions of medical topics. Thus, the benefits and conveniences of cybermedicine are quite apparent. However, there is also the perspective that these new capacities compromise the quality of medical care, as well as the stability and importance of the physician-patient relationship. In industrialised countries and to some extent in poorer countries, internet-based sales of pharmaceuticals are a major source of counterfeit medicines, threatening those who seek cheaper, stigmatised or unauthorised treatments.

Some internet pharmacies are completely legal operations, set up to offer clients convenience and savings. They require patient prescriptions and deliver medications from government licensed facilities. Illegal internet pharmacies on the other hand sell medications without prescriptions and may use unapproved or counterfeit products. In some cases, internet pharmacies are operated internationally and sell products that have an unknown or vague origin (WHO, 2006 b).

1.1.15 What is the nature of the Counterfeit medicine market?

The massive growth of Chinese manufacturing has been one of the key drivers of the twenty-first century global economy (UN report 2009). Much of this growth is the result of outsourcing by overseas companies, attempting to take advantage of China's high productivity and low costs. Most of the retail value of these products accrues to the

companies doing the outsourcing, while the Chinese manufacturing firms retain a relatively small share (UN report 2009).

This mutually beneficial arrangement is only possible because most Chinese firms respect the intellectual property rights of the outsourcing companies. Unfortunately, this situation – in which the designers and manufacturers of a product often live on different continents – has fostered the growth of counterfeiting. Counterfeiting is an attractive alternative to licit commerce because costs are reduced to manufacturing, transport and distribution (Counterfeit product: Case studies of transnational threats: 173. 8: 176-177 WHO, 2003).

The costs involved in research, design and marketing are all avoided. Because counterfeiters are essentially unaccountable and have no interest in building a brand reputation, costs can be additionally reduced by cutting corners in the production phase, such as employing sweatshop labour, engaging in environmentally unsound manufacturing processes and using inferior-grade materials. Profits can be further maximised by avoiding taxes. Thus, import duties are evaded through customs fraud or outright smuggling, and sales taxes are avoided via informal retailing, which itself often makes use of illegal migrants working for little compensation. The end result is a product that can look very much like the original, but which can be sold for much less while generating a larger profit (Counterfeit product: Case studies of transnational threats: 173. 8: 176-177 WHO, 2003).

Mass-scale counterfeiting for export in China seems to be mainly a product of the last decade – in 2000, (See Figure 1.8) China ranked fourth among national sources of counterfeits to the EU, responsible for only 8% of the cases (Saywell, 2002).

The problem of counterfeiting is, of course, not limited to China, and the Chinese Government has taken extensive measures to address it. In 2009, the General Administration of Quality Supervision, Inspection and Quarantine dealt with some 200,000 cases of counterfeit or substandard products, dispatching nearly two million quality inspectors and seizing an estimated US$490 million worth of goods (United nation report: 2012).

The State Administration for Industry and Commerce announced seizing US$221 million in counterfeits in 2008 (Mara, 2010). In addition, Chinese Customs annually seize tens of millions of dollars worth of counterfeits bound for export. Those who were convicted faced stiff sentences and the ringleader of one software piracy operation was sentenced to seven years imprisonment in 2009 (WHO Substandard and counterfeit medicines, 2003).

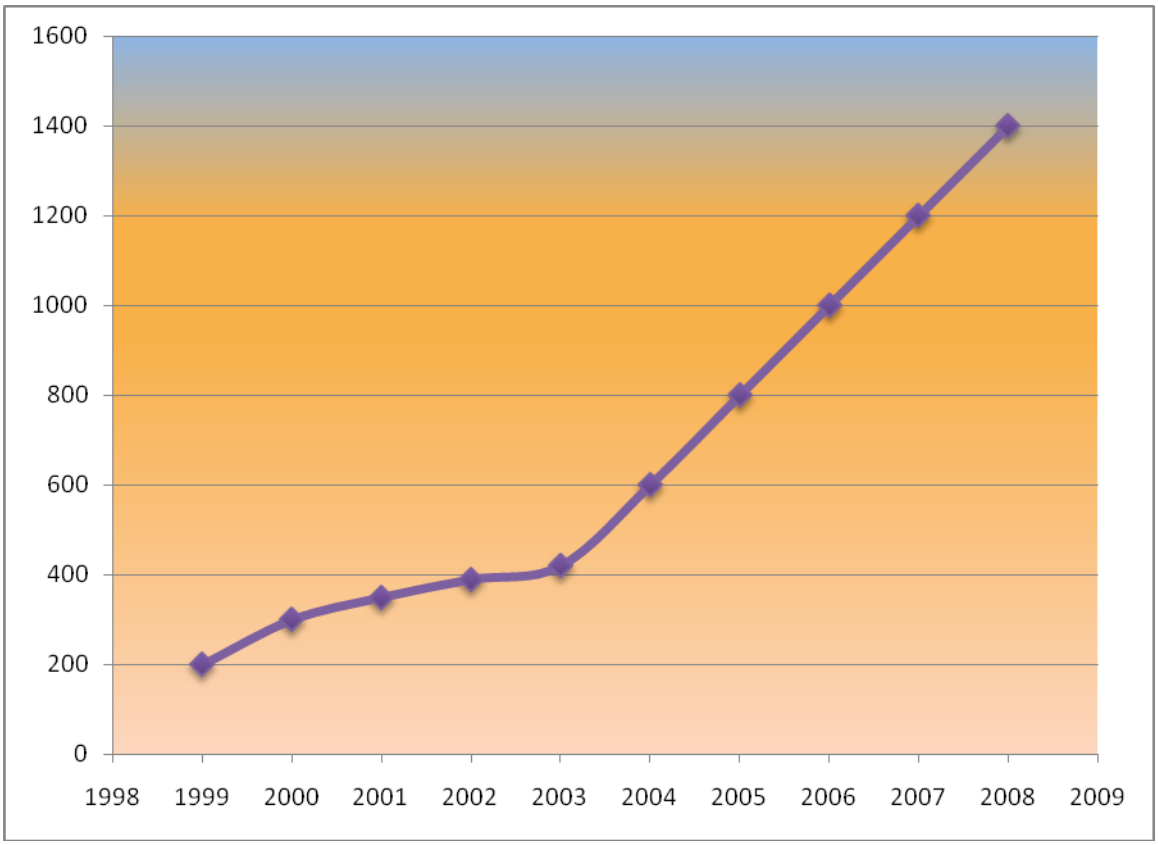


Figure 1.8: The value of exports from China 1999 - 2008: Source- Chinese Customs

1.1.16 What Does the Future Hold for Counterfeit Drugs in Africa?

Presently, there is no agreement on how to define a counterfeit drug, let alone a scheme in international law to make counterfeiting a crime and pursue its perpetrators around the globe. (Bate and Attaran, 2010).

Drug counterfeiting is not an issue that is unique to these countries but an issue that affects most of Sub-Saharan Africa. These countries may have made strides to combat the issue within their own borders, and they may even have made vast improvements, but there is only so much that one country can do to tackle a regional problem. The porous borders between many African nations means that even if one country, for example, Nigeria, manages to resolve the issue of counterfeit drugs within its own borders, counterfeit drugs will still be prevalent, albeit to a lesser extent, unless it is neighbouring countries do the same.

Eradicating counterfeit drugs from the continent will entail the effort of all affected countries. To start, perhaps, the African Union can plan a definition of what a counterfeit drug is, within the context of the African continent.

Once all the countries have a clear idea of what they are looking to eradicate, they can then form a legal collective, such as the Africa and the East African Society, and create laws that impose more deterrent punishments on the drug counterfeiters. Many African officials see tougher penalties as the next logical step towards the eradication of this lethal trade (Ahmed and Dillard, 2011).

There are no estimates on when Africa will be free of counterfeit drugs; however, even without an end in sight, many African countries are taking the necessary steps to safeguard the welfare of their people (Ahmed and Dillard, 2011).

Controlling the entry of fake drugs into a country can be done, but it is a technological and human resource challenge. Renewed international understanding and cooperation is essential if we aim to control the fake drug problem. This will not be accomplished with just another international conference to discuss the issues. (Shepherd, 2010)

1.1.17 Geographic Back Ground of the13 Countries that Studies Were Done:

Figure 1.9: Show the map of 13 countries (Middle East and East Africa countries)

Source: Perry-Castañeda Library Map Collection

1.1.18 Saudi Arabia

Saudi Arabia is the largest Arab country of the Middle East and bordered by Jordan and Iraq on the north and northeast, Kuwait, Qatar, Bahrain and the (UAE) United Arab Emirates on the east, Oman on the southeast, and Yemen on the south (See Figure 1.9). The Persian Gulf lies to the northeast and the Red Sea to its west.

The Saudi Food and Drug Authority (SFDA) were established under the Council of Ministers resolution no (1) dated 2003 and Islamic calendar 07/01/1424 H, as an independent body corporate that directly reports to The President of Council of Ministers. The Authority objective is to ensure safety of food and drug for man and animal, and safety of biological and chemical substance as well as electronic products.

1.1.19 Emirates (UAE):

The United Arab Emirates (UAE) is a federation situated in the southeast of the Arabian Peninsula in Southwest Asia on the Persian Gulf, bordering Oman and Saudi Arabia and sharing sea borders with Iraq, Kuwait, Bahrain, Qatar and Iran (See Figure 1.9). The UAE consists of seven states, termed emirates, (because they are ruled by Emirs) which are Abu Dhabi, Dubai, Sharjah, Ajman, Umm al-Quwain, Ras al-Khaimah and Fujairah. The capital and second largest city of the United Arab Emirates is Abu Dhabi. It is also the country's center of political, industrial, and cultural activities. In 1974 the first law relating to the sale of medicine and pharmaceutical practice was passed, superseded by the second and current law in 1983 (Abu-Dhabi-Gov, 1995)

1.1.20 Qatar:

Qatar is an Arab country, known officially as an Qatar, in the Middle East, occupying the small Qatar Peninsula on the northeasterly coast of the much larger Arabian Peninsula. It is bordered by Saudi Arabia to the south (See Figure 1.9); otherwise, the Persian Gulf surrounds the state. A strait of the Persian Gulf separates Qatar from the nearby island nation of Bahrain. Qatar is an oil- and gas-rich nation, with the third largest gas reserves, and the first or second in the world. An absolute monarchy, Qatar has been ruled by the al-Thani family since the mid-1800s and has since transformed itself from a British protectorate noted mainly for pearling into an independent state with significant oil and natural gas revenues.

1.1.21 Yemen:

Yemen is a country located on the Arabian Peninsula in Southwest Asia. It is bordered by Saudi Arabia to the north, the Red Sea to the west, the Arabian Sea and Gulf of Aden to the south, and Oman to the east (see Figure 1.9).

Yemen has population approx. 19.7 Million inhabitants, 71% of whom live in rural areas. The illiteracy rate is high and reaches about 55.7%. Yemen is a low-income country with per capita GDP of US 659. Ministry of Public Health and population is responsible of regulating, registering and controlling medicine that is used in Yemen (Anon, 2008 a).

1.1.22 Bahrain:

Bahrain is a small island country in the Persian Gulf ruled by the Al Khalifa Royal family. While Bahrain is an archipelago of thirty-three islands, the largest (Bahrain Island) is 55 km (34 mi) long by 18 km (11 miles) wide. Saudi Arabia lies to the west and is connected to

Bahrain via the King Fahd Cause way, which was officially opened on 25 November 1986. Qatar is to the southeast across the Gulf of Bahrain (See Figure 1.9).

In Bahrain, petroleum production and processing account for about 60% of export receipts, 60% of government revenues, and 30% of GDP (Word Fact Book). Ministry Health (MOH) is responsible of regulating, registering and controlling medicine that is used in Bahrain. There is no independent regulatory agency, like Saudi Arabia and Yemen.

In 1978 a Registration Committee was established to regulate medical practice and service in pharmaceutical area (Anon, 2012)

1.1.23 Oman:

Oman is an Arab country in southwest Asia on the southeast coast of the Arabian Peninsula. It borders the United Arab Emirates on the northwest, Saudi Arabia on the west and Yemen on the southwest. The coast is formed by the Arabian Sea on the southeast and the Gulf of Oman on the northeast. The country also contains Madha and Musandam, two exclaves on the Gulf of Oman, south of the Strait of Hormuz and surrounded by the United Arab Emirates on the land side (See Figure 1.9). Ministry of Health (MOH) is responsible of regulating, registering and controlling medicine that is used in Oman. There is no independent regulatory agency, like Saudi Arabia and Jordan.

1.1.24 Egypt:

Egypt is a country mainly in North Africa, with the Sinai Peninsula forming a land bridge in Southwest Asia. Egypt is thus a transcontinental country, and a major power in Africa, the Mediterranean region and the Islamic world. Covering an area of about 1,010,000 square kilometers (390,000 sq mi), Egypt is bordered by the Mediterranean Sea to the north, the

Gaza Strip and Israel to the northeast, the Red Sea to the east, Sudan to the south and Libya to the west (See Figure 1.9). The Egyptian Drug Authority (EDA) is the pharmaceutical regulatory body of the Egyptian Ministry of Health (MOH) and it is responsible for cooperation with relevant international organizations (such as the WHO) in order to improve standards of pharmaceutical products and practices.

1.1.25 Ethiopia:

Ethiopia is the second-most populous nation in Africa with over 85.2 million people and the tenth-largest by area with its 1,100,000 km^2. The capital is Addis Ababa. Ethiopia is bordered by Eritrea to the north, Sudan to the west, Djibouti and Somalia to the east, and Kenya to the south (See Figure 1.9). Ethiopia has shown a fast-growing annual GDP and it was the fastest-growing non-oil-dependent African nation in 2007 and 2008. (Anon, 2008 b) retrieved on 16-04-2010).

Ethiopia has agency call Drug Administration and Control Authority of Ethiopia which claims that this agency its job is to promote and protect the public health by ensuring safety and quality of products and health service through registration, licensing and inspection of health professionals, pharmaceuticals food establishments and health institutions and provision of up-to-date regulatory information while promoting rational medicine use

1.1.26 Somalia:

Somalia: formerly known as the Somali Democratic Republic under communist rule, is a country located in the Horn of Africa. It is bordered by Djibouti to the northwest, Kenya to the southwest, the Gulf of Aden with Yemen to the north, the Indian Ocean to the east, and Ethiopia to the west. With the longest coastline on the continent, its terrain consists mainly of plateaus, plains and highlands (See Fig 1. 9). For 1994, the CIA estimated the GDP at $3.3

billion. In 2001, it was estimated to be $4.1 billion. By 2009, the CIA estimated that the GDP had grown to $5.731 billion, with a projected real growth rate of 2.6%. (Somalia; World Fact book. Central Intelligence Agency. 2009-05-14). Somalia does not have regulatory agency at all.

1.1.27 Kenya:

Kenya is a country in East Africa. Lying along the Indian Ocean to its southeast and at the equator, Kenya is bordered by Somalia to the northeast, Ethiopia to the north, Sudan to the northwest, Uganda to the west and Tanzania to the south. Lake Victoria is to the southwest and is shared between Kenya, Uganda and Tanzania. Kenya has numerous wildlife reserves, containing thousands of animal species (See Figure 1.9).

The Pharmacy and Poisons Board is the Drug Regulatory Authority established under the Pharmacy and Poisons Act, Chapter 244 of the Laws of Kenya. The Board regulates the Practice of Pharmacy and the Manufacture and Trade in drugs and poisons. Their aims is to implement the appropriate regulatory measures to achieve the highest standards of safety, efficacy and quality for all drugs, chemical substances and medical devices, locally manufactured, imported, exported, distributed, sold, or used, to ensure the protection of the consumer as envisaged by the laws regulating drugs in force in Kenya. (Ministry health web site)

1.1.28 Uganda:

Uganda is a landlocked country in East Africa. Uganda bordered on the east by Kenya, on the north by Sudan, on the west by the Democratic Republic of Congo, on the southwest by Rwanda, and on the south by Tanzania (See Figure 1.9). The southern part of the country

includes a substantial portion of Lake Victoria, which is also bordered by Kenya and Tanzania.

In Uganda, the National Medical Stores and National Public Health Laboratories, regulatory functions handled by professional councils, National Drug Authority (NDA) and other regulatory bodies and one of its functions is the implementation of the Policy.

1.1.29 Tanzania:

Tanzania is a country in central East Africa bordered by Kenya and Uganda to the north, Rwanda, Burundi and the Democratic Republic of the Congo to the west, and Zambia, Malawi and Mozambique to the south. The country's eastern borders lie on the Indian Ocean (See Figure 1.9).

1.1.30 Overview background information for drug regulation of these 13 Countries:

The regulation of medicine has evolved over the last five decades in response to serious adverse events in relation to medicinal products. The early regulatory standards were mainly related to ensuring the quality of pharmaceutical products and subsequent advances in the early 1960s led to the developing of new standard for assessing the efficacy and safety of new medicines (Hill and Johnson, 2004)

Currently pharmaceutical companies are required to obtain a marketing licence prior to the sale of new medicine in a particular market or country. This licence, issued by the governing

regulatory authority, follows a review process designed to ensure that only safe and effective drugs reach the market and the patient.

Currently approximately 20% of countries have fully operational medicine regulation whereas 50% have regulation of varying capacity and 30% have either none or very limited drug regulation. Many developing countries are incapable of ensuring safety, efficacy and quality of the pharmaceutical product available in their markets and this due to the resource constrained in terms of staffing, standard system and training

1.1.31 UAE:

In 1974 the first law relating to the sale of medicine and pharmaceutical practice was passed, superseded by the second and current law in 1983 (HAAD, 2013).

1.1.32 Bahrain:

In 1978 a Registration Committee was established to regulate medical practice and service in pharmaceutical area (Anon, 2012)

1.1.33 Qatar:

The pharmaceutical area has been controlled by the Ministry of health since 1971 and Pharmacy and Drug Control Department at the Supreme Council of Health is the department who regulates the Medicine in Qatar (WHO 2006)

1.1.34 Kenya:

In Kenya, there are legal provisions establishing the powers and responsibilities of the Medicines Regulatory Authority (MRA), which is the Pharmacy and Poisons Board (PPB).

The PPB operates as a department of the Ministry of Health, but there are initiatives to establish it as a semi-autonomous agency under the Ministry of health. The MRA is involved in harmonization/collaboration initiatives, which include the African Medicines Regulatory Harmonization and the Harmonization of Medicines Registration in the EAC. An assessment of the medicines regulatory system was conducted in 2006.

1.1.35 Tanzania:

Tanzania Food and Drugs Authority (TFDA) is a regulatory body under the Ministry of Health and Social Welfare which is responsible for regulating the quality and safety of food, drugs, cosmetics and medical devices.

It is established under Tanzania Food, Drugs and Cosmetics Act No. 1 of 2003, after repealing the Pharmaceutical and Poisons Act No. 9 of 1978 (which established the Pharmacy Board) and Food {Control of Quality} Act No. 10 of 1978 (which established the National Food Control Commission). TFDA, a semi-autonomous body under the Ministry of Health and Social Welfare, became operational on 1st July 2003 (TFDA web site: http://www.tfda.or.tz).

1.1.36 Uganda:

The National Drug Authority (NDA) a regulatory body under the Ministry of Health and Social Welfare which is responsible for regulating the quality and safety of food, drugs, cosmetics and medical devices.

NDA mandated with the responsibility of ensuring that the population accesses medicines that are of good quality, safe and efficacious, wishes to inform the general public that it has

received information from World Health. NDA was established on 1986. (NDA Web site http://www.nda.or.ug).

1.1.37 Ethiopia:

Reformation in the Ethiopian Food, Medicine and Health care Administration and control authority was establishes on 2009.The Ministry of Health is

The Ministry of Health is responsible for the accessibility of quality health service to all citizens throughout the country. Although, a number of special programs have been operational, in the last few years, the Primary Health Care quality still requires due attention. However, various challenges, assumptions and bureaucratic hurdles have been hampering the progress in quality health care delivery system. Because of this the health care service was haphazardly regulated inefficiently.

In recognition to the health sector reform in Ethiopia, the regulation of all health care elements are clearly delineated from the provider and purchaser, and is redesigned to provide the public a dramatic result with respect to low cost, short time, high quality, and large amount of service. Accordingly, health and health related services and products quality regulation core process is redesigned in the purpose of protecting the public from any emerging health risks (Food, Medicine and Health Care Administration and Control Authority Ethiopia website FMHACA) accessed on 10/10/2012.

1.1.38 Somalia:

Somalia does not have any regulatory agency, they do have a ministry health

The three zonal Ministries of Health (Ministry of Health of the Transitional Federal Government, Ministry of Health and Labor of Somaliland, and the Ministry of Health of

Puntland) operate with varying and overall limited levels of influence over domestic operations. Somalia is critical for the pharmaceutical trade because its duty-free conditions have made it a major import channel for the Horn of Africa (Kenya and Ethiopia). There are linkages between the pharmaceutical market in Ethiopia and Somalia, but little is known about the routes which are taken or the amount of goods that cross the border. Drug supply routes are the least investigated segment of the health system in Somalia although a study did find that most medicines in the central Bakaarha market in Mogadishu came from Pakistan and India (Capobianco and Naidu 2010).

1.2 AIMS AND OBJECTIVES OF THE STUDY

1.2.1 Aims:

The principal aim of this study was to investigate the performance of health care professionals at the practice level concerning the safety and quality of medicinal products in developing countries focusing on six countries in the East African region and seven countries located in the Middle East.

1.2.2 Objectives:

- To perform some groundwork towards providing a fundamental insight into the extent of drug counterfeiting in these developing countries particularly where data gathering has traditionally been both sparse and challenging.

- To design and evaluate a suitable questionnaires

- To conduct a questionnaire and survey concerning counterfeit medicines in the 13 developing countries.

- To evaluate how developing countries and the authorities in these regions are developing strategies to combat the counterfeit drug problem.

- To establish the activities undertaken to improve safety of medicines in developing countries.

- To compare the safety and use of medicines in developing countries with those of developed countries.

- To address the problem of the counterfeit medicine in developing countries and advocate possible solutions as to how to contend with counterfeit medicines.

- To compare and contrast the data with that in the existing literature.

1.2.3 Hypothesis test:

- To investigate the correlation between the GDP per country/capita against level of counterfeit medicine.

- To investigate the correlation between the counterfeit medicine and education level.

2 CHAPTER TWO

2.1 STUDY RATIONALE AND METHODOLOGICAL FRAMEWORK.

2.1.1 Study Rational

The general introduction to this thesis (chapter one) highlighted the focus of earlier research studies on quality measures regarding the safety medicines and how they tend to be restricted to developed countries such as the USA and Japan in addition to the EU. However, there is a lack of data concerning the quality and safety of medicines and counterfeit medicines in emerging markets such as those of middle-eastern countries and east Africa.

Given the importance of the safety of medicines, and problems of counterfeit drugs in developing countries, it was proposed that data relating to this topic should be collected and analysed from the Middle East and east Africa.

The overall rationale was to:

- Provide an insight into the extent of drug counterfeiting in middle-eastern countries
- Evaluate how the authorities in middle-eastern countries combat counterfeiting.
- Determine the activities undertaken to improve medicines safety
- Compare the safety of medicine in developing countries such as the middle-east and east Africa with those of developed countries

In respect of the above rationale, there is a gap in research in developing countries regarding a valid and reliable instrument to collect comprehensive data on quality performance at the practice level concerning the safety and use of medicines and counterfeit drugs. In view of the above shortcoming, this chapter is intended to review and lead up to an appropriate methodological framework for the proposed study

2.1.2 Study design:

The selection of a study design is one of the most important decisions that need to be made in order to answer any research question. According to Yin (2003), the purpose of any potential academic research may be exploratory, descriptive or explanatory and the following expands on these categories:

2.1.3 Explanatory studies:

The meaning of the word “explanation” is to render complicated concepts understandable by showing how their component parts fit together according to some rules (Miles and Huberman, 1994). Explanatory research is used for studying the relationship between causes and effects as well as factors which together cause certain phenomena to be identified (Yin, 2003).

2.1.4 Descriptive studies:

Descriptive studies are suitable when a problem is clearly structured but the intention is to simplify the matter to make it more understandable rather than identifying the cause of the symptoms. This is performed by reducing the complicated problems into their component parts (Miles and Huberman, 1994).

2.1.5 Exploratory studies:

Exploratory studies aim to gain basic knowledge within a problem area (Zarkesh, 2008). These studies are appropriate when it is difficult to identify the problem and when important characteristics are difficult to determine, they tend to start from a large pool of data that has a narrower focus as the research develops (Saunders et al., 2009).

The current research project aims to investigate the safety of medicines with regard to the counterfeiting in developing countries. Thus the main purpose of the work may be classed as exploratory even though it might also be additionally considered as descriptive research.
When considering the sample populations from which information will be collected, namely healthcare workers and pharmacists, it was decided that the most appropriate technique for data gathering would be through the use of structured questionnaires.

Cross-sectional research involves the collection of data from a whole population or a representative subset, at one specific point in time. There are several advantages of cross sectional studies such as savings in time and costs particularly since this design type has the potential to collect a large amount of data over a short period of time (Anon 2000). Such studies may be short and executed with less difficulty or costs of maintaining subject contact than that associated with longitudinal research, which entails repeated observations over extended periods.

2.1.6 Data Collection:

2.1.7 Data collection techniques:

There are a number of possible data collection techniques and these include structured questionnaires and personal or telephone interviews (Trochim, 2006). A key difference between these two approaches is that in the case of structured questionnaires the respondent completes the questionnaire directly while interviews are completed by the reviewer based on the respondent's verbal answers.

2.1.8 Structured questionnaires:

A questionnaire is useful when information needs to be collected reasonably quickly from respondents in a non-threatening way (McNamara, 1999). It consists of a number of questions in a definite order. The main strengths of questionnaires are the following (McNamara, 1999; Passmore et al., 2002; Bourque and Fielder, 2003; Trochim, 2006):

- Questionnaires are easy to distribute:
- They are relatively inexpensive to administer
- The same instrument may be sent to a large number of people.
- They allow the respondent to respond at their own convenience.
- Large amounts of data can be collected
- They are impersonal and avoid bias which develops as a result of interaction between the researcher and the respondent
- They can be completed anonymously
- The results are easy to compare and analyse.

On the other hand, there are a number of limitations associated with questionnaires. These include (McNamara, 1999; Passmore et al., 2002; Bourque andfielder, 2003; Trochim, 2006):

- Response rates are often very low
- The risk of not obtaining care feedback from some of the respondents
- They can be considered impersonal
- No clarification of items is possible
- The questions may be difficult to develop as they must be drawn up in a way that avoids bias and ambiguity

2.1.9 Personal and telephone interview:

These interviews are used in cases when researchers wish to obtain a full range and depth of information (McNamara, 1999). The method employs an interviewer who telephones or meets in person with respondents, spontaneously or through a scheduled appointment (Diem, 2002).

The main advantages of telephone and personnel interviews include (McNamara, 1999; Diem, 2002; Passmore et al., 2002; Bourque and Fielder, 2003; Bowling 2005; Trochim, 2006):

- Opportunity to obtain quick responses
- The personal element and trust that can be developed through interview.
- Clarification and explanation of items is possible
- Few incorrectly completed questionnaires
- High response rate

In contrast, there are a number of limitations associated with interviews and these include (McNamara, 1999; Diem, 2002;Passmore et al., 2002; Bourque and Fielder, 2003; Bowling 2005; Trochim, 2006).

- The risk that the interviewer biases the respondent's replies
- Responses are not private
- Can be costly to administer each interview
- Time consuming if the interviews are conducted at the participants locations
- Difficult to analyse and compare the responses.

Some these potential weaknesses are avoidable by careful selection, training and monitoring of interviewers (Bourque and Fielder, 2003; Bowling, 2005).

Although personal or telephone interviewing may be a suitable and powerful method, a number of factors, such as cost, time required, and nature of the data gathered and the geographic dispersion of the respondents make this option less feasible. As a consequence, the questionnaire technique is preferred due to the confidential nature of the information required, as well as the high volume of data likely to be collected from different sources.

2.1.10 Data collection method using the questionnaire technique:

There are a number of methods available for collecting data using the questionnaire technique (McNamara, 1999; Diem, 2002), these include questionnaires that are paper based or electronically mailed, group administered, telephone-administered and web-based. Several factors should be considered when selecting the most suitable method such as the type and size of the population being studied, the purpose of the study, timelines, budget and resource (Diem, 2002).

2.1.11 Paper or electronically delivered questionnaires:

This method uses a printable document that is posted or mailed electronically to participants for them to complete at their own convenience, before returning the questionnaire.

This method can be advantageous because it (Diem, 2002: Bourque and Field, 2003 and Trochim, 2006):

- is highly cost –effective
- requires minimum resource
- allows privacy of responses
- reduces bias

However, there are a number of challenges that need to be addressed if this method is used. These include (Diem, 2002; Bourque and Field, 2003; Bowling, 2005):

- The difficulty in obtaining accurate mailing lists
- The time required to receive the responses
- The extra time involved in following up non-respondents
- The possibility of obtaining a low response rate
- The risk of encountering problems with collected data due to the limited flexibility permitted through the questionnaire.

2.1.12 Group-administered questionnaires:

This method brings together a group of respondents who are asked to respond to a structured sequence of questions. Each person is expected to complete the questionnaire without consulting with other persons in the group, but the researcher is available to provide introductory instructions, answer questions and monitor the extent to which the questionnaires are completed (Diem, 2002; Bourque and Field, 2003; Trochim, 2006). The strengths of this approach are that the response rates are high invariably since respondents may request clarification from the researcher, and the qualities of responses tend to be of a higher standard. The limitations include (McNamara, 1999; Bourque and Fielder, 2003)

- The required information can be gathered quickly
- Data can be collected over a large geographic area
- There is some personal contact between the interviewer and the respondent
- It allows for flexibility with the respondent

- Follow-up questions can be asked by the interviewer

Limitations of this method include (Diem, 2002; Bourque and Field, 2003; Trochim, 2006):

- The intrusion of a call might not be liked by some respondents
- The need to establish the credibility of the caller
- The questionnaires have to be relatively short
- Restricted time for respondents to compile the answers
- The interviewer can bias the participant's responses
- Greater auditory demands which may be burdensome to some respondents
- The willingness to disclose sensitive information is low

2.1.13 Telephone-administered questionnaires:

Calling the participants by telephone, typically spontaneously, or by scheduling an appointment can be used to collect data. It may be possible to use an automated system where users reply via a touch-tone telephone to a computer-based interview system. A rapid response is possible using this approach and it can be inexpensive if calling locally. Some of the problems encountered with this method include access limitation from answer machines, reliance on correct numbers and instantaneous credibility of the caller being established in order to complete the call.

Time zones differences and language can also be a barrier (Diem, 2002; Trochim, 2006). In addition, the time differences between different countries can be one of the problems, which may lead to it being inconvenient to answer questions from the researcher's point of view. This type of method was not selected by the researcher and was not used this study.

2.1.14 Web-based questionnaires:

This method involves posting a questionnaire on a website and respondents replying remotely (Diem, 2002). The advantages of this method include: quick responses are possible, it can be inexpensive if the correct software and tools are available; postage is reduced or eliminated; and it is easy for respondents to reply. The limitations of this method are that the respondents must have internet access, require basic computer literacy and reminders are still needed (Diem, 2002 and Bowling 2005).

Taking into consideration the above factors, paper questionnaires were the preferred option due to the fact that many subjects in developing countries do not have computer access. In the execution of the study, either the author or an agent administered the questionnaires (See Figure 2.1).

2.1.15 The study Method:

The methodology used in this study employed a questionnaire survey for information gathering (See Figure 3.1). The questionnaires were delivered to the respondents either by post, personally or via e-mail. Pharmacists returned their questionnaire forms directly on the same day or by e-mail. The data were analysed with regard to the types of questions.

Nine countries in the Middle East were chosen to conduct the pilot questionnaires as the most appropriate source for evaluating the performance of healthcare professionals on the safety of medicine in developing countries.

Pilot questionnaires were developed and tested within the Middle Eastern countries for the following reasons:

- The author was already working with one of the most prestigious Saudi hospitals (King Faisal Hospital and Research Centre) as a Clinical Research associate (CRA) and this necessitated business visits to the Middle East twice per month.
- The cost of field trips was covered by the employer.
- Accessibility: there was easy access to all cities and villages in the KSA (Kingdom of Saudi Arabia) as well as the rest of the Middle Eastern countries apart from Iran and Iraq.
- Political /Government issues: Middle Eastern countries tended to be less corrupt and more politically stable than those in East Africa and it was perceived as much safer to conduct the pilot study in the Middle East.

Probability sampling methods and simple/multistage random sampling was carried out: a sample was drawn randomly from a list of individuals in a population.

Regarding the multistage random sampling: initially, a sampling set of geographic areas was taken then, a subset of regions within those areas was sampled and so on. Pharmacies and clinics were randomly visited and questionnaires were administered to the respondents. At this time, respondents were informed that the questionnaires were for research purposes only. Ten to fifteen pharmacies were visited randomly per day during data gathering visits. Questionnaires that were administered in Iraq, Iran and Oman were sent by e-mail due to time constraints and accessibility issues. Questionnaires that were administered in Yemen, Saudi Arabia, Emirates, Egypt, Jordan and Qatar were administered personally. Respondents were presented either with hard or electronic copies of the questionnaires.

Participants were encouraged to reply honestly, openly and without fear. Interviewers explained to respondents that there would be no future repercussions based on their responses and that all information would be handled maintaining utmost confidentiality in accordance with the stated research purpose.

2.1.16 Background information for the agents collecting the Data:

The first agent was Mr. Abdi-Rizak Ali who was a graduate of Salford University in Manchester and studied media and communication and was employed by Horn Relief (NGO). He travelled regularly between Kenya, Djibouti, Ethiopia and Somalia and was based in Somalia. He was appointed and asked to help in data collection in Somalia, Djibouti, Kenya and Ethiopia.

The second agent was Hassan Ahmed who was based in Saudi Arabia. Mr. Hassan was employed as a Medical device sales person. Hassan travelled regularly within Saudi Arabia and could reach all the small cities as well as villages; he also used travel for business to UAE and Egypt, Hassan and I covered all the Middle East countries.

The third agent was Mohamed Ali Warsame who was based in Uganda. Mohamed was a pharmacy student and he wanted to be part of this project in order to gain experience for his third year thesis. I appointed and asked him to help me in Uganda.

Lastly, the fourth agent was Farah Yunus who was based in Tanzania and had a background in Biological Science and I appointed him to help me in Tanzania.

2.1.17 Training the agent received:

All the agents were provided with training, before they started collecting the data and to avoid bias. They were instructed not to pose leading questions during the interview.

- General information about the project (e.g., the study's background and goals,) was discussed with all the agents.
- How to introduce the survey to respondents
- Agents were familiarised with the questionnaire before administration in the study in and were well informed about the project objectives.

During data collection, there were monthly teleconferences to discuss the progress of the data collection.

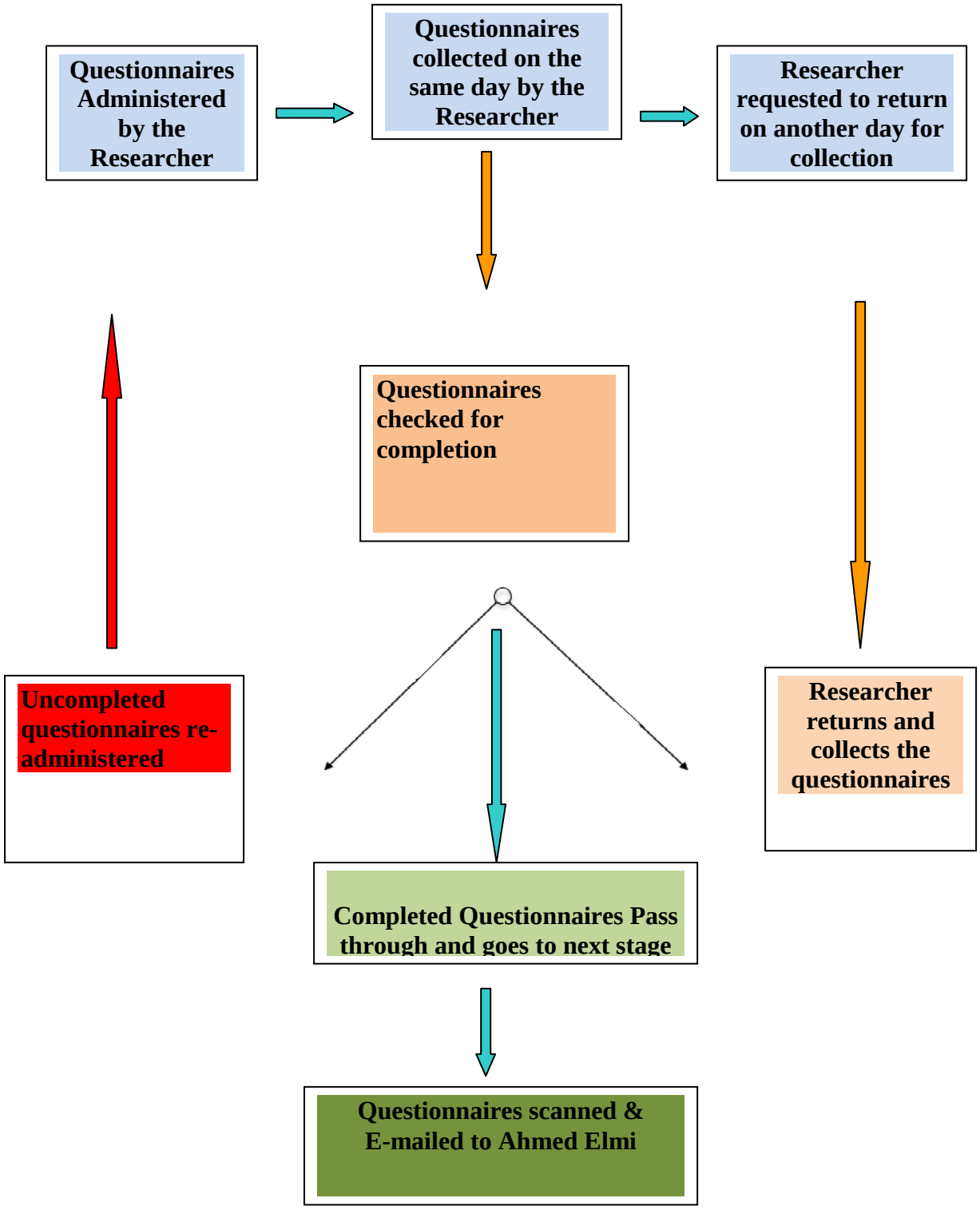
2.1.18 Questionnaire development:

A questionnaire was developed based on the one tested and evaluated previously in a pilot study. This was worked up through a series of consultations with health care workers and the project supervisors.

- The first step was to identify the two leading hypotheses about the source of the problem.
- The second was to distinguish between “What would I like to know” versus “What do I need to know.”

The Third step was to identify the logistical needs of field questionnaires and then start implementation early in the process.

Figure 2.1: Method of administration and collection of questionnaires



2.1.19 Information source:

The developing countries chosen for the study were the following countries: Bahrain, Djiboute, Ethiopia, Egypt, Kenya, Qatar, Saudi Arabia, Somalia, Tanzania, UAE, Uganda and Yemen

Thirteen countries were selected, either because of ease of access entry of these countries as determinant.

- Easy to mobiles a team of workers who will administer the questionnaires.
- Middle East countries were easy and safe to travel between cities.
- Easy African countries were less safe to travel between cities but the logistics were cheaper than compare to Middle East countries.

2.1.20 Study Instrument

A literature search using published databases was instigated to find any existing questionnaire(s) with established psychometric properties to assess performance at the practice level concerning the safety and use of medicines and counterfeit drugs in developing countries. The intention was to use any accessible instrument and modify it for the objectives of the study. However, no relevant questionnaire emerged from the literature search, so the decision was made to develop a bespoke questionnaire specifically for the study purpose.

Between 2009 and 2011, the safety of medicines survey was administered to all healthcare workers in 13 countries (Middle East and East Africa). The survey covers level of counterfeit medicine and quality and safety of medicine sold in these countries.

2.1.21 Psychometric evaluation of the study instruments:

There are a number of fundamental principles that need consideration when developing measurement instruments. In the study, seven psychometric principles will be assessed: applicability, acceptability, practicability, confidentiality, validity, reliability and sensitivity.

2.1.22 (i) Applicability and (ii) acceptability

Applicability of the study instrument ensures the appropriateness of its content for the purpose of the research being conducted. Furthermore, applicability describes the suitability of an instrument for its intended use in terms of wording, clarity and simplicity of language (Higginson and Carr, 2001). Another critical aspect is the acceptability of the study instrument by the study participants and whether they are willing to respond to the questions. It also considers the time required from the participants to complete the questionnaires and whether the questions are clear, concise and easy to understand (Valovich et al, 2008).

2.1.23 (iii) Confidentiality and anonymity of study participants

Anonymity and confidentiality of participants are central to ethical practice in social research. Where possible, participants in this study will be assured that every effort will be made to ensure that the data provided by them cannot be traced back to them in reports or publications (Crow and Wiles, 2008).

There are two possible issues that such practices raise. One is that it is occasionally difficult for researchers to know how far to take anonymisation in order for the participant not to be identifiable (given that research findings may be presented to a variety of audiences).

Secondly, research participants hold differing views about the desirability of anonymisation, presenting researchers with difficult choices between respecting the preferences of those participants who wish to be identifiable and those was preferring to remain anonymous (Crow and Wiles, 2008).

2.1.24 (iv) Practicality

The practicality of the instrument must also be considered when assessing its appropriateness for the purpose of the study. Practicality issues include the participant's comfort, cost and mode of administration of the study instruments (e.g. interview or self administered), convenience and ease of understanding of the questions (Ware et al., 1981). Indicators of the participants' lack of comfort include low response rate, high refusal rate, missing responses and administration time (Ware et al., 1981).

2.1.25 (v) Validity

Kaiser and Smith (2001) define validity as, the most fundamental consideration in developing and evaluating a test. The concept refers to the degree to which evidence and theory support the interpretations of test scores entailed by proposed uses of tests.

Essentially, the concept of validity is whether or not an indicator/instrument measures what it claims it does and when investigating sensitive issues, this can be a complex matter. There are varieties of methods by which validity can be assessed. The three types of validity most commonly used are content-, criterion- and construct-validity.

2.1.26 Content Validity:

This assesses the extent to which questions in a survey serve to encompass the important facets of the notion the indicator is supposed to represent in a balanced way. The weighting of the results are also reviewed with the set of indicators (Anon, 2001).

2.1.27 Criterion Validity:

This assesses how an observed indicator compares with other measures or outcomes (the criteria) already held to be valid. The aim is to correlate a new indicator with reference to a previously well-established indicator (gold standard) (Anon, 2001). In piloting the questionnaires before using the final version in the main study, participants assess the practicality and applicability of questions and this helps to ensure that they are clear, feasible and unambiguous.

2.1.28 Construct validity:

This is the most rigorous approach to establishing validity (Guyatt et al, 1993) and necessitates the assembly of empirical evidence to support the inference that a particular instrument measures what it is supposed to measure.

Construct validity involves comparisons between measures and examines the logical relations that should exist between a measure and the characteristics of the system being studied (Guyatt et al. 1993). Sub-types of construct validity include convergent validity (positive correlation with a related measure) and discriminant validity (a low correlation coefficient is obtained when the measures are the unrelated constructs (Saw, 2001).

2.1.29 (vi) Reliability

Assessing the reliability of the instrument is essential in determining its ability to measure something in a consistent and reproducible manner. In other words, reliability is concerned with how consistently an instrument measures the concept of interest (Pinar, 2002). It therefore assesses whether the instrument produces results that are reproducible and internally consistent (Valovich et al 2008).

2.1.30 (vii) Sensitivity

Sensitivity is related to the instrument's ability to detect and measure change when it has occurred (Higginson and Carr 2001). Differences among groups (approval times, milestones, quality measures, strategic parameters, years of study and the authorities) are checked to test the instrument's ability to detect differences if they really exist (Dimoliatis et al., 2010).

The questionnaires will be developed based on established psychometric principles to collect data from the participating health care workers in the chosen developing countries. Pilot testing is a critical step to increase the confidence about the clarity, feasibility and suitability of the questions for the particular country. Following the pilot study, changes will be made to the questionnaires to incorporate the feedback obtained and the lessons learned, once the appropriateness, convenience, relevance and clarity of the questionnaires are ensured from the pilot study. Questionnaires will then be distributed to the rest of the countries for completion.

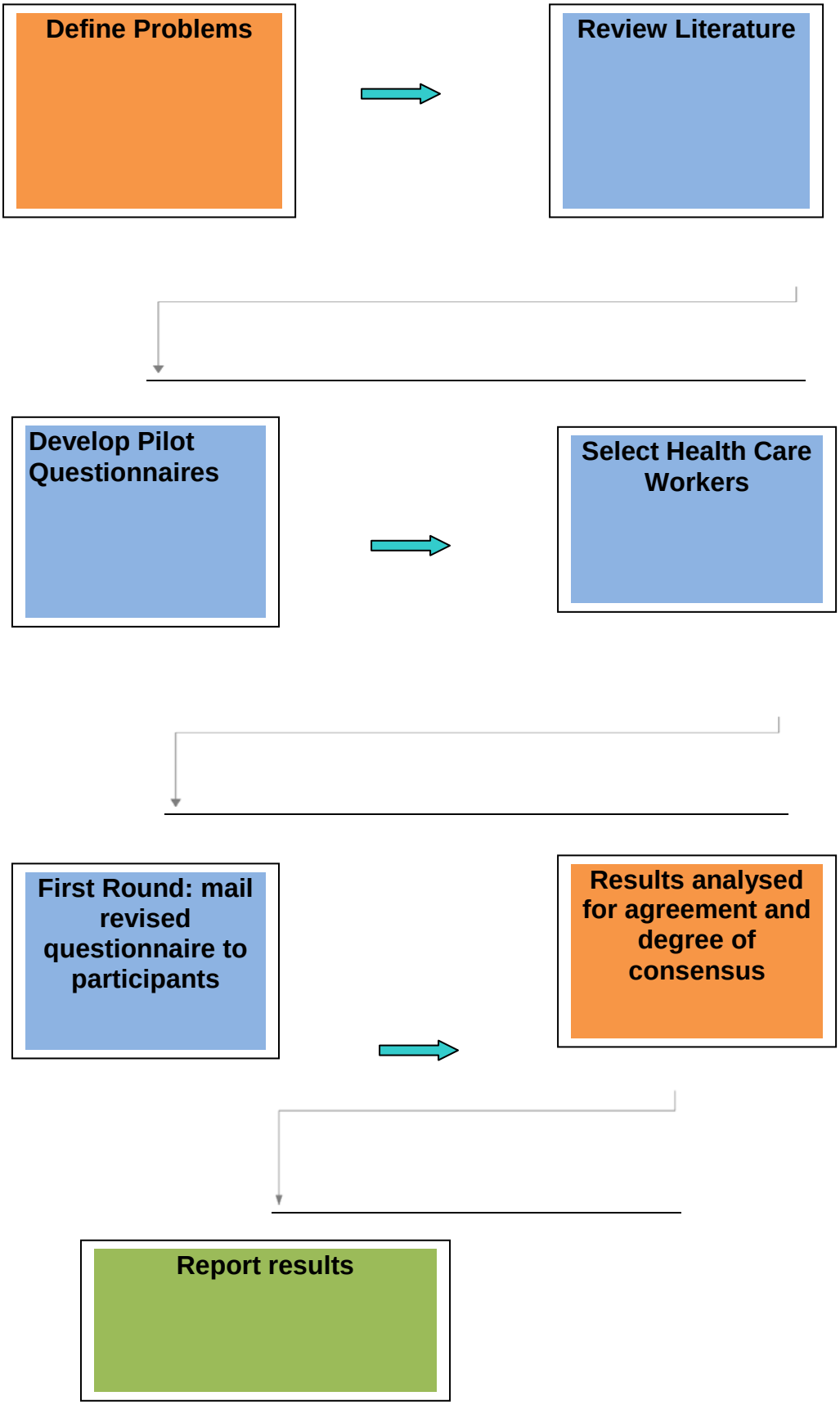
There were no standard questionnaires available to use and therefore the researcher designed and developed new questionnaires. One has to have quantitative information to test specific hypotheses that have previously been generated and in this case, there is none available to use.

2.1.31 Study Plan:

A comprehensive review and critical analysis of the literature reported in chapter one demonstrated a significant problem concerning counterfeit medicines in developing countries. So in order to discover the source(s) of the problem and improve safety aspects of medicines in these developing countries. Therefore, the following study plan was developed to capture data on the safety of the medicines in these countries. The data were then subjected to a substantial scrutiny to fulfill the objectives of the study.

The Thesis consists of three main chapters that investigate the major areas of the safety medicines with respect to drug counterfeiting in developing countries (Middle East and East Africa)

Figure 2.2: The Delphi Approach to be used in this study:



3 CHAPTER THREE

3.1 PILOT STUDY TO VALIDATE THE QUESTIONNAIRE FOR EVALUATING A STUDY OF THE SAFETY OF MEDICINES WITH RESPECT TO DRUG COUNTERFEITING IN DEVELOPING COUNTRIES ESPCIALLY THE MIDDLE EAST:

3.1.1 Introduction:

Pilot studies offer a good opportunity to assess the feasibility of large full-scale studies and are almost an essential prerequisite. Conducting a pilot prior to the main study can enhance the likelihood of success within the main study and potentially improve the quality of the main study. They should be well designed with clear feasibility objectives, logical analytical plans, and explicit criteria for determining feasibility.

In this Chapter therefore, questionnaires were tested in a pilot study performed in Saudi Arabia, Emirates, Bahrain, Iraq, Yemen, Jordan, Egypt, Iran and Qatar. The aim was to detect any flaws in questioning and correct these prior to the main survey. The piloting was intended to facilitate the conversion of open-ended- to closed questions by determining the range of possible answers. There was also a chance to perform a trial analysis on the pilot sample and having performed the pilot survey, amendments could then be made in order to maximize the response rate and minimise the potential error rate on answers.

3.1.2 Reasons for Conducting Pilot Studies:

Van Teijlingen e et al have provided an overview of the reasons for performing a pilot study. In general, the rationale for such a preliminary study can be grouped under several broad classifications (Van Teijlingen et al., 2001).

Resources: This deals with assessing time and budget problems that may occur during the main study. The idea is to collect pilot data on such things as the length of time to mail or fill out all the survey forms.

• Management: This covers potential human and data optimisation problems such as personnel and data management issues at participating centres.

• Scientific: This discusses the assessment of treatment safety, determination of dose levels and response as well as estimation of treatment effect and its variance.

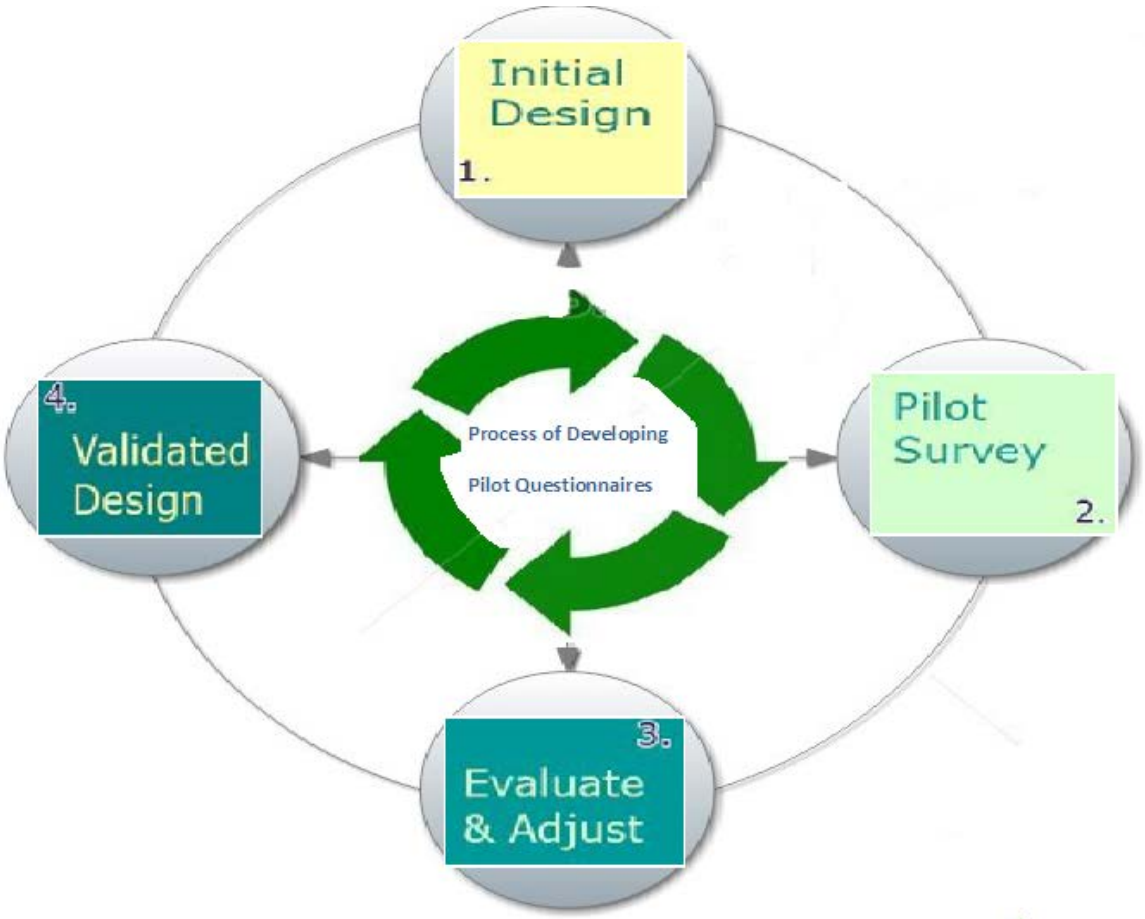
3.1.3 Aim of the Pilot study:

- The aim of this Pilot study was to detect any flaws in questioning and correct these prior to the main survey.
- To gather information prior to a larger study, in order to improve its quality and efficiency.
- To identify the information needed for the logistics of the main study and identify possible sources of error.

3.1.4 Method:

See Section 2.1.15 more details.

Figure 3.1 shows stages in the Development of Pilot Questionnaires.



3.1.5 Materials:

The instructional materials used in the survey consisted of:

- Questionnaires,
- Clipboard pen,
- Paper clips,
- Staplers
- Pen and pencils
- Maps for each area

- Laptop computer.
- Umbrellas
- Letters of introduction
- Hard copies of the questionnaires.
- Envelopes to store completed field questionnaires

Hard copies were employed to administer the questionnaire personally to participants. In those countries where travel was not feasible, a laptop computer was used to send e-mails.

The information needed for the logistics of the pilot study as shown above and also possible sources of errors i.e. incomplete list, non-response bias, response bias and wording as well as error solution was discussed.

Strategy

- To ensure the sample was representative of the population under study
- To follow-up on leads of "where to find" sample

3.1.6 Results:

A total of 100 pharmacy owners and healthcare workers including private clinics were interviewed per country. The majority of the respondents that answered questionnaires were within the age range 34-45. The overall ratio of male to female participants was unequal in that it was heavily skewed by almost a four fold factor towards males (figure 4.1). Thus, out of those pharmacy owners or staff who participated in the pilot study, 74% were male whereas only 22% were female. This disparity was largely attributable to the culture and religion in the Middle East whereby the vast majority of the women were housewives and it was not customary to find them in the workplace. No responses were received from Iraq or

Iran due to people being reluctant to answer questionnaires and also the lack of an interviewer or agent.

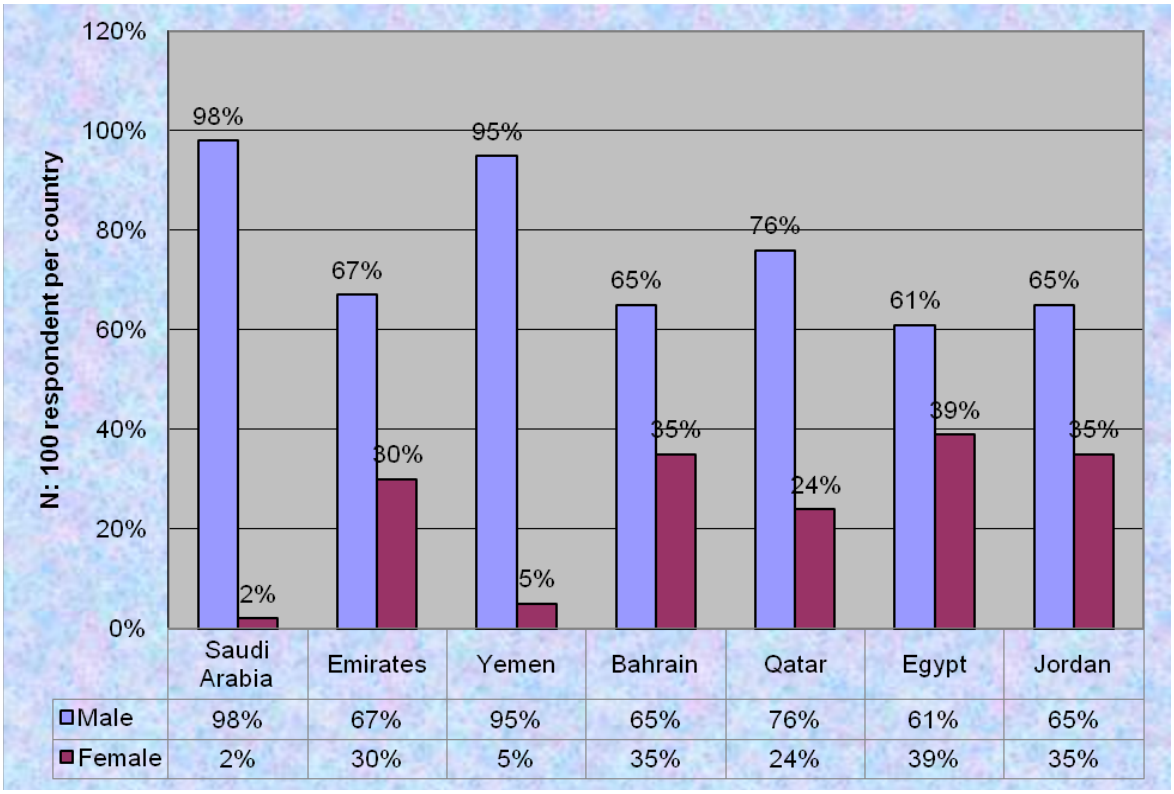
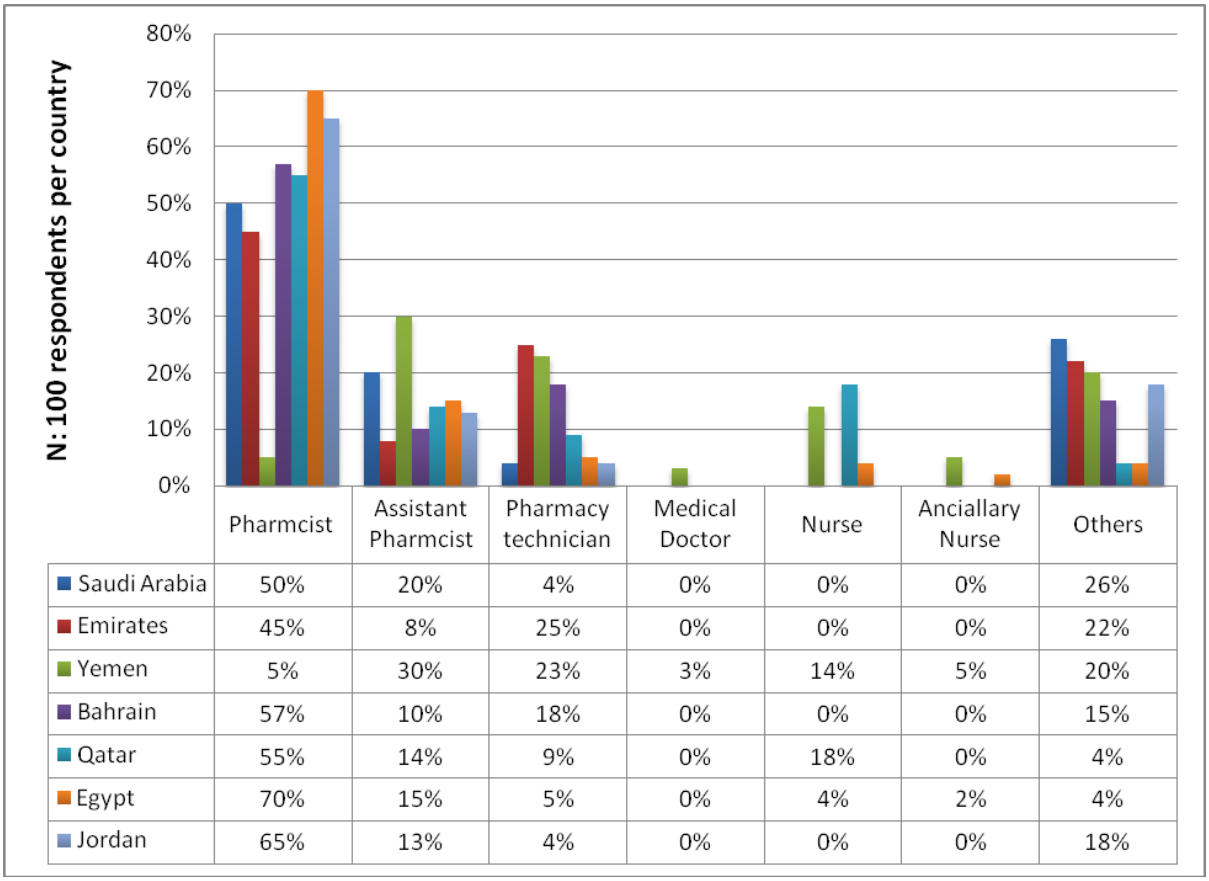


Figure 3.2: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: gender of the pharmacist or pharmacy owners.

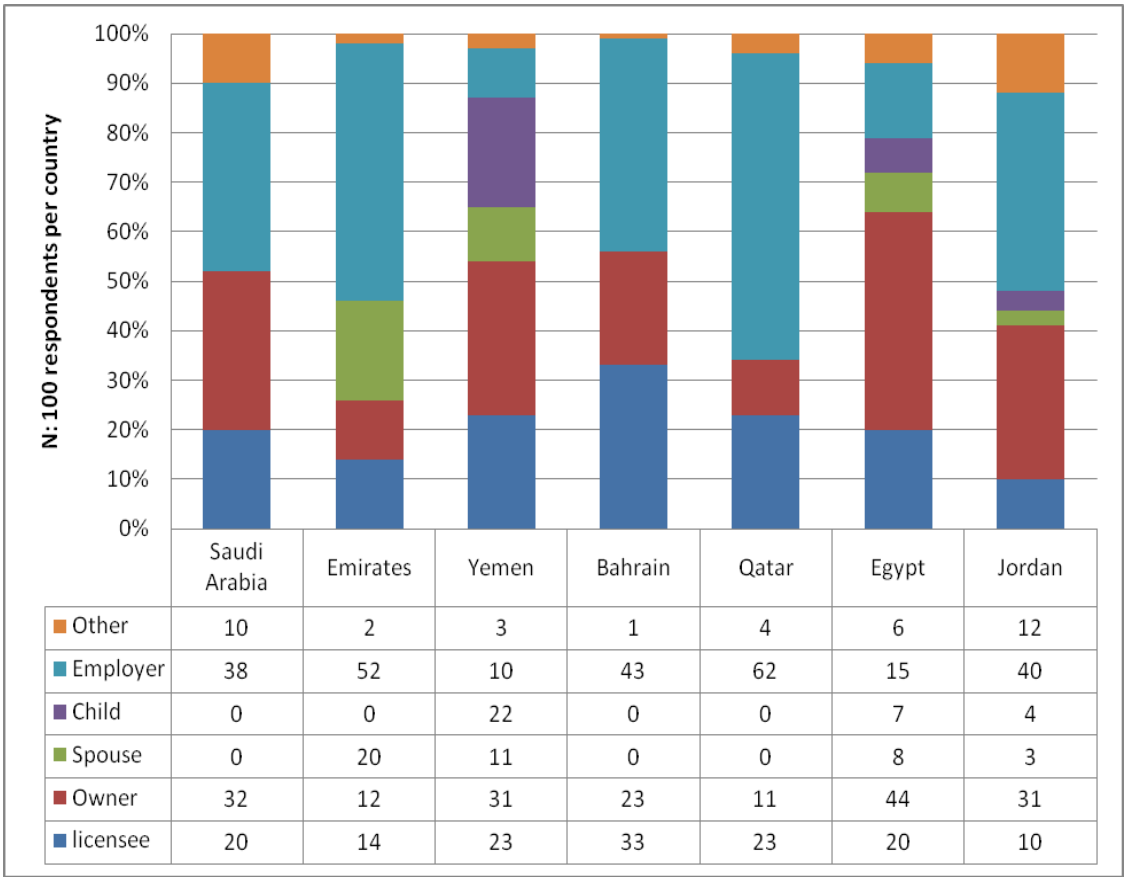
Although the study participants were derived from a variety of backgrounds or professions which included doctors, nurses, pharmacists, pharmacy assistants, pharmacy technicians or ancillary nurses (See figure 3.2), a mean of the majority were pharmacists (50%), pharmacy technicians (12.5%) or pharmacy assistants (16%). Bearing in mind that Iraq and Iran have not responded throughout the pilot survey and zero (0) respondents were received.



	Pharmcist	Assistant Pharmcist	Pharmacy technician	Medical Doctor	Nurse	Anciallary Nurse	Others
Saudi Arabia	50%	20%	4%	0%	0%	0%	26%
Emirates	45%	8%	25%	0%	0%	0%	22%
Yemen	5%	30%	23%	3%	14%	5%	20%
Bahrain	57%	10%	18%	0%	0%	0%	15%
Qatar	55%	14%	9%	0%	18%	0%	4%
Egypt	70%	15%	5%	0%	4%	2%	4%
Jordan	65%	13%	4%	0%	0%	0%	18%

Figure 3.3: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: "What is your level of education?"

Graph 3.4 shows that majority of the responds were employer as compare to rest of the respondents, the lowest responds were others. Some of the others were relatives of the pharmacy owners and a few of them were voluntary workers including students from different colleges and universities. A mean of preponderance of the respondents consisted of employers (approx. 37%) see (figure 3.3) and only 4.7% were children or the offspring of employers. Less than 3% were excluded from the study either because of insufficient time available to complete the questionnaires or the questionnaires remained unattempted.



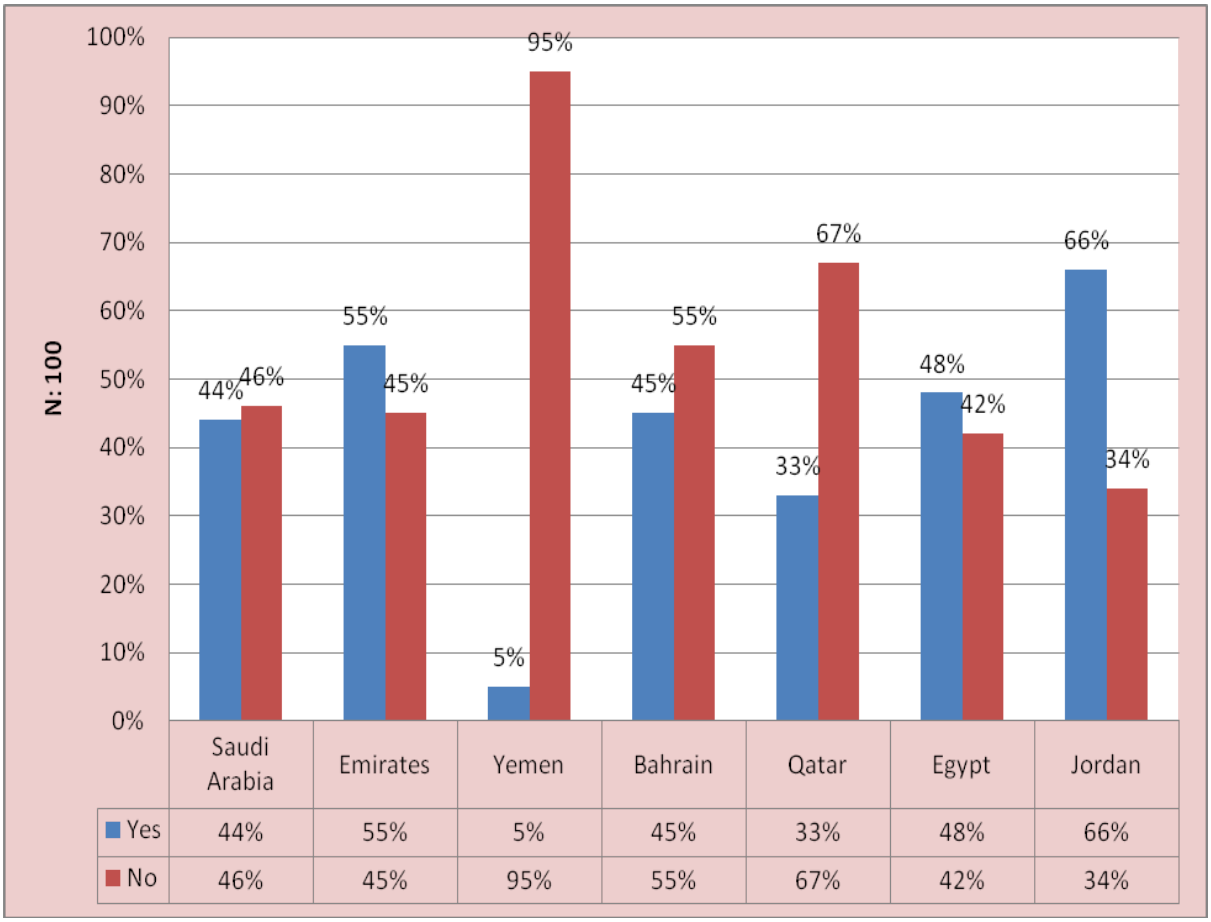
	Saudi Arabia	Emirates	Yemen	Bahrain	Qatar	Egypt	Jordan
Other	10	2	3	1	4	6	12
Employer	38	52	10	43	62	15	40
Child	0	0	22	0	0	7	4
Spouse	0	20	11	0	0	8	3
Owner	32	12	31	23	11	44	31
licensee	20	14	23	33	23	20	10

Figure 3.4: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: "What is your status?"

Regarding data concerning drug regulation, amongst those countries surveyed, a mean of 42% of the respondents stated that they had received some information relating to drug regulation compared to 32% who had received none (figure 3.5). This is a relatively high proportion of responses indicating a non-reception of regulatory information and may be ascribed to the low level of regulatory inspection as shown in Figure 3.6.

In essence, a mean value of 30% of respondents had undergone no inspection within the previous 5-year period and in the case of Yemen, only 5% stated that they had been inspected whilst 95% reported no inspection.

In terms of competency and expertise, over 25 - 30% of respondents indicated that their knowledge of drug dispensing was very good or excellent compared to 12% who described their knowledge of dispensing as fair to good (see figure 3.7).



	Saudi Arabia	Emirates	Yemen	Bahrain	Qatar	Egypt	Jordan
Yes	44%	55%	5%	45%	33%	48%	66%
No	46%	45%	95%	55%	67%	42%	34%

Figure 3.5: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: "Have you received any information related to drug regulation

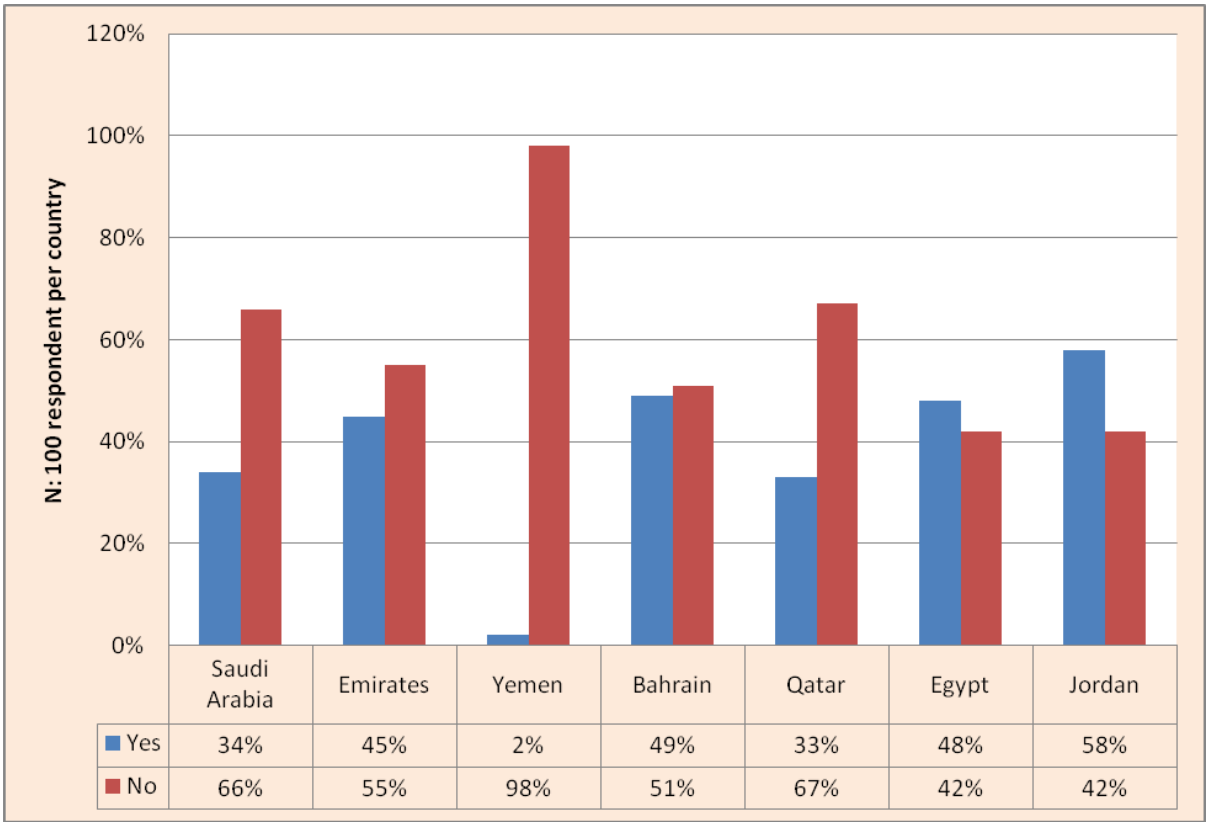


Figure 3.6: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: "Have you been inspected by regulatory agency within the last 5 years"

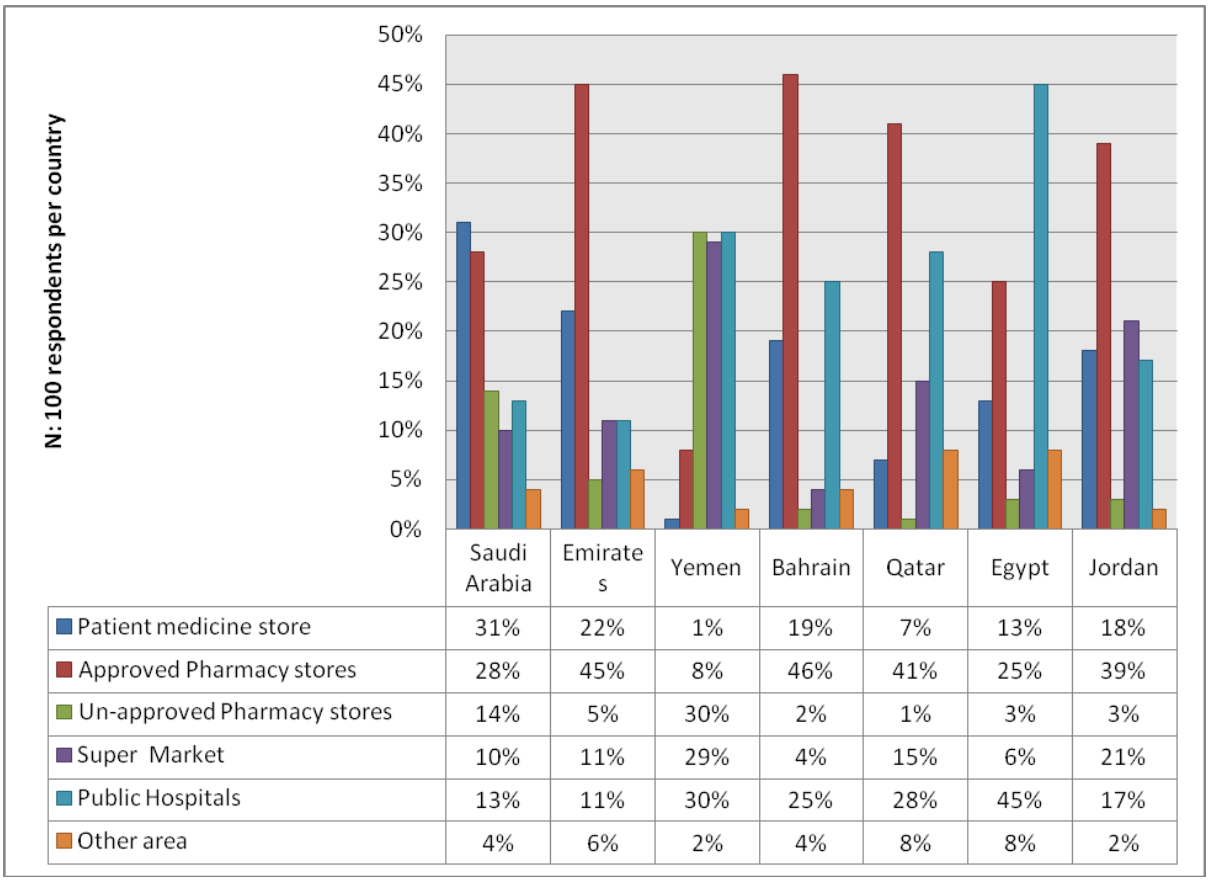
When the responders were asked; if they have been inspected by regulatory agency for the last five years, the majority of the respondents said they had one or two inspection last five years, Yemen were exception where 98 respondents said that they have not had any inspection and this is due to a lack of inspectors available and weak enforcement of intellectual property regulations.The World Health Organisation (WHO) estimates that only one in six countries have fully drug regulatory agency (WHO 2006).

	Saudi Arabia	Emirates	Yemen	Bahrain	Qatar	Egypt	Jordan
Fair	18%	16%	20%	12%	10%	18%	15%
Good	26%	17%	43%	25%	22%	9%	8%
Very Good	23%	28%	21%	27%	37%	25%	48%
Excellent	33%	39%	16%	36%	31%	48%	29%

Figure 3.7: Responses to the question asked of 100 healthcare workers per country and pharmacy owners: would you say that your knowledge of drug dispensing is?

The broad majority of participants in those Middle Eastern countries surveyed bought their medicines from approved pharmacy outlets, the percentage proportions ranging from 25% in Egypt up to 46% in Bahrain. The exception to this finding was the case of Yemen where only 8% of individuals bought medicines in registered pharmacies, 30% purchased them in unapproved pharmacies, 29% in supermarkets and 30% in hospitals (Figure 3.9). However, this is not a reliable indication of whether registered pharmacies had been supplied with or encountered counterfeit medicines. Few countries in the Middle East suffer poverty to the degree of Yemen, so it might be speculated that one solution to the problem of counterfeit

medicine sales in such countries is product price reduction to the consumer instigated by pharmaceutical companies.

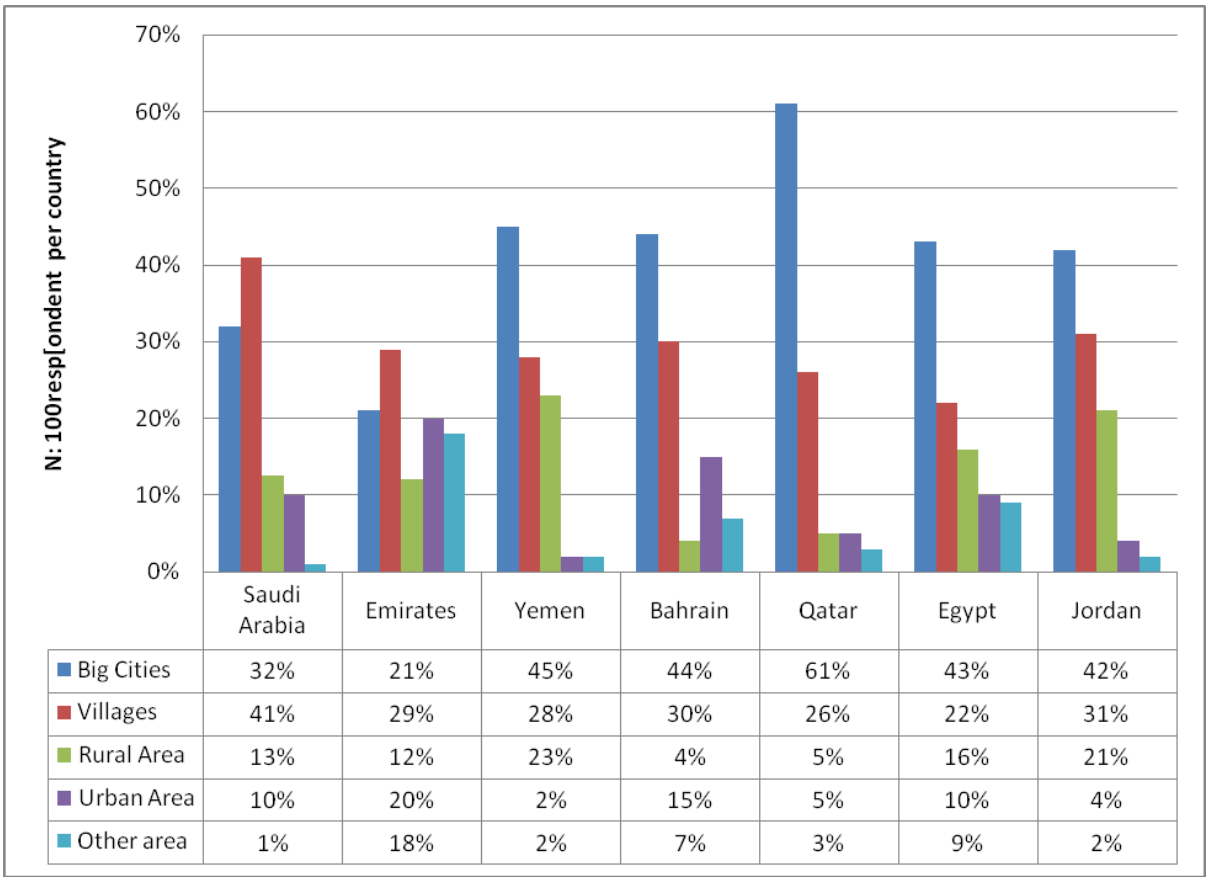


	Saudi Arabia	Emirates	Yemen	Bahrain	Qatar	Egypt	Jordan
Patient medicine store	31%	22%	1%	19%	7%	13%	18%
Approved Pharmacy stores	28%	45%	8%	46%	41%	25%	39%
Un-approved Pharmacy stores	14%	5%	30%	2%	1%	3%	3%
Super Market	10%	11%	29%	4%	15%	6%	21%
Public Hospitals	13%	11%	30%	25%	28%	45%	17%
Other area	4%	6%	2%	4%	8%	8%	2%

Figure 3.8: Responses to the question asked of 100 healthcare workers per country and pharmacy owners (analysed by country): "Where do most patients buy their medicines?"

The problem of counterfeit medicines is universal whether it is in big cities, villages or rural areas. However, the perception of counterfeit incidence in this survey did vary between the locations. The majority of the respondents indicated that villages and rural areas were the localities to find counterfeit medicines most frequently (Figure 3.8). It is tempting to suggest

that poverty and subsequent lack of education contributed towards this result but there is no direct evidence to substantiate this supposition from the survey.



	Saudi Arabia	Emirates	Yemen	Bahrain	Qatar	Egypt	Jordan
Big Cities	32%	21%	45%	44%	61%	43%	42%
Villages	41%	29%	28%	30%	26%	22%	31%
Rural Area	13%	12%	23%	4%	5%	16%	21%
Urban Area	10%	20%	2%	15%	5%	10%	4%
Other area	1%	18%	2%	7%	3%	9%	2%

Figure 3.9: Responses to the question asked of 100 healthcare workers per country and pharmacy owners (analysed by country): "Where are fake medicines most likely to be sold?"

More than half of the respondents admitted that it was easy to buy medicine from Middle East Countries (see Figure 3.10). In the same context, the rank order of countries reporting that it was fairly/very easy to buy medicines was: Yemen (78%) > Egypt (53%) > Bahrain/Saudi Arabia (34%) > Qatar (33%) > Emirates (30%) > Jordan (16%) (Refer to Figure 3.10).

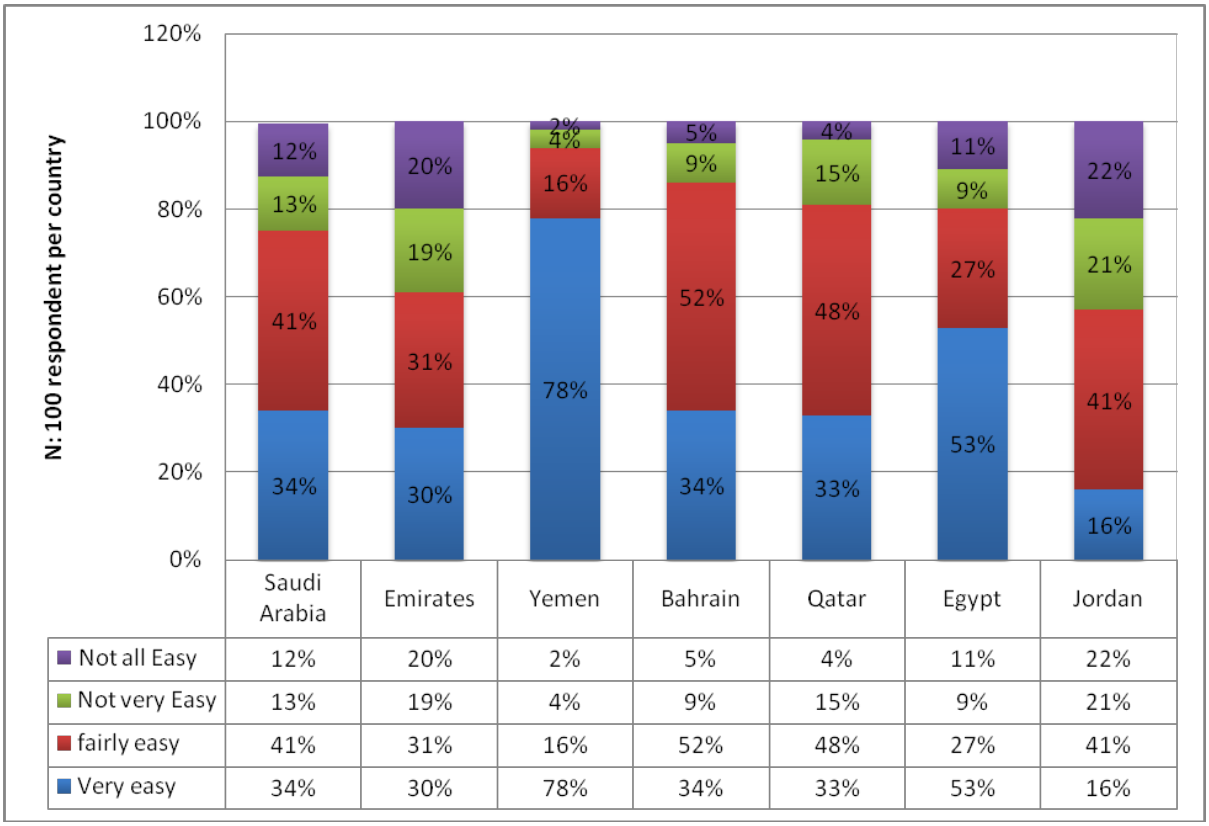


Figure 3.10: Responses to the question asked of 100 healthcare workers per country and pharmacy owners (analysed by country): "How easy is it to buy medicines in your country?"

To better understand the data in this survey and to establish the size and extent of the problem of counterfeit medicines, is difficult for several reasons:

- The problem of poor drug quality caused by adulteration, poor manufacturing or decomposition has always been present in developing countries (Caudron et al 2008)
- Over the last 20 years, direct counterfeiting of prescription drugs has increasingly been added to that list (Wertheimer et al., 2003)
- Whether this represents a true increase in counterfeiting or is simply new attention being paid to a problem that has always existed is difficult to determine from the limited published research (Newton et al., 2006)

Nevertheless, the survey has shown that 78% see figure 3.9 the counterfeiting drug cases affect poorer countries; for example Yemen is poorer than either Qatar or the Emirates and some respondents indicated that, this is really a public health issue, principally because counterfeit medicine is very difficult to identify.

Patent medicine stores are owned by the holders of patent and proprietary medicine vendors licenses. Ordinarily the patent medicines should be sold in their original packs. Over the Counter (OTC) drugs are the only drugs authorised to be sold by the vendors but they generally sell all types of drugs as determined by their financial capability. Considering the knowledge base of these vendors, whose minimum academic requirement to obtain a license is the first school-leaving certificate, they are not in a good position to differentiate between fake and genuine product.

Community pharmacies are statutorily registered with the Pharmacists Council of their country. With such pharmacies, there should not be any serious problem of the sale of fake drugs. Unfortunately however, there are many unregistered “pharmacies” special Yemen flourishing. In addition, in such premises drugs are purchased from doubtful sources with its attendant danger to the health of the public.

Poor patients are at risk from using expired and fake medicines in Yemen according to one of the responders in Yemen. He added that almost all counterfeit drugs – which are considerably cheaper than drugs manufactured in the west – are smuggled into the country, mostly from India and China.

According to one anonymous health worker, most of these cheaper imitation drugs have not been tested in laboratories and even if they were genuine, they had often exceeded their expiry dates. Additionally, they seldom met international standards for proper storage.

One of the respondents complained that counterfeit drugs were killing their business. He said "This is really a serious problem for us as an emerging medicine supplier. We cannot compete with smuggled and counterfeit medicines that are sold at low prices. It is also affecting the importers of medicines." The respondent added that part of the problem was the absence of any legal provision with regards to prescribing or dealing with counterfeit medicines.

3.1.7 Discussion:

In this pilot study, the recruitment rate was adequate, and the individual response rate for each country was comparable, the range being between (100%; 100/100) Bahrain – (90%; 90/100). Qatar was the exception along with Iran and Iraq from whom a zero response was received. A response rate of nearly 100 of the pharmacists returning questionnaires out of the 100 per country initially targeted might raise the question of potential bias because questionnaires were shorter and quick to complete. Response rates tended to be higher for the questionnaires administered personally rather than by e-mail and values for this parameter ranged from 72% down to 20% between these modes of delivery.

This research pilot survey has provided some useful data that will assist in the initiation of the main studies. Two countries, namely Iran and Iraq did not return their questionnaires. Therefore, these two countries were eliminated from the main study.

While the questionnaires highlighted the ease of purchase of medicines without a prescription from some pharmacy outlets, they may have also reflected the possible imperfections in registering a large number of drugs in these countries. Thus, the registration number of a regulatory body may be easily faked; bureaucracy, internal policies and the inability of some small and medium enterprises to meet the cost of registration may additionally delay or even deny certification of some companies and their products. Furthermore, it is unclear from the pilot study to what extent regulatory bodies monitored drugs and companies after initial certification.

Although the sample sizes are too small to make broad conclusions and/or generalisations about counterfeit drugs in Middle Eastern countries, they do provide at least one reasonable scenario of the cities sampled. The failure of effective regulation could be the result of deliberate counterfeiting, or substandard production, transport or storage. The researcher discussed these results with several local counterfeit drug investigators. The conclusions of these discussions were as follows: the wide variation in lower medicine safety rates among pharmacies suggests that most pharmacists were buying good quality drugs and storing them properly. However, some pharmacists were buying, either wittingly or unwittingly, substandard drugs, expired drugs that had had their packaging possibly re-stamped with new expiry dates, or they were incapable or unwilling to store drugs correctly.

Additionally, there were too few drug inspectors in these Middle Eastern Countries especially Yemen, while the number of licensed manufacturing and selling premises increases exponentially. Pharmacists are not required to register with professional bodies or state boards and do not need to maintain continuing education after their initial qualification.

Furthermore, there is a strong general culture of self-prescription in the Middle East, which is enabled by pharmacists willing to sell drugs without a prescription.

Middle East governments should make efforts to harmonise regulatory requirements across states and consolidate regulatory functions, as recommended by the WHO (WHO 2006 a). They should also increase penalties for those involved in the sale of substandard products as recommended by their governments. In addition, they should also consider requiring that all drug manufacturers receive licenses from central government, even while allowing states with sufficient regulatory capacity to continue licensing sales establishments.

There was concern that the authorities might be defensive about working with external independent researchers and would be slow to give permission (or perhaps refuse permission) to collaborate in the research. Some investigators also suggested that their authorities might be part of the problem – for example, one of the investigators expressed that authorities often advised pharmacies of visits prior to the arrival of inspectors, which might bias collected samples. In addition, there have been reports that the authorities are currently conducting extensive drug quality surveys and therefore small scale independent surveys from outsiders are discouraged.

This pilot study will be followed by a larger study to explore the extent of the availability of substandard and counterfeit drugs in the market. The pilot study calls for an investigation of pharmacies located in different parts of the country - rural, semi-urban, peri-urban - where the problem may be more rampant due to less stringent drug quality enforcement.

Finally, there were two parameters that worked well within this pilot study and these were the design of the questionnaires and face to face interview.

The questionnaires were too short and modifications were made. Hence, it was expanded in order to include more questions addressing the problem of the counterfeit medicines.

There was no background introduction and no identification the person or organization doing the survey in the pilot study. Consequently, an introduction, study purpose and an indication of the individual performing the study was added to the first page of the main study questionnaire. The underlying strategy was to train interviewers and build in quality checks when the main study commenced.

Hence, it is important to ensure an overall high response rate, for example by offering incentives to participate or send reminders to non-responders (Silman and McFarlane, 2002). Therefore, it was decided to offer incentives to participators especially in Yemen and Egypt. And this approach worked well and encouraged more respondents to return or complete the questionnaires.

In the case of disease-curing drugs, consumers may be aware that products are available and they are obviously highly motivated to get these products. Where governments have placed artificial price controls or import duties on these drugs counterfeiters may step in to supply the demand, offering far less effective or even dangerous products at affordable prices. According to Morris and Stevens 2007combined total duties and taxes on retail medicines in 11 developing countries in 2003 ranged from 24%. Many high-tariff countries have a serious problem with counterfeit medicines and the authors state, “it is unlikely that this is entirely coincidental

3.1.8 Summary of Chapter 3:

- A pilot study was conducted in order to detect any flaws in the design and wording of the questions and improve these prior to the main survey
- To determine preliminary testing of the hypotheses that lead to testing more precise hypotheses in the main study.
- To determine ideas, approaches, and items that may not have been foreseen before conducting the pilot study. Such ideas and items tend to increase the chances of getting clearer findings in the main study.
- To determine a thorough check of the planned statistical and analytical procedures, providing a chance to evaluate the usefulness for the data.
- To reduce the number of unanticipated problems and to have an opportunity to redesign parts of the study in order to overcome difficulties that the pilot study unveiled.
- To save time (specially travelling) and finances in the long term.

4 CHAPTER FOUR:

4.1 A STUDY ON SAFETY OF MEDICINES WITH REGARD TO DRUG COUNTERFEITING IN MIDDLE EASTERN COUNTRIES: (BAHRAIN, EGYPT, EMIRATES, QATAR, SAUDI ARABIA, OMAN AND YEMEN)

4.1.1 Introduction:

Medicine counterfeiting in seven Middle Eastern countries was studied in order to obtain some form of indirect evaluation of potential outcome hazard. The reasons underlying study country choice were as follows:

- Valid data availability regarding counterfeit drugs was either sparse or non-existent in each of the countries
- There was an anecdotal impression that there are high levels of counterfeit medicines available throughout the Middle East and North East Africa.
- Statistics from the World Health Organisation suggest that drug counterfeiting may attain a level approaching thirty five % of all drugs in the Middle East compared to <1% in the US A and Western Europe.

Points to be considered throughout the chapter included:

- The reasons why counterfeit medicines exist and the extent of the problem
- Counterfeit drug production (which drugs are counterfeited where?) and the channels of distribution
- Consequences of counterfeit medicines
- The possibility of a correlation between national illiteracy rate and severity of medicine counterfeiting
- The relationship between rank order of gross domestic product (GDP) for a country versus its regulatory ranking.

4.1.2 AIMS AND OBJECTIVES OF THE STUDY:

4.1.3 Aim:

The overall aim of this chapter is to present a concise, authenticated and up-to-date snapshot of the problem of counterfeit drugs in developing countries with a focus on the Middle East (Yemen, Saudi Arabia, Emirates, Qatar, Bahrain, Oman and Egypt).

4.1.4 Objectives:

- To estimate the level of medicine counterfeiting present in these countries
- To obtain an indirect assessment of potential outcome hazard in these countries which might ensue from counterfeiting
- To investigate any possible link between counterfeit medicines and degree of national education.
- To examine any potential correlation between the regulatory ranking and GDP ranking.

4.1.5 Methodological Framework:

4.1.6 Methods:

(i) Questionnaire distribution to seven Middle East countries

4.1.7 Study participants:

The study involved pharmacists in hospitals, private clinics and owners or managers of stores such as supermarkets who provided or sold medicines in each individual country.

4.1.8 Data Collection:

During the period 2009 to 2010, 4 persons were appointed as agency researchers in order to administer questionnaires to the study participants (See information in Chapter two – methodology).

They administered informal questionnaires to two hundred fifty healthcare personnel (including doctors, pharmacists and other health care workers) as well as outlet owners/managers in each of the seven study countries (total n= 1750). Participants were informed that they were being asked to complete the questionnaire in order to obtain information and data concerning the level of medicine counterfeiting present in their respective country and that the results would only be used for research purposes.

Pharmacies, health care clinics or other outlets were selected in areas that the field researchers considered representative of each village, town or city. Each city was divided into 10 area and villages were divided into two areas.

They approached the personnel and requested that they complete questionnaires straightaway or they offered to retrieve the questionnaires several days later. Twenty-five percent (25%) (437/1750) of those who completed the questionnaires responded immediately and 14% (250/1750) requested that the researchers return in order to retrieve the completed forms.

Researchers assisted 18% (315/1750) of the respondents by guiding them through the questionnaire form. This was done if the respondent indicated that they had questions or did not understand what was being asked. The overall response was 63.3%.

Thirty six percent (636/1750) of healthcare personnel refused to complete the questionnaires indicating either that they did not feel safe or comfortable or that they would need prior clearance from their superior i.e. their supervisor or the outlet owner. Following completion,

the agent collected the questionnaires then they were submitted to initial screening and sorting.

Questionnaires were then scanned and sent by e-mail to the thesis author. In the case of those questionnaires that were administered by mail or electronically, the participants were re-contacted on several occasions where necessary by the agents and there was a direct correlation between the number of follow-up contacts and the response rate. Finally, questionnaires were sorted by country and groups and they were then analysed by country and subgroups.

Figure 4.1

Map of the Middle East countries studied and showing the distribution of collection sites with 1250 of pharmacies and 500 ploy clinic that participated. Countries coloured green and orange were those sampled in the first phase of collection and the rest were sampled in a second phase. Countries in purple (Iran), grey (Iraq) and light red (Jordan) were not sampled due to travel difficulties and the absence of a local research agent.

(ii) Analysis of possible factors such as national gross domestic product (GDP), degree of regulatory control and level of education on the occurrence of drug counterfeiting in Middle East countries.

In the second part of this chapter, data was extracted from the literature regarding national GDP, the degree of regulatory control as assessed by the Pearson Product Moment Correlation model and the general level of education in each Middle East country was then ranked. This was then analysed with respect to the rank order of drug counterfeiting level as assessed by the Pearson Product Moment Correlation model.

4.1.9 Results and analysis:

(i) Results from the questionnaire

It is noteworthy that from the information obtained via questionnaires, approximately two thirds (63.3%; 1115/1750) (see table 4.1) of the respondents returned the questionnaires. Individual response rate for each countries was comparable the range between (57%; 143/250) Qatar – (73%; 184/250) Yemen and there was little variation between the countries. 79% (880/1115) of the respondents were men and only 21.0% (235/1115) of whom were women and this is due to cultural and religious factors. More men are in employment than women in Middle Eastern countries and the majority of the respondents (37.1%) were Arab so this finding was somewhat expected. 13.9% of respondents were of Asian origin whereas 2.1% were Caucasian and 7.5% were black/Africans (see table 4.1). More men were employed fulltime than women and again this was expected as it is due to cultural and religion practise since it is not customary for women to take up employment. (Source: Adopted from World Bank 2011).

Table 4.1 Characteristics of the study population.

	Women		Men		Total	
	n	%	n	%	n	%
(Age)						
18- 24 years	46	4.1	98	8.9	144	13
25- 34 years	55	5	137	12.2	192	17.2

35- 44 years	90	8.1	246	22	336	30.1
45- 54 years	34	3	145	13.1	179	16.1
55- 64 years	10	0.9	240	21.5	250	22.4
65- 74 years	0	0	14	1.3	14	1.3
85 over	0	0	0	0	0	0
Total	235	21	880	79	1115	100
(Race)						
White	10	0.9	29	2.6	39	3.5
Arab	81	7.2	570	50.6	651	58.4
Asian	34	3	211	19	245	22
Black/African	23	1.3	109	6.2	132	11.8
others	37	3.3	11	1	48	4.3
Total	185	19.4	930	80.6	1115	100
	Women		Men		Total	
	n	%	n	%	n	%
Full time	117	10.5	620	55.6	737	66,1
Part time	54	4.8	324	29	378	33.8
Total	171	15.4	944	84.6	1115	100

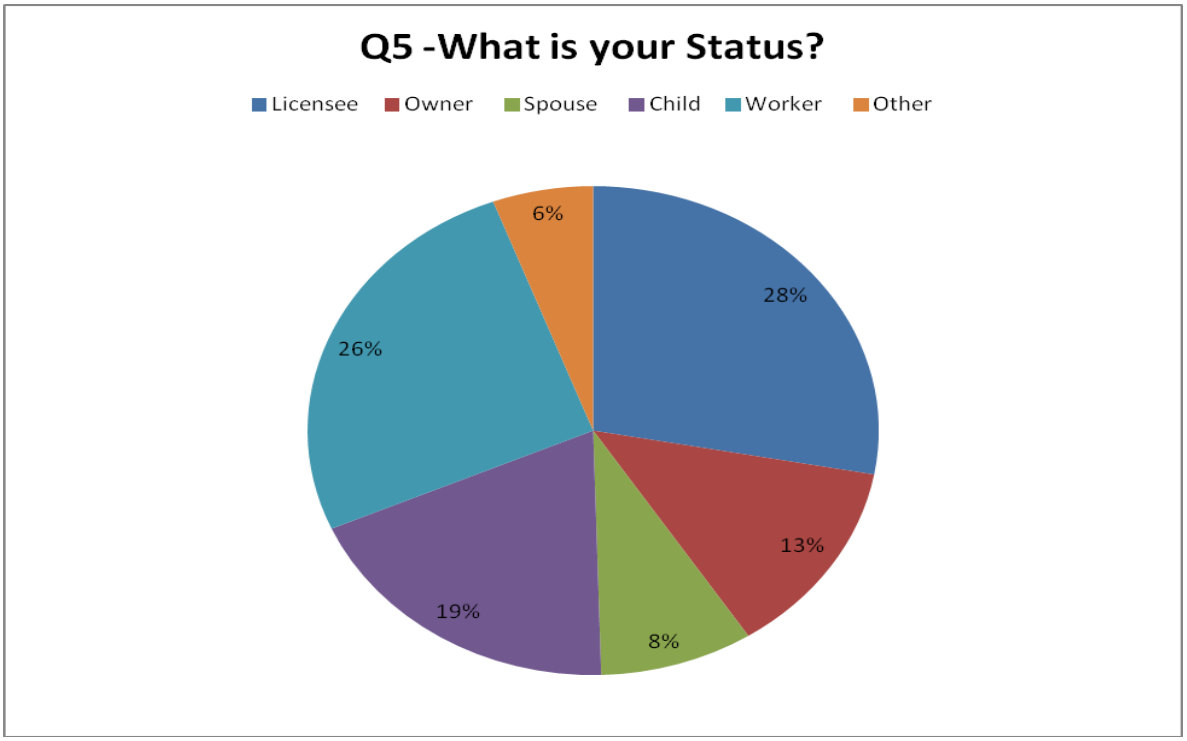


Figure 4.2 Status of respondents in the survey

Apparently 28 % of the respondents were licensees compared to 13% of whom were pharmacy or clinic owners (see Fig 4.2). Actually 26% were employed workers, 19% were children or offspring of the clinic or the pharmacy owners and this is predictable because in local culture, a high proportion of children look after their family business.

Finally 8 % of respodents were spouses of the clinic or the pharmacy wheres as an additional 8% were other such relative of the owners and co-owners .

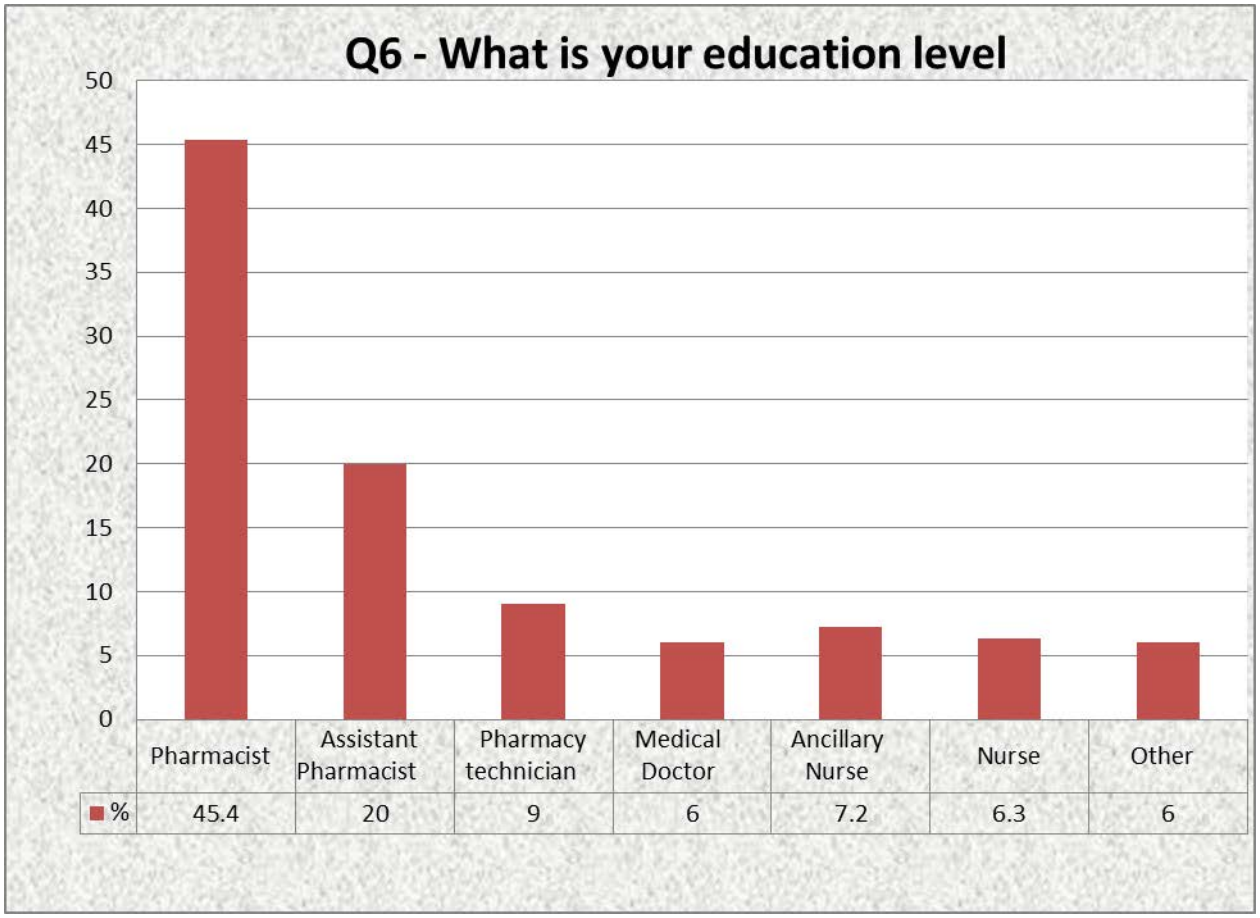


Figure 4.3 Education levels of respondents in the survey

Although 45.4% of respondents were pharmacists, 20% were pharmacy assistants and 9% were pharmacy technicians resulting in a total of 74.4% of pharmacy-related participants and this indicated the highest proportion of such staff in the supply of pharmaceuticals. Hence 6% of the respondents were medical doctors, especially in Yemen where many practitioners also own pharmacies and some of the doctors who were working as pharmacists were not registered to practise in the Gulf Country Cooperation (GCC) (figure 4.3). Furthermore, 7.2% of respondents were ancillary nurses who were working in pharmacy and they were found mainly in the rural areas and villages.

Yemen has the highest rate of illiteracy (46%) of those countries studied according to the United Nations, whereas Qatar has the lowest illiteracy rate (11%) which is closely followed by the UAE (11.3%). Approximately 17.1% of the Saudi population is illiterate as are 28% of Egyptians. Out of the two remaining countries, 18% of the Oman population and 13% of the Bahrain population are illiterate.

(Sources: United Nations, 2009 World Almanac, the Economist)

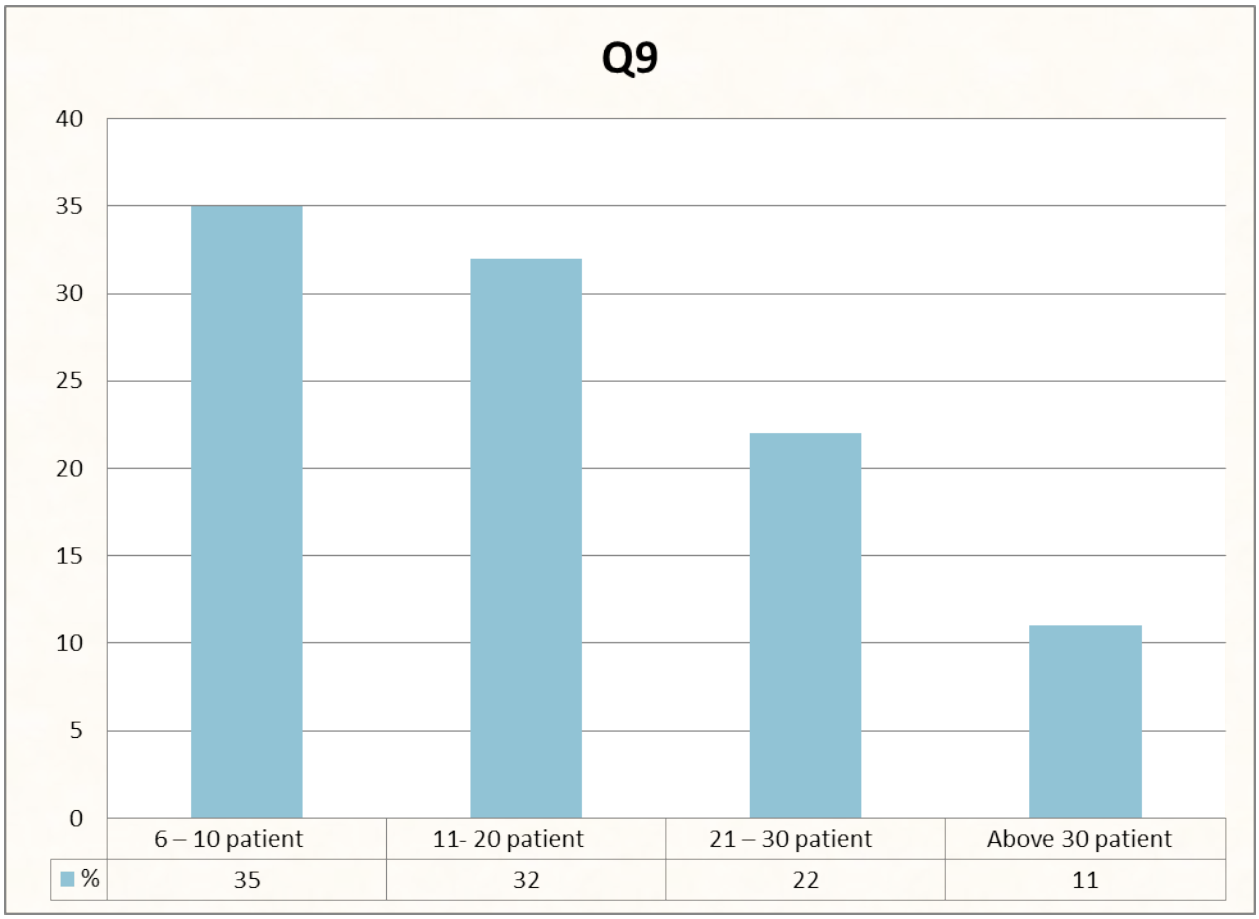


Figure 4.4 The numbers of patients seen daily at clinics or by pharmacies who usually bought medicines or requested treatment.

The commonest range of patient numbers seen daily at clinics or by pharmacists (6-30 patients daily) was reported by the majority of respondents. However, at the busier end of the scale, (11%) respondents reported that >30 patients daily came to buy medicines at their pharmacy or clinic. (Figure 4.4).

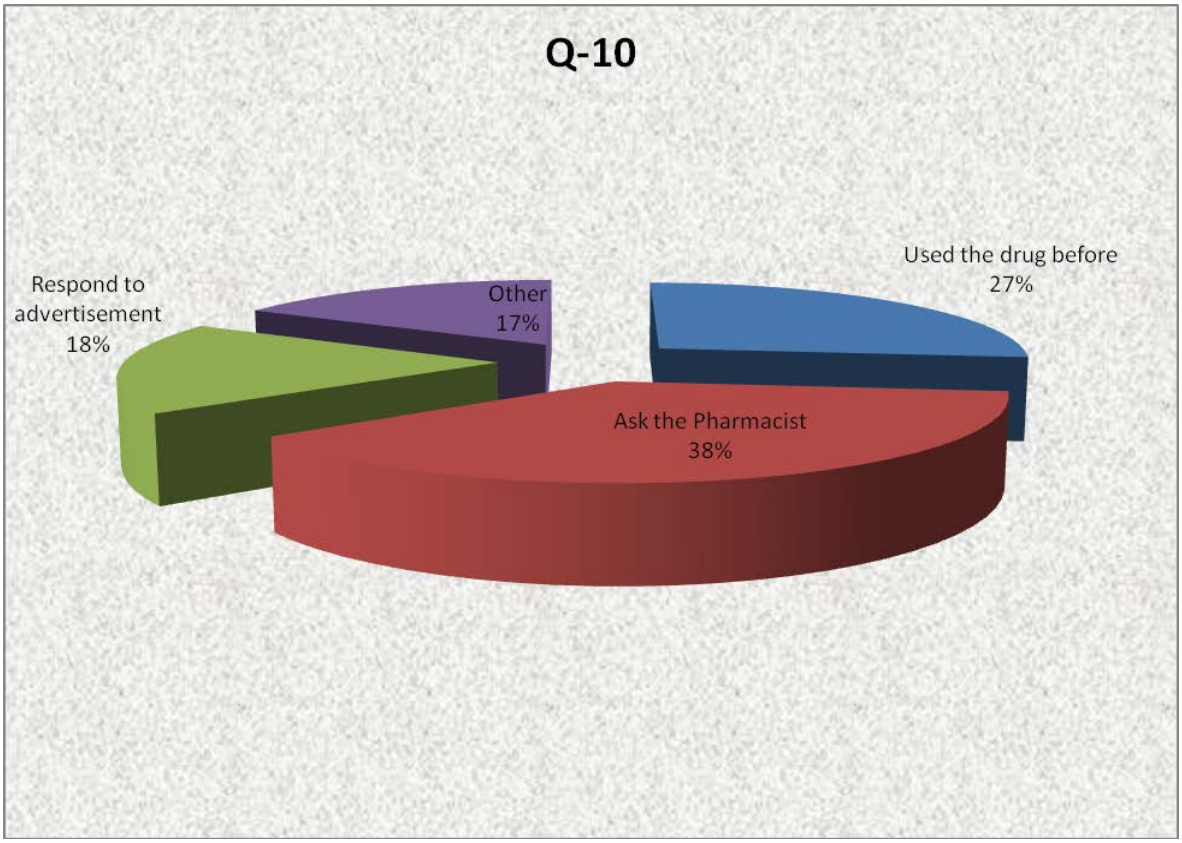


Figure 4.5 Questionnaire responses regarding proportions of patients with knowledge of appriopriate drugs to buy.

The majority of the respondents (38%) stated that patients asked the pharmacist for advice regarding what medication to buy compared to 27% who indicated that patients already knew or had used the drug before i.e. a repeat precription. Therefore, 18% of respondents thought that patients were influenced by advertisements and only 17% indicated that other factors

influenced their use e.g. the doctor prescribed the medicine to patients. The majority of respondents reported that patients trusted the pharmacist and always sought advice (Figure 5.5).

Counterfeit medicines represent a significant threat to the whole healthcare system, contributing towards a risk of a deterioration in patient health or even death and affecting the public (end user) image of physicians, pharmacists, nurses and private and government institutions (WHO 2010).

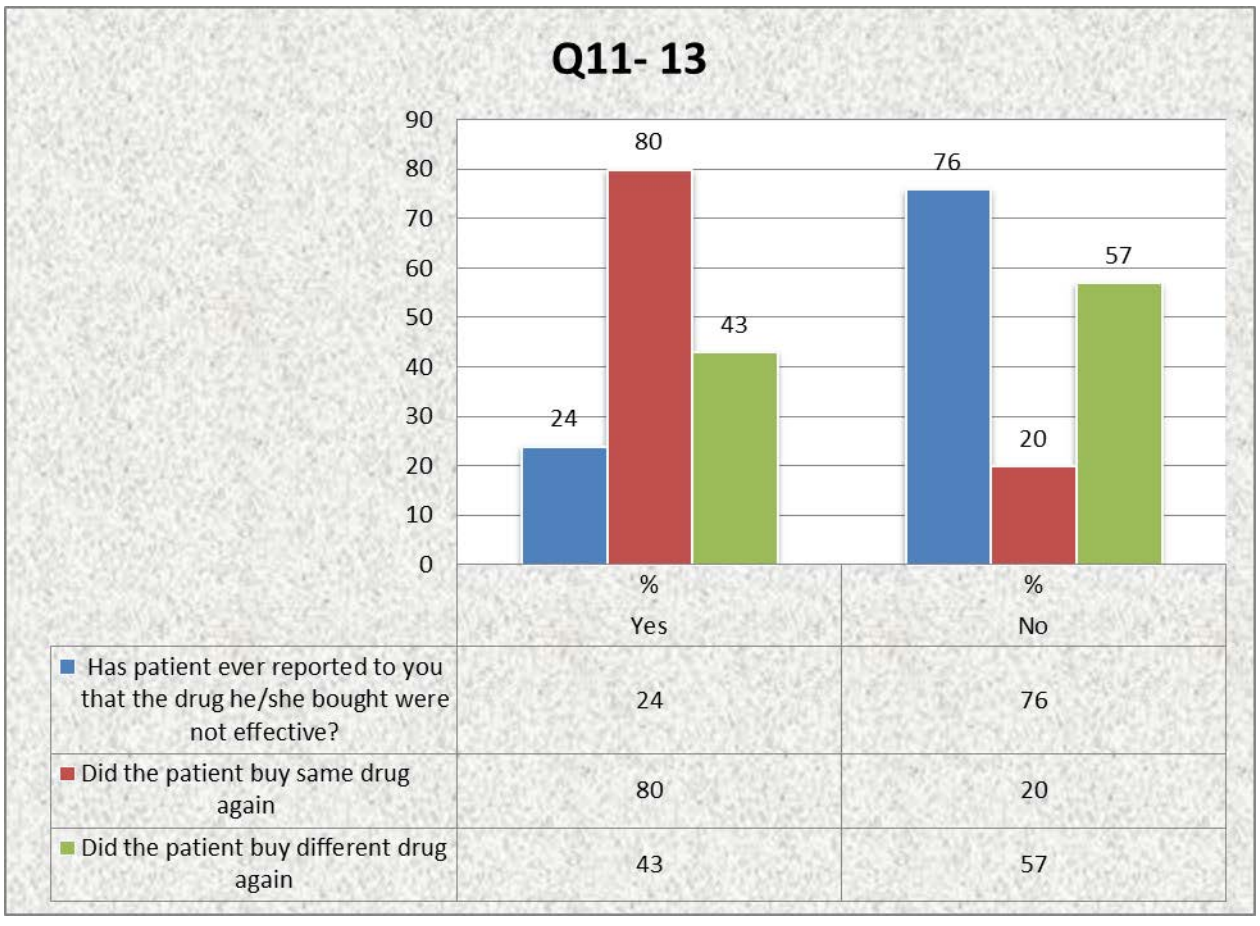


Figure 4.6 Questionnaire responses regarding whether patients report to the pharmacist or doctor that a drug purchased was not effective

Surprisingly, 17% of respondents replied that patients do not complain or report if a drug is not effective compared to 5% who stated that patients reported and requested another brand of medicine. Hence, 24 % of respondents replied that patients bought the same drugs again compared to 5% who said that patients changed the brand name of drugs bought on the first occasion or selected another type of medicine. This latter option corresponded with the percentage of patients who reported drug inefficacy.

Thus, 6 % of the respondents reported that patients bought different drugs on their subsequent visit to the pharmacy or clinic whereas 8% replied that patients bought the same drug on their next visit. In the majority of instances, patients only report when a pain persists or a morbidity is worsened and some of them may experience a placebo effect.

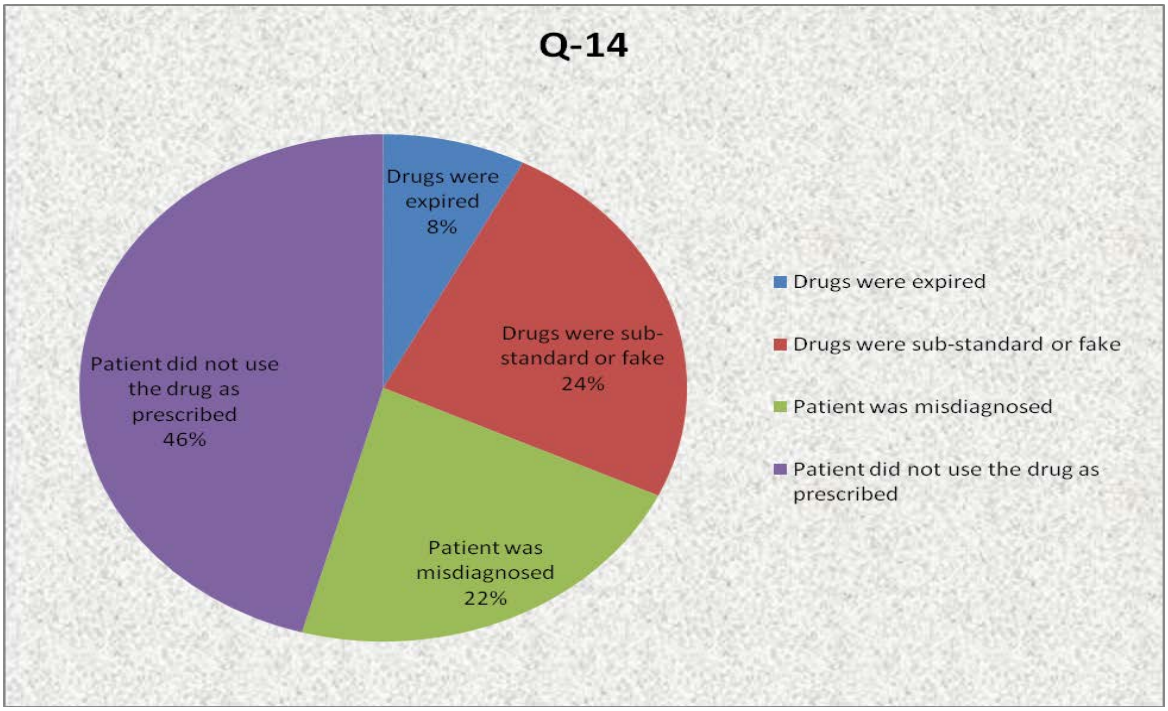


Figure 4.7 Questionnaire responses regarding possible reasons reported why drugs were not effective in patients.

To start with 46% of the respondents stated that patients did not use their medicines as prescribed. This would be a compliance issue e.g. they did not take the drug everyday or did not finish the course of treatment.

On the other hand, 21% of respondents reported that patients were misdiagnosed and consequently given the wrong type of medicine. Moreover, 24% of respondents stated that drugs taken by the patient were probably sub-standard or fake and this is an alarming figure. Eight per cent of respondents said that medicines were expired and therefore were not effective by asking their patients.

Physicians and nurses tend to have a low index of suspicion that a fake drug may be the cause of therapeutic failure and they are more likely to attribute poor clinical outcomes to human variation. Similarly, patients, their physicians, and their families may not know that they have been harmed by a fake drug and worst case scenario is that a patient might even die without even knowing that they had a treatable illness.

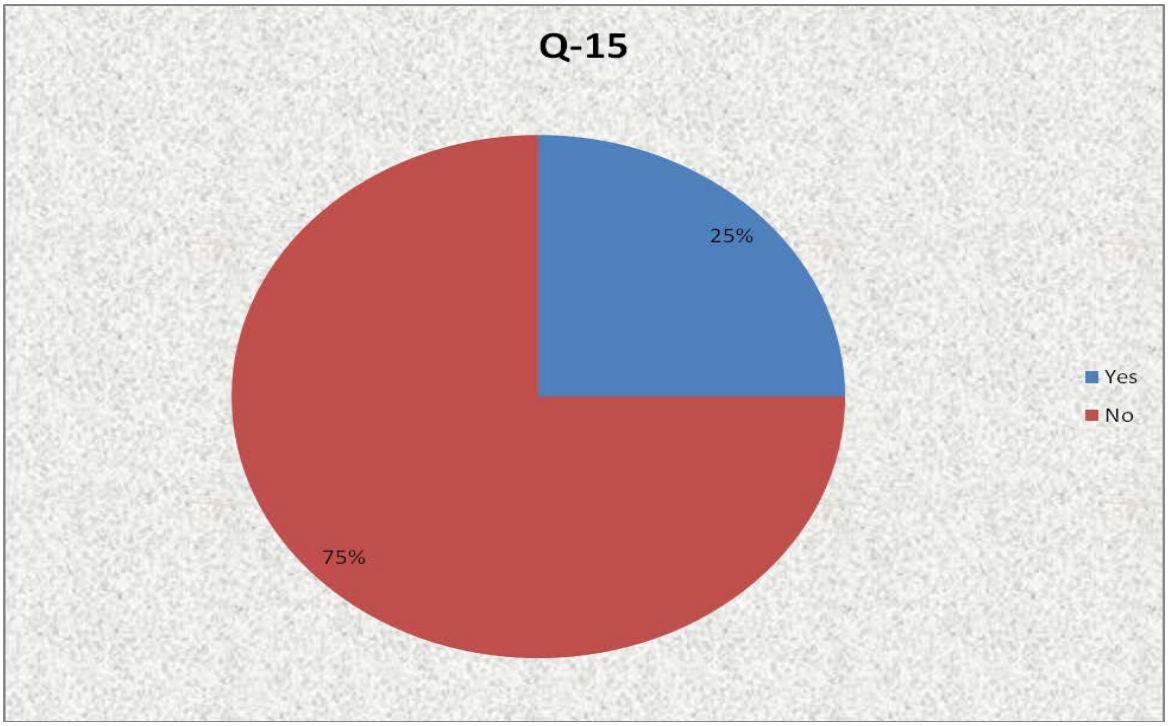


Figure 4.8 Questionnaire responses regarding Respondents view on whether patients obtain their drugs from unapproved or approved outlets.

Therefore, 75% of respondents stated that patients do not obtain their drugs from approved outlets which poses the question whether they even realise or are aware of the risk involved in buying medicines from unapproved or unregistered places.

In general, more products are available without a prescription in the Middle East region than in the western world. Along with these "relaxed" regulations comes a greater responsibility for community pharmacists to function in a "triage" role to ensure safe and effective medication use and to ensure patients seek medical attention when appropriate (Kheir et al. 2008). The extent to which pharmacists are meeting these responsibilities is unknown and beyond the scope of this thesis in the Middle East setting.

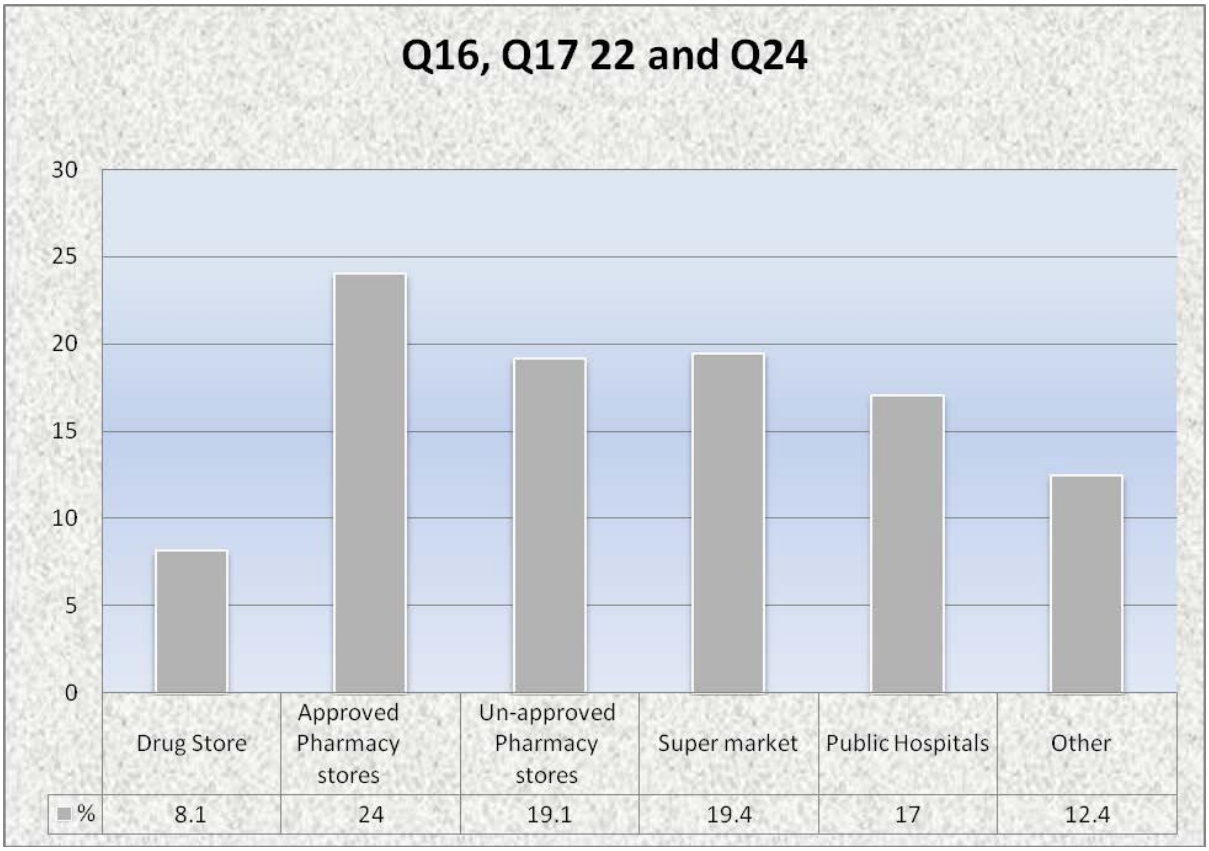


Figure 4.9 showing responses to three combined questions Q16 -where is the cheapest patient buy their medication Q17 - most patient buy their medicine and Q22 where is fake medicine is distributed to.

Evidently, 17% of respondents indicated that patients bought their medicines at public hospitals and this is largely due to the fact that they were supplied on a subsidised basis. 24% of respondents stipulated that patients bought medicines at approved pharmacy stores whereas 19.1% of respondents reported that patients obtained their medicines at unapproved outlets such as a local store or corner shop (figure 4.9).

Manifestly, 8% of the respondents expressed the view that patients bought their medicines at Drug store_and 19.4% of respondents indicated that they thought that patients bought their medicines from supermarkets. This last statistic may reflect a convenience of medicine purchase whilst shopping.

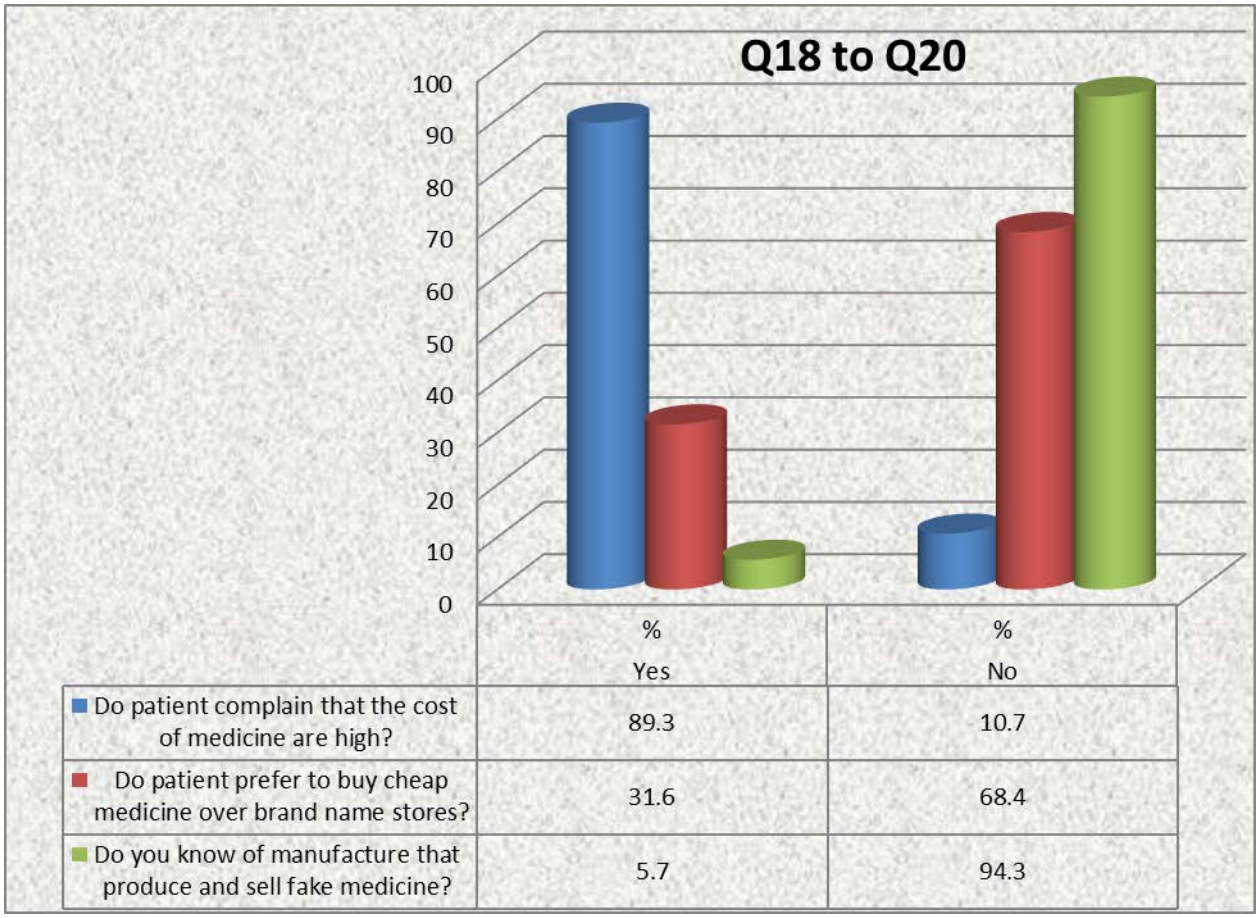


Figure 4.10 Responses to the questions "Do patients complain that the cost of medicines are high", "Do patients prefer to buy cheap medicines over brand names" and "Do you know of a manufacturer that produces and sells fake medicines?"

Purposefully, 89.3% of respondents reported that patients always complained about the high cost of medicines compared to 10.7% of respondents who said patients did not complaint.

68.4% of responses indicated that patients bought cheaper or generic medicines in preference to brand names whilst 31.6% of responses specified purchases of brand names and this might be attributed to the high per capita income of these countries (Cockburn et al., 2005).

Although, 94.3% of respondents did not know of manufacturers that produced and sold fake medicines compared to 5.7% who responded affirmitively to this question and this might be ascribed to a political reason or a fear of government (Cockburn et al., 2005).

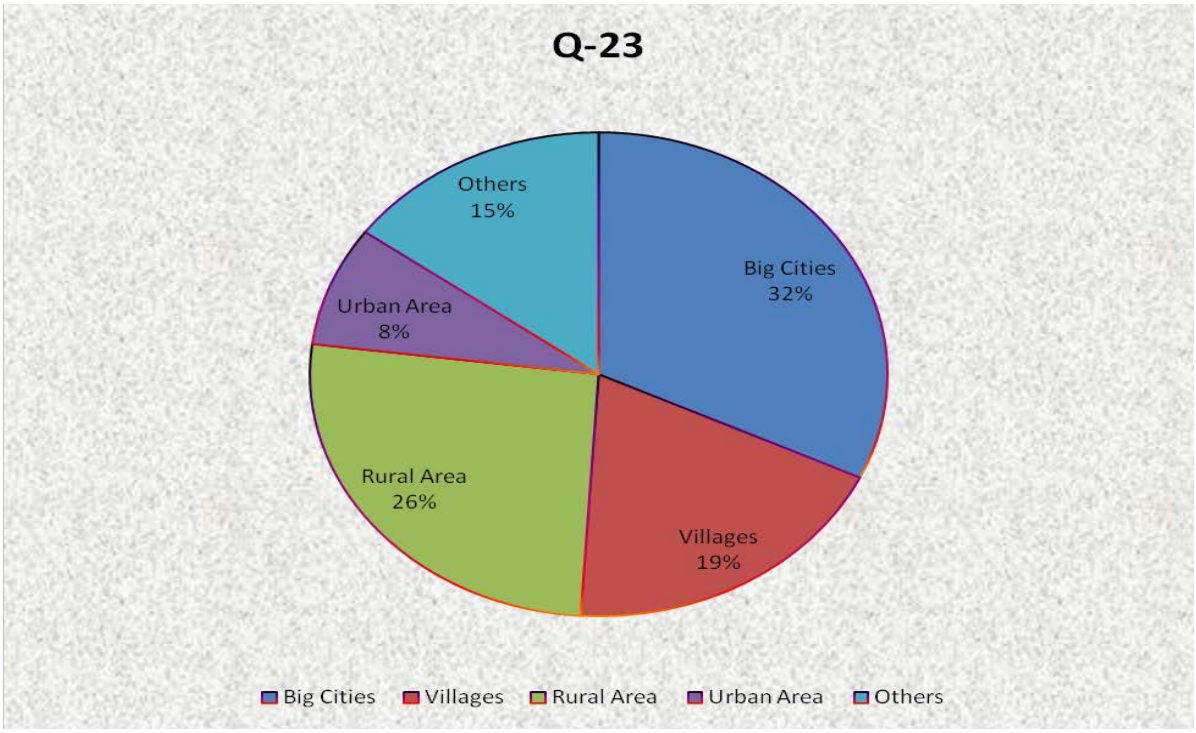


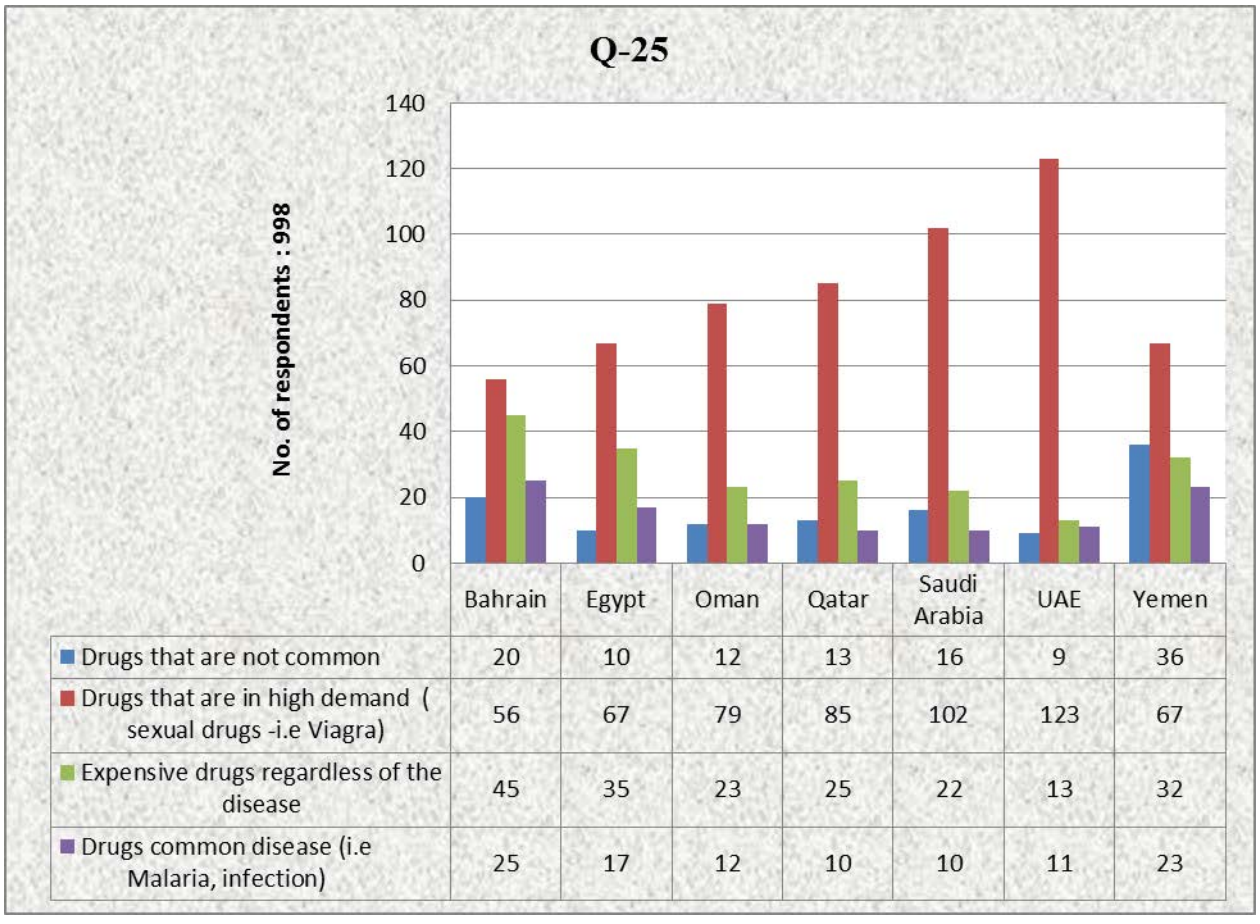
Figure 4.11 Questionnaire responses regarding the most likely location of counterfeit medicine sales.

The majority of respondents indicated that patients did not only buy drugs based on prescription. Hence, the health care personnel reported that most patients bought their drugs

from well-established pharmacies or clinics which were required to be appropriately licensed to obtain patent and proprietary pharmacy licence to operate or approved supermarket stores.

In rural areas and villages, approximately one-third (26%) of the respondents also testified that patients bought medicines from unapproved pharmacies or stores. The most common types of medicine to be substandard or counterfeit were those sold in big cities (32%) see figure 4.11.

Interestingly, one-fifth of respondents (19%) indicated that fake medicines were sold in villages whereas only 8% claimed that fake medicines were sold in rural areas. A further 8% of respondents indicated that other places were where counterfeit medicines were sold and such places specified included service stations and kiosks.



	Bahrain	Egypt	Oman	Qatar	Saudi Arabia	UAE	Yemen
Drugs that are not common	20	10	12	13	16	9	36
Drugs that are in high demand (sexual drugs -i.e Viagra)	56	67	79	85	102	123	67
Expensive drugs regardless of the disease	45	35	23	25	22	13	32
Drugs common disease (i.e Malaria, infection)	25	17	12	10	10	11	23

Figure 4.12 showing questionnaire responses regarding the types of medicines most prevalently counterfeited in Middle Eastern countries.

Surprisingly, the majority of respondents reported that recreational drugs (sexual medicines e.g. Viagra) were not only in high demand but most frequently counterfeited. The second most faked medicines were expensive drugs regardless of the disease they were intended to treat. Furthermore, other drugs that were used to treat common diseases such as malaria and infections were least likely to be counterfeited and this is ascribable to their pervasiveness in the region.

Reliable data on these issues are scarce in order make comparisons with the current findings. Given that the situation is likely to vary widely from country to country, it is difficult to extrapolate from these figures to a reliable global estimate.

In many parts of the Middle East countries, there is a high demand for medicines, which cannot always be met by official healthcare systems. In addition, where resources are limited, consumers will look to secure low-cost alternatives to genuine products. Both of these factors tend to promote black-market sales and a ready outlet for counterfeit medicines (WH0 2003).

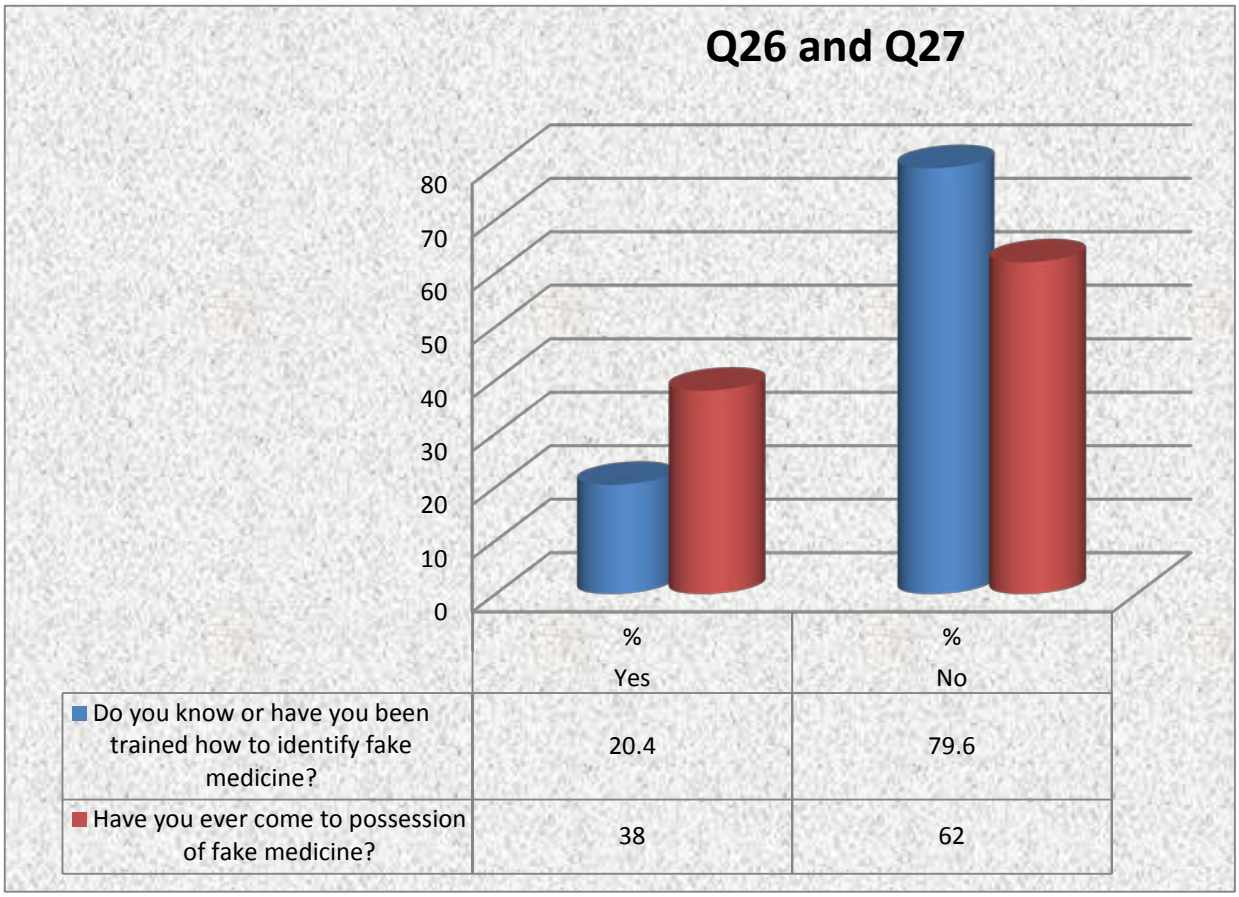


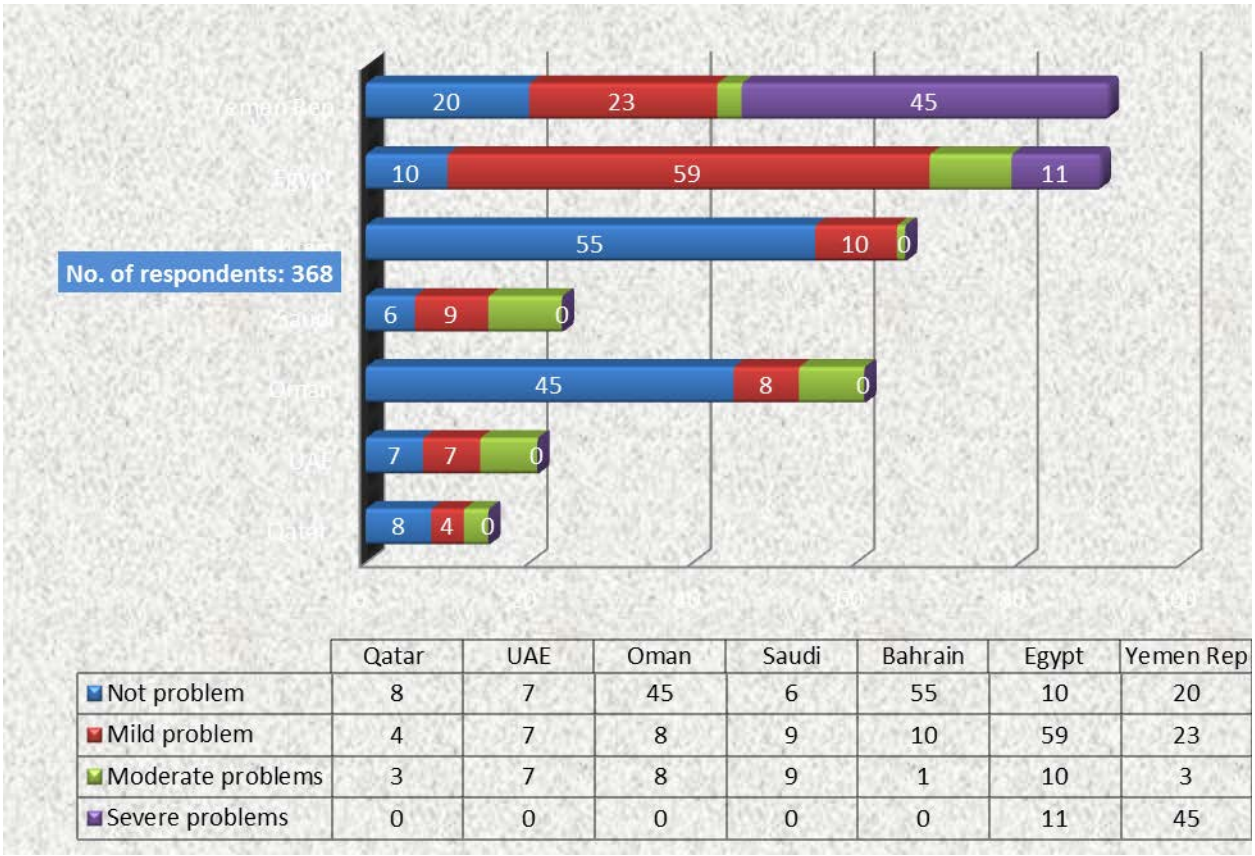
Figure 4.13 Questions whether respondents knew or had been trained to identify counterfeit medicines or whether they had ever come to possess fake medicines.

Hence, 79.6 % of respondents reported that they had no training to identify fake medicines whereas 20.4% of respondents said they had training and attending seminars. On other hand, 62% of respondents answered that they had not come into possession of fake medicine indirectly or directly, compared to 38% of respondents who responded that they come across medicines counterfeits and the majority of these respondents were from Yemen and Egypt.

The public have a key role to play. There is an educational need, to encourage patients to choose reputable suppliers of drugs and to be aware of the risks of counterfeit medicines. In

this instance, the majority of the respondents replied that, it was not always easy, and some counterfeit drugs mimicked legitimate drugs so well that, without running a laboratory test, it is very difficult to tell the difference. However, we were informed by the trainers to look for signs of counterfeit drugs that should raise suspicion. These signs included unanticipated side effects and changes in packaging, labeling, color, taste, and pill shape.

Q29



	Qatar	UAE	Oman	Saudi	Bahrain	Egypt	Yemen Rep
Not problem	8	7	45	6	55	10	20
Mild problem	4	7	8	9	10	59	23
Moderate problems	3	7	8	9	1	10	3
Severe problems	0	0	0	0	0	11	45

Figure 4.14: Responses to the question regarding the seriousness of medicine counterfeiting

The majority of respodents claimed that there was a mild counterfeit medicine problem in their country compared to a few respodents who reported that the problem was severe (figure 4.14).

Given its clandestine nature, and a lack of effective reporting logistics, it was difficult to obtain a clear estimate of the scale of the counterfeit medicine problem in the Middle East Countries. Nevertheless, the evidence suggested that it is a significant problem and is not receiving the attention it deserves.

Counterfeit medicines are a much greater problem in less well developed countries. However, it is difficult to extrapolate from these figures to a reliable global estimate. Suggestions that 10–30 per cent of all medicines across all developing countries are counterfeit might therefore be plausible but difficult to verify.

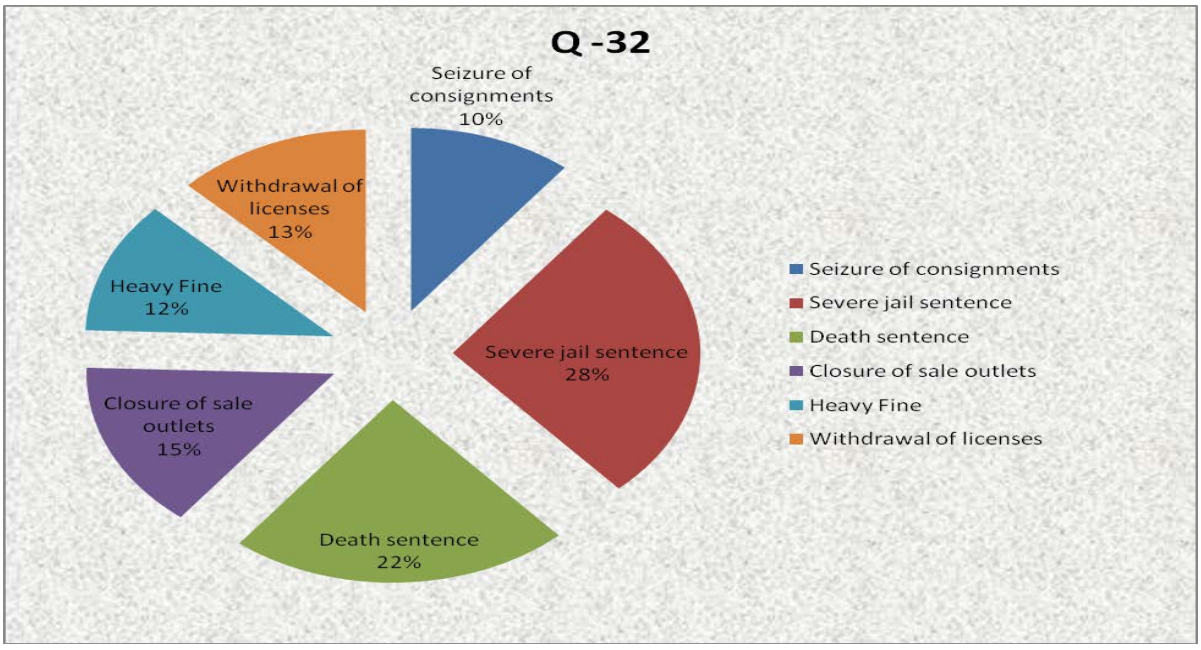


Figure 4.15: Questionnaire responses by health care workers as to what measures would be most appropriate to check the incidence of medicine counterfeiting

Surprisingly, 22% of respondents answered either that the death penalty was the best method of stopping the counterfeiters, or that it was the most appropriate punishment and this may have been attributed to cultural and religious reasons. Only 13% respondents perceived

withdrawal of the licence as appropriate. Clearly, 15 % of those questioned indicated that closure of their outlets would be the most appropriate method to deal with counterfeiters while 10% of respondents indicated that seizure of consignments would stop re-offending.

Although, 28% of the respondents indicated that a severe jail sentence was the best method to stop culprits. Interestingly, 12% of the respondents said that a heavy fine would abolish or reduce medicine counterfeiting. In this context, India plans to introduce the death penalty for the sale and manufacture of fake and counterfeit medicines that cause grievous harm. The move follows widespread concern that existing regulations pose little deterrence to unscrupulous drug vendors (Mudur et al., 2003).

The vigilance of healthcare professionals is paramount and often, in most primary care settings, the pharmacist is the most readily accessed healthcare provider. As such, this individual needs to be able to pick up signs and symptoms from patients and other people with whom interaction occurs in the pharmacy and at the bedside

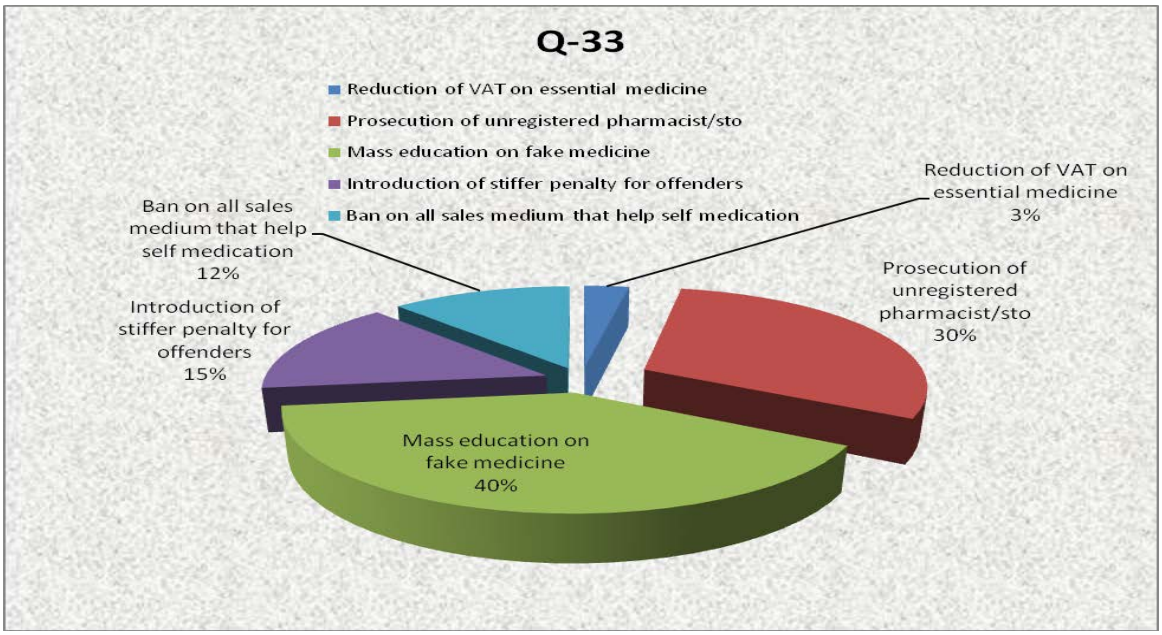


Figure 4.16: Questionnaire responses of healthcare workers regarding the best way to tackle the problem of Medicine counterfeiting

Remarkably, 40% of respondents believed that mass education on fake medicines were needed to reduce counterfeiting, whereas 3% of respondents believed that reduction of Value added Tax (VAT) on essential medicines was the best way to reduce or tackle the problem of counterfeiting and it was notable that Middle Eastern countries do not charge VAT at all.

Extraordinarily, 15% of respondents indicated that introduction of stiffer penalties for offenders might be the best solution although 30% suggested that prosecution of unregistered pharmacist was the best answer. Nevertheless, the majority of respondents agreed that measures of some sort were required to stop or reduce counterfeiting (figure 4.16).

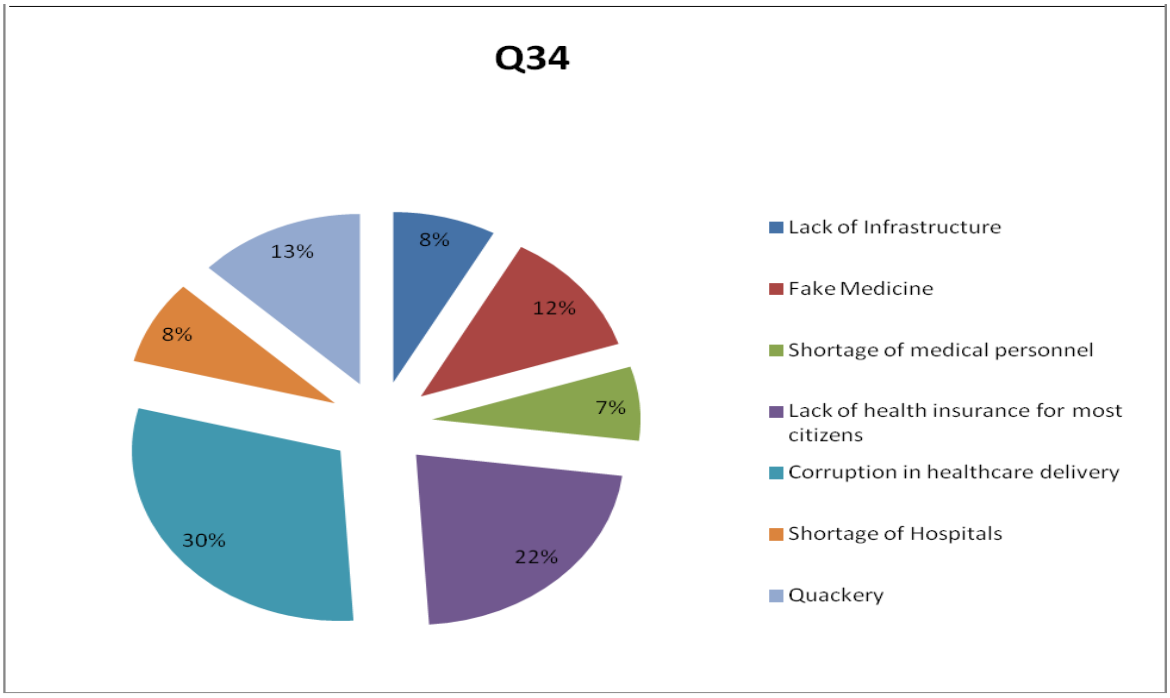


Figure 4.17: Questionnaire responses to the question asked of 1115 healthcare workers regarding perception of problems with the health care system in the 7 Middle East Countries:

Although, 22 % of responses indicated that a lack of health insurance for most citizens was problematic with the healthcare system in their country and this may well have been due to the culture and the islamic religion which do not allow insurance. In addition, 8% of respondents reported lack of healthcare infrastructre as a problem, and this may suggest that the majority of the Middle Eastern countries had a good infrastructre .

Eventhough, 30% of respondents believed that corruption was prevalent in their health care system and that bribery was rife whilst 12% thought that counterfeit medicines were a problem and only 7% claimed that a shortage of medical personnel was at the root of their difficulties.

However, 8% of respondents held the view that shortage of hospitals was problematic and this particularly applied to Yemen while 13% thought quackery was a hindrance in their health care system.

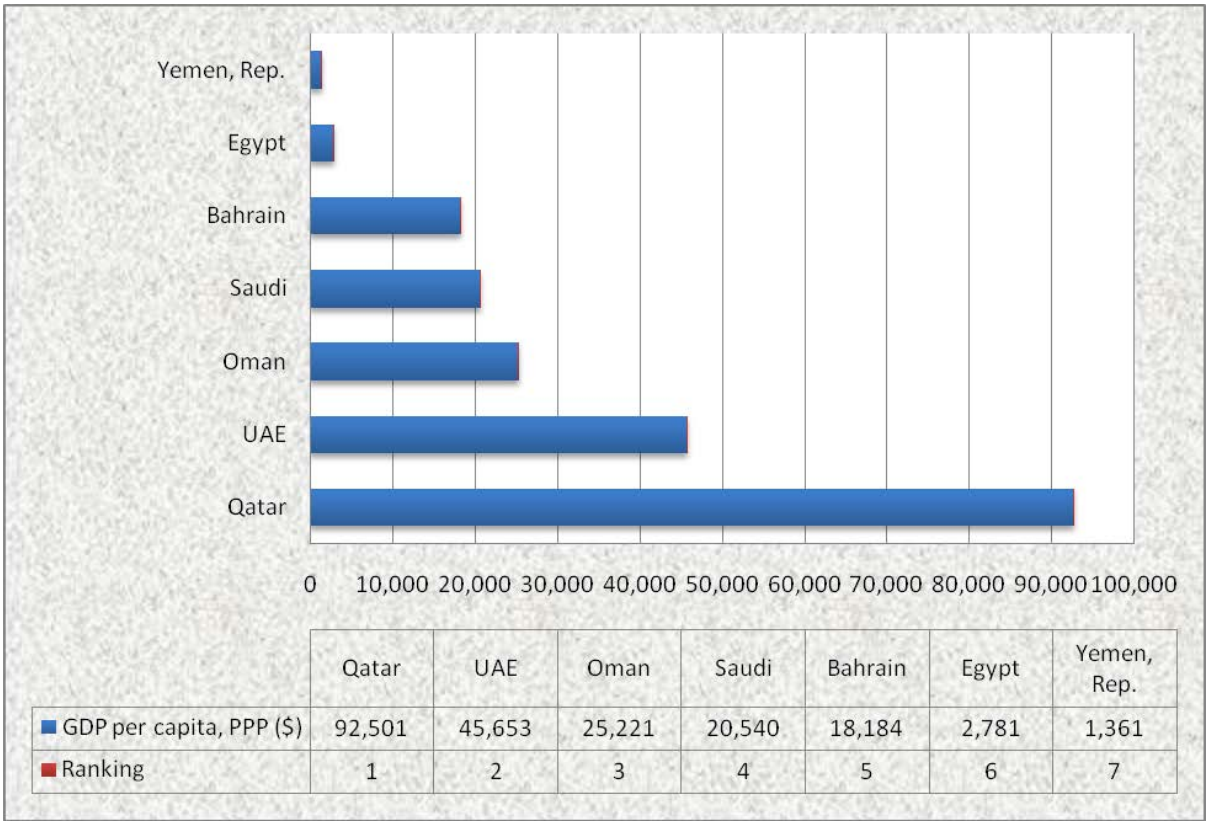
Table: 4.2 Scorecard developed to measure the quality of medicine in Middle East.

	7 Middle East Countries						
	Bahrain	Egypt	Oman	Qatar	Saudi Arabia	Yemen	UAE
Effective Regulatory agency (man power)	X	✓	✓	✓	✓	X	✓
Effective Border control of counterfeit medicine	✓	X	✓	✓	✓	X	✓
Healthcare Personnel Awareness	✓	X	✓	✓	✓	X	✓
Patient Awareness	X	X	X	✓	X	X	X
Drug quality testing	✓	✓	✓	✓	✓	X	✓
High degree counterfeit problems	X	X	X	✓	X	X	✓
Lack of adequate civil liability	X	X	X	✓	✓	X	✓
Weak or Absent rule of law	X	X	X	X	X	X	X
Price Control	✓	✓	✓	✓	✓	✓	✓
Taxes and tariffs	✓	✓	✓	✓	✓	✓	✓
Total number of quality measures (0ut of 10)	5	4	6	9	7	2	8

✓ = quality present

X = quality lacking

(ii) Analysis of possible factors such as national gross domestic product (GDP), degree of regulatory control and level of education on the occurrence of drug counterfeiting in middle eastern countries



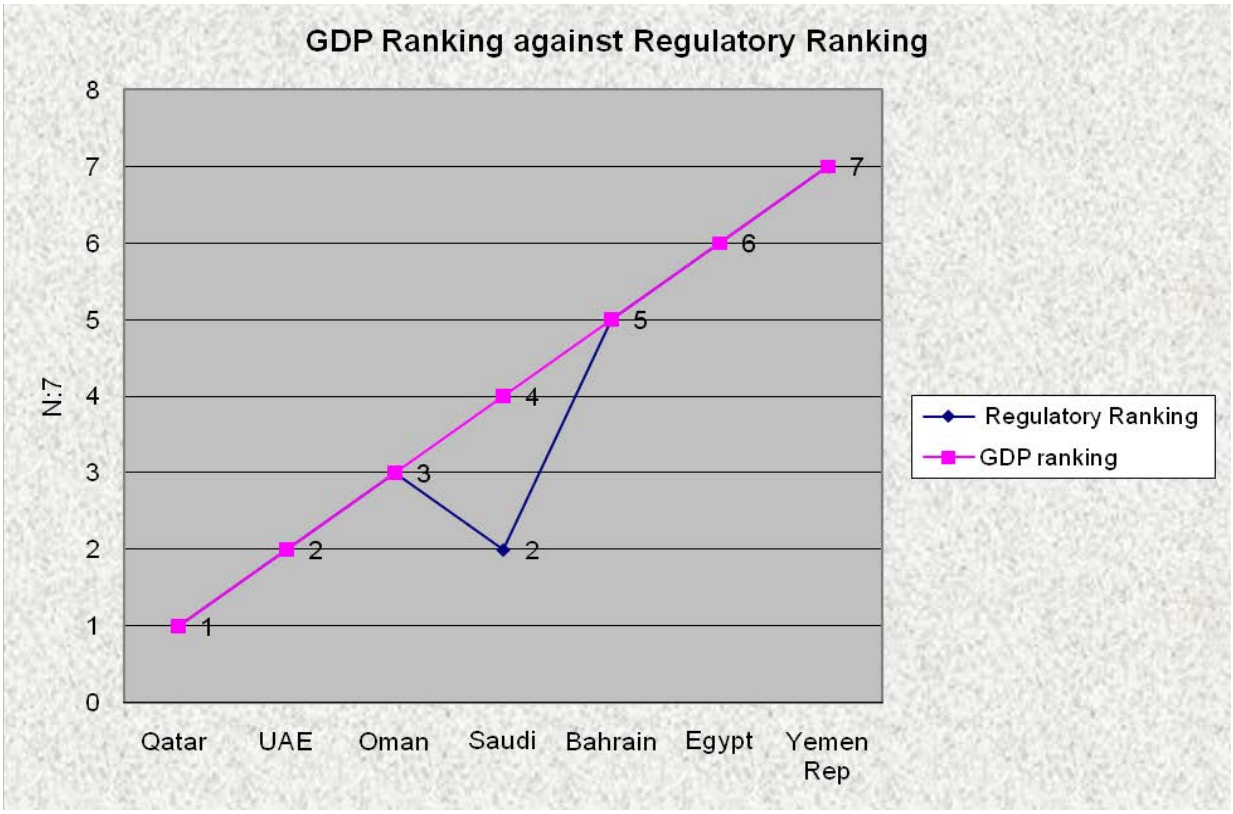
	Qatar	UAE	Oman	Saudi	Bahrain	Egypt	Yemen, Rep.
GDP per capita, PPP ($)	92,501	45,653	25,221	20,540	18,184	2,781	1,361
Ranking	1	2	3	4	5	6	7

Source: (World Fact Book)

Figure 4.18: GDP per capita and the rank of 7 Middle East countries.

According to the world bank, Qatar is ranked number one in the middle east in the ranking of GDP per capita and Yemen is ranked last (i.e. 7th of those countries studied) (See figure 4.18). However, even though countries such as Qatar, UAE and Saudi Arabia are rich, they are still classified as “developing” according to the world bank. In this context, the economic

impact of drug counterfeiting on legitimate companies is enormous and they must have an influence on governments, their policies, and society at large.



Correlation	0.943
Determination	0.890
T-Test	6.390
p-value	0.001

Figure 4.19: Correlation between GDP rank against regulatory rank for the 7 Middle East countries

Statistical analysis using the Pearson Product Moment Correlation model showed that there is a significant correlation between the GDP ranking and regulatory ranking as shown above ($P < 0.001$).

The plot suggests that the richer countries tend to spend more money on regulatory affairs than poorer countries. The structures of the individual Middle East regulatory authorities were explored through with key regulatory authorities in the region. Five authorities were under the autonomy of the ministry of health and they were financed by their governments. Saudi Arabia and Yemen had independent stand-alone authorities. These regulatory authorities had a variety of other responsibilities depending on the size and resources available for each authority.

The increased urbanisation and elevation of per capita income in Middle East countries has probably led citizens to have unhealthy diets and aggravated lifestyle-related diseases such as diabetes and cardiovascular ailments. This has increased the market for drugs such as insulin, statins and antihypertensives. Although patents for medicines ultimately expire, increasing lifestyle-related diseases would maintain revenue of the prescription medicines market in the long-term and encourage prospects for generic medicine manufacturers in the near future (Capital, 2010).

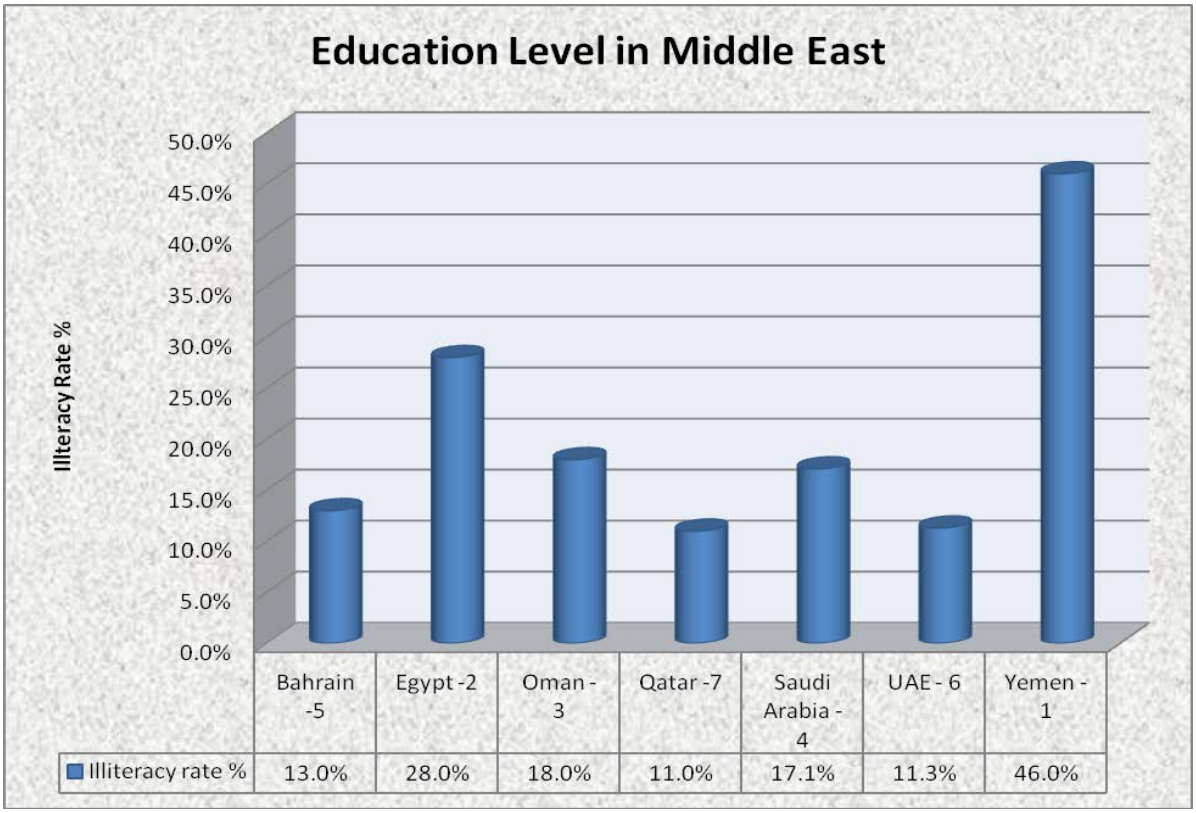


Figure 4.20: Level of education in the seven Middle East countries studied.

Sources: United Nations, 2009 World Almanac, the Economist

As a result of government investment in education, the average educational attainment of the labor force in general in the Middle East has increased.

However, due to the rising number of young students, especially in rural areas, countries such as Yemen and Egypt face a serious obstacle towards achieving universal basic education.

In Egypt, guaranteeing education for those aged below 15 is an enormous challenge since more than a third of the population is between 6 and 14 particularly in rural areas. In the mountainous areas of Yemen, despite substantial efforts to build new schools or repair existing ones, classes may have to be held outdoors.

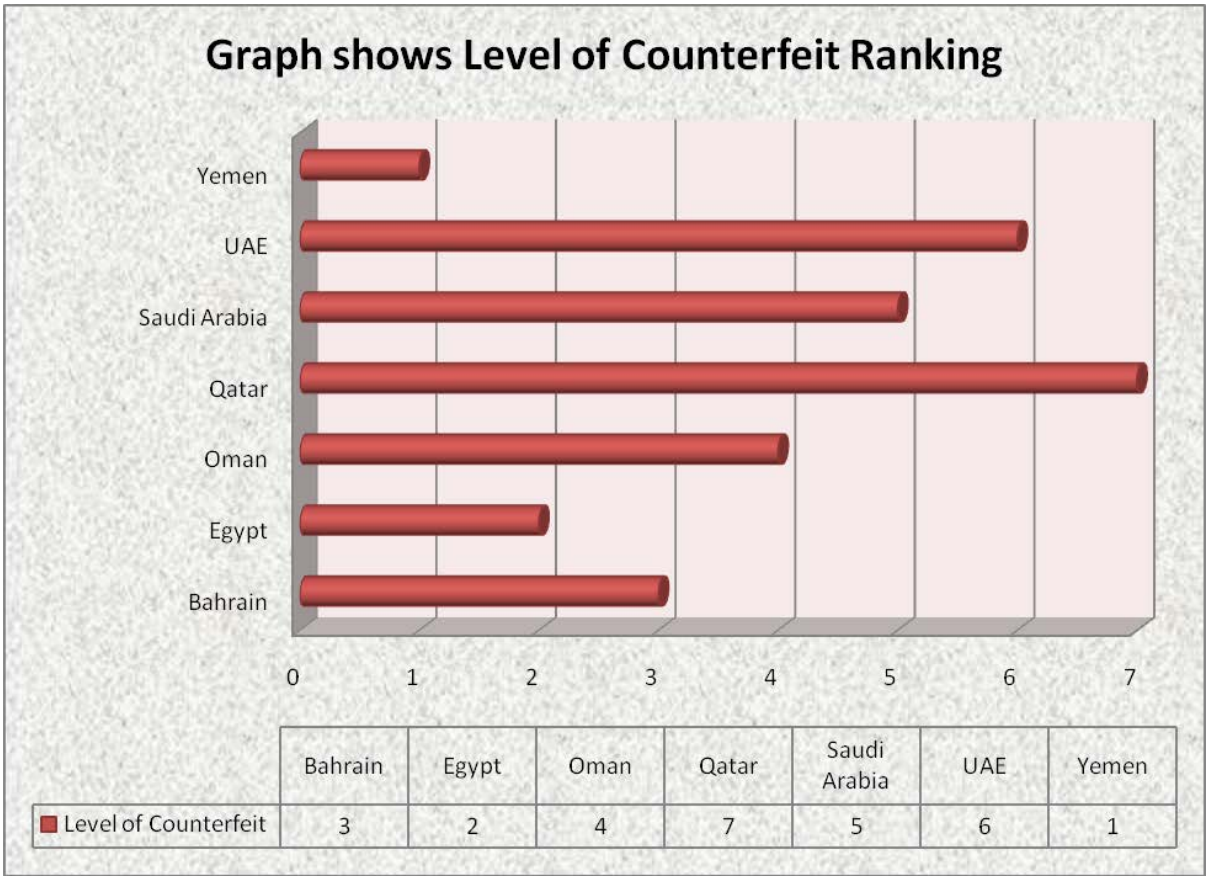


Figure 4.21: The suspected level of drug counterfeit ranking for the 7 Middle East countries in the study (n.b. the lower the number of ranking, the higher the counterfeit drugs present in that country).

Attempting to measure the effects of drug counterfeiting is extremely difficult and discovering and measuring output is a real challenge. As can be seen from the graph shown above, more counterfeit medicines were found in Yemen and it was ranked least (1) compared to Qatar which was ranked number 7; there is no agreement on factors that should be considered when calculating the scale of counterfeiting (Chaudhry, Zimmerman, 2009). While there are strict laws against counterfeiting in the UAE, the scourge of fake medicines is all too common. It was in the early 1990s that the UAE first implemented anti-counterfeiting laws. Before 1990s, one could see any variety of pirated goods openly displayed - from

Lacoste shirts, Rolex watches and Prada handbags and medicines up to a vast array of audio and videotapes. The majority of the Yemeni respondents indicated that they felt there are insufficient regulations in their country.

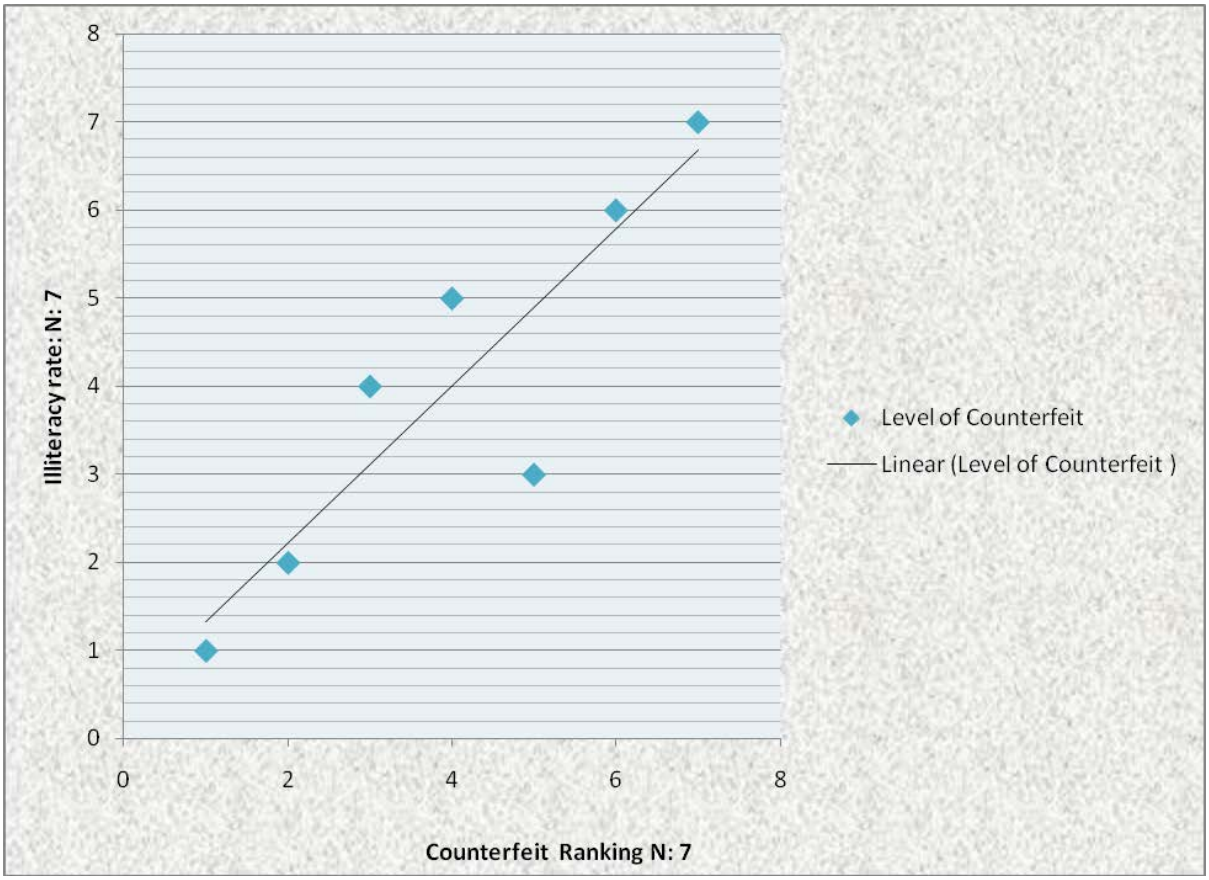


Figure 4.22: The rank level of drug counterfeiting plotted against the rank level of education in 7 Middle East Countries:

Statistical analysis using the Pearson Product Moment Correlation model showed that there are also significant correlation between the level of counterfeit medicines and education level as shown above ($P < 0.79$). Therefore, the higher the level of education in a particular country, then less medicine counterfeiting was present.

Health care providers and pharmacist need to educate patients and the general public on counterfeit medicines and the appropriate and efficient reporting systems available for suspected cases.

4.1.10 Discussion:

This study, according to the authors' knowledge, is the very first to demonstrate the extent of the vast threat of the presence of the illegal counterfeit drugs trade in the Middle East. Thus, it has not been feasible to compare the current results with the findings of others as such studies simply do not exist and any verification of such studies has been a fruitless exercise.

The findings of this study suggest that there are disparities between healthcare workers and lay persons in their appreciation of the counterfeit medicines phenomenon.

Firstly, the findings revealed a lower awareness amongst healthcare professionals than among lay persons about the dangers of purchasing illegal medicines or dietary supplements outside pharmacies i.e. through illegal channels. The fact is that lay persons, nurses and physicians are claiming that, more awareness is needed.

Therefore, it also suggests that there may be unreasonable use of drugs in Middle East countries. Pharmacists reported that some patients purchased medicines without a valid prescription and obtained them from unregistered channels. Nearly 90% of healthcare workers (i.e. pharmacists, Nurses and other health care workers) acknowledged writing prescriptions for patients even though the law in these countries only permits prescribing by qualified doctors.

Given that unregistered channels – such as roadside hawkers or commercial vehicles were cited by respondents as the most likely source of poor quality medicine, it is reasonable to conclude that a proportion of patients are exposed to these substandard medicines. The law in these countries requires that every pharmacy have a qualified pharmacist, registered with the government healthcare agency to oversee day to day operation. One example is Yemen where, despite national regulations which demand legal prescriptions for drugs, people tend to buy from illegal but cheaper street vendors where, according to WHO sources, one in five drugs is counterfeit.

The number of respondents indicating that they would not do anything when they discovered a counterfeit medicine is a concern because most of the citizens access drugs through their neighborhood chemist particularly when they are poorly educated .

The fact that respondents who indicated that they would not report a counterfeit incident to their respective regulatory agency or to the police may be attributed to the perception that corruption is widespread in the country. Thus, in such cases, reporting an incident could jeopardise their personal safety or economic wellbeing and this applied especially to a country like Yemen.

The UAE was the third largest importer of counterfeit medicines after India and Syria. They were shipped from China via Hong Kong to Dubai and then distributed all over the world, especially to developing countries. Therefore, Dubai (UAE) is a major gateway for counterfeit medicines.

Counterfeit medicine initially went into a free zone warehouse at Dubai airport owned by a fictitious company, and were later moved to the Jebel Ali free zone. The UAE government is therefore considering increasing inspections and raids and a federal pharmaceutical law would be introduced to tighten penalties and introduce jail terms and larger fines. The belief is that the law should deter pharmacies from knowingly stocking counterfeit drugs thus stopping importers from targeting the UAE market.The UAE will also set up a committee to investigate the nature of the trade in the Middle East, and has banned re-exporting of medicines without Ministry approval, in order to prevent the country being used as a staging post for counterfeits.

According to a member of the parliamentary health committee, about 70 percent of the drugs available in Yemen are contraband and "there is no quality control checking (United nation report 2006). Some health experts claim that smuggled medicines enter the country mainly from the Horn of Africa, particularly Djibouti, from where they are brought by sea to the Yemeni coast. "Trading in counterfeit drugs is a lucrative business worldwide (United Nation report, 2006). Unfortunately, a proportion of pharmacies in Yemen do not buy medicines from the original manufacturers and in one instance, a respondent reported some years ago that they discovered a bottle filled with water in place of a medicine which is potentially dangerous.

Yemen spends approximately US $117m per annum on medicines, according to the country's Supreme Drugs Authority (United nation report, 2006). Most of this money is spent on importing medicines from a total of 50 countries via 400 importers, since local pharmaceutical plants only produce 17 percent of Yemen's requirements.

The Middle East market in general has witnessed an increasing demand for drugs such as Viagra which are employed in the treatment of erectile dysfunction which affects about 150 million people around the world and they are not limited to adults only, but to varying age groups. Men, women, and young people across all socio-economic divisions look to these drugs to create an enhanced sexual experience. About 250 sexual stimulant medications are produced by seven local factories, which has stabilised the medical situation in Yemen.

These drugs should be taken according to the prescription. As much as it is useful for certain situations, these are a great danger especially to people who suffer from heart disease and diabetes (United Nation report 2006). Hence it has been noted that the type of Viagra registered with the supreme body of medicines that contains the substance sildenafil, which is expensive, but the rest of the drugs are cheap, ranging from only Yemen riyal (YR) 100-200 as a collection of vitamins, minerals and chemical components that help build the body's cells (United Nation report 2006).

Overall, the Middle East market is flooded with legal and illegal, effective and ineffective drugs as well as smuggled and locally crafted sexual stimulants. Some local producers make excellent products, but it is difficult for consumers to know which drugs are beneficial and which could harm their health. Many people have little or no knowledge about their disease state, so pharmacists should be able to advise them or suggest consultation with a clinician.

While proven drugs such as Viagra are imported from India and Switzerland, they are often too expensive for the Middle Eastern population especially in Yemen and Egypt. Consequently, the majority resort to the drugs produced by factories in their own country. These drugs are not of lower quality than the imported drugs according to some local pharmacists who have claimed "there is a difference in the mechanics of how these drugs

work." While the drugs were originally crafted to help older men or those with illnesses to retain sexual prowess, many young men have enthusiastically embraced them. In addition to the pharmaceuticals sold in Yemen there are stimulants derived mostly from Yemeni honey.

Yemeni honey contains natural substances that many people believe can help them maintain an erection. Thus, materials derived from this honey are often referred to as "Yemeni Viagra." The smuggling and counterfeiting of such erotic stimulants throughout the Arab world is a major threat to the health of the people. These drugs do not undergo adequate testing, and may be at best ineffective and at worst, lethal.

Moreover, the view of many clinicians is that in order to protect the health of citizens, it is the responsibility of government officials to address the problem of smuggling and counterfeiting of medicines.

Ministries of Health must ensure somehow that only individuals issued with a doctor's prescription can receive these drugs, and that the drugs are authentic. Resolving this issue will require the cooperation of all workers in the health sector including, pharmacists, drug store operatives and hospitals. Furthermore, educating the public on the awareness of the dangers of these drugs will also help in this respect to settle this issue.

In Yemen, there is a specific local problem, which does generalise to other parts of the Middle East. This is exemplified by Khat (the leaves of catha edulis) which is a stimulant when chewed. Many men feel an increased sexual desire when they chew Khat (The leaves of *Catha Edulis*), however, this bitter leaf can also prevent an erection and it is likely that in rural regions even this herb is traded under false pretenses.

On a more formally prescribed drug, a study performed in some Arab countries in the Middle East (Kyriacos et al., 2008) examined the quality of amoxicillin formulations the aim being to investigate the quality of locally produced and imported amoxicillin products in the Lebanese, Jordanian, Egyptian and Saudi markets. The authors found that a substantial proportion of the amoxicillin was outside USP limits especially Jordan and Egypt and as such, it was considered unsafe (See Figure 4.23).

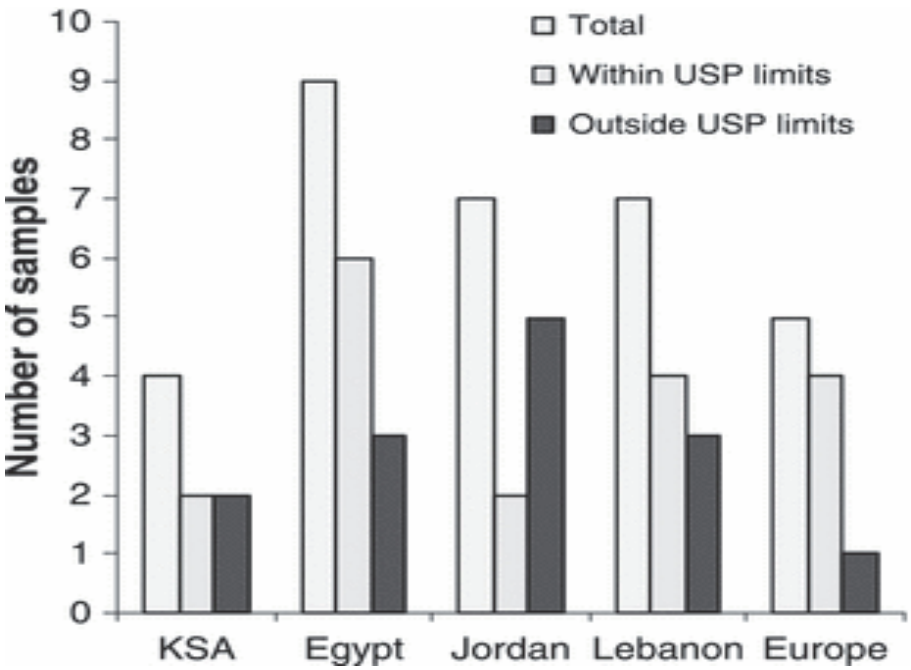


Figure 4.23 Quality of amoxicillin formulations in some Arab countries

Source: (Kyriacos,. et al 2008)

4.1.11 Conclusions:

The higher-income countries in the Middle East as can be seen from my findings have stringent regulations and more rigorous legal control than those countries that are not fortunate enough to be rich. Such rich countries represent greater rewards to the counterfeiter. One reason why drug counterfeiting has thrived in the Middle East is that authorities have been unprepared for the sheer scale and sophistication of counterfeiting and had neither the appropriate law enforcement framework nor the legislation to tackle them.

Smuggling of drugs remains a widespread and dangerous problem. Figures from the World Health Organization show that it can reach 35% of all drugs in the Middle East, compared to less than 1% in the U.S and Western Europe. One confiscated shipment by the Syrian ring to Egypt contained counterfeit copies of one brand of a leukemia drug with a street value of over $4 million -- equivalent to 50% of the annual sales of the brand (WHO, 2006a). Counterfeiters now also target the most lucrative markets, copying high-value, high turnover, high-demand drugs where huge profits are possible.

As stated earlier, counterfeit drugs are a threatening and dangerous problem in the Middle East. In most of the Middle East countries, about half of the total drugs produced are counterfeit drugs. Poor public health conditions and high prices of drugs have provided a chance for the industries producing counterfeit drugs and selling them at cheap prices. As a result, in some Middle East countries, the governments and pharmaceutical industries have begun to expend more effort in combating the problem. Some pharmaceutical companies including GlaxoSmithKline, considering introduced holograms on their product packaging in order to differentiate them from counterfeit or substandard fakes. Technology however is not

a “magic bullet” that will stop the counterfeiting problem on its own. It needs to be combined with other measures including tough legislation and regulations against counterfeiting, rigorous enforcement, stiffer penalties, and diligent surveillance on the part of the authorities (GSK, 2011)

To conclude, in order to crack down on the number of counterfeit drugs and irrational drug use in the Middle East, healthcare workers and patient awareness must be increased. Patients especially must be better educated on the potential dangers of self prescription. Pharmacists must be also reinforced and made even more aware of the importance of buying and distributing only high quality drugs that have not exceeded their expiry date or been counterfeited.

One initial step in the process is overcoming inadequacies within the drug supply system, by improving parts of the supply chain, including local production, storage, distribution and retail outlets. In addition, higher investment in the logistics and operation of medicines regulatory agencies which are often taken for granted in rich nations.

A second step is to overcome inadequate legal powers, or instigate better enforcement of those powers, to protect patients from the criminality or negligence, with actions ranging from improving the regulatory environment to helping police, customs and intelligence agency investigations.

India, China, Pakistan, Far East Asia, Brazil, Mexico and Chile are the main countries that produce counterfeited drugs, one particular example is the occurrence of fake Viagra which is

often sold in Middle East Countries in forged packages with forged Pfizer trademark and seals (United Nation Report 2006)

Pharmaceutical companies should be more open about the drugs that are counterfeited; notwithstanding the negative implications that such disclosures often carry. Health professionals should note any failure of a drug to bring about effective treatment, and encourage their members to use only trusted sources of supply. Consumers must also be educated about the scope and dangers of counterfeiting. Whereas, again, these recommendations are directed toward individual nations battling counterfeiters within their borders, there are at least two steps that should be taken at the international level. These include:

- The creation of an international database of all known sources of counterfeits, whether substantiated or not. This database would become a reference point for all countries whether importing from or exporting drugs to the specified country.
- Pharmaceutical companies need to open the lines of communication with all relevant parties and should divulge all counterfeiting information to agencies such as INTERPOL, or to the national police force of the country that they suspect has counterfeits of their drug.

Without the cooperation of the pharmaceutical companies, it will be very tough to confront offenders. A certain degree of immunity from publicity needs to be given to the companies. Consumer education will no doubt become more important as companies agree to disclose more sensitive information.

The problem of drug counterfeiting is likely to increase in the future as healthcare costs continue to escalate around the globe and trends of globalisation and deregulation continue to

open new markets (WHO 2010). As new markets emerge, demand for pharmaceuticals is likely to increase and with it, the supply of substandard or counterfeit drugs. Furthermore, increased globalisation will require improvements in communications between governments and, thus, between drug regulatory authorities. With new lines of communication, buttressed by stricter penalties for counterfeit drug traffickers, along with technological improvements to track drugs along the distribution chain, counterfeiters may be kept at bay.

Although it is unlikely that counterfeiting will ever cease to be a thorn in the side of governments, drug regulatory authorities, licit pharmaceutical manufacturers and the patients at the end of the chain, improved communication and extended collaboration among all of the relevant parties across national boundaries provides the best opportunity for curtailing the seemingly exponential potential of the counterfeit trade in the future.

4.1.12 Summary of Chapter 4:

- In this chapter the awareness of the extent of the counterfeit medicine problem in the Middle East was identified.
- The illegal trade and manufacture of medicines is a global problem, disproportionately affecting low- and middle-income Middle East countries were highlighted in this Chapter.

- Countries in the Middle East with weak regulatory oversight and law enforcement attract illegal manufacturers, while countries with strict law enforcement prevent them were highlighted in this Chapter.
- Awareness of the threats that might be caused by counterfeit medicine.
- Awareness of the scale of counterfeit medicines and dietary supplements sold outside pharmacies.

- Further research is needed to determine the consequences of counterfeit drugs and identifying health risks in Middle East.

- Additional research is recommended to create standardised research instruments that may help to identify specific interventions that may best enhance the safety of patients and further substantiate best practices.
- These findings suggest that healthcare professionals need to become better educated about counterfeit medicines and be trained in skills to readily identify counterfeit medicines.

5 CHAPTER FIVE:

5.1 A STUDY ON SAFETY OF MEDICINES WITH REGARD TO DRUG COUNTERFEITING IN SIX EAST AFRICAN COUNTRIES: (DJIBOUTI, ETHIOPIA, KENYA, SOMALIA, TANZANIA AND UGANDA)

5.1.1 Introduction:

Counterfeit and substandard drugs are a serious and growing problem around the world – especially in East African Countries. There are many reasons for this phenomenon, including illegal imitation, inappropriate packaging, poor manufacturing processes, and improper conditions during transportation and storage. At the point of supply or purchase, such drugs share the common feature that they are not what they purport to be, so for simplicity we class them all as 'fakes or counterfeits' in this study.

The scale of the problem remains unclear. The World Health Organisation (WHO) estimates that counterfeit drugs constitute up to 25 per cent of the total medicine supply in less developed countries (LDCs) (Harris et al 2009). In Africa and South East Asia, more detailed sampling has revealed that between 30 and 60 per cent of medicines were substandard (WHO, 'Counterfeit medicines', Fact sheet No. 275). The largest producers and suppliers of counterfeit medicines were India and China and fake drugs existed in most therapeutic classes and posed direct threats to patients.

Counterfeit medicines fail to provide effective treatment. Largely because fake drugs often contain insufficient bioavailable active ingredient. Thus, a patient who believes he is addressing his disease is in fact remaining untreated or exposed to sub-therapeutic doses. The disease thus progresses, often leading to death, especially in children and the elderly.

However, it has been estimated that approximately 700,000 deaths from malaria and tuberculosis are attributable to counterfeit drugs in East African countries, adulteration with toxic chemicals, often leading to death or injury. There have been numerous deaths due to

consumption of cough syrup contaminated with anti-freeze, including 84 children in Nigeria in 2008 (Kelesidis et al. 2007).

In 2008 contaminated Heparin from China killed 62 people in the US (FDA 2008).
If for example an anti-infective drug contains some active ingredient, but too little to kill the invading organism, it can lead to the emergence of drug resistance. This is a serious problem with tuberculosis where extremely drug resistant strains have now been found in 49 countries (Keshavjee and Farmer, 2012). In addition, malaria, parasites in much of Africa and Asia are now resistant to most drugs, except those based on artemisinin and there are even worrying signs of emerging resistance to these drugs too. Resistance is also a serious problem for HIV medications and how much counterfeiting contributes towards this is an unknown factor (Keshavjee and Farmer, 2012)

East African countries have been unwilling to accept that they have a problem with counterfeit medicines. There is little respect for trademarks or copyright, and this encourages pirating activities (including counterfeiting of medicines). They do not have the infrastructure or resources necessary for effective detection and consequently, the process of enforcement is invariably weak.

Definitions of counterfeiting set a very high burden of proof, making it difficult to collect enough evidence for successful prosecutions. Additionally, in East African countries, regulatory and legal systems are inadequate or too slow to respond (Castell and Brickwood, 2009)

Legitimate drug manufacturers know which distributors to whom they supply stock. However, farther down the supply chain, drugs may be traded repeatedly, making it difficult to follow the movement of products so the supply 'chain' more closely resembles a network. Efforts to deal with counterfeit medicines may be hampered by corruption inside these East African Countries either at high-level, when the trade in medicines is associated with politically powerful individuals, or at a more local level, when corrupt staff with regulatory or enforcement roles compromise enforcement programs (Morris and Stevens 2006).

In many poor countries, like those in East Africa, fake drugs often displace or crowd out real drugs, especially in street markets where vendors have no reputation to protect. The solution must, therefore, be to enable patients to distinguish between what is real and what is not. Another measure is to enable manufacturers to protect the identity and quality of the drugs they produce through the supply chain all the way to the ultimate consumer. This chapter and study is concerned with examining potential solutions and recommendations to limit the amount of counterfeit medicines sold in areas like East Africa.

5.1.2 AIM AND OBJECTIVE OF THE STUDY:

5.1.3 Aim:

The aim of this work was to perform a study on the safety of medicines in relation to drug counterfeiting from the perspective of clinicians, pharmacists, and other healthcare workers and owners of drug outlets in East African countries: (Djibouti, Ethiopia, Kenya, Somalia, Tanzania and Uganda)

5.1.4 Objectives:

- To determine at least partially, the level of drug counterfeiting present in these countries
- To assess the perception on the safety of medicines in relation to counterfeiting
- To understand any possible link between medicine counterfeiting and the level of education.
- To understand any possible link between the regulatory ranking and GDP ranking in each country.

5.1.5 Methodological Framework:

5.1.6 Study design:

This section outlines the methodology and the selection of a study design is one of the most important sections in a thesis in order to answer the research questions. According to Yin (2003), the purpose of any academic research can be exploratory, descriptive or explanatory. In this study, it was initially exploratory using questionnaires administered to healthcare workers including pharmacists and clinicians as in the previous chapter firstly regarding

counterfeit medicines and then a correlative analysis was performed on the relationships between GDP, regulatory ranking and educational levels.

5.1.7 Data Collection:

Data collection was performed between 2009 and 2011 in order to reach all regions including some rural areas in each of the study countries. A number of individuals were recruited to be agency researchers and to help in the administration of questionnaires (see more details in chapter 2). Pharmacies, other drug outlets and other health care workers were randomly selected in townships by the field researchers who considered them to be representative of each state.

They approached concerned personnel, with the request that they complete the questionnaires and if they could not complete them immediately, the researchers offered to retrieve the questionnaires several days later. Forty-four per cent (660/1500) of those who completed the questionnaires responded immediately and 21% (315 of 1500) requested that the researchers return to pick them up.

In the case of 10% (150 of 1500) of the questionnaires, researchers assisted respondents by guiding them through the form. This was done when the respondents indicated that they had queries or that they did not understand what was asked. 26% (435of 1500) of healthcare personnel refused to fill out the questionnaires with some saying that they did not feel safe or comfortable or would first need clearance from their superiors.

5.1.8 Results and Analysis:

The results from the questionnaires and correlative analysis of potential medicine counterfeit influencing factors are presented in the following order:

(i) **Questionnaire distribution to six East African countries**

i. Characteristics of the study population
ii. About their patients, medicine costs and fake medicines.
iii. Types of fake medicines and the medicines most likely to be faked
iv. Possible measures to stop or reduce the occurrence of sub-standard counterfeit medicines.

(ii) Analysis of possible factors such as national gross domestic product (GDP), degree of regulatory control and level of education on the occurrence of drug counterfeiting in East African countries.

i. Correlative ranking of GDP and education versus level of medicine counterfeiting

A breakdown of the total characteristics of the study population for all 6 East African countries is shown in Table 5.1 below.

Table 5.1 Characteristics of the study population.						
	Women		Men		Total	
	n	%	n	%	N	%
(Age)						
18- 24 years	52	4.8	45	4.3	97	9.1
25- 34 years	78	7.3	137	12.8	215	20.1
35- 44 years	85	8	274	25.7	359	33.7
45- 54 years	108	10.1	123	11.5	231	21.6
55- 64 years	7	0.65	105	9.9	112	10.5
65- 74 years	0	0	51	4.7	51	4.7
85 over	0	0	0	0	0	0
Total	330	31	735	69	1065	100
(Race)						
White	0	0	0		0	
Arab	23	2.2	176	16.5	199	18.7
Asian	106	10	111	10.4	217	20.4
Black/African	78	7.3	508	47.7	586	55
others	23	2.2	40	3.7	63	5.9
Total	230	21.6	835	78.4	1065	100

	Women		Men		Total	
	n	%	n	%	N	%
Full time	119	11.2	302	28.3	421	39.5

Part time	98	9.2	546	51.3	644	60.5
Total	217	20.4	848	79.6	1065	100

It is significant that from the information obtained through questionnaires overall that more than two thirds of the respondents (71% 1065/1500) (see table 5.1) returned the questionnaires and 69% respondents were men compare to 31% respondents who were women. Individual response rate for each countries was comparable the range between (66%; 164/250) Tanzania – (77%; 192/250) Somalia and there was little variation between the countries.

This gender difference is largely due to culture and religion. More men are in employment than women in East African countries. The majority of the respondents (55%) were black African and this was expected. One fifth (20.4%) of respondents were Asian whereas 18.5% were Arab and 5.9% were of other ethnic origins (see table 5.1).

More men were employed fulltime than women and again, this was expected as it was due to cultural and religious practice and the fact that more males than females received school education. The status of each respondent in the East African countries is shown in figure 5.1 below:

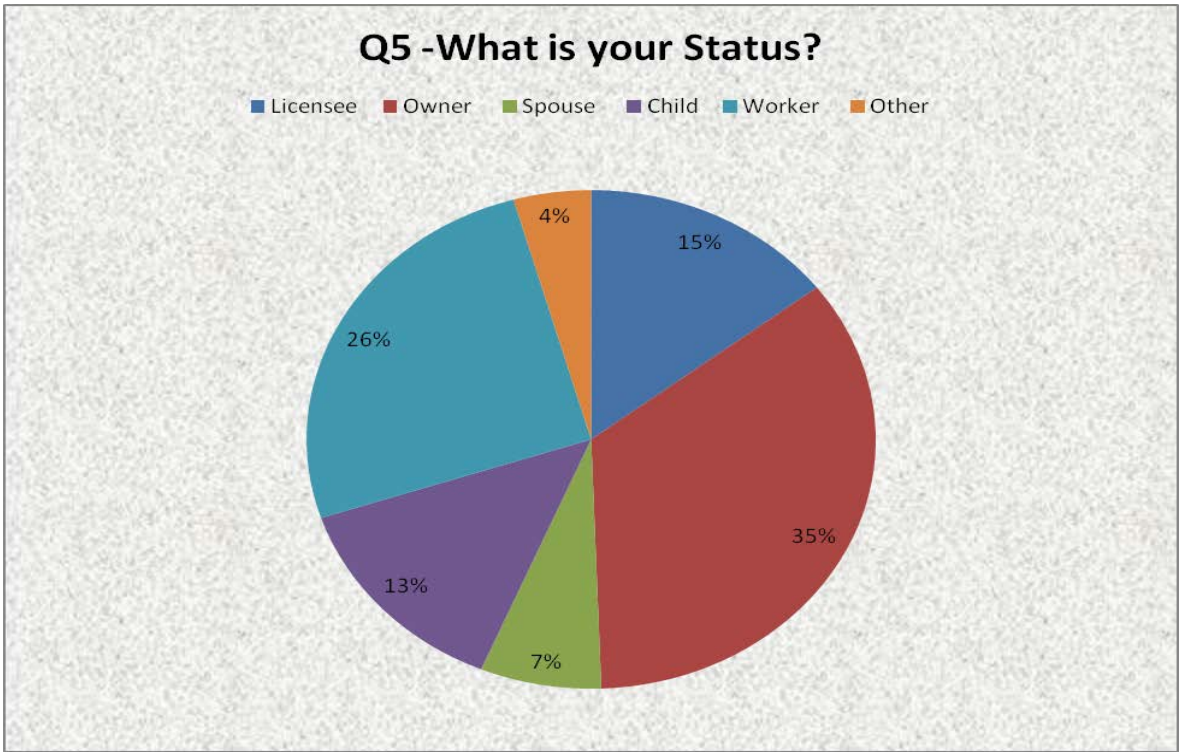


Figure 5.1 shows overall status of questionnaire respondents in the East African countries studied.

The majority of the respondents (35%) were owners of the pharmacies or clinics, whereas 15% of the respondents were licensees. On the other hand, 13% of the respondents were children and 7% were spouses see fig 5.1. On the other hand, 26% of the respondents were workers compared to 4% who were of other categories, i.e. volunteers and co-owners.

In the context of the above data, a study conducted in Laos on the knowledge and perception of medicines quality among sellers and consumers concluded that sellers lacked adequate scientific knowledge. The study tested knowledge of medicine quality using four criteria: correct labelling, testing, registration of medicines, and knowledge of active ingredients noted on the label. Of 59 sellers interviewed, only one had full and adequate knowledge of what constituted a high-quality medicine. 51% of urban sellers, 53% of rural sellers, and 39% of remote sellers could identify at least two of the four criteria for a quality medicine (Syhakhang et al., 2004)

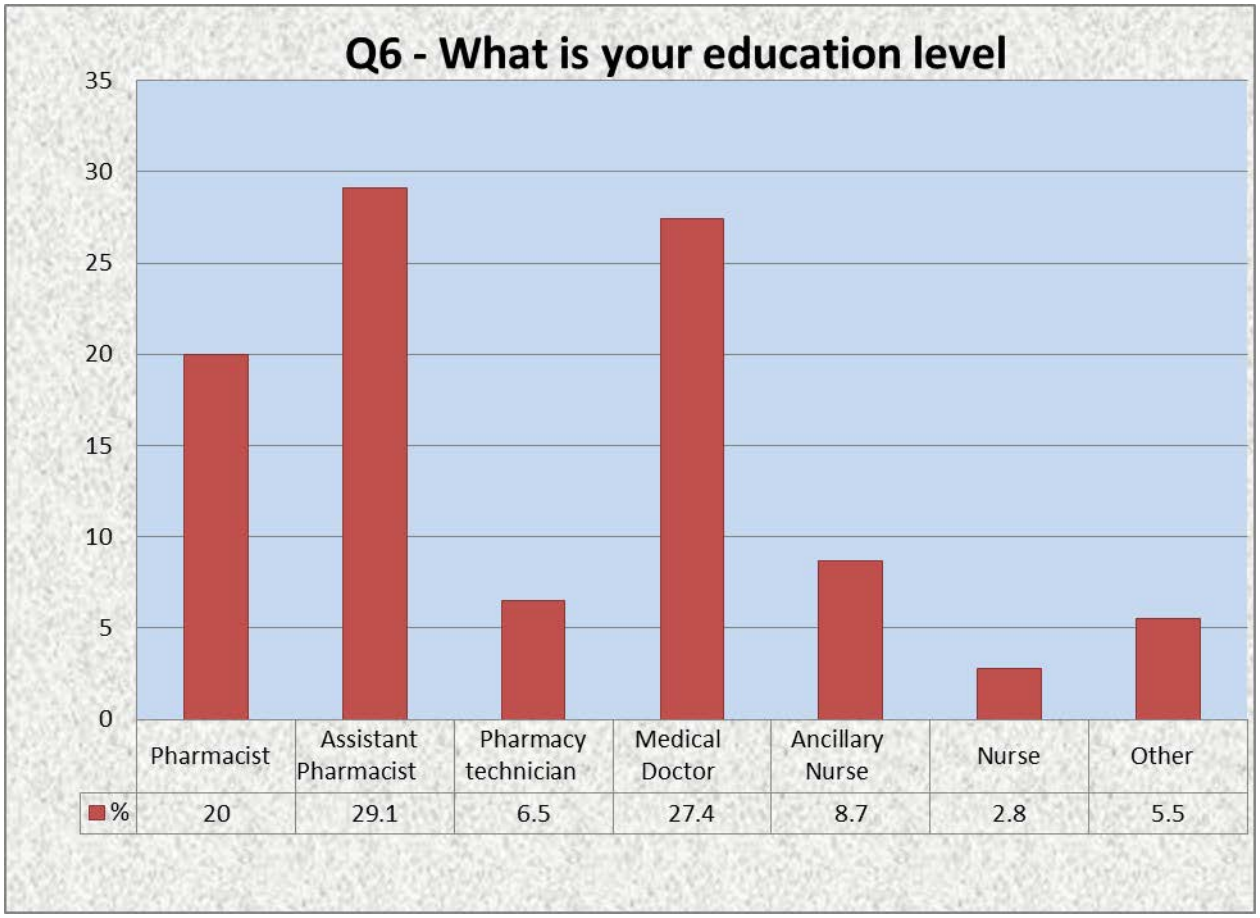


Figure 5.2 Education level (professional qualification status) of respondents to the questionnaire.

Surprisingly, 27.4% of the respondents were medical doctors, the majority of whom worked in clinics which sold medicines see figure 5.2. In contrast, 13% of respondents were pharmacists whereas 29.1% were pharmacy assistants. Only 6.5% of respondents were pharmacy technicians, suggesting that the pharmacy technician role is not prevalent in East African countries (see figure 2).

On the other hand, 2.8% of respondents were qualified nurses compared to 8.7% who were ancillary nurses. Lastly, 5.5% of respondents were from other education categories, like engineers, dentists and former farmers/nomads. Regrettably, in this region of Africa still, there are many pharmacies working without pharmacy qualification. This study is significant

because the people rights to health includes the right access to a reliable standard of health care and assure the medicines received are not only genuine but also safe, effective, of good quality and affordable (Erhun et al., 2001)

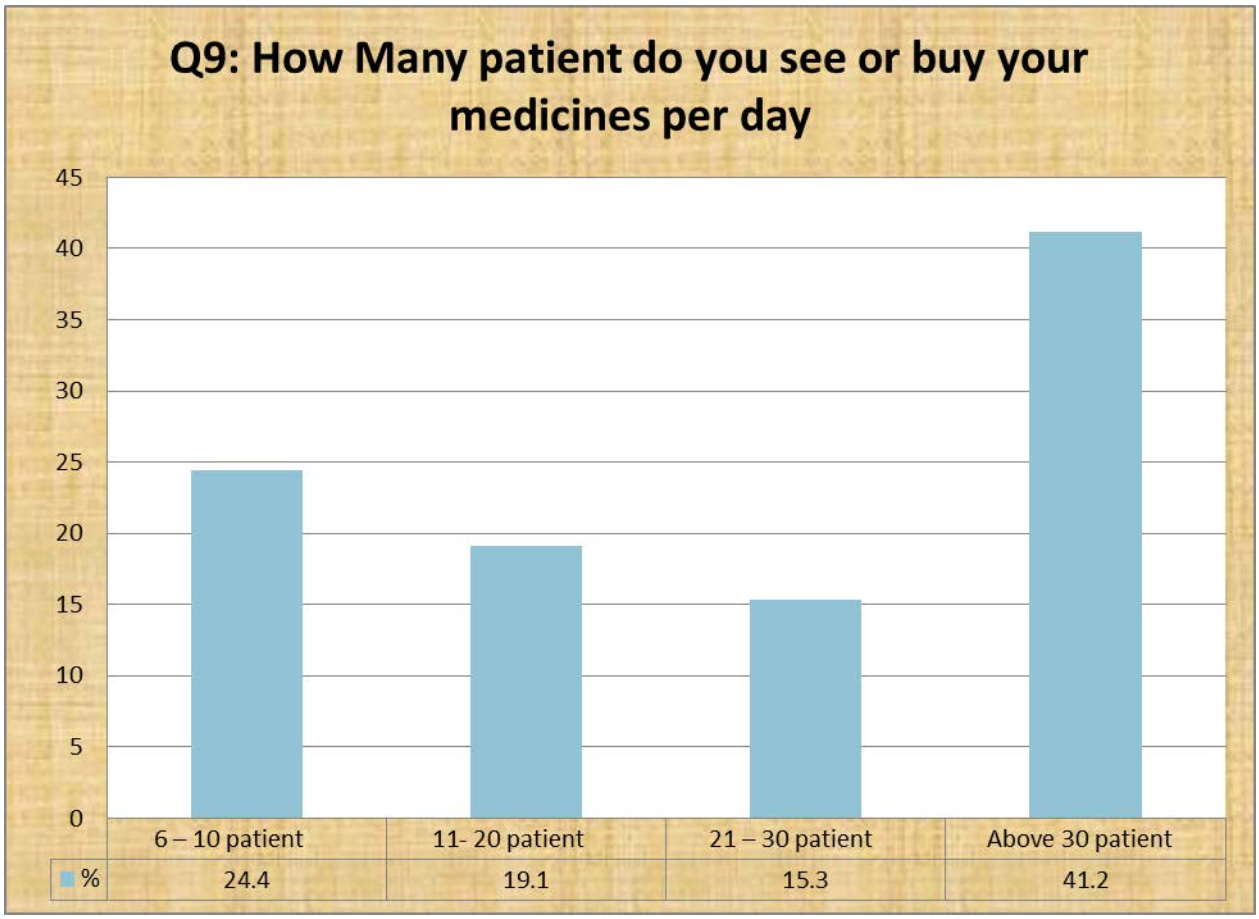


Figure 5.3 Responses to question asked of 872 healthcare workers in 6 East African countries regarding the number of patients they saw weekly.

Hence, 41.2 of the respondents (i.e. the majority) indicated that more than 30 patients visited their clinic or pharmacy to have treatment or buy their medicines weekly whereas 24.4% of those who responded specified that 6-10 patients per week came to their clinic or pharmacy to obtain medicines. Respondents that were from big cities tended to see more than 30 patients per week as a consequence of the high catchment population, see figure 5.3.

Respondents to the questionnaire indicated that due to the rapidly rising cost of healthcare and the prices of medicines, there was growing concern in this region of Africa where patients had to pay for healthcare commodities such as medicines. Hence, those patients visiting clinics were limited by these factors and a proportion of the remainder sought help from traditional healers.

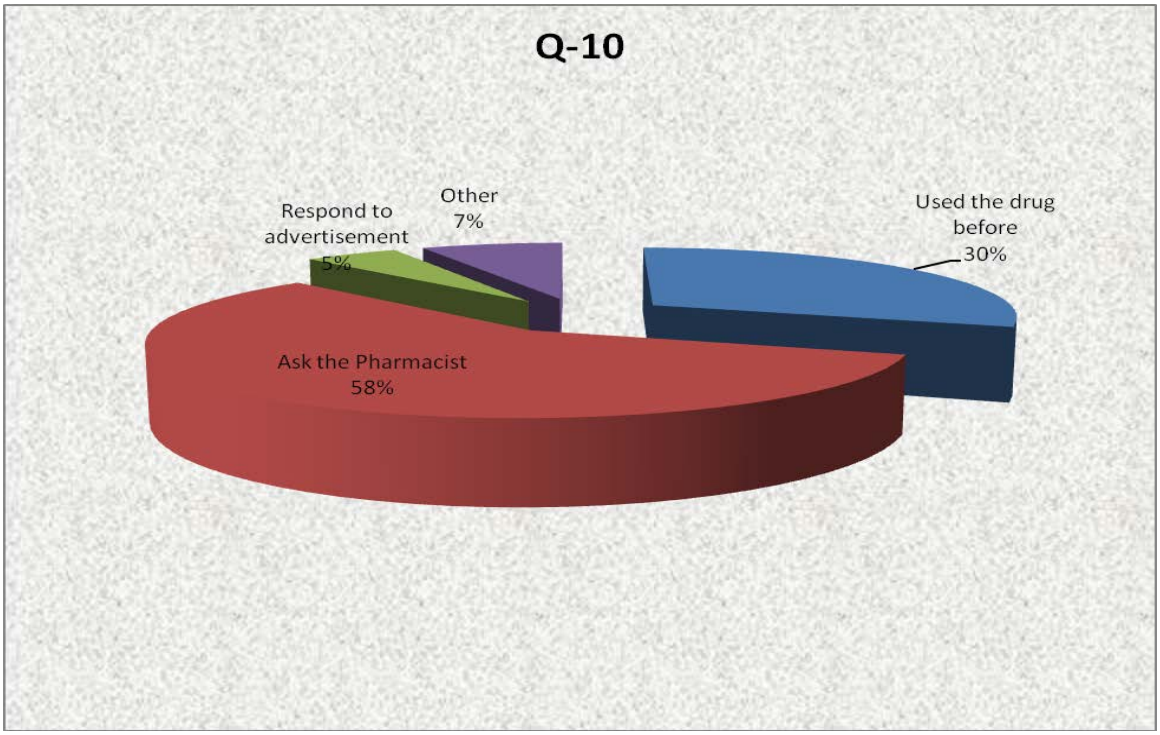


Figure 5.4; Responses to question asked of 750 health care workers in 6 East African countries "how do patient know the appropriate medicine to buy."

The majority of the respondents (58%) to the questionnaire replied that patients sought advice from the pharmacist/healthcare professional about the appropriate medicine to buy, see figure 5.4. This was in contrast to 30% of respondents who reported that patients had used the medication previously and they were aware of what they wished to select. Only 5% of respondents indicated that patients responded to an advertisement, and this may suggest that patients trusted their local pharmacist to provide suitable advice on the selection of a medicine.

While it is impossible to evaluate the extent to which patients are exposed to counterfeit medicines, it is therefore also challenging to establish how many of those adverse events reported are linked to counterfeit drugs. Patients in this region of the world do not tend to question that the drugs they receive from a pharmacist or healthcare specialist are legitimate or that they will cure disease and alleviate symptoms rather than causing serious harm or even death.

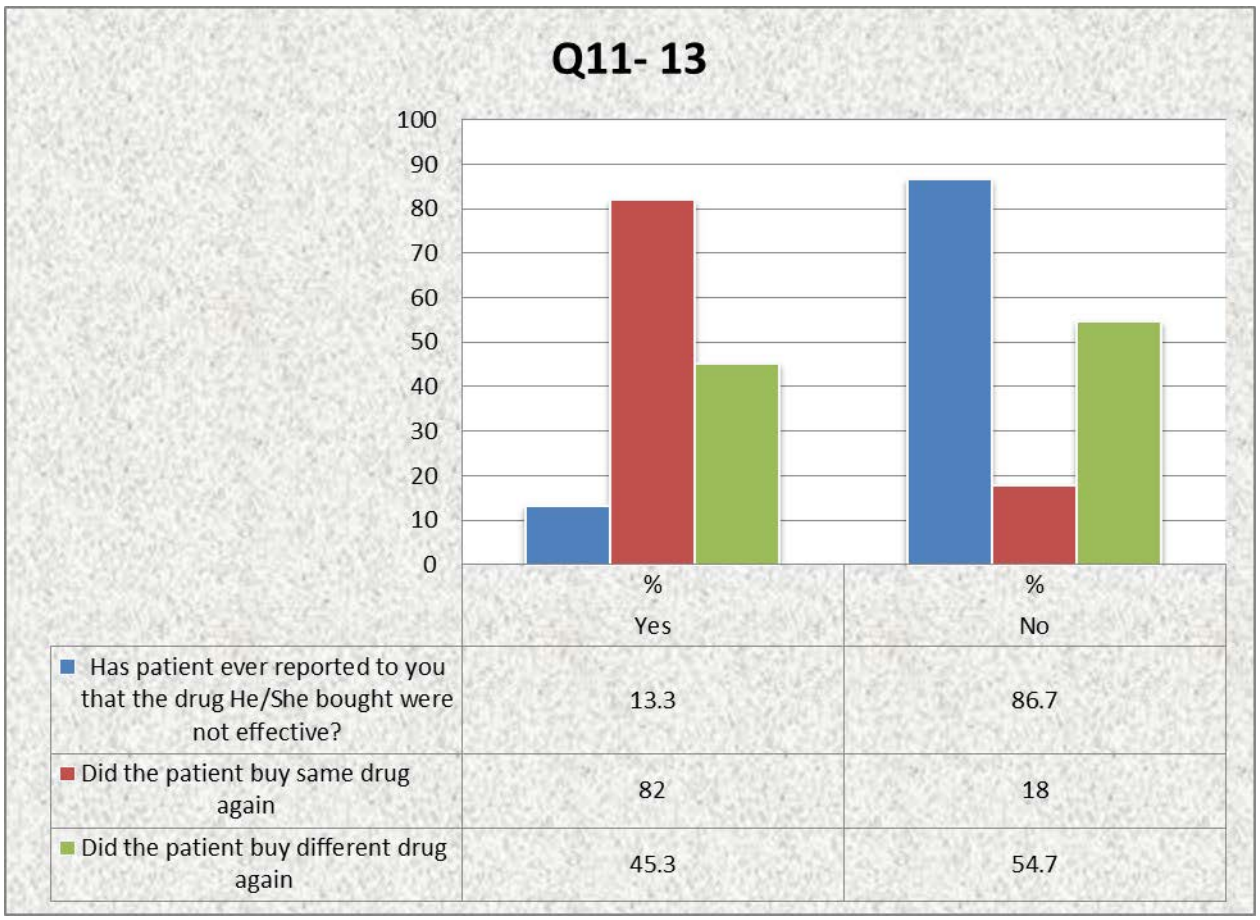


Figure 5.5 showing responses to questions asked of healthcare workers "has the patient ever reported that drugs bought were not effective and did the patient buy the same drugs or a different drug."

Although, 13.3% of respondents indicated that patients reported that the medicine they were using was not effective and did not help their condition at all whereas 86.7% of respondents specified that patients did not report to them if the medicine they were using was not effective, see figure 5.5.

The other two questions were linked to the first question which was that if patients reported to their local clinic or pharmacy that the medications they bought was not effective (or in other words not improving their condition). Thus, 82% of respondents reported that patients bought the same medicine every time they visited their clinic or pharmacy compared to 45.3% of respondents who replied that patients bought a different medicine.

Consequently, the survey found that patients generally did not report to their local pharmacy or clinic if the medicines were not effective or did not help them.

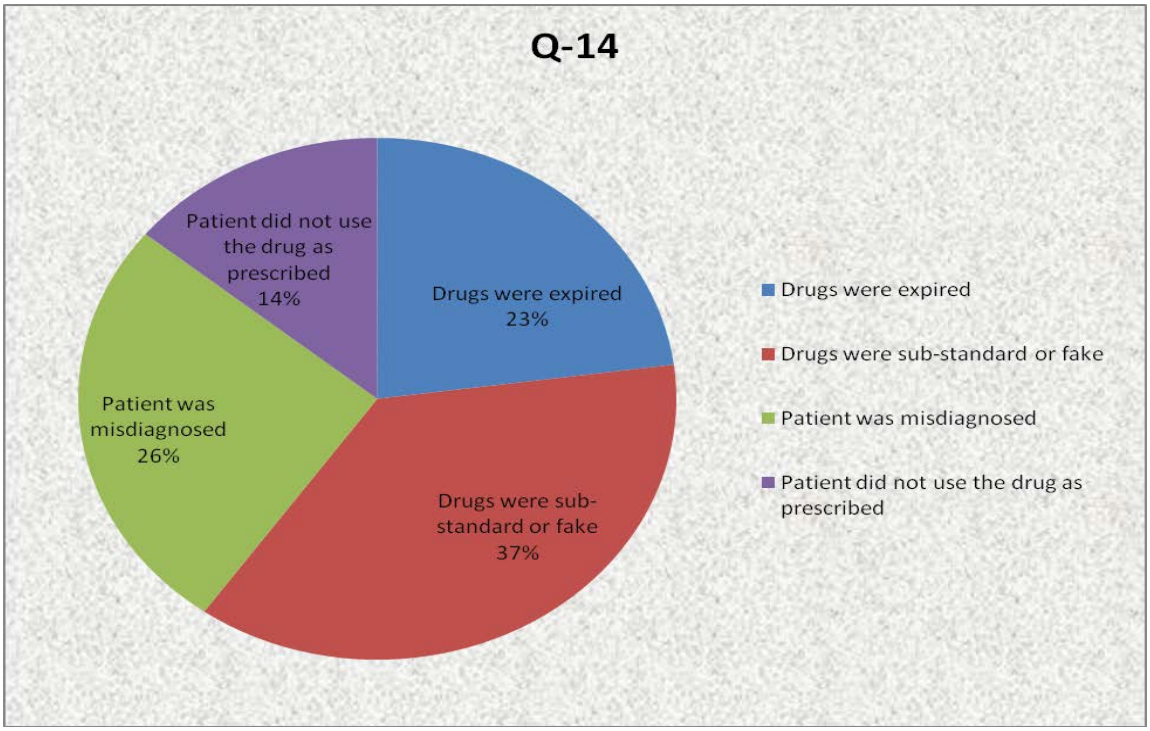


Figure 5.6; Responses to the question asked of 1500 healthcare workers in 6 East African countries "What are some likely reasons that drugs were not working".

Surprisingly, 37% of respondents claimed that medicines sold and used to treat patients were sub-standard, whereas 14% of respondents said that patients did not use their drugs as prescribed, see figure 5.6. According to the WHO, an estimated 25% of medicines consumed in developing countries were believed to be counterfeit. In some African countries, the figure is thought to be as high as 50%. Therefore the current findings are not too dissimilar from those of the WHO.

Whereas, 23% of respondents revealed that many drugs were beyond their expiry date and this may have explained their non-effectiveness. In many parts of Africa, medicines are sold in coffee shops, kiosks, corner shops and also by vegetable sellers which may explain why 26% of respondents thought patients were misdiagnosed, and continued receiving the wrong medication.

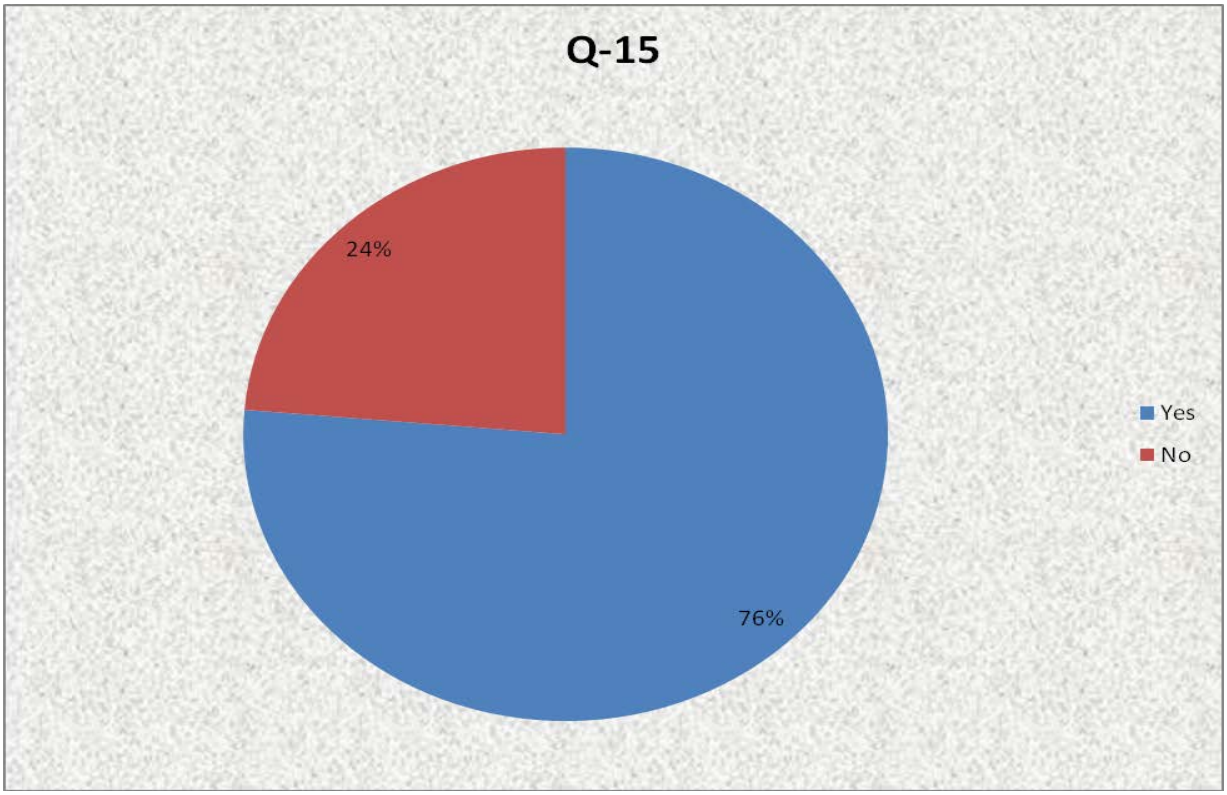


Figure 5.7; Responses the question asked of 1500 healthcare workers in 6 East African Countries "do patients buy their drugs from unapproved places."

The majority of respondents (70%) were in accord with the available literature and specified that most patients bought their medicines from unapproved outlets such as kiosks, coffee shops or corner shops, see figure 5.7.

On the other hand, 24% of responses indicated that patients bought their medication from approved outlets such as pharmacies or government hospitals. These tended to be patients who were compliant with government laws and therefore preferred to buy their medications from approved outlets. Trade in these products is more prevalent in countries with weak drug regulation control and enforcement, scarcity and/or erratic supply of basic medicines, unregulated markets and unaffordable prices. However, as counterfeiting methods become more sophisticated, counterfeits are increasingly present in better-controlled markets (WHO 2003).

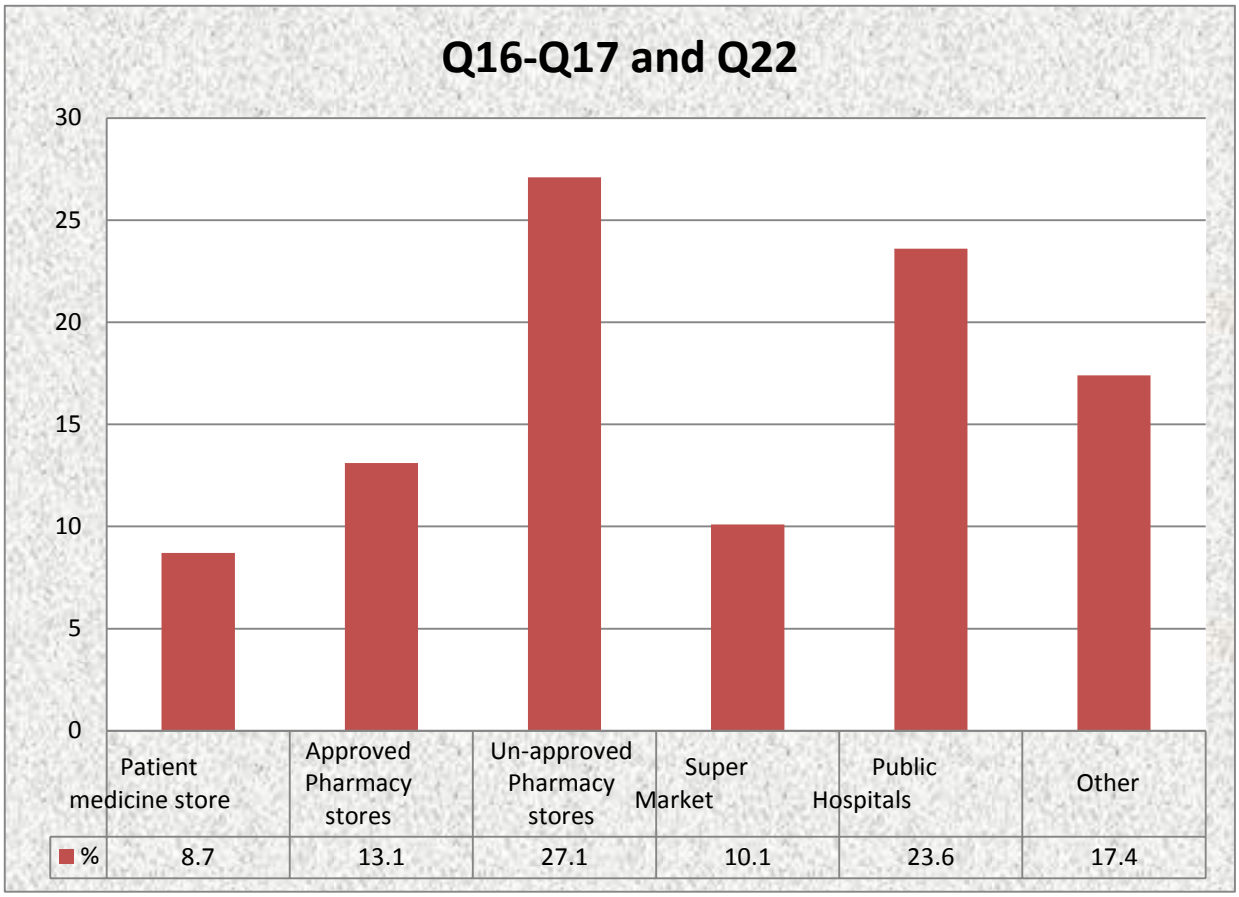
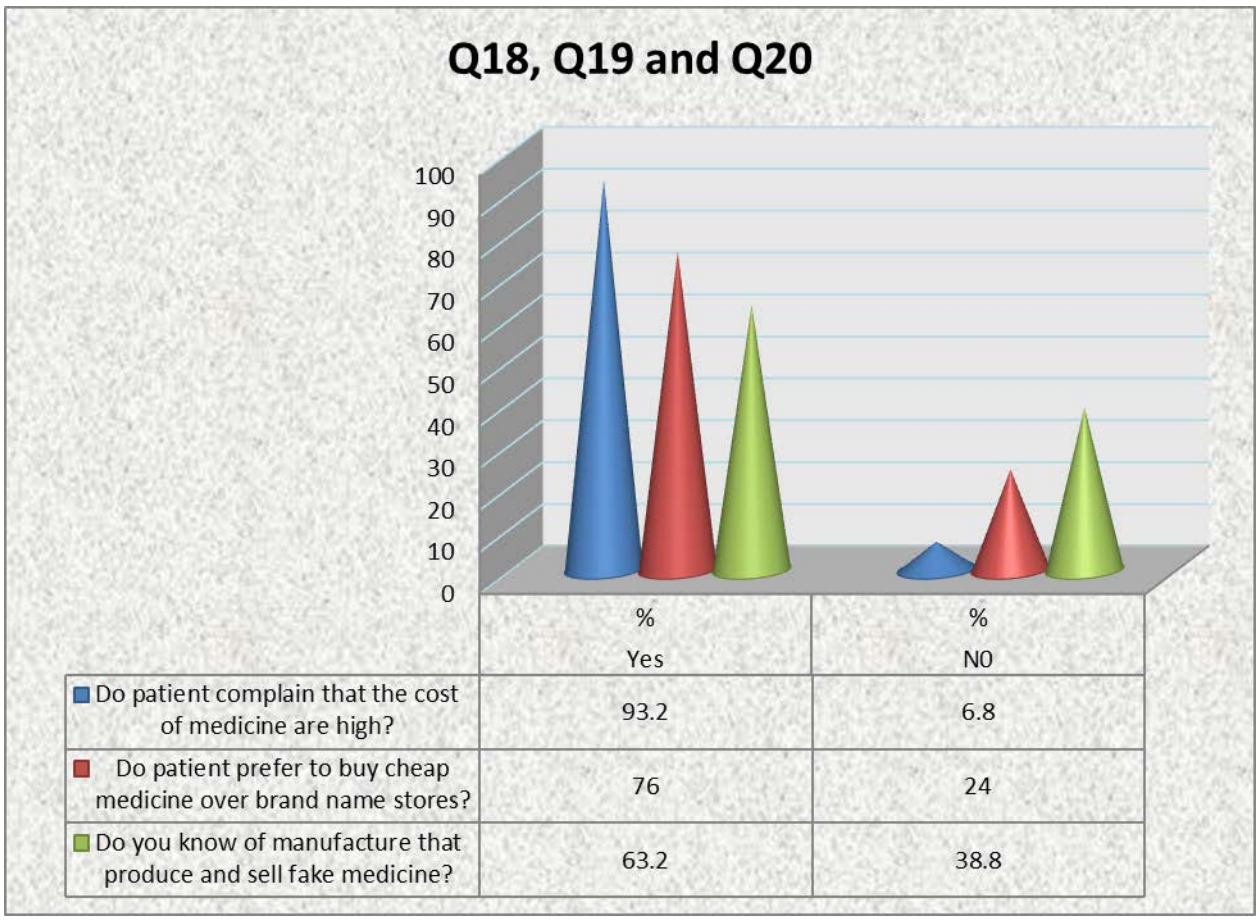


Figure 5.8 showing responses to the question asked of 1500 healthcare workers in 6 East African countries "Where is the cheapest place that most patients buy their medicines and where are fake medicines distributed."

While, 10.1% per cent of respondents said that unapproved pharmacy stores were where patients obtained their medicines and this was attributable to the cheaper prices, whereas 24% of respondents indicated that patients procured their medicines in public or government hospitals, the principal reason being that poor patients either were given free or subsidized medicines at these sources, see figure 5.8. Seventeen point four per cent of respondents said patients got their medicines at other outlets, like kiosks, coffee shops, internet shops, local corner shops, at vegetable markets or on the buses.

The majority of the respondents did not want to comment on where fake medicines were distributed and this was due to fears concerning the government. The main reason for counterfeiting medical products is that huge sums of money can be made because of the low manufacturing costs. However, in many countries, legislation or enforcement is inadequate and counterfeiters face extremely low risks of being punished.

This makes counterfeiting attractive for criminals. The expansion of trade and deregulation offers greater opportunities to introduce fake products into official channels (Chan et al., 2008)



	% Yes	% N0
Do patient complain that the cost of medicine are high?	93.2	6.8
Do patient prefer to buy cheap medicine over brand name stores?	76	24
Do you know of manufacture that produce and sell fake medicine?	63.2	38.8

Figure 5.9 showing responses to the questions asked of 1500 healthcare workers in 6 East African countries; "Do patients complain that the cost of medicines are high"; "Do patients prefer to buy cheap medicines over brand names" and "Do you know of manufacturers that produce and sell fake medicines?"

While, 93.2% of responses indicated that patients complained that the cost of medicine was too high compared to only 6.8% of respondents who said patients did not complain and even some of the patients haggled to reduce the cost of their medicines, see figure 5.9.

This study showed that, 76% of respondents claimed that patients preferred to buy cheap medicines or a generic medicine rather than a brand name. Thus again, the survey emphasized just how expensive medicines can be in poor African countries. While, 63.2 % of respondents indicated that they were aware that some manufacturers sold substandard medicines. On other hand, they were conscious of overseas producers selling fake medicines though 36.8% of them reported that they did not know of any manufacturers in their own country in this respect. The majority of the respondents indicated that they were of the opinion that China and India were the two leading countries from which sub-standard medicines were sourced.

Prescription medications have become a powerful tool in the medical arsenal against disease and promotion of health and quality of life. Yet the success of prescription drugs and their extensive use has attracted unsavoury characters interested in exploiting vulnerable patients and the market for medicines. Some countries, such as Tanzania for example, rely on the International Dispensary Association's quality assurance for testing their essential medicines

and since 2006 the Association has tested batches of medicines made overseas (Mackintosh et al., 2011).

It is not unusual for people in developing countries to pay, on average, proportionately more for medicines through out-of-pocket expenditure than consumers in the developed world, including those individuals who pay insurance premiums regardless of their health status. It just so happens, that one third of the global population lacks reliable access to essential drugs (WHO, 2004) and this sector directly overlaps with those in developing countries. Governments should have a role to play beyond enforcing the rule of law and many East African government interventions in the pharmaceutical market have restricted supplies of quality medicines, driving up prices and simply leading to gaps in the market.

This situation has then been exploited by purveyors of fake medicines. Governments could substantially reduce these problems by removing impediments to the supply of quality medicines, such as taxes, tariffs, price controls and arbitrary regulations (Harris, 2009).

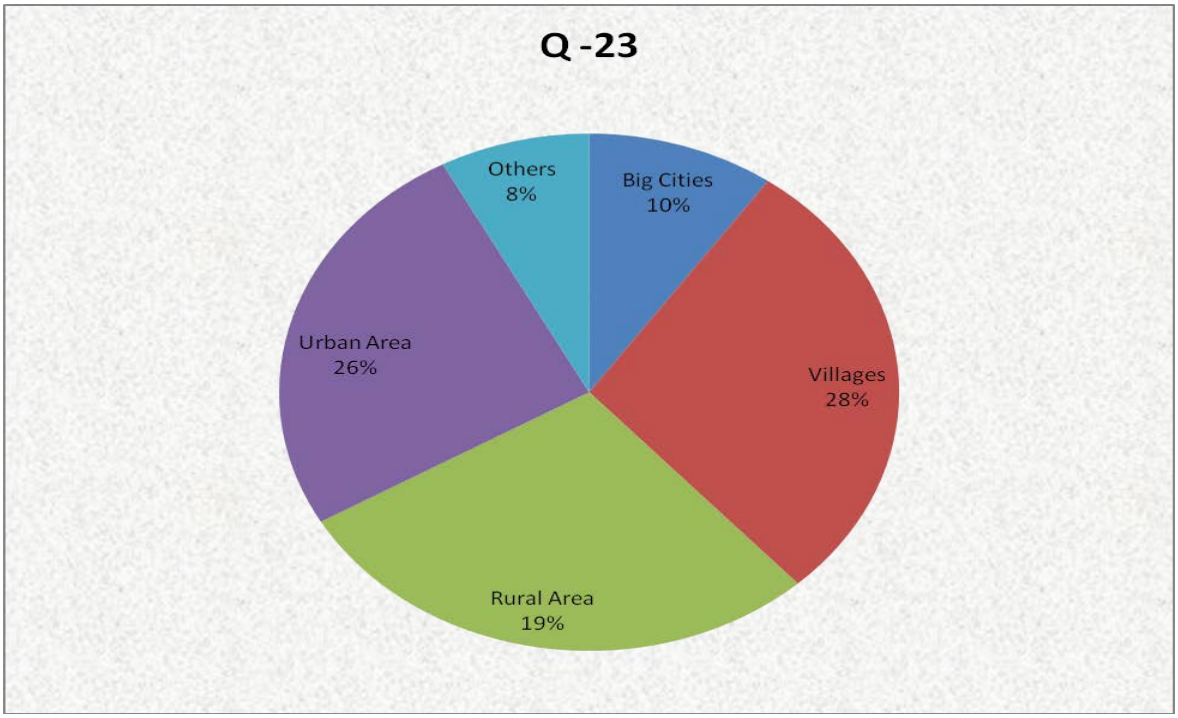
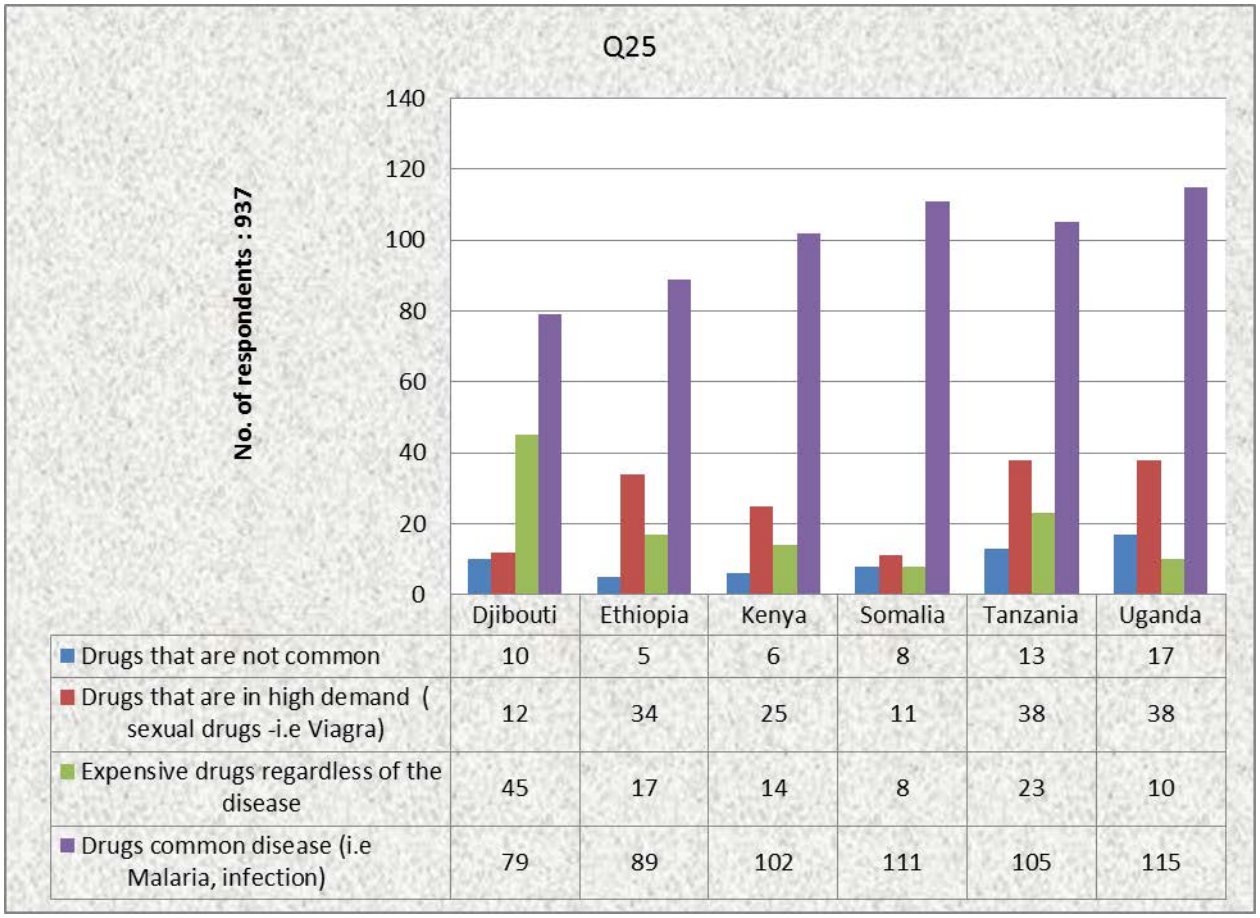


Figure 5.10 showing responses to question asked of 1500 healthcare workers in 6 East African countries "Where are fake medicines most likely to be sold."

Across those East African countries studied, villages were the most likely places where counterfeit medicines were likely to be found. Thus, 28% of respondents indicated that the village setting was a safe haven where sub-standard or fake medicines were sold compared to only 10% of respondents who thought that big cities were the locations where such counterfeits were to be encountered, see figure 5.10.

Some respondents feared that harmful counterfeit medicines could impel rural communities in Africa to re-adopt traditional medicines in order to address their needs and it was somewhat telling that 19% of respondents answered that it was rural areas where most counterfeit medicines were traded. Only 8% of respondents indicated that other unusual places such as buses, on the streets, vegetable markets and laundry shops were credible places for counterfeit medicine sales.



	Djibouti	Ethiopia	Kenya	Somalia	Tanzania	Uganda
Drugs that are not common	10	5	6	8	13	17
Drugs that are in high demand (sexual drugs -i.e Viagra)	12	34	25	11	38	38
Expensive drugs regardless of the disease	45	17	14	8	23	10
Drugs common disease (i.e Malaria, infection)	79	89	102	111	105	115

Figure 5.11 showing responses to the question (Q25) asked of 1500 healthcare workers in 6 East African countries:

Africa is fraught with challenges as was apparent from this survey question. There is a substantial lack of previous data from which to judge the types of medicine most frequently counterfeited and few objective studies have been conducted in the continent (Caudron, J.M. et al., 2008). Moreover, from the graph shown above (Fig 5.11), the majority of respondents, ranging from to generally reported that drugs used in widespread disease areas i.e malaria and infectious diseases, were most commonly faked. The quality of antimalarial drugs is particularly important in this context since it affects the ability to effectively manage one of the most prevalent diseases in East Africa (Amin et al., 2005).

Hence, it has been reported that sub-standard and counterfeit antimalarial drugs are present in the markets of developing countries and a small sample study of this drug group across Africa in 2008 found that over 30 per cent of these drugs originating from Asia failed quality checks. However, locally-produced drugs fared even worse, with nearly half being discovered as substandard (Bate et al., 2008). On the other hand, the number of counterfeited recreational drugs such as Viagra in this region of Africa, are on the increase and according to the current survey, respondents specified this type of drug as the second most faked group of medicines encountered in their country. Moreover, expensive drugs and those that are uncommon, regardless of the disease area of treatment, are also faked but not too the same extent as more the common drugs.

Counterfeit medicines in East African countries were originally focused upon life-saving medicines including those for infectious diseases, antimalarials and cardiovascular drugs. However, it might be hypothesised from the survey that there may be an increasing trend towards ‘lifestyle’ medicines such as those for erectile dysfunction as mentioned above and there were even reports of agents for weight loss.

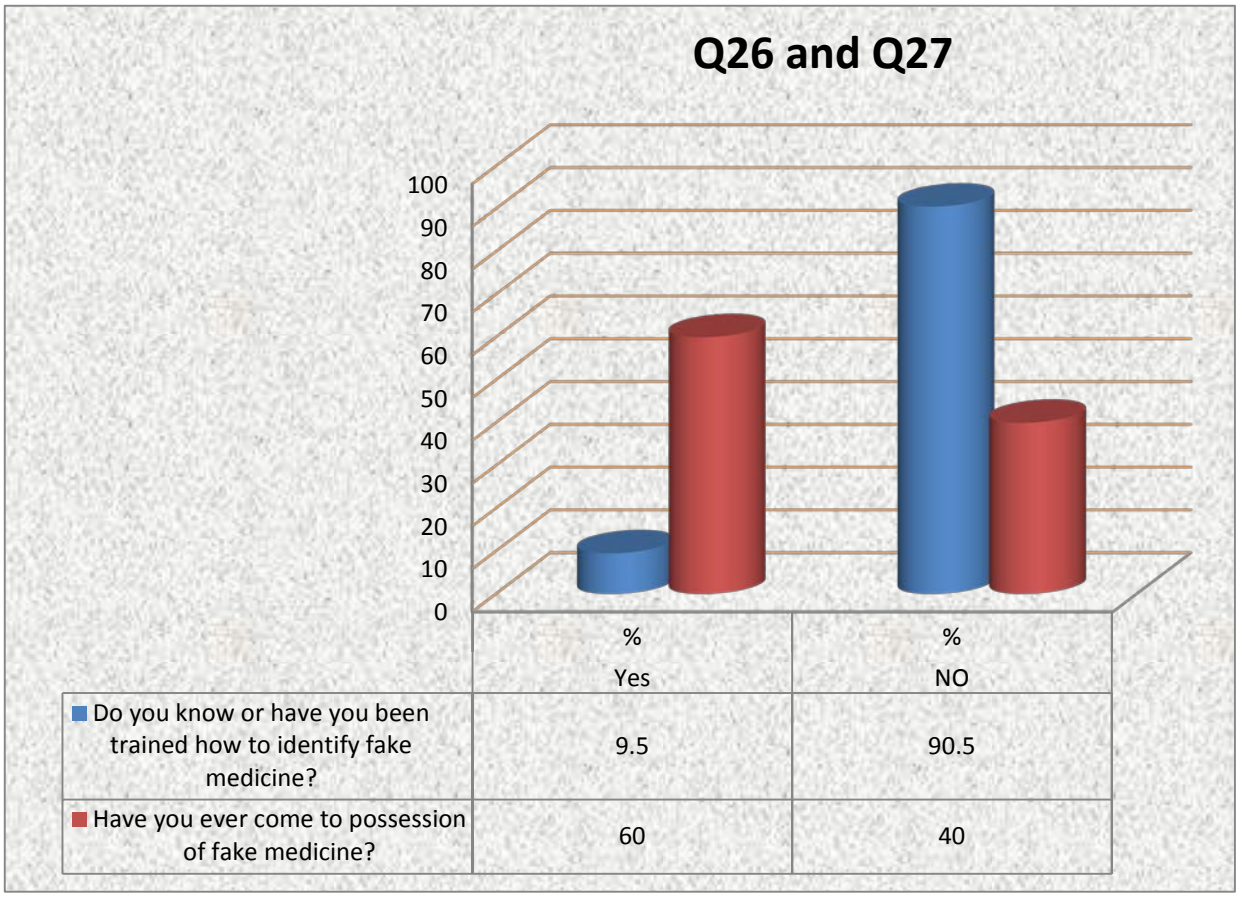


Figure 5.12. Responses to questions asked of 1500 healthcare workers in 6 East African countries: "Do you know or have you been trained how to identify fake medicines?" and "Have you ever come into possession of fake medicines?" If their answer was "yes" to the second question, respondents were asked "What have they done about it."

The results showed that, 90.5% of respondents signified that they had not been trained or did not know how to identify fake medicines compared to only 9.5% who claimed that they had been on a training course or were self-trained and knew how to identify counterfeit medicines, see figure 5.12.

East African governments need to increase public awareness about identifying counterfeit medicines but this will only be productive if the counterfeits are poor and easily detectable. In

such cases, patients should have sufficient information concerning the existence of counterfeits, be given advice on how best to avoid them and what they should do if they are suspicious about the authenticity of a medicine or medical device.

Unfortunately, many counterfeits are extremely good copies designed to deceive the patient and visual examination alone is unlikely to identify the fake. Consequently, it is sometimes only laboratory analysis that is capable of establishing whether a medicine is authentic or counterfeit.

The results also showed that 60% of respondents signified that they had come into possession of fake medicines as opposed to 40% of individuals who said they had not come into possession of fake medicine or even if they had, they were not aware of it.

The majority of the respondents suggested in the comment section of the questionnaire, that governments should establish or launch a 24 hour hotline to enable the public (assuming they had communications access), healthcare professionals, those engaged in the supply chain and industry to report directly, and where necessary, confidentially to a regulatory agency. The reporting of any suspicions concerning counterfeit medicines or medical devices could be accomplished via telephone or through a Ministry of Health website. Another suggestion from the respondents was that, governments needed to instigate a national conference held yearly to raise awareness of the domestic efforts to tackle these issues.

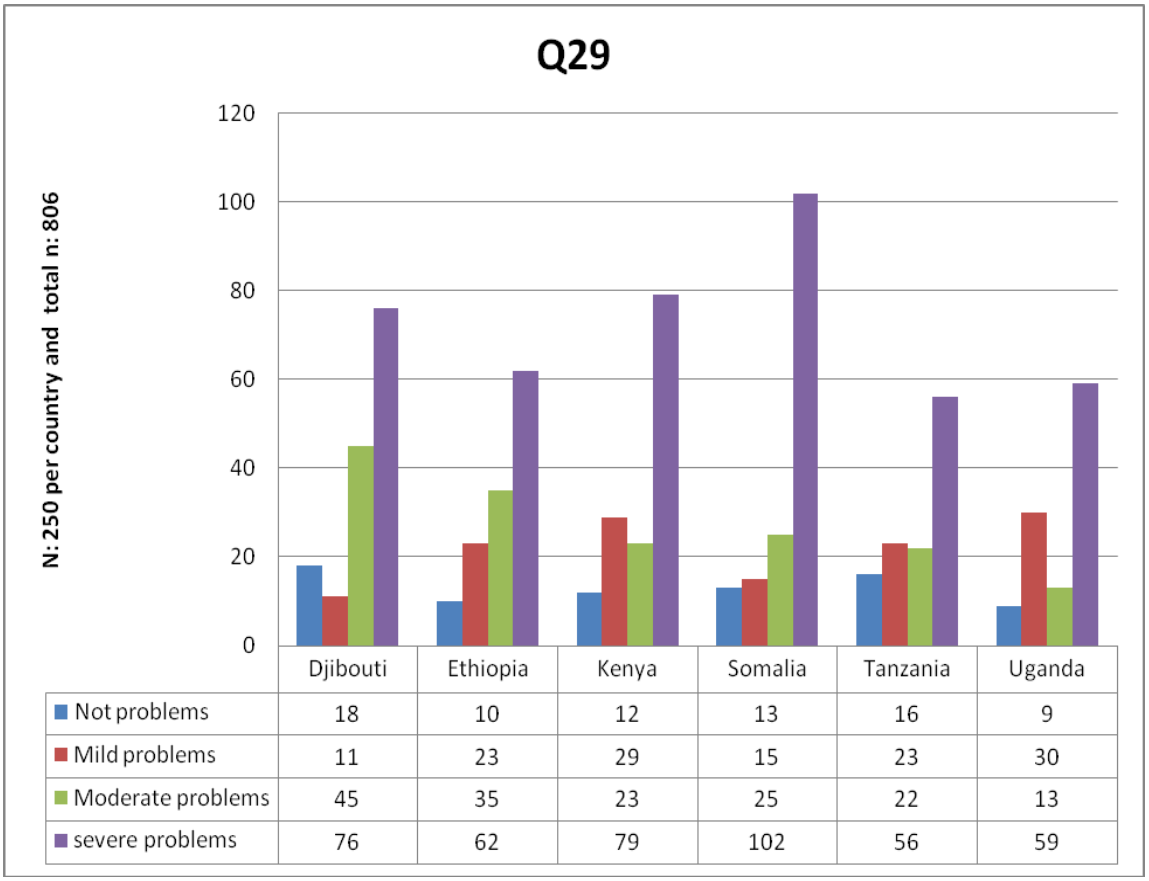


Figure 5.13: Responses to the question regarding the seriousness of medicine counterfeiting

The majority of respodents claimed that there was a severe counterfeit medicine problem in their country compared to a few respodents who reported that the problem was mild (figure 5.13).

However, the evidence suggested that it is a significant problem and is not receiving the attention it deserves. Counterfeit medicines are a much greater problem in less well developed countries. However, it is difficult to extrapolate from these figures to a reliable global estimate. Suggestions that 10–30 per cent of all medicines across all developing countries are counterfeit might therefore be plausible but difficult to verify.

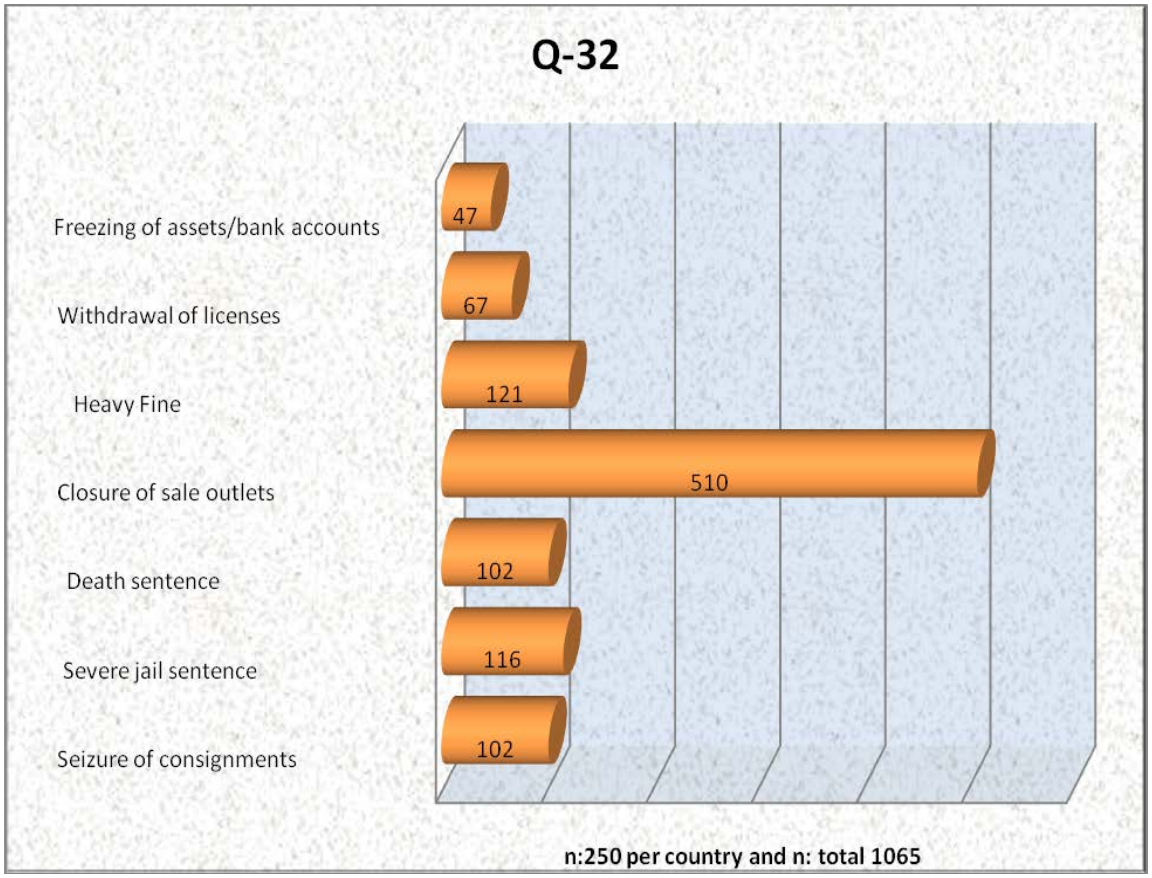


Figure 5.14. Responses to the question asked of 1500 healthcare workers in 6 East African countries "What measures are in place to check the incidence of fake medicines in your country.

Arising from the results presented in figure 5.14, it can be seen that 510 out of 1065 respondents replied that closure of certain selling outlets would reduce the number of illegal transactions with fake medicines whereas 67 out of 1060 respondents indicated that withdrawal of a trade license would stop further illegal trade. Out of 1065 respondents, 102 were of the opinion that a death sentence would definitely reduce medicine counterfeiting, the rationale being that a fake medicine has the potential to kill a patient so the punishment should be the death sentence. On the other hand, 102 of the respondents also indicated that

seizure of consignments would stop the offenders repeating the crime, whereas 121 subjects said that a heavy fine would be as equally effective as other penalties. Only 47 respondents thought that freezing offenders assets and bank accounts would stop reoffending compared to 116 who thought that a severe jail sentence would deter the would be counterfeit seller.

Overall, respondents strongly believed that rigorous measures were needed in order to curtail or completely stop the growth of sales and manufacturing of counterfeit medicines.

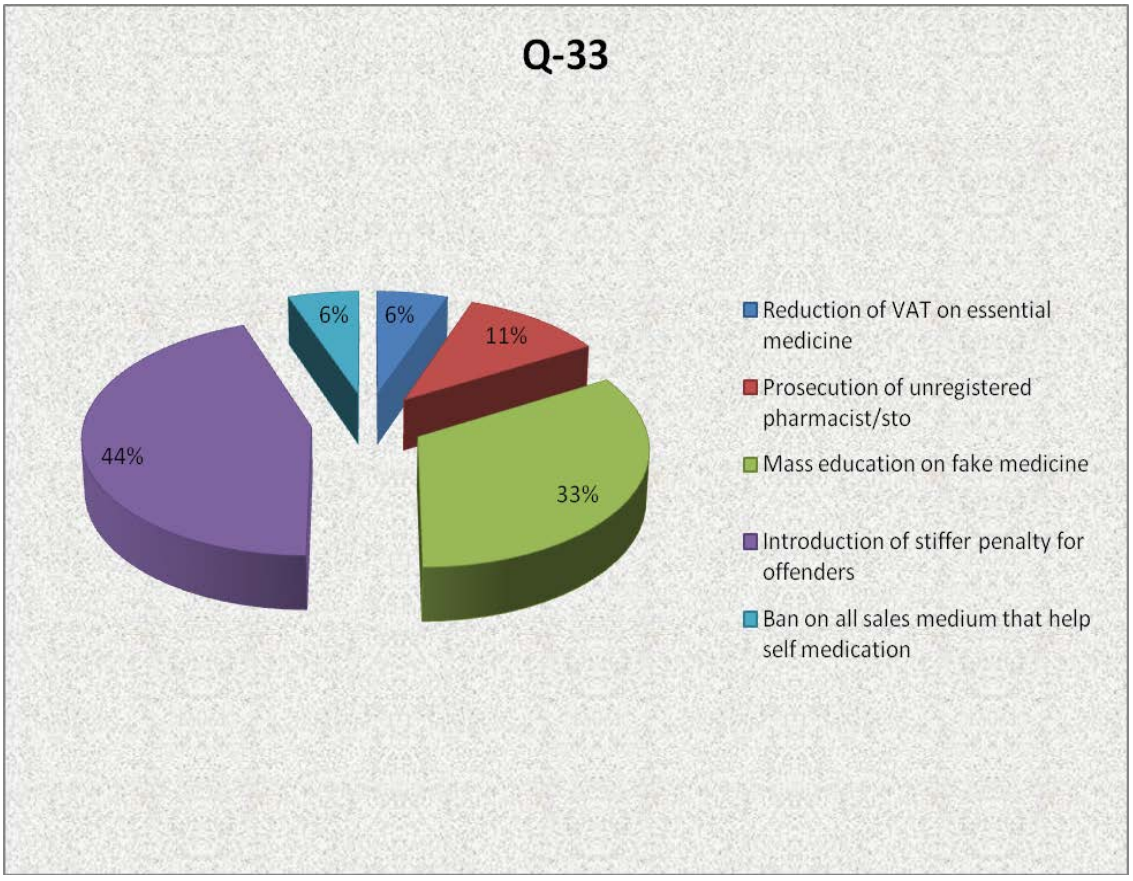


Figure 5.15 showing responses to questions asked 980 healthcare workers in 6 East African countries; "How best to tackle the problem of fake medicines in East African Countries."

The research presented that, 33% of respondents thought that mass education about counterfeit medicines was the best way to combat this problem. The public have a key role to play and there is an educational need, to encourage patients to choose reputable suppliers of drugs and to be aware of the risks of counterfeit medicines.

The largest proportion (44%) of respondents signified that the introduction of stiffer penalties for offenders was the best way to tackle the growth of fake medicines. Successful enforcement calls for collaboration between different agencies, such as customs officials, law enforcement agencies and drug regulatory bodies. Often, these bodies have not previously worked together or are inadequately resourced. The success of INTERPOL's training programmes in East Africa suggests a model by which joint working can be accomplished (WHO, 2010). On a smaller scale, 6% of respondents indicated that a reduction of VAT on essential medicines and prosecution of unregistered pharmacies or stores was a good way to reduce the trade in counterfeit medicines.

Legal systems in East African countries are often not equipped to deal with the extremely serious consequences of counterfeit medicines and penalties for counterfeiters are too light to act as deterrents. Stronger legislation would help empower those who have to deal with purveyors of counterfeits and counterfeiters in the course of their work; namely, the police, customs officials and the judiciary.

(ii) Analysis of possible factors such as national gross domestic product (GDP), degree of regulatory control and level of education on the occurrence of drug counterfeiting in East African countries.

Arising from the analysis and the graph shown in Fig 5.15 below, Kenya is ranked number one in the GDP ranking of East African countries, whereas Somalia is ranked number 6 due to a combination of problems, such as a lack of central government and a long running civil war.

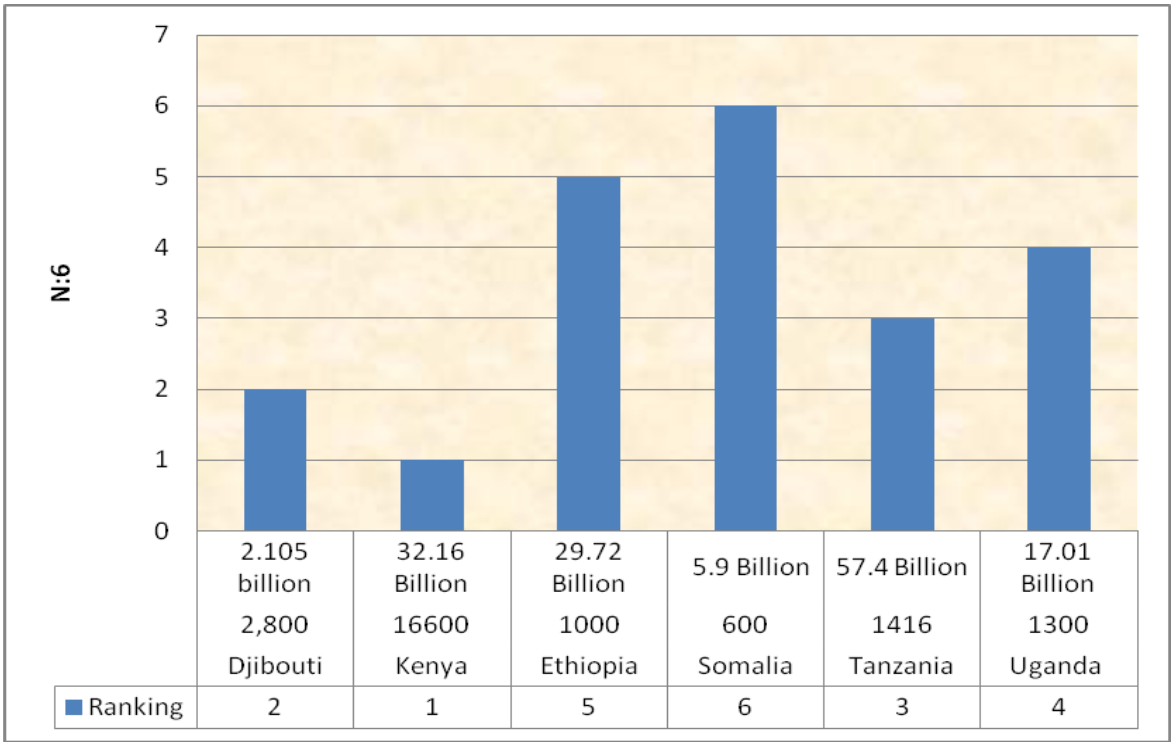


Figure 5.16 GDP per Capita ranking of 6 East African Countries.

Source: (World FactBook: https://www.cia.gov/library/publications/the-world-factbook/rankorder/2004rank.html)

The criteria for ranking of the six East African countries with respect to regulatory control was performed using several parameters which are shown by the scorecard in Table 5.2 below.

Table 5.2 Showing the scorecard used to rank the quality of the regulatory control in 6 East African countries:

	6 East African Countries					
	Djibouti	Ethiopia	Kenya	Tanzania	Somalia	Uganda
Effective Border control of counterfeit medicine (Man Power)	X	X	✓	X	X	X
Healthcare Personnel Awareness (Education level)	X	X	✓	✓	X	✓
Patient Awareness (Education level)	X	X	✓	✓	X	✓
Drug quality testing	✓	X	✓	✓	X	✓
Man Power to police the fake Medicine	X	X	X	X	X	X
Lack of adequate civil liability	X	X	X	X	X	X
Weak or Absent rule of law	X	X	X	X	X	X
Price Control	✓	✓	✓	✓	✓	✓
Taxes and tariffs	✓	✓	✓	✓	X	X
Effective Regulatory agency	X	X	X	X	X	X
Total number of quality measures (10 0ut of 10)	3	2	6	5	1	4

✓: this quality is present X: this quality is not present or lacking

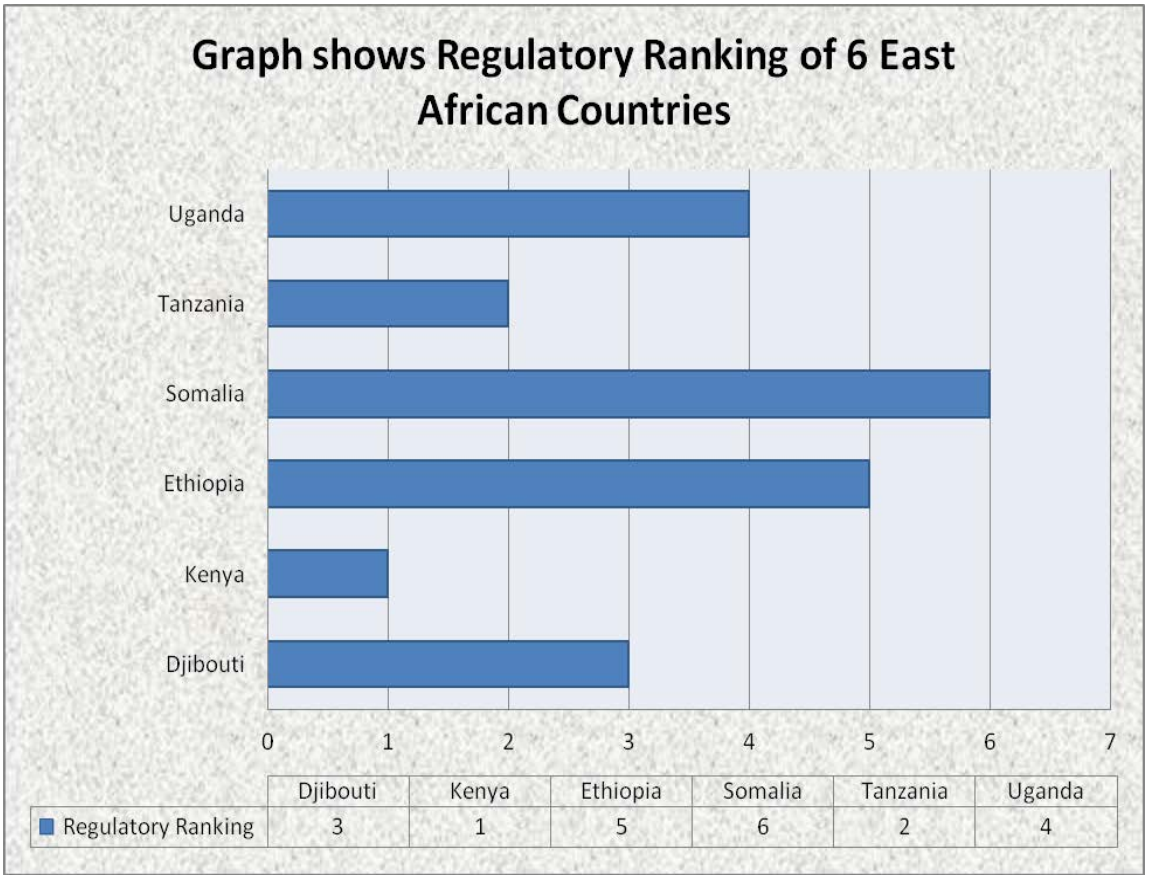


Figure 5.17: Regulatory control ranking of 6 East African countries based on the scorecard shown above

East African economies have large informal sectors, which are not integrated with the formal economy or large business. Research has suggested that promised investments in the region's overwhelmingly poor rural infrastructure is lacking, with the significant exception of agro-industrial firms embracing out-grower schemes or those that otherwise contribute to the coordination of smallholder production and trade. (Booth et al., 2007)

East Africa is a solid economic bloc with a combined population of over 120 million and it is estimated that at least 50% of the populace regularly use medicines. Traders are solely interested in profit, but this is a human rights issue because the possible consequences of the counterfeit business are really immense. Take, for example, a person with severe malaria if

s/he cannot access the genuine drug, then it may be a life threatening situation. Hence, the priority should be to boost weak drug regulatory systems, and provide the resources to help them to routinely track down and test the quality and safety of drugs before they reach patients.

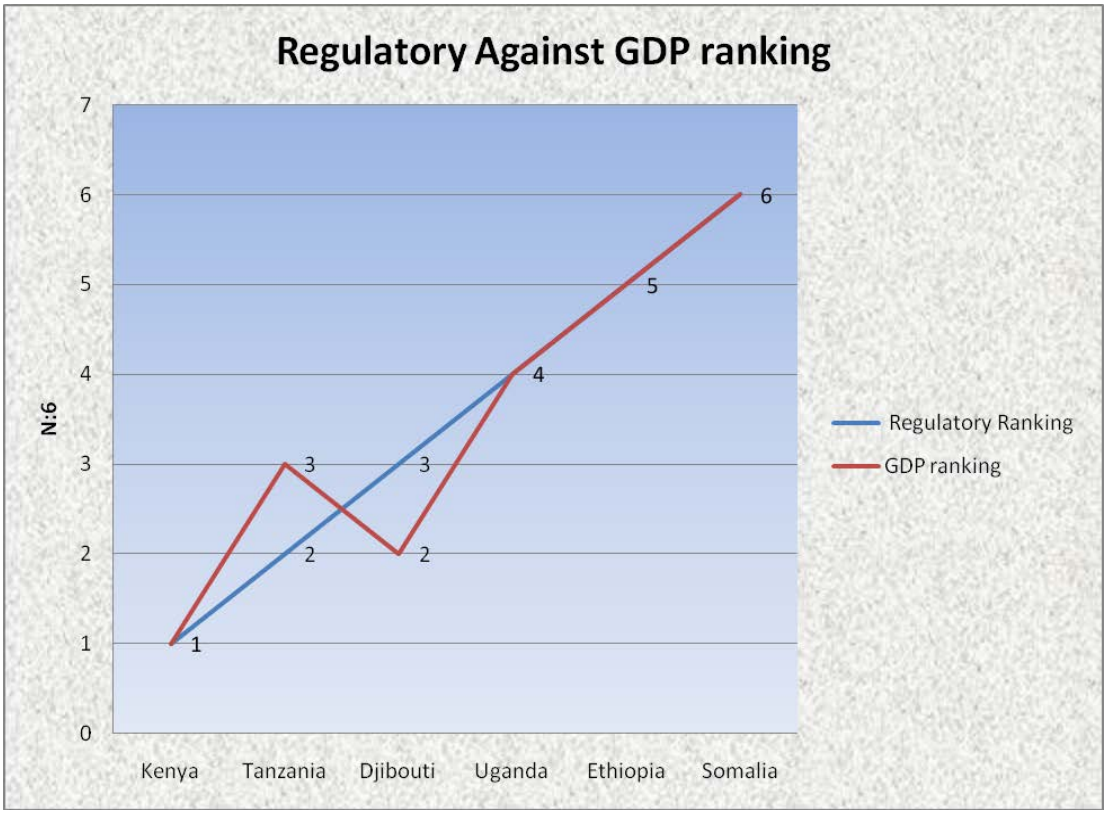


Figure 5.18 showing correlation between regulatory control and GDP ranking in 6 East African Countries

Statistical analysis using the Pearson Product Moment Correlation model showed that there was a significant correlation ($P < 0.001$) between the GDP and regulatory control rankings (derived from the scorecard shown in Table 5.1) as shown above.

Developing countries are particularly vulnerable, in part because regulatory officials often lack the capacity (See figure 5.3) or political will to curb the distribution of fake goods.

Additionally, because legitimate drugs can be expensive, poor consumers also fuel demand by knowingly or unwittingly turning to cheaper counterfeit varieties.

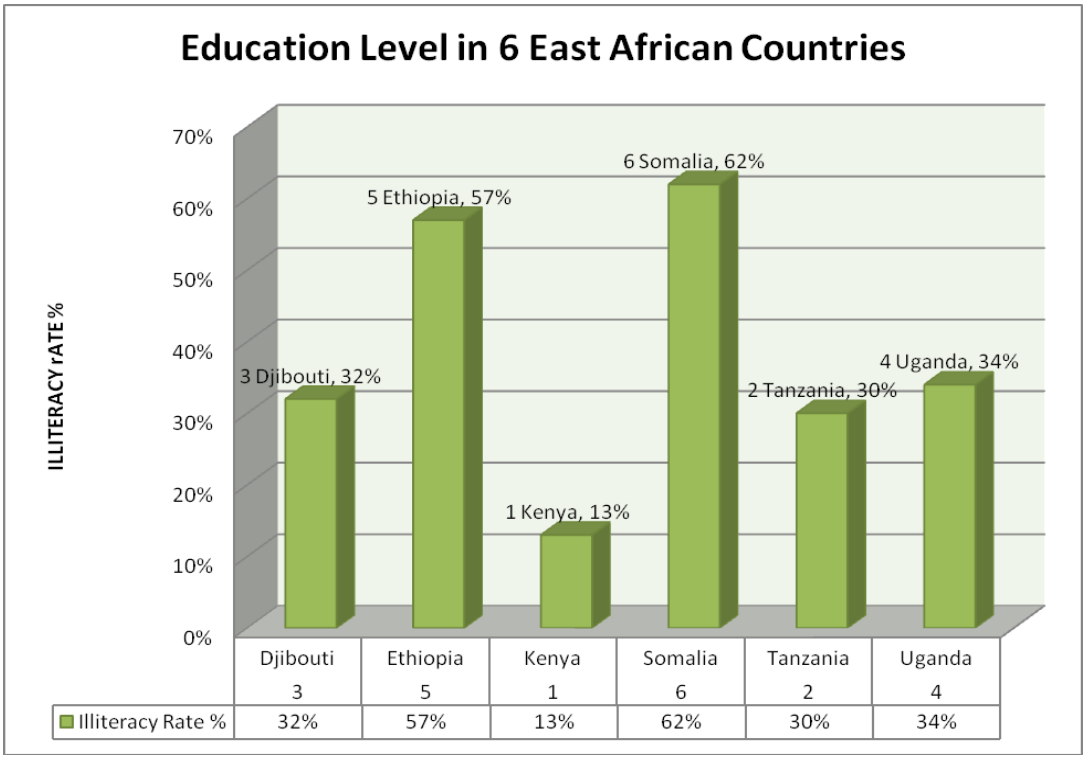


Figure 5.19 showing Illiteracy rates in 6 East African Countries (CIA World Book, 2012).

Illiteracy and access to knowledge are two of the key problems that inhibit socio-economic development in developing countries. Rural people lack the vital information they need to improve their lives, and because most are illiterate, they cannot benefit from many educational methods. Furthermore, lack of electricity and poor roads isolate these regions and further complicate development efforts rural schools aim to teach literacy skills but insufficient funding makes this very challenging. Furthermore, children rely solely on these schools to gain literacy skills because most have illiterate parents.

More than two out of every three pupils who have finished two years of primary school in East Africa fail to pass basic tests in English or numeracy, according to a new report. The survey by (Agwunobi et al., 2009) conducted for a civil society group that monitors educational achievement, reported that despite significant gains in enrolment, pupils did not learn core skills expected at their age and grade level. In part, the difference between Tanzania and the other countries is likely to be driven by the much smaller share of pupils attending private schools, even among the non-poor, suggesting they must be particularly selective, claimed the report. In Kenya, the pass rate in private schools was 83%, compared with 75% in government schools, while in Uganda the gap was 53% to 36%.

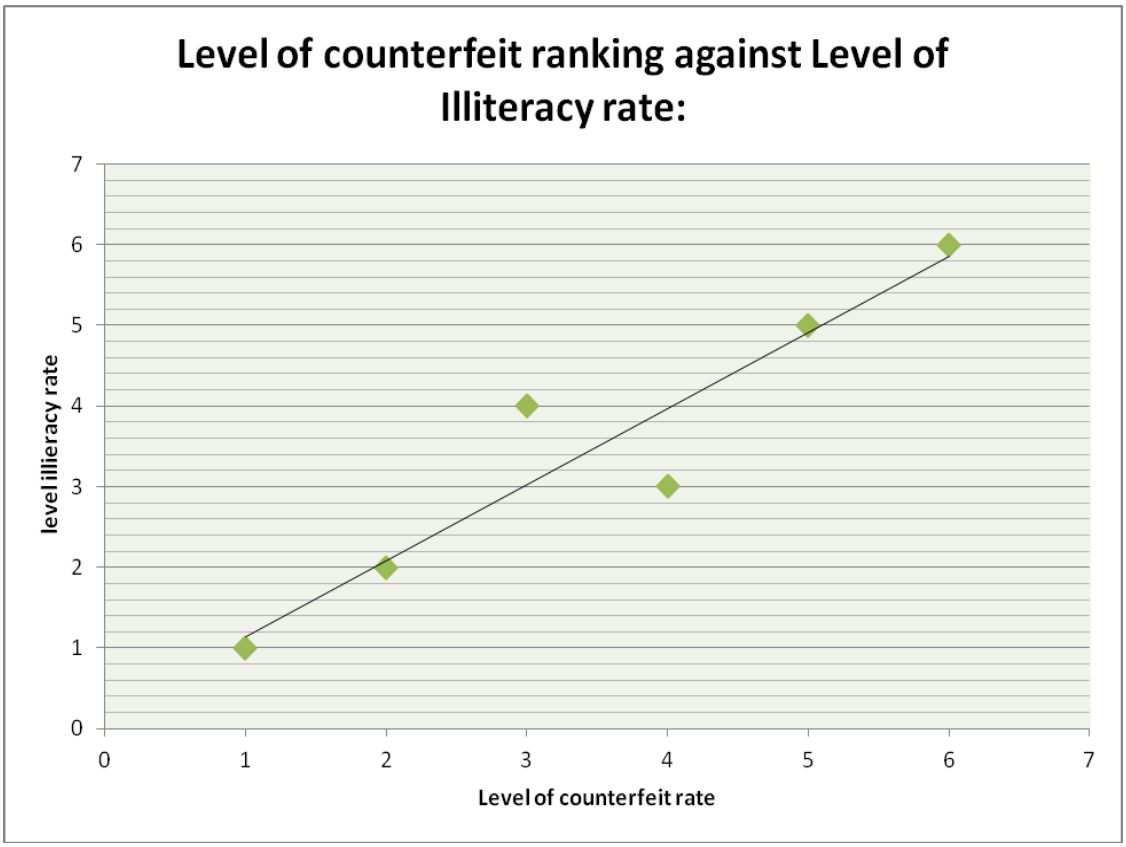


Figure 5.20: Level of counterfeit ranking against level of education in 6 East African countries.

Statistical analysis using the Pearson Product Moment Correlation model showed that there was a significant correlation between the level of counterfeit medicines and education level as shown above (P <0.89) Thus, a positive rank correlation between education level and counterfeiting exists across those East African countries studied though it should be noted with caution that correlation does not establish causation. On average, governments in these developing countries spend approximately 3% of gross national product (GNP) on education (Knight and Sabot, 1990) and spending on combatting counterfeit medicines is largely an unknown quantity.

5.1.9 Discussion:

Poor countries, such as those in East Africa, tend to have highly inefficient, slow and expensive legal systems to enforce the control of medicine counterfeiting and so it even more challenging for patients to be assured of the quality of the medicines with which they are supplied.

The major sources of fake medicines are most likely to be from India and China. One set of figures from the European Commission showed that 75 per cent of drugs being imported from 22,000 small drug producers in India were counterfeit and supplied through informal channels (Bate, 2008). The Associated Chamber of Commerce and Industry of India estimated that this market was growing by 20-25 per cent per annum and in order to have some appreciation of the scale of this problem, India's global pharmaceutical exports totaled $10.3 billion in 2010 (Nair, 2012). A large proportion of these fake medicines are life-saving drugs but surprisingly recreational drugs are catching up and in the future they may be the most common type of counterfeit drug found in East Africa. Nigeria is an example of a

country in West Africa that has been very successful in combating the problem, whereas Kenya and Tanzania are East African countries that are only at the elementary stages of dealing with it (Ahmed and Dillard, 2011).

Pharmacists and other health care workers have reported that some patients acknowledge purchasing medicines without valid prescriptions and through unregistered channels. Given that unregistered outlets – such as roadside hawkers or commercial buses were cited by respondents as the most likely source of poor quality medicines, it is reasonable to conclude that some patients at least may be exposed to these substandard medicines via these routes. Indeed, a preponderance (approximately 70%) of healthcare workers (i.e. pharmacists and nurses and even non-educated healthcare workers) conceded to actually writing prescriptions for patients even though the law in these countries only permits qualified doctors to prescribe drugs and that every pharmacy should have a qualified and registered pharmacist to oversee day to day operations.

Outlets authorized only to sell over-the-counter medicines often illegally stock prescription medicines. For example, in Tanzania, stocking of prescription medicines without a permit is the norm. Additionally, while medicines sold in shops should be packaged and labelled, they are sometimes sold loose as individual tablets. Loose tablets of painkillers and antimalarial medicines were found in 29 and 22 drug stores respectively, often packaged in homemade envelopes labeled with a hand-written note (Goodman et al., 2007)

The number of healthcare workers who indicated that they would not take any action when they discovered a counterfeit medicine is worrying because most citizens access drugs through their neighborhood chemist, particularly when they are poorly educated. The number

of respondents who indicated that they would not report a counterfeit incident to the respected regulatory agency or police may be ascribed to the perception that corruption is widespread in the country, or that reporting the incident could jeopardize their personal safety or economic wellbeing and this was particularly the case in Somalia and Ethiopia.

There are certain factors about medicines in this African region which should be noted. For a predominant proportion of patients, medicines are too expensive thus forcing individuals to search for cheaper alternatives. For some, they are inconvenient prompting the quest for doctor-free alternatives. Counterfeit drugs of every description have an impact on nations of every population and income level. No drug appears to be invulnerable and no country is immune (WHO, 2013).

While data are limited, there is little doubt that counterfeit drugs are an increasing problem globally, with hundreds of thousands of people dying annually as a result. East African countries and all developing countries represent a lucrative market for counterfeiters of medicines and medical devices. Weak economies, increasing prices, a large market, (as the current survey found) and also increased internet connectivity, inconsistent regulatory oversight and a complex supply chain all conspire to encourage those engaged in the manufacture and supply of counterfeit medicines and devices **(**Akunyili, 2011).

Even with reforms, developing countries, especially those examined in this study (East Africa), face significant logistical and social challenges in cracking down on counterfeit production. The existing situation has been facilitated by the lack of coordinated anti-counterfeiting initiatives by various national and multinational regulatory agencies and

professional organizations. Health professionals must take an active role in evaluating and implementing both revised and new responsibilities that further protect patient safety

The problem of counterfeit medicines in the world's pharmaceutical drug supply is growing and will not disappear in the foreseeable future. However, as discussed in the last two chapters, there are measures and tactics that can facilitate efforts of the pharmaceutical industries and governments to combat this serious problem.

Given the lack of previous hard data on the proportion of fakes and the patchiness of precise information on the incidence of disease in East Africa, any attempt to estimate the impact of fake medicines is inevitably as much art as science. Nevertheless, the scale of the problem is such that estimates serve a useful purpose of calling attention to the issue and as long as they are approached with caution, then approximations have some value. The likely impact of counterfeit medicines on mortality in East Africa is overwhelming especially in a country like Somalia where there are governmental problems and a long running civil war. In addition to mortality, fake medicines also have an impact on morbidity though assessing such an impact is equally difficult.

If private companies are able to implement solutions to the problem of identity preservation and quality assurance, such as those described above, they would then have strong incentives not only to advertise their products but also to educate the public about the nature of the problem. In addition, there may be a role for third party groups, such as health advocacy NGOs. Such groups have done important work educating the public in Sub-Saharan Africa about the problem of HIV-AIDS. In view of the scale of the problem of fake medicines, it seems plausible that such groups could be persuaded to get involved in proactive education campaigns describing the nature of the problem and the need to ensure that medicines are

supplied from reputable sources and are, so far as can be ascertained, what they say they are (WHO, 2010).

Counterfeit drugs on the market may well amplify any humanitarian disaster and the poorest countries are most likely to suffer from a lack of legitimate medication in such a crisis especially since access to services is severely restricted. The producers focus on profit while exploiting the limited availability of health services to the poor.

Reports of counterfeit pharmaceuticals in Africa indicate that there are a wide variety of detrimental effects. In addition to poor public health, these include lost revenues to firms that might otherwise be used to develop newer and better products, lost taxes to governments responsible for public health, additional costs firms and governments incur to protect supply chains from counterfeit products. This results in disincentives to foreign investment, and consequent loss of jobs and economic opportunities.

WHO launched a taskforce in late 2006 to fight a thriving multimillion dollar illegal trade in counterfeit drugs, vaccines and other medical products and this was called the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) its aim being to put a stop to the deadly trade in fake drugs. However, some NGO's and countries like India, Brazil do not agree with the work offered by IMPACT. Its areas of focus are:

- Legislative and regulatory infrastructure
- Regulatory implementation
- Enforcement

- Technology

- Communication

There is need to strengthen the theme that there should be some world treaty organization to counteract with the global health care threat of counterfeit medicines (WHO, 2006a).

In an ideal developing world, everyone would obtain their pharmaceuticals from reliable pharmacies, which would in turn be sourced from reputable distributors, who would use dependable logistics companies, and so on back to the manufacturer. Meanwhile, at each point in the chain, the pharmaceuticals would be stored and handled according to standards established by the manufacturer and their identity through the chain secured using technologies such as those described above.

Unfortunately, we do not live in an ideal world and at least for the time being, many patients are likely to continue to source their medicines from non-qualified street hawkers. These sellers have usually purchased the medicines from distributors that move them from place to place in small vehicles at ambient temperatures approaching 40^{C} for extended periods of time. Furthermore, these distributors invariably purchase their medicines from wholesalers, many of whom store medicines for months in warehouses lacking air conditioning and who often take consignments from intermediaries of dubious repute. Hot and humid climates in these countries pose serious problems, with at least some medicines showing decreased concentrations of the active ingredient upon testing (Hogerzeil et al., 1992)

Some respondents who took part of this study recommended that medicine counterfeiting should be legislated as a specific crime against humanity. Currently, a crime against humanity is known as ‘extermination’ which is defined in international law as ‘the intentional infliction of conditions of life, inter alia the deprivation of access to food and medicine, calculated to bring about the destruction of part of a population’. No instance of medicine counterfeiting has ever exterminated a population, but even so, it is highly notable that within the definition, denying access to a medicine can be considered as a component method of attacking a civilian population, and may be at the root of a crime against humanity. Hence, denying access to a medicine is exactly what counterfeiters do when they supply a fake medicine lacking the therapeutic qualities of a real medicine.

In summary, while there is no crime against humanity specifically for medicine counterfeiting, current legal doctrine defines it as possibility. However, in reality, to crack down on the number of counterfeit drugs and irrational drug use in East African countries, the awareness of healthcare workers and patients must be increased and patients in particular, must be educated on the potential dangers of self-prescription. Some pharmacists and outlet managers should also be re-educated and be made more aware of the importance of buying and distributing only high quality drugs that have not passed their expiry date or are discernible counterfeits.

The problem of counterfeit drugs should be discussed overtly by concerned professionals and a good example of this was given by a meeting held in Nairobi, Kenya, in 1985. However, since that time, the counterfeit market has rapidly expanded, largely as a result of the widespread use of internet marketing which is increasingly accessible especially in larger cities. Counterfeit drug rackets are most common in regions where the regulatory and

policing infrastructure for drug control are at their weakest. Thus, one of the key battlegrounds in the fight against organized counterfeit crime is Africa as a whole, where drugs are counterfeited on a huge scale (Newton et al., 2010).

Evidence from this study is exceptionally alarming because it discloses to some extent, the size of the medicines counterfeiting challenge in East Africa, the magnitude of which needs to be fully appreciated by healthcare professionals. Therefore, the preventive role of healthcare professionals has to increase and continue to develop for the benefit and safety of patients. This research survey may possibly lay some groundwork for further studies on the prevalence of counterfeit drugs in East Africa and neighbouring countries. By assessing the scale of this phenomenon in East Africa, an effective collaboration in detecting and preventing counterfeit medicines is needed. Sharing responsibility by setting up an anti-counterfeit network to include governments, international institutions, pharmaceutical companies and other interested bodies, would be helpful in decreasing the phenomenon of counterfeit medicines in this region (WHO, 2006a). This was identified as a major issue for the future by nurses and physicians in the current study.

Additional data gathering and analysis revealed significant rank correlations between GDP, regulatory control and levels of education across countries in the region respectively versus counterfeiting. These correlations were interesting and though their outcomes were not surprising it should be emphasised that they did not establish causation

5.1.10 Summary of Chapter 5:

- This Chapter reviews the extent of the counterfeit drug trade in East Africa and what aspects of it were particularly unique.

- The Survey found that the majority of the faked medicines were drugs intended to treat diseases, which were common to the area, like malaria and infections.

- The survey also indicated that, the counterfeit problem was more pronounced in countries where the manufacture, importation, distribution, supply and sale of drugs were less regulated and enforcement was weak.

- According to the report the prices of the medicine are too high and patient complain and find to buy medicine unapproved stores.

- This survey also found that citizen of these countries would like to see stiffer penalties to be introduced such as death, prison and closure of their outlets and stores for those violating the drug laws.

6 CHAPTER SIX:

6.1 GENERAL DISCUSSION

The main objective of the questionnaire surveys conducted in this thesis was to provide an overview of the safety of medicines in developing countries with respect to the problem of counterfeiting. The data collected from the (1065) respondents in East African and (1115) Middle Eastern countries (total n: 2180) confirmed that, medicine counterfeiting is a substantial problem. Systematic records regarding the global incidence of counterfeit medicines were not abundant in the literature; consequently, a re-examination of individual reports on medicine quality with respect to counterfeiting was timely. The current literature evaluation presents some additional information on counterfeiting in East African and the Middle East countries. While it is anticipated that drug quality is often compromised in developing countries, the current research does pinpoint the level of perception and some of the likely causes of the problem. Although it is a possibility that the research protocol and the questionnaires circulated in this study may be a valuable starting point for others mounting subsequent work in this field.

Hence, it is important to bear in mind that there is increasing awareness of escalating medicines counterfeiting in industrialised countries as the current study found (see figures 4.12 and 5.13) in addition to those in the developing world and the legal supply chains within these nations receive increased pressure every year. This study showed that the Middle Eastern respondents recounted only a mild counterfeit medicine problem in their country compared to East African respondents who reported that the problem was severe (see figures 4.14 and 5.13).

The majority of the respondents were owners of pharmacies or clinics and the rest of those surveyed were mainly employers or relatives of the owners. In the context of the current

study, the knowledge and perception of medicines quality among suppliers and consumers revealed that sellers often lacked adequate scientific knowledge. Thus, still the findings highlighted the fact that, in this area of Africa and the Middle East, there are many pharmacies working without an appropriately qualified pharmacist in charge. This outcome is significant because people's rights to health include the right of access to a reliable standard of health care and an assurance that medicines they receive are not only genuine but also safe, effective, of good quality and affordable.

Healthcare workers indicated that due to the rapidly rising cost of healthcare and the price of medicines, there was mounting concern in East African and Middle Eastern countries since patients invariably had to pay for healthcare commodities such as medicines. Hence, those patients visiting clinics were limited mainly by the numbers of the patients seeking help from traditional healers and herbalists.

Although it is challenging to evaluate the extent to which patients are exposed to counterfeit medicines, it is an even greater test to establish how many of the adverse events reported are linked to counterfeit drugs. Patients in East Africa and the Middle East do not tend to question whether the drugs they receive from a pharmacist or healthcare specialist are legitimate or that they will cure disease and alleviate symptoms rather than causing serious harm or even death. Therefore, the survey found that patients generally did not report to their local pharmacy or clinic if the medicines were not effective or that they did not help them.

The view of those surveyed indicated that in East Africa, at least 70% of the drugs distributed were thought to be counterfeit and in the Middle East, more than 60% of medicines issued

were considered fake. These figures are alarming to say the least and should raise concern among the authorities of the countries in question.

Whereas substandard medicines have been with us since they were first compounded, they are an inevitable consequence of inadequate pharmaceutical industry regulation and inspection in much of the developing world. For example, substandard antimalarials were identified in Yemen, Cameroon, Nigeria, Kenya, Senegal, Uganda and Tanzania (Abdo-Rabbo et al., 2005)

The present survey found that from a total of 2180 respondents in 7 Middle Eastern and 6 East African countries there was an overall opinion that at least sixty per cent of patients had been supplied with counterfeit drugs. This was in comparison with 5% of patients who had received a counterfeit prescription while only 1% believed that they had been exposed to a counterfeit drug according to a previous marketing survey of more than 5000 consumers across five European countries including the UK. (Jackson et al., 2010)

The present study reflected the view that most classes of therapeutic drug were counterfeited. When examining the differences in the prevalence of fake medicines between regions within these developing countries, it should not be forgotten that, there is an uneven distribution of governmental control (i.e. policing) in urban compared to rural areas as suggested by the current findings.

An alarming trend for industrialised countries is the fact that they appeared to be more heavily targeted by drug counterfeiters. The numbers of seized goods as well as the counterfeit cases in different well developed countries have undergone a fast rise leading to

the assumption that the magnitude of counterfeiting on their markets has risen considerably (FDA, 2011).

Furthermore, the gap between developed and less developed states concerning the prevalence of counterfeit drugs within their markets remains relatively large. The former have taken clear measures to maintain the incidence as low as possible inside their borders. The WHO has been playing a clear role in aiding countries in their anti-counterfeit efforts, and the World Trade Organization also helps to regulate international drug trade. All these are strengths that can be utilised in combating the global problem (WHO, 2010).

This Study also provides more specific data on medicine safety with regard to counterfeiting in East African countries and the Middle East. Although it is evident from those interviewed that East African countries were affected more than the Middle East and this is due to the different rank of socio-economic factors as seen in the survey. Hence it is very difficult to make a sound judgment about counterfeit medicines in developing countries but within this context, it is recommended that priority to be given to heavier policing of counterfeiting.

The range and geographical diversity of these countries were comparable and there was little variation between them in terms of the number respondents. The majority of respondents in both East African and the Middle Eastern countries were in agreement with the available literature which specified that most patients bought their medicines from unapproved outlets such as kiosks, coffee shops or corner shops (see figures 4.8 and 5.7).

The challenges of addressing how to combat drug counterfeiting in East African and the Middle Eastern countries were not comparable. Twenty-two per cent of Middle Eastern respondents expressed the opinion that the death sentence for offenders would reduce

medicine counterfeiting whereas 48% of East African respondents were in favour of closure of offender's outlets (see figures 4.15 and 5.13). The study also identified major differences between the two continents regarding the best way to combat this problem. Thus, 11% of respondents in East African countries believed that reducing VAT on essential medicines compared to only 3% of respondents in Middle East countries would contend with the problem. However both East African and the Middle Eastern respondents agreed that one unequivocal measure to tackle and reduce the real threat was through mass education (see figures 4.16 and 5.14).

The results also indicated that drugs counterfeited and supplied in villages received little attention compared with those counterfeited and distributed in the big cities in both East African Countries and the Middle East (see figures 4.11and 5.10) and this is not surprising since monitoring and potential control in outlying regions is much more likely to be negligent.

Additionally, and as predicted, the survey findings also showed that respondents felt that prescribing and dispensing as opposed to uncontrolled purchase, were the two most important safety aspects of access to medicines in the majority of East African and the Middle Eastern countries . In the light of these survey results, it is recommended that strengthening medicine regulatory authority control, promotion of national awareness of the problem and obtaining a rigorous resolution to fight counterfeiting are perhaps the crucial primary tasks.

However, the most common deficiency of information the study identified was a lack of pharmaceutical communication in developing countries. Consequently, pharmaceutical

companies need to open the lines of communication with their sources of information to keep track of underground counterfeiting operations and should disclose all information to agencies such as Interpol or to the national police force of any country in which companies suspect counterfeit versions of their products are being sold. Without the pharmaceutical companies' cooperation, it will be very difficult to confront offenders and penalise them (Gupta et al., 2012).

The graphs in chapters 4 and 5 regarding the plots of GDP against education and counterfeiting clearly demonstrate that GDP per capita is positively correlated with level of education and any presence of counterfeiting in these developing countries. Countries with an abundance of natural resources tend to do better than countries with less resource wealth.

Somalia has the lowest GDP per capita of all those countries sampled and it is one of the nations with the highest levels of medicines counterfeiting. The current study demonstrated that GDP influences not only education but other resources such as healthcare expenditure. While the correlation between GDP and counterfeiting is strong, education and regulatory control can be equally powerful though the causality link remains unsettled.

In oil rich countries like the Gulf States, the labour income growth of those with tertiary education exceeds GDP growth, largely as a consequence of a strong shift towards higher skills and the impact of the global economic crisis on overall economic activity in these countries. Lynn and Vanhanen (2012) have convincingly established that national IQs correlate positively with GDP, education, and many other social and economic factors. Once more however, the direction of causality still remains debatable.

6.1.1 Solutions and Recommendations:

There is no standard solution applicable to all countries to eliminate medicine counterfeiting. Each country has to develop a strategy based its own circumstances taking into account the available infrastructure as well as human and other resources. This should be part of the overall national drug quality assurance system.

Harmonised efforts to eradicate trade in counterfeited medicines will be severely hampered by corruption especially in East Africa. Governments must initiate a commitment to protect their citizens by rooting out officials or business leaders involved in the manufacture or trade of counterfeit medicines. In addition, agencies must ensure that their enforcement activities are not compromised by corrupt officers (Castell and Brickwood 2009).

The importance of raising public awareness about acquiring medication only from known sources (pharmacies) and also the exposure and reporting of names of individuals and companies involved in trading fake drugs must be stressed. As an example of this, the Saudi Food and Drug Association has requested all drug companies to report any counterfeited drugs and provide SFDA with samples along with the necessary documentation (SFDA, 2011).

Governments should contest such national problems as counterfeiting as part of their responsibilities. It should be recommended that all African countries establish a central drug administration which would regulate the licensing of all drugs in lieu of the current licensing system whereby state drug regulatory agencies allow the manufacture of drugs which are not approved. Stiffer penalties such as death, 10 years minimum prison sentence and higher fines should be recommended for those violating the drug laws (Ramchandran, 2003).

Accepting that counterfeit drugs are a global and persistent problem, prompts the concept that it can only be combated by international collaboration. During 2006, in the WHO international conference on (Combating counterfeit drugs: Building effective international collaboration') held in Rome, it was declared that the WHO should lead the establishment of an International Medical Products Anti-counterfeiting Taskforce (IMPACT) of governments, non-governmental and international institutions aimed at encouraging and coordinating anti-counterfeiting initiatives.

In February 2004, the U.S. FDA issued a report entitled 'Combating Counterfeit Drugs: A Report of the Food and Drug Administration (FDA, 2004). This report identified six critical measures to combat fake drugs. This included securing the actual drug product and its packaging, securing the movement of the product through the drug distribution chain, enhancing regulatory oversight and enforcement, increasing penalties for counterfeiters, heightening vigilance and awareness of counterfeit drugs and increasing international collaboration (FDA, 2004). The U.S. FDA also recommended the use of Radio Frequency Identification (RFID) tags started on 2007 and it was suggested that the drug supply chain in the U.S. would be RFID-secure following its introduction (FDA, 2004).

Legal frameworks are under revision to boost anti-counterfeiting measures in many countries including European Member States, India and the United States. In Britain, there are proposals for the introduction of a charge of corporate killing' for companies who have contributed to the deaths of customers and this could also apply to drug companies if they did not take reasonable steps to warn the public of a fake product . Some countries such as Vietnam, the United Arab Emirates, Oman, Bahrain, Kuwait and Qatar even have provisions

of death sentence as punishment for counterfeit drugs related offences (Anonymous, Lancet, 2003).

Many research-based companies are working through the Pharmaceutical Security Institute (PSI), a counterfeit intelligence forum that conducts worldwide investigations. Information on illegal activity obtained by PSI is provided to governments and international agencies, which are responsible for proceeding against counterfeiters (PS1 Web site).

The International Pharmaceutical Federation (IPF) and International Federation of Pharmaceuticals Manufacturer Association (IFPMA) are actively involved as observers of WHO activities aiming to establish guidelines and rules for policies against substandard medicines (WHO, 2010).

The German Pharma Health Fund (GPHF) has developed basic training methods for about 35 commonly used essential medicines in their finished dosage forms. International agencies like Interpol, the World Customs Organization (WCO), the World Intellectual Property Organization (WIPO) and the International Chamber of Commerce (ICC) have contributed significantly in addressing the problem. More and more pharmaceutical companies have adopted sophisticated techniques like holograms, watermarks and tamper proof packaging to safeguard their products (Parry, 2005).

An international coalition is working for consumer awareness and also to educate the end users to differentiate between genuine and fake versions of drugs. The overall goal of WHO support has been to promote the regular availability and accessibility of affordable essential medicines of good quality. WHO provides support to countries to strengthen pharmaceutical legislation, Good Manufacturing Practice (GMP), national drug regulatory capacity and

performance, to promote information exchange among drug regulatory authorities and to strengthen drug procurement (WHO, 2002). Update references needed.

The Malaysian ministry of health has also introduced such holograms on their pharmaceutical products as a security measure. These holograms are tagged and registered with a security device known as Meditag. Each Meditag has a unique serial number and can be scanned with a special device to verify its authenticity. However, these holograms are not too dependable as it is possible to copy them. Hence, they are not adequate in stopping counterfeiting (Perry, 2005). Another technique mentioned previously is radio frequency identification or RFID which contains a chip with an antenna affixed to the drug packaging.

The exact location of the drug can then be detected using radio waves. This technology is not cheap, but is said to be one of the most effective techniques developed so far to uproot and stop counterfeiting. Some pharmaceutical companies such as Purdue Pharma and Pfizer have already employed RFID technology to trace their respective products, OxyContin and Viagra (Parry, 2005).

6.1.2 Mass Education and Raising Awareness:

If private companies are able to implement solutions to the problem of identity preservation and quality assurance, such as those described above, they would then have strong incentives not only to advertise their products but also to educate the public about the nature of the problem.

In addition, there may be a role for third party groups, such as health advocacy NGOs. Such groups have done important work educating the public in Sub-Saharan Africa about the

problem of HIV-AIDS. Given the scale of the problem of fake medicines, it seems plausible that such groups could be persuaded to get involved in proactive educational campaigns describing the nature of the problem and the need to ensure that medicines are from reputable sources and are genuine. A qualitative study of Sudanese policy makers and pharmacists suggested that awareness of counterfeit is lowest among the poor and people living in remote areas (Alfadl et al., 2013)

Other private companies might also be encouraged to join such campaigns. Manufacturers of retail goods, for example, are acutely aware of the problems created by fakes, so they might be willing to support a general campaign educating the public about the importance of buying the authentic medicine. (Harris et al., 2009).

6.1.3 Limitation of the Study:

There were limitations in the current study, which could be classed into three categories: the lack of localized funding in rural regions for manpower restricting data acquisition, travel difficulties and security issues.

One of the main limitations regarding safety of medicines in developing countries is the lack of funding and manpower, which in this study, restricted the availability of data particularly in the more rural regions. Therefore, it may also have skewed the findings towards the urban areas and it would have been advantageous to obtain data from every urban rural area in East Africa and Middle East countries that was surveyed. However, the impact was probably minimal due to the complete data set that was available and easily obtained from other cities and rural areas.

In order for questionnaires to be practical, a good response rate invariably necessitates it being of reasonable length. This tended to moderate the possibility of evaluating certain components in greater depth. On the other hand, this study covered the majority of relevant topics and is one of the first studies to identify the perceived severity of medicine counterfeiting in the developing countries of East Africa (especially Somalia).

In Somalia and Ethiopia above all, travel between cities, and even within cities, was very difficult and hazardous because of civil wars involving the Somali Transitional Federal Government, the Eritrean-Ethiopian conflict and inherent ongoing inter-tribal clashes. This limited free movement within these two countries, though it was a definite positive aspect that local agents could be enlisted to administer the questionnaires.

The level of government corruption was also part of the study limitation and this made it additionally challenging to collect data in a timely manner from government hospital pharmacists expecting to receive bribes. Many health care workers were concerned for their safety and were reluctant to answer the questionnaires. However, it was made perfectly clear to respondents at the outset that the questionnaires were confidential and intended for research purposes only.

6.1.4 Future Work:

Given that the topic of safety of medicines with respect to counterfeiting in developing countries is likely to remain a key issue for the foreseeable future, it would be advantageous and beneficial for prospective studies to use similar study instruments or adapted versions for future work. Although it might not be feasible to curb counterfeit medicines completely, it

should be possible with the right will and appropriate measures, to lower the rate of counterfeiting in developing countries considerably.

However, it is clear that the aim and objectives of this study have been achieved and the findings have demonstrated the potential for combating counterfeit medicines both in the Middle East and East Africa. This may also contribute to other similar initiatives in other regions of the world such as Latin America and Far East Asia where counterfeiting is a problem.

As mentioned earlier, more research is needed to quantify the effects of trade in counterfeit medicines, to support advocacy and to inform policy making. Without good data, it is also hard to plan education or intervention campaigns or to know what works. There is certainly a need for testing and validation of devices for assessing drug quality in the field. Health systems research may also help to identify ways in which prevention, monitoring and enforcement can be integrated into healthcare delivery (Hyder et al, 2008).

The studies where analysis of GDP against drug counterfeiting along with education and regulatory control are useful as a prompt to those countries where any upgrading of GDP occurs since a proportion of the subsequent wealth benefit could be invested in the controlling measures.

6.1.5 Conclusions:

Therefore, I would like to conclude that, counterfeiting of medicines is of international concern. There is therefore, a need to implement intercountry, sub-regional and regional cooperation to combat counterfeiting of medicines. Counterfeit drugs have a long history. As early as 400 B.C., there have been warnings of their existence (WHO 1999) and Dioscorides,

a Greek physician, pharmacologist and botanist who lived from 40–90 AD, wrote in his 'Materia Medica' about the detection of counterfeit drugs (WHO, 1999). The threat of counterfeit medicines therefore is hardly a new one and has persisted through the ages. The 'modern' issue of counterfeit medicines emerged in the 1980s when more and more member states of the WHO reported the incidence of medicine counterfeiting. Hence it was first brought to greater attention in developing countries through an international conference on the rational use of drugs in Nairobi 1985 (WHO, 2003).

Both branded and generic drugs are likely to be subject to counterfeiting, however, a patented high-priced medication is more likely to be faked in either an industrialised or developing country (Harris et al., 2009). The difference between these types of country will depend very much on the level of drug regulation control and enforcement as well as the prices in the legal supply chain.

In most industrialised countries like the USA, Japan or members of the EU, the extent of drug counterfeiting is below 1% of the share of the total medicines market value. An exemption is the former Soviet Union where up to 20% of the market may consist of counterfeit drugs (WHO, 2010). In contrast, in extensive parts of Africa, the Middle East and Asia, between 10-30% of available medicines are fakes and this figure could be even higher (WHO, 2010).

The data presented in this thesis suggests that 71% of medicines available in East African countries, especially in Somalia, are counterfeit and this largely due to a lack of regulatory control. Both in developed countries and those that are developing (especially the Middle East) it is often lifestyle medicines such as slimming agents and anabolic drugs that are faked. The best known symbol of counterfeit medicines is of course, the widely known drug for

erectile dysfunction ‘Viagra®’. In developing countries, however, it is often more crucial medicines that are faked. Examples include antibiotics and drugs against very prevalent diseases such as malaria, HIV/AIDS or tuberculosis (Kelesidis et al., 2007).

Therefore it may be concluded that the problem in developing countries is with all substandard medicines and not just counterfeits. What is needed first and foremost is for each country to have a medicines regulatory framework which:

Prohibits distribution of any medicine unless it is first licensed in that country.
Only issues licenses to a particular person or company who will be held responsible for the quality of that particular product.
Restricts the importation/distribution of a medicine to the individual or company who holds the license.

Hence, the aim of this project was primarily to increase awareness in developing countries (especially East Africa) in terms of the perception of the growing market in counterfeit medicines and the public health risks associated with this illegal practice. Moreover, the current findings are only a starting point and larger studies regarding medicine counterfeiting in different developing countries are needed alongside strategies to combat the problem.

7 REFERENCES:

Abdo-Rabbo, A., Bassili, A., Atta H. (2005). The Quality of antimalarials Available in Yemen. Malaria J. 4:28.

Abu Dhabi-Gov, (1995). Book 8 Pharmaceutical Profession and Medicines Pages 3 http://www.haad.ae/haad/Portals/0/Health%20Regulation%20Laws/Book8_En/index.html#/3/zoomed (accessed 01/02/2013)

Ahmed Abushouk, L and Dillard M (2011) Health and sickness in Africa: medicine that kills. pp 1-26. http://digitalcommons.providence.edu/cgi/viewcontent.cgi?article=1010&context=auchs (accessed 10/10/13)

Agwunobi, J., London, P. A. (2009). Removing costs from the health care supply chain: lessons from mass retail. Health Affairs 28:1336-1342.

Akindeinde, O. (2010). Attack simulation and threat modelling: online Logas: free software foundation: Available from: http://www.docstoc.com/docs/34284016/attack-simulation-and-threat-modeling.

Akunyili, MT., Garcia-Buitrago, J., MacIntyre, J., Levi, J., Rocha Lima, C. M. (2011). Sustained response to FOLFOX and Bevacizumab in metastatic bronchial carcinoid - A case report and review of the literature. J Gastrointest Oncol. 2: 117–121.

Alan, S. Counterfeit drugs a menace keeps growing.US Pharmacist Vol. No: 28:01: Jan 15 2003

Alfadl, A. A., Hassali, M. A, Ibrahim M. I. (2013). Counterfeit drug demand: Perceptions of policy makers and community pharmacists in Sudan. Res Soc Admin Pharm. 9:302-10.

Aldhous, P. (2005). Murder by medicine. Nature. 434:132–136.

Amin, A. A., Snow, R. W., Kokwaro, G. O. (2005). The quality of sulphadoxine-pyrimethamine and amodiaquine products in the Kenyan retail sector. J Clin Pharm Ther. 30: 559–565.

Hall, K. A., Newton, P. N., Green, M. D., De Veij, M., Vandenabeele, P., Pizzanelli, D., Mayxay. M., Dondorp, A., Fernandez, F. M. (2006). Characterization of counterfeit artesunate antimalarial tablets from south east Asia. Am J Trop Med Hyg. 75: 804–11.

Anon. (2000). Guidelines for planning effective surveys (Online) reading: Statistical service centre: http:// www.reading.ac.uk/ssc/ (accessed on 01/4/2009).

Anon. (2001). Approaches to the analysis of survey data (Online) reading: Statistical service centre: http:// www.reading.ac.uk/ssc/ (accessed on 02/4/2009).

Anon. (2003). Who will take responsibility for corporate killing? Lancet. 361(9373):1921.

Anon. (2005). Combating counterfeit medicines and protecting patients through a partnership approach. Europe Fed Pharm Ind Assoc. PP 1-10. http://efpia.org/Objects/1/Files/counterfeit2005.pdf (accessed 9/10/13).

Anon. (2008 a). Country profile Yemen: Library of congress – Federal Research Division. pp1-26. http://lcweb2.loc.gov/frd/cs/profiles/Yemen.pdf (accessed 01/02/2013).

Anon. (2008b). Afrol news, Ethiopia sees Africa's fastest growth. http://www.afrol.com/articles/28991 (accessed 9/10/13).

Anon. (2008 c). The pills that kill http://www.telegraph.co.uk/health/3354135/Counterfeit-medicines-the-pills-that-kill.html

Anon. (2012) Bahrain MOH pharmacy & drug control directorate. http://www.moic.gov.bh/MoIC/En/MoIC+Centers/BahrainInvestorsCenter/Licensing+Authorities/MinistryOfHealth/PharmacyandDrug+ontrolDirectorate/: (accessed 01/12/12).

Atemnkeng, M. A., De Cock, K., Plaizier-Vercammen, J. (2007). Quality control of active ingredients in artemisinin-derivative antimalarials within Kenya and DR Congo. Tropic Med Int Health 12:68–74.

Athumani, R. (2012). Tanzania: Factory closed over fake ARVs. Tanzania Daily News. http://allafrica.com/stories/201210110213.html (accessed 9/10/13)

BASCAP. (1996). Fake vaccine leads to 3,000 deaths in Niger. http://www.iccccs.co.uk/bascap/article.php?articleid=363 (accessed 3/06/12).

Ba, A., Bauer, M., Hamdani, H., de la Torre, N., Videau, J. Y., Yameogo, O. (2005) Comparative behavioural study in dissolution of various Glibenclamide generic tablets with princeps drugs. STP Pharma Pratiques 15:213–230.

Bagozzi D. (2006) Facts Sheet 275: Counterfeit medicines. World Health Organization: Geneva, Switzerland. http://www.who.int/mediacentre/factsheets/fs275 (accessed 9/10/12).

Bate, R., Attaran, A. (2010). A counterfeit drug treaty: great idea, wrong implementation. Lancet. 376 (9751): 1446-1448.

Bate, R., Boateng, K. (2007): Bad medicine in the market. Am Enterprise Inst Pub Policy Res. 8:1150.

Bate, R. (2008) Making a killing: the deadly implications of the counterfeit drug trade. Pub l American Enterprise Inst. pp 1-113. http://counterfeiting.unicri.it/docs/Making%20a%20Killing.the%20Deadly%20implications%20of%20%20the%20Counterfeiting%20Drug%20Trade.%20Roger%20Bate.pdf (accessed 9/10/13)

Bate, R. (2012) Counterfeit drugs: a growing global threat. Lancet. 379:685

Bank, W. (2005). Democratic republic of Congo health, nutrition and population: country status report. DC: Washington. http://siteresources.worldbank.org/INTAFRREGTOPEDUCATION/Resources/444659-1212165766431/H_CSR_DRC.pdf (accessed 9/10/13)

Bauer, M., Couteau, A., Montjanel. F., Pages, M., Videau, J.Y., Yameogo, O. (2002) Effects of the physical characteristics of frusemide on its release from generic tablets. STP Pharma Pratiques 12: 76–84.

Booth, D., Cammack, D., Kibua T., and Kwek, J, Rudaheranwa, N. (2007) East African integration: How can it contribute to East African development overseas development Institute: http://www.odi.org.uk/publications/100-east-african-integration-can-contribute-east-african-development. (accessed 18/10/2013).

Bourque, L.B., Fielder, E.P. (2003). How to conduct self administered and mail surveys. 2nd ed. London: Stage Publication, Inc. pp 1-264.

Bowling, A. (2005). Mode of questionnaire administration can have serious effects on data quality. J Publ Health. 27:281-291.

Capobianco, E., Naidu, V. (2010). A decade of aid to the health sector in Somalia (2000-2009). Washington: The World Bank working paper 215. pp1-68. http://www-wds.worldbank.org/external/default/WDSContentServer/WDSP/IB/2011/05/18/000333037_20110518004532/Rendered/PDF/618980WP0Aid0S000public00BOX358355B.pdf (accessed 9/10/13)

Castell, W., Brickwood, D. (2009). Opinion farmers conference counterfeit medicines: perspectives and action report. Wellcome Trust.

http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/WTX057518.pdf (accessed on 01/11/2012)

Caudron, J-M., Ford, N., Henkens, M., Mace, C., Kiddle-Monroe, R., Pinel, J. (2008). Substandard medicines in resource-poor settings: a problem that can no longer be ignored. Tropic Med Int Health 13:1062–1072.

Centers for Disease Control and Prevention (CDC). (2009). World malaria report. http://www.cdc.gov/malaria/features/world_malaria_report_2009.html (accessed 9/10/13)

Charatan, F. (2001). Fake prescription drugs are flooding the United States. Brit Med J. 322:1443.

Chaudhry, P., Zimmerman, A. (2009) The economics of counterfeit trade: governments, consumers, pirates and intellectual property rights. publ. Springer pp 1-194.

Chan, X., Hoek, T., Reggi, V. (2008). Counterfeit medicines – it will never happen to me. J Eur Assoc Hosp Pharmacists. 14:55- 57.

Chaplin S. (2008) The MHRA's three-pronged strategy to tackle counterfeits. Prescriber. 19: 51–3.

Cheng, M. M. (2009). Is the drugstore safe? counterfeit diabetes products on the Shelves. J Diabetes Sci Technol. 3:1516-1520.

Clark, E. Counterfeit medicines: the pills that kill. (2008). http://www.telegraph.co.uk/health/3354135/Counterfeit-medicines-the-pills-that-kill.html (accessed 01/02/10).

Cockburn, R., Newton, P. N., Agyarko, E. K., Akunyi, D., White, N. J. (2005). The global threat of counterfeit drugs: Why industry and governments must communicate the dangers. PLoS Medicine 2:302-308.

Cockburn, R. (2002). Leading world organizations to seek solutions in first global pharmaceutical anticounterfeiting forum Geneva, Switzerland. http://www.thefreelibrary.com/Leading+World+Organizations+to+Seek+Solutions+in+First+Global...-a087846280 (accessed 9/10/13).

Counterfeit product: Case studies of transnational threats: United Nations on drugs and crime 8: 176-177. http://www.unodc.org/documents/data-and-analysis/tocta/8.Counterfeit_products.pdf (accessed 9/10/13)

Crawford, S. Y. (2003). Internet pharmacy: issues of access, quality, costs and regulation. J Med Sys 27:57-65.

Crow, G., Wiles, R. (2008). Managing anonymity and confidentiality in social research: The case of visual data in community research. Southampton: E.S.R.C National Centre for Research Methods.

http://eprints.ncrm.ac.uk/459/1/0808_managing%2520anonymity%2520and%2520confidentiality.pdf. (accessed 9/10/13).

Caudron, J.-M., Ford, N., Henkens, M., Mace, C., Kiddle-Monroe, R., Pinel, J. (2008). Substandard medicines in resource-poor settings: a problem that can no longer be ignored. Tropic Med Int Health. 13:1062–1072.

Erhun, W.O., Babalol, O. O., Erhun, M. O. (2001). Drug regulation and control in Nigeria: The counterfeit drugs. J. Health Popul Dev Countries. 4:23– 34.

Dahiya, S. (2008). Counterfeit medicines: the global hazard. pharmainfo.net 6:1. http://www.pharmainfo.net/reviews/counterfeit-medicines-global-hazard (accessed 9/10/13).

Danzon, P. M., Kim, J. D. (1998). International price comparisons for pharmaceuticals. measurement and policy issues. Pharmacoeconomics 14:115–28.

Davison, M. (2011). Pharmaceutical anti Counterfeiting: combating the real danger from fake drugs. 1st ed. publ John Wiley. pp 25-27.

Cavenaghi, R. (1989). Rifampicin raw material characteristics and their effect on bioavailability. Bull Int Union against Tuberc Lung Dis. 64:36–37.

Diem, K.G. (2002). Choosing a data collection method for survey research. Fact sheet FS996. Online (USA): the state University of New Jersey Rutgers Cooperative Extension. New

Jersey Agriculture Experiment Station.
http://njaes.rutgers.edu/pubs/publication.asp?pid=FS996 (accessed 9/10/13).

Dimoliatis, I. D. K., Vasilaki, E., Anastassopoulos, P., Ioannidis, J. P. A., Rolf, A. (2010). Validation of the Greek translation of the Dundee ready education environment measure (DREEM). Educ Health. 23:348.

Dutton, G. (2004). How Pharma is tightening its supply chain to avoid counterfeiting. World Trade. 17:26-30.

Easton, V., McColl, J. (2004). Steps Statistics Glossary V1.1.
http://www.stats.gla.ac.uk/steps/glossary/ (accessed 5/08/11).

Faucon, B., (2010). No Cure for Fake Drugs: The Middle East struggles with an influx of counterfeit medicines. Wall Street J.
http://online.wsj.com/news/articles/SB10001424052748704533204575047282075703998 (accessed 20/0510).

FDA. (2006). Guidance for industry testing of glycerin for diethylene glycol. US Food and Drug Administration, Rockville, MD.
http://www.fda.gov/downloads/Drugs/.../Guidances/ucm070347.pdf (accessed 10/10/13)

FDA. (2008). Heparin in China.
http://www.fda.gov/NewsEvents/Testimony/ucm115242.htm (accessed 12/12/2011).

FDA. (2004). Combating counterfeit drugs. http://www.fda.gov/downloads/Drugs/DrugSafety/UCM169880.pdf (accessed 12/12/2011).

FDA. (2009). Initiative to combat counterfeit drugs. http://www.fda.gov/Drugs/DrugSafety/ucm180899.htm (accessed 26/02/11).

Food, Medicine and Health Care Administration and Control Authority Ethiopia website FMHACA. http://www.moh.gov.et/English/Information/Pages/Food%20Medicine%20and%20Health%20Care%20Adminstration%20and%20Control%20Authority.aspx (accessed on 01/09/2013)

Goodman, C. S., Kachur, S. P., Abdulla, S., Bloland, P., Mills, A. (2007). Drug shop regulation and malaria treatment in Tanzania - why do shops break the rules, and does it matter? Health Policy Plan 22:393-403.

GSK, (2011) Global public policy issue GlaxoSmithKline's position the counterfeiting of healthcare products. http://www.gsk.com/content/dam/gsk/globals/documents/pdf/GSK-on-counterfeiting-of-healthcare-products.pdf (accessed on 01/10/2012).

Gupta, P. Singhal, Pandey, A. Counterfeit (fake drugs and new technologies to identify it in India. Int J Pharm Sci Res. (2012) 3: 4057-4064

Guyatt, G. H., Feeny, D.H., Patrick, D. L. (1993). Measuring health-related quality of life. Annals Int Med. 118: 6622-629.

HAAD (2013). http://www.haad.ae/haad/tabid/1013/Default.aspx (accessed 10/10/13)

Hall, K. A., Newton, P. N., Green, M. D, De Veij. M. Vandenabeele, P., Pizzanelli, D., Mayxay, M., Dondorp, A., Fernandez, A. M. (2006). Characterization of counterfeit artesunate antimalarial tablets from southeast Asia. Am J Trop Med Hyg. 75:804-81.

Harris, J., Stevens, P., Morris, J. (2009). Keeping it real: Combating the spread of fake drugs in poor countries: International Policy Network, London, pp30. http://search.asksource.info/cf/display/bibliodisplay.cfm?db=biball&ID=37438&StartRow=1&search=meta&display=full (accessed 10/10/13).

Higginson, I. J., Carr, A. J. (2001). Measuring quality of life using quality of life measures in the clinical setting: Brit Med J. 322:1297-3100.

Hill, S., Johnson, K. (2004). Emerging challenges and opportunities in drug registration and regulation in developing countries. London: DFID Health Systems Resources Centre. 1-47. http://www.hlsp.org/LinkClick.aspx?fileticket=0TXMdaAk5KA%3D&tabid=1643 (accessed 10/10/13).

Hogerzeil, H. V., Battersby, A. Srdanovic, V., Stjernstrom. N. E. (1992). Stability of essential drugs during shipment to the tropics. Brit Med J. 304:210-212.

Hyder, A. A., Merritt, M., Ali, J., Tran, N. T., Subramaniam, K., Akhtar, T. (2008). Integrating ethics, health policy and health systems in low- and middle-income countries: case studies from Malaysia and Pakistan. Bull World Health Organ. 86:606–611.

IMPACT/Counterfeit Medicines: an update on estimates. (2006). http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf : (accessed 16/04/09).

IMPACT / WHO. Counterfeit drugs kill. (2008). http://www.who.int/impact/FinalBrochureWHA2008a.pdf (accessed 16/04/09).

International Police Organization (INTERPOL). (2008b). Operation Mamba (IMPACT) – targeting counterfeit medicines in Tanzania and Uganda. http://www.INTERPOL.int/Public/News/2008/mamba20081029.asp (accessed 28/09/10).

Prebble, J. (2003). Thieves take the wrap. http://www.keionline.org/misc-docs/deisingh_pharmaceutical_counterfeiting.pdf

Jackson, G, Arver, S., Bank, I., Stecher, V. J. (2010). Counterfeit phosphodiesterase type 5 inhibitors pose significant safety risks. Int J Clin Pract. 64:497-504.

Jahnke, R, W. O. (2004). Counterfeit medicines and the GPHF-Minilab® for rapid drug quality verification. Pharm Indust. 66:1187-1193.

Jakobsson, A. (2010). Problems of fake medicine in developing countries could be solved. Lund University. http://www.alphagalileo.org/ViewItem.aspx?ItemId=83846&CultureCode=en (accessed 10/10/13).

Kaisier, P.D., Smith, K. (2001). The Standards for Educational and Psychological testing: Zugzwang for Practising Professionals? The International Personnel Management Association Council (IPMMAAC). http://annex.ipacweb.org/library/conf/01/kaiser.pdf (accessed 10/13/10)

Kelesidis, T., Kelesidis, I., Rafailidis, P. I., Falagas, M. E. (2007). Counterfeit or substandard antimicrobial drugs: a review of the scientific evidence. J Antimicrob Chemother. 60:214-236.

Keshavjee, S., Farmer, P. E. (2012). 200th Anniversary article tuberculosis, drug resistance, and the history of modern medicine. New Eng J Med. 367:931-936

Khan, M. H., Akazawa, M., Dararath, E., Kiet, H. B., Sovannarith, T., Nivanna, N., Yoshida, N Kimura, K.E. (2011). Perceptions and practices of pharmaceutical wholesalers surrounding counterfeit medicines in a developing country: a baseline survey. BMC Health Serv Res. 11:306.

Kheir, N., Zaidan, M., Younes, H., El Hajj, M., Wilbur, K., Jewesson, P. J. (2008). Pharmacy education and practice in 13 middle eastern countries Am J Pharm Educ. 72:133.

Kibwage, I.O., Otego, J.O., Maitai, C. K., Rutere, G., Thuranira, J., Ochieng, A. (1992). Drug quality control work in Daru: observations during 1983-6. East African Med J. 69: 577–580.

Knight, J. B., Sabot, R. H. (1990). Education, productivity and inequality: The east African natural experiment. Human development and public services. publ World Bank, Washington. pp 94. http://econ.worldbank.org/external/default/main?pagePK=64165259&theSitePK=477916&piPK=64165421&menuPK=64166093&entityID=000178830_98101901431421

Kohler, J. C., Pavignani, E., Michael, M., Ovtcharenko, N., Murru, M., Hill, P. S. (2012). An examination of pharmaceutical systems in severely disrupted countries. BMC Int Health Hum Rights 12:34.

Kubic, T. T., Mollo, S. J. (2006). Pharmaceutical counterfeiting trends: understanding the extent of criminal activity. J Biolaw Bus. 9:51–56.

Kyriacos, S. M., Mroueh, M., Chahine R. P., Khouzam O. (2008). Quality of amoxicillin formulations in some Arab countries J Clin Pharm Ther. 33:375-379.

Laserson, K. F., Kenyon, A. S., Kenyon, T. A., Layloff, T., Binkin, N. J. (2001). Substandard tuberculosis drugs on the global market and their simple detection. Int J Tubercle Lung Dis. 5:448–454.

Liang, B. A. (2006). Fade to black: Importation and counterfeit drugs. Am J Law Med. 32:279–323.

Lon, C.T., Tsuyuoka, R., Phanouvong, S., Nivanna, N., Socheat, D., Sokhan, C., Blum, N., Christophel, E.M., Smine, A. (2006). Counterfeit and substandard antimalarial drugs in Cambodia. Trans Roy Soc Trop Med Hyg. 100:1019–1024.

Ly, T., Selgelid, M. J., Kerridge, I. (2007). Pandemic and public health controls: Toward an equitable compensation system. J Law Med. 15:296-302.

Lynn, R., Vanhanen, T. (2012). National IQs: A review of their educational, cognitive, economic, political, demographic, sociological, epidemiological, geographic and climatic correlates. Intelligence. 40(2): 226-234

SFDA (2011). http://www.sfda.gov.sa/en/Pages/default.aspx (accessed 11/10/13)

Mackintosh, M., Chaudhuri, S., Mujinja. P. G. M. (2011). Can NGOs regulate medicines markets? Social enterprise in wholesaling, and access to essential medicines. Globaliz Health. 7:1-13.

Mackey, T. K., Liang, B. A. (2011). The global counterfeit drug trade: patient safety and public health risks. J Pharm Sci. 100: 4571–4579.

Mara, K. (2010) Coverage of Anti-Counterfeit Policy Debate Varies Widely Across Global Media, Intellectual Property Watch: http://www.ip-watch.org/2010/08/02/coverage-of-anti-counterfeit-policy-debate-varies-widely-across-global-media/ (accessed 10/10/13).

Marchal, R. (2002). A survey of Mogadishu's economy. Nairobi: European Commission/Somali Unit (Nairobi). http://eeas.europa.eu/delegations/somalia/documents/more_info/mogadishu_economic_survey_en.pdf (accessed 10/10/13).

Maponga, C., Ondari, C. (2003). The quality of antimalarials. A study in selected African countries. WHO, Department of Essential Drugs and Medicines Policy. pp 1-54. http://libdoc.who.int/hq/2003/WHO_EDM_PAR_2003.4.pdf (accessed on 01/12/2012)

Mendis, S., Fukino, K., Cameron, A. (2007). The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. Bull WHO. 85:279–87.

Meliza, 0. (2013). Making counterfeiting unprofitable Published: February (Sporxil blog) 20, 2013 accessed on 22Feb2013 http://www.sproxil.com/blog/ (accessed 11/10/13).

McNamara, C. (1999). Overview of basic method to collect information. http://intraserver.nurse.cmu.ac.th/mis/download/course/lec_566823_Handout%20-%20Jan%2017.pdf (accessed 11/10/13).

Miles, M.B and M. Huberman, (Eds). (1994). Qualitative data analysis. London Sage Publication.

Minzi, O. M., Moshi, M. J., Hipolite D., Massele, A. Y., Tomson, G., Ericsson, G. Ö., Gustafsson, L. L. (2003) Evaluation of the quality of amodiaquine and sulphadoxine / pyrimethamine tablets sold by private wholesale pharmacies in Dar Es Salaam Tanzania. J Clin Pharmacol Ther 28: 117–122.

Ministry health Website (Kenya) http://www.pharmacyboardkenya.org/index.php?id=28 (accessed 01/08/12)

Morris, J., Stevens, P., (2006). Counterfeit medicines in less developed countries. International Policy Network, Lond. http://counterfeiting.unicri.it/docs/Ctf%20medicines%20in%20less%20developed%20countries.pdf (accessed 11/10/13).

Moride, Y., Haramburu, F., Requejo, A. A., Bégaud, B. (1997). Underreporting of adverse drug reactions in general practice. Brit J Clin Pharmacol. 43:177–181.

Mudur, G. (2003). India Introduce death penalty for peddling fake drugs. Brit Med J. 327:414.

Nair, A. (2012). India to double pharmaceutical exports by 2014. http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=757923

Nazerali, H., Hogerzeil, H. V. (1998). The quality and stability of essential drugs in rural Zimbabwe: controlled longtitudinal study. Brit Med J. 317:512–513.

Newton, P. N., Green, M. D., Fernández, F. M. (2010). Impact of poor-quality medicines in the 'developing' world. Trends Pharmacol Sci. 3:99–101.

Newton, P. N., White, N. J., Rozendaal, J. A., Green, M. D. (2002). Murder by fake drugs: Time for international action: Brit Med J. 324:800:801.

Newton, P. N., Green M. D, Fernandez F. M, Day, N. P., White, N. J. (2006). Counterfeit anti-infective drugs. Lancet Infect Dis. 6:602–613.

Newton, .P.N., Proux, S., Green, M. D., Smithuis, F, Rozendaal J. A. (2001). Fake artesunate in southeast Asia. Lancet 357:1948–1950.

Newton, P.N. (2008). A collaborative epidemiological investigation into the criminal fake artesunate trade in south east Asia. PLoS Medicine 5:e32.

O'Brien, K. L., Selanikio, J. D., Hecdivert, C., Placide, M. F., Louis, M., Barr, D. B., Barr, J. R., Hospedales, C.J., Lewis, M.J., Schwartz, B., Philen, R. M., St Victor, S., Espindola, J., Needham, L. L., Denerville, K. (1998). Epidemic of paediatric deaths from acute renal failure caused by diethylene glycol poisoning. JAMA 279:1175–180.

Onoja, A. L., Adu, F. D., Tomori, O. (1992). Evaluation of measles vaccination programme conducted in two separate health centres. Vaccine 10:49–52.

Parry, J. (2005). WHO, Combats counterfeit malaria drugs in Asia. Brit Med J. 330:1044.

Patouillard, E., Hanson, K. G., Goodman, C. A. (2010). Retail sector distribution chains for malaria treatment in the developing world: A review of the literature.” Malaria Journal 9: 1-14.

Patil, D. D., Pandit, V. S., Pore, S. M., Chavan, C. S. (2012). Fighting counterfeit and substandard drugs at periphery; the utility of basic quality control tests. Pharmacie Globale. Int J Comprehen Pharm. 3:1-3.

Passmore, C., Dobbie, A. E., Parchman, M., Tysinger, J. (2002). Guidelines for construction survey. Fam Med 34:281-286.

Perks, B. (2011). Faking it. Chemistry World 2011; 56–59. http://www.rsc.org/images/Counterfeit%20Drugs%20-%20Faking%20It_tcm18-196053.pdf (accessed 11/10/13).

Pincock, S. (2003) WHO tries to tackle problem of counterfeit medicines in Asia. Brit Med J. 327:1126.

Pinar, R. (2002). A Study on the reliability and validity of the Turkish version of the MQOLS-CA2 in People with Cancer. Turkish J Cancer. 32:148-163.

Ramchandran, R. (2003). Dealing with fake drugs, Frontline. 20:18.

ReMeD. (1995) La qualite´ des me´dicaments sur le marche´ pharmaceutique africain: e´tude analytique dans trois pays: Cameroun, Madgascar, Tchad. Action Programme on Essential Drugs. WHO, Geneva. (Cited in Caudron 2008)

Reggi, V. (2007). Counterfeit medicines: an-intent to deceive, Int J Risk Safety Med. 19:107-108.

Roy, J. (1994).The menace of substandard drugs. World Health Forum 15:406–407.

Rudolf, P. M. (2004). Counterfeit drugs. New Eng J Med. 350:1384-1386.

Saywell, T., McManus, J. (2002). What is in that pill? Far Eastern Economic Review. (21 Feb):34-40. Hong Kong.

Saw, S. M. (2001). The Design and assessment of questionnaires in clinical research. Singapore Med J. 42:131-135.

Saunders, M., Thornhill, A and Lew, P. (Eds) (2009). Research method for business students. Publ Essex, Pearson Education Limited.

Schofield, J. (2001). Counterfeit pharmaceuticals flood Russian market. Brit Med J. 322:1564.

SFDA (2011). http://www.sfda.gov.sa/en/Pages/default.aspx (accessed 11/10/13).

Shakoor, R. B., Taylor, R. H., Behrens, R. H. (1997). Assessment of the incidence of substandard drugs in developing countries. Tropical Med Int Health. 2:839–845.

Shah, S. (2007). Drug giants accused of ignoring fake medicines that kill millions. http://www.independent.co.uk/news/world/africa/drug-giants-accused-of-ignoring-fake-medicines-that-kill-millions-444466.html (accessed 11/10/13).

Shabsigh, R., Perelman, M. A., Laumann, E. O., Lockhart, D. C. (2004). Drivers and barriers to seeking treatment for erectile dysfunction: a comparison of six countries BJU Int. 94:1055-65.

Shepherd, M. (2010). Beef up international cooperation on counterfeits. Nature Med 16:366 2010

Silman, A. J., Macfarlane, G. J. (2002). Epidemiological studies: A practical guide. Cambridge University Press. 2nd Ed. pp 132-137.

Singh, J., Dutta, A. K., Khare, S. et al., (2001) Diethylene glycol poisoning in Gurgaon, India, 1998. Bulletin WHO. 79:88–95.

Singh, S., Mohan, B. (2003). A pilot stability study on four-drug fixed-dose combination anti-tuberculosis products. Int J Tubercle Lung Dis. 7:298–303.

Siva, N., (2010). Tackling the booming trade in counterfeit drugs. Lancet 376:725-1726.

Skulmoski, G. J., Hartman, F.T. (2007). The Delphi method for graduate research. J Information Technol Educ. 6:1-21.

Solomon, S. (2007). BC woman killed by fake drugs bought online: 'Metal toxicity' from counterfeit pills reinforces danger of internet meds. National Review of Medicine. http://www.nationalreviewofmedicine.com/issue/2007/07_30/4_policy_politics_13.html. (accessed 11/10.13)

Spies, A. R. (2003) Counterfeit drugs a menace keeps growing. US Pharmacist 28:01. http://legacy.uspharmacist.com/index.asp?show=article&page=8_1014.ht (accessed 9/10/13)

Stenson, B., Lindgren, B. H., Syhakhang, L., Tomson, G. (1998). The quality of drugs in private pharmacies in the Lao People's Democratic Republic. Int J Risk Safety Med. 11:243–249.

Syhakhang, L., Freudenthal, S., Tomson, G., Wahlström, R. (2004). Knowledge and perceptions of drug quality among drug sellers and consumers in Lao PDR. Health Policy Plan 19:391-401. http://heapol.oxfordjournals.org/content/19/6/391.abstract. (accessed 15/05/11).

Taylor, R. B., Shakoor O, Behrens R.H., Everard, M., Low, A. S., Wangboonskul, J., Reid, R. G., Kolawole, J. A. (2001). Pharmacopoeial quality of drugs supplied by Nigerian pharmacies. Lancet 357:1933–1936.

Taylor, P. 2011. Fake HIV medications uncovered in Kenya. http://www.securingindustry.com/pharmaceuticals/fake-hiv-medications-uncovered-in-kenya/s40/a1095/?cmd=PasswordRetrieval (accessed 11/10/13).

Ten Ham, M., (1992). Counterfeit drugs: implications for health. Adverse Drug React Toxicol Rev 11:59-65.

Tim, K., MackeY Bryan N A. Liang. Mackey, T. K., Liang, B. A. (2011). The Global counterfeit drug trade: Patient safety and public health risks Publ Wiley Online Library. http://onlinelibrary.wiley.com/doi/10.1002/jps.22679/pdf (accessed 11/10/13).

Trochim, W. M. K. (2006). Types of surveys. Available from: http://www.socialresearchmethod.net/kb/survtype.php.

The World Fact book; Central Intelligence Agency. Somalia 2009-05-14 https://www.cia.gov/library/publications/the-world-factbook/geos/so.html (accessed 11/10/13).

Valovich-Mcleod, T. C., Synder, A. R., Parsons, J. T., Bay, R. C., Michener, L. A., Sauers, E. L. (2008). Using disablement models and clinic outcomes assessment to enable evidence-based athletic training practice, part II: Clinical outcome assessment. J Athletic Training. 43:437-440.

Van Teijlingen, E. R., Rennie, A. M., Hundley, V., Graham, W. (2001). The importance of

conducting and reporting pilot studies: the example of the Scottish Births Survey. J Adv Nurs 34:289-295.

United Nation report. (2006). Yemen: Counterfeit, obsolete drugs pose safety risk, say health experts United Nations. http://www.irinnews.org/report/27101/yemen-counterfeit-obsolete-drugs-pose-safety-risk-say-health-experts (accessed 11/10/13).

United nation report 8. (2012). Counterfeit products. http://www.unodc.org/documents/data-and-analysis/tocta/8.Counterfeit_products.pdf (accessed 11/10/13).

United Nations, 2009 World Almanac, the economist: http://middleeast.about.com/od/middleeast101/a/me090425b.ht (accessed 11/10/12).

Ware, J., Brook, R. H., Davies, A.R., Lohr, K. N. (1981). Choosing measures of health status for individuals in general population. Am J Public Health. 71:620-625.

Weimer, D. L., Vining, A. R. (2011). Policy Analysis: concepts and practice. (5th ed). Boston: Longman.

Wertheimer, A, Chaney, M., Santella, T. (2003). Counterfeit pharmaceuticals: current status and future projections. J Am Pharm Assoc. 43:710–718.

WHO (2013) Where are counterfeit medicines found? http://www.who.int/medicines/services/counterfeit/faqs/11/en/index.html (accessed 14/10/13).

WHO. (2003). Alert no. 110: Counterfeit triple antiretroviral combination product (Ginovir 3D). http://www.who.int/medicines/publications/drugalerts/DrugAlert110.pdf (accessed 14/10/13).

WHO. (1999). Counterfeit Drugs - Guidelines for the development of measures to combat counterfeit drugs. http://whqlibdoc.who.int/hq/1999/WHO_EDM_QSM_99.1.pdf (accessed 14/10/13).

WHO (2003). Substandard and counterfeit medicines. http://www.who.int/mediacentre/factsheets/2003/fs275/en/ (accessed 12/04/10).

WHO (2010). Growing threat from counterfeit medicines. Bull WHO. 88(4):247–248. http://www.who.int/bulletin/volumes/88/4/10-020410/en/ (accessed 14/10/13).

WHO report (1998). Counterfeit drugs: WHO/DRS/CFD/98.1:Geneve. http://apps.who.int/medicinedocs/pdf/h1456e/h1456e.pdf

WHO Counterfeit medicines. (2006a). Fact sheet No.275. http://whqlibdoc.who.int/fact_sheet/2006/FS_275.pdf (accessed 14/10/13)

WHO (2006b). Counterfeit medicines: an update on estimates. IMPACT http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf (accessed 14/10/13).

WHO (2002). Effective drug regulation- A mulitcountry study and Annex 1: guide for data collection to assess drug regulatory performance. http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf (accessed 14/10/13).

Wondemagegnehu, E. (1999). Counterfeit and substandard drugs in Myanmar and Viet Nam. WHO, Geneva. http://apps.who.int/medicinedocs/pdf/s2276e/s2276e.pdf (accessed 14/10/13).

World Bank (2011). http://siteresources.worldbank.org/EXTANNREP2011/Resources/8070616-1315496634380/MiddleEastandNorthAfrica.pdf (accessed 14/10/13).

WHO. (2000). Global comparative pharmaceutical expenditures with related reference information (Health Economics and Drugs EDM Series No. 3). (Document EDM/PAR/2000.2). http://apps.who.int/medicinedocs/documents/s18569en/s18569en.pdf (accessed 14/10/13).

(World Fact Book: https://www.cia.gov/library/publications/the-world-factbook/rankorder/2004rank.html (accessed 11/10/12).

Yin, R. K. (2003). Case study research: Design and methods: applied social research methods. Thousand Oaks, (2nd ed) pp1-181. Sage Publ.

Zarkesh, M. (2008). Customizing strategic planning model for Iran's cement industry. Department of Business Administartion and Social Science. Luleå University of Technology

Sweden Master Thesis. http://epubl.ltu.se/1402-1552/2008/104/LTU-DUPP-08104-SE.pdf (accessed 14/10/13).sis.

8 Appendix 01

PILOT QUESTIONNAIRES FOR A STUDY ON SAFETY OF MEDICINES WITH REGARD TO DRUG COUNTERFEITING IN DEVELOPING COUNTRIES (SPECIALLY – MIDDLE COUNTRIES)

Data Collection form for Safety of medicines with to drug counterfeiting in developing countries:
State:
Country:
City:
Village: **Name of Pharmacy or Clinic:** **Date of Interview:**

Q1 Sex	Male ☐ Female ☐
Q2 – What is your age Group:	18-24 ☐ 24-35 ☐ 35- 45 ☐ 46-54 ☐ 55-64 ☐ 65+ ☐
Q3 - What is your race?	White ☐ Arab ☐ Asian ☐ Black African ☐ Other ☐ Specify_____
Q4- Employment status?	Full Time Work ☐ Part time Work ☐

	Other:_____
Q5 - What is your Status:	Licensee ☐ Owner ☐ Spouse ☐ Child ☐ Other ☐ Specify_____
Q6- What is your level Education	Pharmacist ☐ Assistant Pharmacist ☐ Pharmacy technician ☐ Medical Doctor ☐ Nurse ☐ Ancillary Nurse ☐ Other ☐ Other ☐ Specify_____
Q7 - Years of Work Experience?	

Q8- Have you received Any Training in drug dispensing	Yes ☐ No ☐
If yes Please where and when did you receive it	
Q9 – have you received any information related to drug regulation	Yes ☐ No ☐
If yes who gave it to you:	
Q10 - Please specify those regulation you know about	FDA ☐ EMEA ☐ Your Own Country regulatory ☐ WHO ☐ Other ☐
Q11 -Have you been inspected in the last five years?	Yes ☐ No ☐
If yes Please specify who inspected you and when:	

Q12-In general would you say your knowledge of drug dispensing is?	Excellent ☐ Very Good ☐ Fair ☐ Poor ☐
Q13: Where do most patients buy their medicines?	Patient medicine store ☐ Approved Pharmacy stores ☐ Un-approved Pharmacy stores ☐ Super Market ☐ Public Hospitals ☐ Other ☐ Specify:_____

Q14- Where are fake medicines most likely to be sold?	Big Cities ☐ Villages ☐ Rural area ☐ Urban area ☐ Others ☐ Specify:_____
Q15– How easy is it to buy medicines in your country?	Very easy ☐ Fairly easy ☐ Not very easy ☐ Not at all easy ☐

9 Appendix: 02

Doctors, Health care Workers and Pharmacist Survey:

This questionnaire has been designed to better understand the safety of medicines with regard to drug counterfeiting in the development countries. Your responses to these questionnaires will be made confidential and mainly for research purpose.

Data Collection form for Safety of medicines with to drug counterfeiting in developing countries:
State:
Country:
City:
Village: **Name of Pharmacy or Clinic:** **Date of Interview:**

About Yourself (Q1 – Q7)	
Q1- What is your gender?	Male ☐ Female ☐
Q2- how old are you?	18- 24 years ☐ 25- 34 years ☐ 35- 44 years ☐ 45- 54 years ☐ 55- 64 years ☐ 65- 74 years ☐ 85 over ☐
Q3 - What is your race?	White ☐ Arab ☐ Asian ☐ Black African ☐ Other ☐ Specify_____
Q4- Employment status?	Full Time Work ☐

	Part time Work ☐ Other:_____
Q5- What is your Status?	1- Licensee ☐ 2- Owner ☐ 3- Spouse ☐ 4- Child ☐ 5- Worker ☐ 6- Other ☐ Specify_____
Q6- What is your level of Education	1- Pharmacist ☐ 2- Assistant Pharmacist ☐ 3- Pharmacy technician ☐ 4- Medical Doctor ☐ 5- Nurse ☐ 6- Ancillary Nurse ☐ 7- Other ☐

	Specify_____
Q7 – Years of work Experience:	
Q8- Have you received Any Training in drug dispensing	Yes ☐ No ☐
If yes Please where and when did you receive it	
About Your Customer or Patient (Q8 – 18)	
Q9- How Many patients do you see or buy your medicines per day?	1 – 5 patient ☐ 6 – 10 patient ☐ 11- 20 patient ☐ 21 – 30 patient ☐ Above 30 patient ☐

Q10 – How do patients know the appropriate drug to buy?	Used the drug before ☐ Ask the Pharmacist ☐ Respond to advertisement ☐ Other ☐ Specify: _____
Q11 –Has any patient ever reported to you that the drug He/She bought was not effective?	Yes ☐ No ☐
Q12 – Did the patient buy the same drug again	Yes ☐ No ☐
Q13 -Did the patient buy a different drug again	Yes ☐ No ☐
Q14 – What are some likely reasons that drugs were not working?	Drugs were expired ☐ Drugs were sub-standard or fake ☐ Patient was misdiagnosed ☐ Patient did not use the drug as prescribed ☐
Q15 – Do the patients buy drugs from unapproved places:	Yes ☐ No ☐

If yes: what is the reason? **(check all that apply)**	Drugs are Cheaper ☐ Convenient for the patient ☐ It is the only place to buy ☐ Other ☐ Specify: _____
Q16: Where do most patients buy their medicines?	Drug store ☐ Approved Pharmacy stores ☐ Un-approved Pharmacy stores ☐ Super Market ☐ Public Hospitals ☐ Other ☐ Specify:_____

Q17- Where is cheapest place to buy medicines?	Drug store ☐ Approved Pharmacy stores ☐ Un-approved Pharmacy stores ☐ Super Market ☐ Public Hospitals ☐ Other ☐ Specify:_____
Q18 – Do patients complain that the cost of medicines are high?	Yes ☐ No ☐
Q19- Do patient prefer to buy cheap medicines over brand names?	Yes ☐ No ☐
About the Fake Medicines (Q19 – Q33)	
Q20- Do you know of a manufacturer that produces and sells fake medicines?	Yes ☐ No ☐

Q21- If yes: Where is it located?	Within your Country ☐ Outside of the country ☐ Other ☐ Specify:_____
Q22 – Where are fake medicines distributed?	Drug store ☐ Approved Pharmacy stores ☐ Un-approved Pharmacy stores ☐ Super Market ☐ Public Hospitals ☐ Other ☐ Specify:_____

Q23- Where are fake medicines most likely to be sold?	Big Cities ☐ Villages ☐ Rural area ☐ Urban area ☐ Others ☐ Specify:_____
Q24 –Where are patients most likely to buy fake medicines?	Patient medicine store ☐ Approved Pharmacy stores ☐ Un-approved Pharmacy stores ☐ Super Market ☐ Public Hospitals ☐ Other ☐ Specify:_____

Q25 – What type of medicines are most commonly faked?	Drugs Common disease: i.e. Malaria, infections etc ☐ Drugs that are expensive regardless of the disease ☐ Drugs that are in high demand i.e. Viagra ☐ Drugs that are not common ☐ Other ☐ Specify:_____
Q26 – Do you know or have you been trained how to identify fake medicines?	Yes ☐ No ☐
Q27 – Have you ever come into possession of fake medicines?	Yes ☐ No ☐

Q28 – If you have answered Q 26 yes. What have you done with the fake medicine?	Reported to superior officer ☐ Alerted police ☐ Reported to Authority (regulatory agency) ☐ Destroyed the medicine ☐ Did nothing ☐
Q29 - How serious is the problem of fake medicines in health care delivery?	Not problem ☐ Mild problem ☐ Moderate problem ☐ Severe Problem ☐

Q30- What is the reason for the growing trade in fake medicines?	Heavy taxes/ VAT on drugs ☐ Government policies towards health delivery ☐ Poor economic situation ☐ Lack of health insurance for most citizens ☐ Other ☐ Specify:_____
Q31 – In your opinion, could fake medicines be eliminated if the patent rights of the original drug manufacturers were respected	Yes ☐ No ☐

Q32 – What measures could be put in place to check the incidence of fake medicines?	Seizure of consignments ☐ Severe jail sentence ☐ Death sentence ☐ Closure of sale outlets ☐ Heavy Fine ☐ Withdrawal of licenses ☐ Freezing of assets/bank accounts ☐ Other ☐ Specify:_____
Q33 – Rank the best way to tackle the problem of fake medicines in your country? **(1 is the best way and 5 is the worst)**	Reduction of VAT on essential medicine ☐ Prosecution of unregistered pharmacist/store ☐ Mass education on fake medicine ☐ Introduction of stiffer penalty for offenders ☐ Bann on all sales medium that help self medication ☐

Q34 – Rank the following problems with the health care system in order of importance? **(1 is the most important and 7 the worst)**	Lack of Infrastructure ☐ Fake Medicine ☐ Shortage of medical personnel ☐ Lack of health insurance for most citizens ☐ Corruption in healthcare delivery ☐ Shortage of Hospitals ☐ Quackery ☐

Q35 - We want to know your rating of the problems of counterfeit medicines in your country. **Using any number from 1 to 10 where 0 is the worst possible counterfeit medicine problem and 10 is the least possible counterfeit medicine problem in your country,**	1 Worst Counterfeit Medicine found ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Least Counterfeit Medicine found ☐

Q36 **: We want to know your rating of the quality of the regulatory control in your country:** **Using any number from 1 to 10 where 0 is the worst and 10 is the best rating**	
Effective Border control of counterfeit medicines (manpower)	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Healthcare Personnel Awareness (Education level).	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Patient Awareness (Education level)	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Drug quality testing	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Manpower to police fake medicines	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Lack of adequate civil liability	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Weak or Absent rule of law	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Price Control	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Taxes and tariffs	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐
Effective Regulatory agency	1-☐ 2-☐-3 ☐-4 ☐-5 ☐-6 ☐-7 ☐-8 ☐-9 ☐-10 ☐

Q37- General Comments/ additional comments	

10 Appendix 03

COVERING LET TER

Date: _____/_____/_____

Dear Sir/ Madam

The following questionnaire is part of survey and study to better understand the safety of medicine in the development countries. It is recognized and narrated from WHO that the World Health Organization (WHO) estimates that 8% to 10% of the medicines in the global medicine supply chain are counterfeit, reaching as high as 25% to 60% in developing countries.

The questionnaire should only take 15 minutes to complete. Please answer all questions in such a way as to reflect most clearly Counterfeit medicine. Most questions will require you to circle your selected response. Others will require you to write down a number. Do not leave blanks.

Your participation is very much appreciated and we thank you for your contribution to this important research.

Ahmed Elmi MSc MICR Csci