PHARMACEUTICAL QUALITY AND POLICY IN NIGERIA: STAKEHOLDER PERSPECTIVES AND VALIDATION OF THE MOBILE AUTHENTICATION SERVICE

Thesis submitted in accordance with the requirements of the University College London (UCL) degree of Doctor of Philosophy by

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Declaration

I, Chioma Joy Ebenezer confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature..... Date.....

Abstract

Background

Medicines that are of poor quality present a challenge to many countries especially the developing countries. Many interventions against medicines counterfeiting are often not evaluated and qualitative fieldwork to find how stakeholders perceive the problem of poor quality medicines is currently lacking.

Aims

1) To conduct a systematic review of the literature 2) To validate the Mobile Authentication Service (MAS) 3) To explore stakeholder experiences and perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria.

Methods

1) A quantitative study involving Short Message Service (SMS) authentication of tagged Glucophage® (metformin) samples, packaging and chemical (Near Infrared spectroscopyand High Performance Liquid Chromatography) analysis of metformin samples, randomly selected from retail outlets in Lagos, Nigeria 2). A qualitative study involving semi-structured interviews with different stakeholders.

Results

The results of the SMS authentication agree with that of packaging and chemical analyses. The Glucophage® samples were significantly different in quality from the generic versions in terms of the concentration of active ingredient with a p value of 0.006. This difference in quality was in favour of the innovator brand, Glucophage® and it is similar to the findings from the qualitative interviews where majority of the participants perceived innovator brands better in quality than their generic versions.

Majority of the participants felt that the problem of poor quality medicines in Nigeria is decreasing.

Increase in cost of medicines, poor dispensing practices, poor phone network, time constraints, consumer trust in medicine sellers, low level of awareness and complacency by the consumers were identified as factors that may be a barrier to the use of MAS.

Conclusion

MAS seem to be successful in helping consumers authenticate their medicines. However, recommendations arising from this study should be adopted to overcome barriers to its use. Substandard medicines may present a greater challenge than medicines counterfeiting and should therefore not be neglected.

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Abbreviations

ACPN: Association of Community Pharmacists of Nigeria
ACT: Artemisinin Combination Therapy
ACTA: Anti-Counterfeiting Trade Agreement
AFRO: African Regional Office
AIPM: Association of International Pharmaceutical Manufacturers
AMRO: American Regional Office
ASEAN: Association of Southeast Asian Nations
ASHP: American Society of Health System Pharmacists
BI**:** Bamako Initiative
BBC: British Broadcasting Co-operation
BP: British Pharmacopoeia
CD-P-PH/CMED: Experts on Minimizing Public Health Risks Posed by Counterfeiting Medical Products and related crimes
cGMP: Current Good Manufacturing Practice; GMP: Good Manufacturing Practice
CIA: Central Intelligence Agency
CIOPF: Conférence Internationale des Ordres de Pharmaciens Francophones
CWPA: Common Wealth Pharmacists Association
DEG: Diethylene glycol
DFID: United Kingdom Department for International Development
DRA: Drug Regulatory Agency
DRF: Drug Revolving Fund
EAC: East African Community
EDQM: European Directorate for Quality of Medicines and Health Care
EFPIA: European Federation of Pharmaceutical Industries and Associations
EMEA: European Medicines Agency
EMRO: East Mediterranean Regional Office (Majority of the Middle East countries and Pakistan)
EURO: European Regional Office
FIP: International Pharmaceutical Federation
FMOH: Federal Ministry of Health
GMP: Good Manufacturing Practice
GPHF: German Pharma Health Fund
HIV: Human Immunodeficiency Virus
HSRC: Health Systems Resource Centre
IFPMA: International Federation of Pharmaceutical Manufacturers and Associations
IMPACT: International Medical Products Anti-counterfeiting Taskforce
INTERPOL: International Criminal Police Organization
IP: Intellectual Property

IPSF: International Pharmaceutical Students' Federation
IV: Intravenous
LGA: Local Government Area
LMHRA: Liberia Medicines and Health Products Regulatory Agency
MAN: Manufacturers Association of Nigeria
MAS: Mobile Authentication Service
MD-RTB: Multi Drug-Resistant Tuberculosis
MHRA: Medicines and Health Care Regulatory Agency.
MOH: Ministry of Health
NABP: National Association of Boards of Pharmacy
NACDS: The National Association of Chain Drug Stores
NAFDAC: National Agency for Food and Drug Administration and Control
NDP: National Drug Policy
NGO: Non-governmental Organisation
NHIS: National Health Insurance Scheme
NHP: National Health Policy
NIR: Near Infrared
NMA: National Medical Association
NNHP: Nigerian National health Policy
OECD: Organization for Economic Cooperation and Development
OTC: Over the Counter
PCN: Pharmacists Council of Nigeria
PDMA: Prescription Drug Marketing Act
PFIPC: Permanent Forum for International Pharmaceutical Crime
PGM-MAN: Pharmaceutical Group of Manufacturers-Manufacturers Association of Nigeria
PHC**:** Primary Health Care
PhRMA: Pharmaceutical Research and Manufacturer's of America
PMS: Patent Medicine Shop
PMV: Patent Medicine Vendors
PNLP: National de Lutte contre le Paludisme
PSI: Pharmaceutical Security Institute
PSN: Pharmaceutical Society of Nigeria
PTF: Petroleum Trust Fund
RAS: Rapid Alert System
RFID: Radio-frequency Identification
RPSGB: Royal Pharmaceutical Society of Great Britain
R & D: Research and Development
SEARO: South East Asian Regional Office (Includes India)
SFDA: State Food and Drug Administration
SMS: Short Message Service
SOPs: Standard Operating Procedures
SPOC: Single Point of Contact

TB: Tuberculosis
TFDA: Tanzania Food and Drug Authority
TLC: Thin Layer Chromatography
UMI: Unique Medicine Identifier
USAID: United States Agency for International Development
USFDA: United States Food and Drug Administration
USP: United States Pharmacopeia
USP DQI: United States Pharmacopeia Drug Quality and Information Program
UV: Ultraviolet
VHC: Village Health Committee
WADRAN: West African Drug Regulatory Authorities Network
WCO: World Customs Organisation
WHA: World Health Assembly
WHO: World Health Organisation
WHPA: World Health Professional Alliance
WIPO: World Intellectual Property Organisation
WPRO: West Pacific Regional Office (Austria, China, Vietnam and Philippines)
WTO: World Trade Organisation

Chapter 1

Introduction to the thesis

1.1 Introduction to the chapter

This chapter is an introduction to the PhD research. This study seeks to present a systematic review of the literature on quality of medicines, validate the Mobile Authentication Service (MAS) as an anti-counterfeiting intervention aimed at improving the quality of medicines distributed in Nigeria and to explore stakeholder perceptions on issues relating to accessibility to good quality medicines in Nigeria. It was anticipated that the findings of this research will for the first time present a holistic independent evaluation of the utility, capacity and effective mass replication of MAS in Nigeria as well as stakeholder perceptions on how accessibility to good quality medicines can best be ensured. This research employed a quantitative research approach which involved random sampling and analysis of metformin tablets from Lagos, Nigeria and a qualitative research approach which involved semi-structured interviews with different stakeholders (consumers, medicine sellers such as community pharmacists, patent medicine vendors and traders as well as policy makers in pharmacy).

This chapter begins by giving the context in which the research was carried out which includes an overview of current health situation in Nigeria. This is followed by a discussion of drug supply, distribution and regulation in Nigeria, presenting a background to the research. Definition of terms and history of medicines counterfeiting is presented towards the end of the chapter followed by a detailed illustration of the structure of the thesis.

1.2 Background and context

Nigeria is located in West Africa. It is Africa's most populous country (about 177 million people); accounting for a quarter of the population of Africa. It is divided into 6 geopolitical regions namely; south-south, south-east, south-west, north-east, north-west and north-central (see figure 1). The 6 geopolitical regions are further divided into 36 states with Abuja as the federal capital territory and Lagos state as the most populated and ethnically diverse (Central Intelligence Agency (CIA), 2014).

Figure 1: The 6 geopolitical zones of Nigeria (Adapted from Federal Ministry of Health and World Health Organisation, 2010)

1.3 Overview of Current Health Situation in Nigeria

The results of the World Health Organisation (WHO) report on monitoring the world's health system performance which was last released in 2000 ranked the Nigeria's overall health system performance 187th among the 191 member states (WHO, 2000). More recent data from the Nigerian National Health Policy (Federal Ministry of Health, 2004) did not indicate any significant improvement in this position. The Nigerian National Health Policy (NNHP) of 2004 indicated that the nation's poor health state is as a result of communicable (for instance Malaria, Tuberculosis (TB) and Human Immuno deficiency Virus (HIV) and non-communicable (for instance Hypertension and Diabetes) diseases accounting for 72% and 23% of annual deaths respectively while other unknown causes account for the remaining 5%. Recently, Nigeria has been ranked 11th among the 22 countries with high TB burden (WHO, 2013). Malaria in Nigeria accounts for more deaths than it does in any other country globally with about 100 million cases and over 300, 000 deaths per year (United States Embassy in Nigeria, 2011). HIV is also a major public health problem in Nigeria with Nigeria accounting for the second highest number of new infections each year (Avert, 2014). About 3.7% of the population live with HIV (Avert, 2014). According to the Federal Ministry of Health, (2004), these communicable and non-communicable diseases in addition to other factors relating to the poor health care system such as poor ante-natal care have led to an increase in infant and maternal mortality rate and a decrease in life expectancy from 51.01 years in 2003 to 46.94 years in 2010 (Central Intelligence Agency (CIA), 2010).

Table 1 summarizes the key health indicators of Nigeria.

Table 1: Health Indicators of Nigeria

Key Health Indicators	Value
Total Population (2006 census)	144, 720, 000
Annual growth rate	3%
Fertility rate	5.84
Crude death rate per 1000	16
Annual per capita income	$260
Gini index	37.5
Life expectancy at birth	48 years
Healthy life expectancy	42 years
Infant mortality (per 1000 live births)	122
Maternal mortality (per 100, 000 live births)	1000
Contraceptive prevalence rate	6%
Under five mortality per 1000	191
Average rate of immunisation	18%

(Adapted from World Bank, 2000 cited in United Kingdom Department of International Development Health Systems Resource Centre (DFID HSRC), 2000; Federal Ministry of Health and World Health Organisation, 2010; Ogbonnaya, 2009)

Note: Gini index is the extent of inequality among individuals of households within an economy in terms of their income or their consumption expenditure. A Gini index of 0 means a perfect equality while a Gini index of 100 means a perfect inequality (World Bank, 2014). Nigeria has a Gini index of about 37.5 suggesting a high level of income inequality, which is common in many other countries in Africa. The median Gini index value for Africa is 41.5% (Wolfram Alpha, 2014).

The health indicator values presented above are indicative of the poor health status of majority of people living in Nigeria. These figures are even of greater concern when compared to other countries in the West African region that are faced with similar disease burden as Nigeria but has significantly better health indicator values. One of such countries is Ghana. Comparing the health indicator values of Nigeria above with the health indicators of Ghana as published by Ghana Health Service, (2012); Ghana has a life expectancy at birth of 60 years compared to Nigeria with a life expectancy at birth of 48 years. The under-five mortality per 1000 in Ghana is 80, a figure less than half of the

under-five mortality in Nigeria. Infant mortality per 1000 live births in Ghana is 50 compared to 122 in Nigeria and the crude death rate per 1000 in Ghana is 9.4 compared to Crude death rate per 1000 of 16 in Nigeria. Although this comparison of health indicators made here is between Nigeria and Ghana, it mirrors the situation of Nigeria when compared to majority of other countries in sub Saharan Africa.

Furthermore, the National Health Policy revealed that there has been a downward trend in health development since 1993 (Federal Ministry of Health, 2004). This downward trend was among other factors attributed to irregular supply and non-availability of good quality essential medicines. It therefore appears that the National Drug Policy which was adopted and launched in 1990 is yet to achieve its goal of ensuring access to safe, effective and affordable good quality drugs at all levels of health on the basis of health care needs (Federal Ministry of Health, 2003). This failure of the National Drug Policy (NDP) can be attributed to a lot of factors among which include the failure of the National Health Policy (NHP), smuggling and dumping of medicines as well as illegal sourcing of medicines which encourages sale of fake, substandard, adulterated drugs and unregistered drugs, lack of political will and law enforcement, poor funding and poor development of the local pharmaceutical industries (Peterson and Obileye, 2002). Presently local drug manufacturing accounts for about 25% of Nigeria's pharmaceutical markets while the remaining 75% are mainly imports from Asian countries (United Nations Industrial Development Organisation, 2011).

Additionally, it is worthy of note that about 60-80% of health service provision comes from the private sector and the traditional medicine providers whose activities are often unregulated and not standardised (DFID HSRC, 2000). Drug hawkers are found in many places in Nigeria selling medicines that may be fake, adulterated or degraded. Patent medicine shops (PMS) are owned by non-professionals and may operate illicit activities such as unsafe abortions,

injections and unnecessary administration of intravenous (IV) fluids (Dahiru, 2009). The majority of substandard and counterfeit medicines circulating in Nigeria are believed to come from the open markets and these unregulated patent medicine shops (PMS) in the country (Peterson and Obileye, 2002). According to Pharmaceutical Society of Nigeria (PSN), (2001) cited in Peterson and Obileye, (2001), about 49.6% of counterfeit medicines come from the open markets while about 32.8% come from the patent medicine stores. Interestingly, about 58.8% of physicians in Lagos prefer to purchase their medicines from these open markets (Peterson and Obileye, 2002). This shows that these markets may have good patronage by both the illiterates and health care professionals.

Another common feature in most streets and markets in Nigeria are traditional medicine healers (herbalists) who make claims of curing almost all diseases and sell concoctions to patients. Patients often seek the help of traditional medicine healers and street vendors before visiting public health facilities. This may be due to inaccessibility of public health facilities, low standard of care and high cost of services in most available public health facilities (Dahiru, 2009).

1.4 Drug Supply, Distribution and Regulation in Nigeria

The National Drug Policy (NDP) guides public drug supply in Nigeria. The National Drug Policy, which was last revised in 2003, has a major goal of ensuring that medicines which are effective, affordable, safe and of good quality are available for use at all times. It also promotes rational drug use and local production of essential medicines (Federal Ministry of Health, 2003).

Drug distribution in Nigeria is still not well organised. This disorganised nature of drug distribution in Nigeria may in part be attributed to insufficient number of pharmacists around 1960. Due to the lack of pharmacists at the time, some of

the existing pharmacists engaged in multiple registrations of premises with the agreement of the shop owners, thereby creating room for traders and other non-professionals who lack the basic knowledge of drugs to engage in the sale of medicines without supervision (Peterson and Obileye, 2002). With time these traders obtained licenses to trade on patent and proprietary medicines under the liberalisation policy of the government at the time (Toye, 2009). This consequently led to the establishment of big drug markets in major Nigerian cities (Lagos, Kano and Onitsha). Presently there are open drug markets in other cities such as Aba, Enugu, Maiduguri, Gombe, Kaduna and Owerri (Pharmaceutical Society of Nigeria, 2001 cited in Peterson and Obileye, 2002). These markets are unregulated and unlicensed with the majority of the shops failing to meet the standards set by the Pharmacists Council of Nigeria (PCN) (Peterson and Obileye, 2002). They also create a ready market for counterfeit medicines and poor quality medicines as a whole (Nigerian Food and Drug Regulatory Advisor, 2010).

The sources of medicines used by patients include pharmacies of public and private healthcare institutions, retail medicine outlets (retail pharmacies, patent medicine shops, illegal street vendors and hawkers) (Federal Ministry of Health and World Health Organisation, 2010). Although, patent medicine shops are allowed by the law to stock over the counter (OTC) medicines, they often stock all categories of medicines, diagnose, prescribe and administer injections and are a major source of drugs and disease information for patients as they are widely distributed across the nation (Federal Ministry of Health and World Health Organisation, 2010). This means that over the counter, prescription and controlled drugs can be obtained from anywhere including the open drug markets, patent medicine stores, pharmacies and hospitals.

Patent medicine shops are greater in number than pharmacies and pharmacists, which are in short supply. For instance, in comparison to the wide availability of patent medicine shops, there were only about 2,685 registered

pharmacies in Nigeria in 2006, which were unequally distributed in favour of the urban areas (Federal Ministry of Health and World Health Organisation, 2010). In 2001, there were about 9,308 pharmacy graduates in Nigeria; out of which 6,412 were registered. This makes pharmacist patient ratio to be about 1 to 10,743 based on the estimated population of Nigeria at the time. These figures give an idea of the scarcity of pharmacists when compared to the large number of people in Nigeria who need their services. This scarcity may also be one of the reasons why some patients seek their medicines from other sources and may be a contributory to the chaotic nature of medicine supply and distribution in Nigeria.

The majority of the drug distribution outlets are located in the urban areas; urban areas of Nigeria account for 70% of health care workers and facilities (Campbell 1998 cited in Peterson and Obileye, 2002). Lagos alone accounts for 30% of the total number of pharmacies in the country (see Appendix 1). For the states where pharmacies are present, the percentage of pharmacies in urban area of each state of the federation ranges from 50% in states such as Kebbi and Abuja to 100% in other states such as Bayelsa, Ebonyi, Sokoto and Yobe state (see Appendix 1). About 98% of pharmacies in Lagos state are located in the urban areas (PCN, 2000 cited in Peterson and Obileye, 2002).

Several bodies have been established to help improve the quality of medicines supply and distribution in Nigeria. For instance, the National Agency for Food and Drug Administration and Control (NAFDAC) was formed following the resolution by the 1988 World Health Assembly (WHA), which requested engagement of countries in the fight against medicines counterfeiting. It is the responsibility of NAFDAC to control the quality of food, drugs, cosmetics, medical devices, chemicals, detergents and packaged water which are either imported or locally manufactured (Yusuff and Tayo, 2004). The Federal Task Force on Fake and Adulterated Drugs established by decree 21 of 1988 as amended, an arm of NAFDAC is empowered by Section 8 of Decree 25 of 1999

to close down the open drug markets and all unregistered premises (Orivri, 2009) (See Appendix 2). The Pharmacists Council of Nigeria (PCN) is in charge of regulating professional practices including the issuance of licenses to Pharmacists and Patent Medicine Vendors (PMVs) as well as drafting the pharmacy education curriculum (Yusufu, 2008).

The lack of enforcement by the Federal Task force, conflict of responsibilities between PCN and NAFDAC as well as limited access to essential medicines have contributed in making recent efforts to permanently close the open drug markets and improving the quality of medicines in Nigeria futile (Nigerian Food and Drug Regulatory Advisor, 2010). In addition, the increased complexity of the nature of Nigeria's drug distribution network remains an obstacle in the fight against medicines counterfeiting and ensuring the availability of good quality, efficacious and safe medicines in general. Other issues such as lack of good transportation networks, unavailability of funds, erratic power supply and unreliable telecommunication networks constitute a significant challenge to drug dispensing particularly in the rural areas (Peterson and Obileye, 2002).

The problem of poor quality medicines is particularly important in many developing countries such as Nigeria which are faced with an increased burden of both communicable and chronic diseases among other numerous public health issues as described by Beran, (2006). The health workforces in these countries are overburdened, in short supply and are faced with the problem of poor quality medicines.

In addition to medicines being a major target to counterfeiters because of their low bulk despite being of high value, chaotic drug distribution systems, leaky supply chain systems, scarcity and/or erratic medicines supply, high cost of medicines, vested interests both on the part of the regulatory officials and the

counterfeiters, weak laws and lack of enforcement of existing laws, ignorance or low literacy rates, pervasive poverty, poorly equipped laboratories, under-funded regulatory authorities as well as poor handling and manufacturing practices and high level of corruption in the health care system has been identified as the common reasons for the increased prevalence of counterfeit medicines in such countries as Nigeria (Erhun et al., 2001). The high cost of medicines is worsened by high import tariffs on drugs in such countries as Nigeria, Iran, India, Congo, Morocco and Zimbabwe among others that have tariffs of 15% or more (Bate and Boateng, 2006 and Wertheimer and Norris, 2009). This constitutes a significant financial burden to the patients especially where they are forced to pay for the medicines out of their pocket (Wertheimer and Norris, 2009). Poor quality medicines can also result from such factors as degradation of medicines when exposed to tropical weather conditions as well as inadequate quality control on the part of the manufacturers. Furthermore, the problem of lack of human and financial resources needed to tackle the problem of poor quality medicines creates a conducive atmosphere for the proliferation of trade in counterfeit and sub-standard medicines (Caudron et al., 2008).

1.5 Definition of terms

Several factors such as the raw materials used, manufacturing environment, formulation, manufacturing process, equipment, technical know-how for production and packaging of the product, transportation and storage conditions determine the quality of medicines. Quality specifications are usually set by the manufacturers and are published in pharmacopeias (United States Pharmacopiea; USP, 2010). Poor quality medicines refer to medicines (legally registered, generics or counterfeits), which do not meet the official specifications for strength, quality, purity, packaging or labelling (USP, 2010).

There remains a lack of agreement among stakeholders on a universal definition for counterfeit and substandard medicines. This has significantly

hindered initiatives that are aimed at curbing medicines counterfeiting (Caudron et al., 2008).

In an attempt to differentiate counterfeit drugs from substandard medicines which are both categories of poor quality medicines; the World Health Organisation (WHO) defines a counterfeit drug as “a medicine, which is deliberately and fraudulently mislabelled with respect to identity and/or source” (Wondemagegnehu, 1999 cited in Newton et al., 2006a). “Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct or wrong ingredients, without or with insufficient active ingredients or with fake packaging” (World Health Organisation 2010). It has also been found that counterfeiters copy or imitate existing products. They can also manufacture products that they have invented, and are not normally available (IMPACT, 2008). All counterfeits are, by nature, at high risk of being substandard (IFPMA, 2010). According to WHO regional office for the Western Pacific (WPRO) (2005-2010)

Drugs are classed as counterfeit if they fall into any of the following seven categories:

1. Fake packaging and correct quantity of correct ingredient;
2. Fake packaging and wrong ingredient;
3. Fake packaging and no active ingredient;
4. Fake packaging and incorrect quantity of correct ingredient;
5. Genuine packaging and wrong ingredient (deliberate);
6. Genuine packaging and no ingredient (deliberate); or
7. Genuine packaging and incorrect quantity of ingredient (deliberate).

According to the WHO and the United States Pharmacopeia,

Substandard medicines are regarded as “genuine drug products that do not meet the quality specifications set for them” (Wondemagegnehu, 1999; WHO, 2005 and Smine, 2002). They are approved and legally manufactured, but do not meet all quality criteria. They may pose a significant health risk, as they are not of good quality, but should not be regarded as counterfeit.

For instance if there is:

Genuine packaging + incorrect quantity of ingredient (not deliberate). Examples are choloroquine samples with genuine packaging from a genuine manufacturer but with incorrect quantity of active ingredient as shown in Maponga and Ondari, (2003). Another example is when a product from a genuine manufacturer with the correct quantity of active ingredient gets contaminated for example contaminated magnesium sulfate leading to *Serratia septicaemia* and gentamycin-resistant *Pseudomonas aeruginosa* in gentamycin eye drops causing severe infections (Newton et al., 2010)

While a genuine medicine has:

Genuine packaging + correct quantity of ingredient

These definitions above by WHO for counterfeit (falsified or spurious) and substandard medicines were adopted in this research project and form part of medicines regarded as poor quality medicines in this entire report. These WHO definitions clearly show that additional inspection of the packaging of the drugs may be helpful in differentiating which medicines are counterfeit from those that are substandard. However, this may be limited by the sophisticated nature of medicines counterfeiting as the counterfeiters have successfully copied even complex holograms. Further tests such as forensic examinations of trademarks or product designs can be carried out to differentiate counterfeited medicines from substandard medicines as well as to determine the source of the counterfeited products (Newton et al., 2008). The use of techniques such as HPLC and NIR have also proved helpful in detection of counterfeits. This

distinction is vital since the reasons for their production and potential countermeasures are different. For example, the strategies to combat substandard medicines may be more straightforward. In this instance, focus can be placed on the manufacturing and quality assurance processes in production to resolve these issues, which is not the case with tackling medicines counterfeiting where the need to tackle fraud may be obvious (Newton et al., 2010).

Due to the varying nature as well as the complexity of medicines counterfeiting in some countries, the definition of counterfeit medicines also varies from country to country. For instance; The National Agency for Food and Drug Administration and Control (NAFDAC) - Nigeria's drug regulatory agency - has identified counterfeit drugs to be those with;

"Same quantity of active ingredient as the genuine brands which are clones that are unlikely to produce the desired therapeutic effects due to differences in their formulation and bioavailability when compared to the genuine brands or Medicines with insufficient or without active ingredient, expired medicines as well as toxic or ineffective herbal preparations and medicines lacking the name and address of the manufacturer" (Akunyili, 2004).

The Nigerian Counterfeit and Fake Drugs and Unwholesome Processed Foods (1999 Miscellaneous Provisions) Decree defines a fake drug as:

1. "Any drug product which is not what it purports to be;
2. or any drug or drug product which is so coloured, coated, powdered or polished that the damage is concealed or which is made to appear to be better or of greater therapeutic value than it really is, which is not labelled in the prescribed manner or which label or container or anything accompanying the drug bears any statement, design, or device which makes a false claim for the drug or which is false or misleading;
3. or any drug or drug product whose container is so made, formed or filled as to be misleading;

4. or any drug product whose label does not bear adequate directions for use and such adequate warning against use in those pathological conditions or by children where its use may be dangerous to health or against unsafe dosage or methods or duration of use;
5. or any drug product which is not registered by the Agency in accordance with the provisions of the Food, Drugs and Related Products Registration Decree 1993, as amended."

The above definition shows that any medicine that is not registered by NAFDAC is also classed as counterfeit. This means that what may be considered counterfeit in Nigeria may not be considered as such in other countries. It also potrays products that have been genuinely registered by drug regulatory bodies of other countries and imported into Nigeria but sold without further registration with NAFDAC as counterfeit. Other countries such as Pakistan, United States, Brazil, Portugal, Australia, India, The Philippines and Japan have their own definitions for a counterfeit medicine.

Apart from these country definitions of counterfeit medicines, which seem to be rooted in a public health perspective, some other organisations define counterfeiting from an Intellectual Property (IP) right infringement point of view. For example, the World Trade Organisation (WTO) Agreement on Trade Related Aspects of Intellectual Property defines counterfeit trademark goods as “meaning any goods, including packaging, bearing without authorisation a trademark which is identical to the trademark validly registered in respect of such goods, or which cannot be distinguished in its essential aspects from such a trademark, and which thereby infringes the rights of the owner of the trademark in question under the law of the country of importation” (Forzley, 2005).

WHO research into the use of the term “counterfeit” revealed that majority (34) of the member states used the term “counterfeit” in their national legislation. Other terms used include “falsified”, “illicit”, “illegal”, “unregistered”, “unauthorized” and “adulterated”. Besides these variations in terms; the meaning of counterfeit medicines in some of the national legislations includes unauthorised medicines, substandard medicines and intellectual property infringement. The implication of these is that what may be considered a counterfeit in one country may not be viewed as such in another country (Deisingh, 2005).

1.6 History of medicines counterfeiting

Medicines counterfeiting is not new. It can be dated back to the first century in Greece when Dioscorides first classified drugs by their therapeutic use and warned of the dangers of adulterated drugs as well as how they could be detected (WHO, 1999a cited in Newton et al., 2006a). It has also been referred to as the ‘second oldest profession’ (Lybecker, 2008). Other early incidents of counterfeiting includes the adulteration of herbal medicines such as *Valeriana officinalis,* adulteration of *Ferula assa-foetida* with red clay and the adulteration of the Peruvian cinchona bark with other astringent barks and aloes in the 17th century (Newton et al., 2006a). In the mid 19th-century, there was a widespread adulteration of medicines especially quinine which led to the establishment of the code of ethics for pharmacists and guides on the detection of counterfeits in the United States of America (Newton et al., 2006a).

The first case of a documented death which was attributed to fake anti-malarial was in 1999 when a 33 year old man from Cambodia died despite treatment with mefloquine, further testing revealed the mefloquine as fake (Strobel et al., 2010). Since then there have been anecdotal reports of tragedies resulting from the use of poor quality medicines.

In Nigeria, medicines counterfeiting was first observed in 1968 when there was a deregulation of Crown agents as sole distributors of medicines (Akunyili, 2007). Owing to the global economic recession at the time and the consequent devaluation of the Naira, which is Nigeria's official currency, most drugs became unaffordable to the majority of the population leading to the issuance of import licenses for drugs (NAFDAC, 2002-2009). Politicians largely influenced the implementation and issuance of import licenses. This led to its issuance to unqualified persons who lacked adequate knowledge about drugs. This situation coupled with an increase in demand for drugs, limited number of pharmacists and continued irrational drug use led to increased importation of fake drugs by non-professionals since they were cheaper than genuine drugs (Peterson and Obileye, 2002). It then became obvious that the existing laws on medicines distribution could not tackle the problem of drug quality in Nigeria and the Counterfeit and Fake Drugs Decree No.17 of 1989 was promulgated. This established the Federal Task force that is now an arm of NAFDAC. Decree No. 17 of 1989 was later replaced with Decree 25 of 1999 that included a stricter penalty for forfeiture and a fine of N500,000 for offenders (Peterson and Obileye, 2002).

Despite the importance of tackling medicines counterfeiting, it was not given international recognition until about 30 years ago when it was first discussed at an international health meeting; the WHO Conference of Experts on Rational Drug Use (WHO, 2006c). Since then several efforts have been made by the WHO to help tackle the problem of poor quality medicines. WHO held a conference in Rome in 2006, which led to the formation of International Medical Products Anti-counterfeiting Taskforce (IMPACT) as a collaborative effort among a range of stakeholders to curb medicines counterfeiting. IMPACT focused on major technical areas which were identified as needing action nationally and internationally; legislative and regulatory infrastructure, regulatory implementation, enforcement, technology development for detection of counterfeits and technology transfer to developing countries as well as

communication of risk and innovations/strategies aimed at curbing counterfeiting (WHO, 2010a). What is now unique about medicines counterfeiting when compared to what was reported prior to the 20th Century is the international nature and scope of the problem as well as the sophisticated technology and strategies the counterfeiters currently use (Forzley, 2005).

1.7 The thesis structure

This research project sought to conduct a systematic review of the literature on medicines quality in addition to validation of MAS; an anti-counterfeiting intervention and exploring stakeholder perspectives on issues relating to quality of medicines distributed in Nigeria. The main sections of the thesis are the Introduction, Methodology, Results, Discussion and Recommendations for future research and Conclusion. The results section was divided into two chapters in order to give a clearer understanding of the results arising from the different phases of this research. Figure 2 illustrates how the thesis is structured.

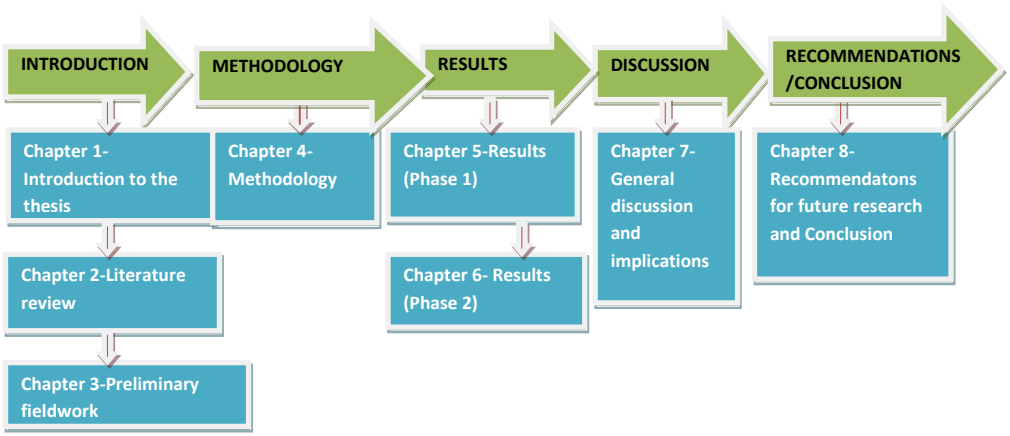


Figure 2: The thesis structure

1.8 Conclusion

This chapter presents a background to the research by describing the context in which the research was carried out, giving an overview of the health system of Nigeria as well as drug supply, distribution and regulation in Nigeria. Inefficiencies such as availability of poor quality medicines are also discussed.

In order to systematically examine the extent and impact of the use of poor quality medicines in Nigeria as well as the strategies in place to tackle the problem and to provide a focus for the research, a systematic review of the literature was conducted. The details of the literature are formally presented in Chapter 2.

Chapter 2

Review of the literature

2.1 Introduction to chapter

A systematic review of the literature was necessary in order to find out what has been done in the field of medicines quality and how the present research can add to the existing body of knowledge. The review was continually updated throughout the data collection, data analysis and synthesis phases of the study. This chapter of the thesis starts by stating the objectives of the literature review. It goes ahead to describe the procedure for the review. This is followed by a discussion of the results obtained from the literature review based on the literature review objectives. The limitations of the review and future areas of research identified were also presented. At the end of review, the objectives and rationale for conducting the research as well as the research approach were presented.

The literature review aimed at identifying the extent of medicines counterfeiting and poor quality medicines in Nigeria and other low-income countries such as other sub-Saharan countries that may be facing similar developmental challenges as Nigeria. This review did not explore in details the extent of counterfeiting in developed regions such as Europe and the United States of America. However, the worldwide impact and strategies in place to combat this public health threat were reviewed.

2.2 Objectives of the systematic literature review

The objectives of the literature review were to identify;

i) The extent of poor quality medicine

ii) The impact of poor quality medicine

iii) The strategies in place to curb the existence of poor quality medicine

iv) The barriers hindering the fight against poor quality medicines and

v) Existing evaluation of interventions against poor quality medicines.

Publications that described the extent and impact of poor quality (counterfeit and substandard) medicines in Nigeria and other parts of the world as well as strategies in place to combat medicines counterfeiting and the problem of poor quality medicines as a whole were searched for in order to determine what has been done in these areas.

2.3 Methods

2.3.1 Search strategy

In order to obtain the articles relevant to meeting the review objectives, an electronic, English language search of PUBMED and EMBASE databases were carried out. Entering the key words; substandard and drug and Nigeria yielded 7 relevant articles; Onwujekwe et al. (2009), Taylor et al. (2001), Verduin-Mutiganzi and Verduin-Mutiganzi, (1998), Garuba et al. (2009) and Bate and Hess et al. (2010), Osadebe and Akabogu (2003) and Shakoor et al. (1997) which provided links to 15 other relevant studies.

A bibliographical search of Onwujekwe et al. (2009) retrieved Atemnkeng (2007), Amin et al. (2005), Amin and Kokwaro (2007), Basco (2004), Bate et al. (2008), Kaur et al. (2008), Newton et al. (2006a) and Wondemagegnehu (1999) while bibliographical search of Shakoor et al. (1997) yielded Ifudu (1989) (the first systematic study conducted to examine the quality of drugs on sale in Nigerian street markets), OgohAlubo (1994), Okuonghae et al. (1992), Roy (1994), Abdi et al. (1995), Sowunmi et al. (1994) and Hanif et al. (1995). WHO (2011) was retrieved in Geneva when the researcher attended the WHO

advanced technical briefing seminar on quality assurance and safety of medicines at the WHO headquarters in Geneva. It was from this study that Hebron et al. (2005) was obtained. Minzi et al. (2003) was obtained from the citation in Hebron et al. (2005).

When the key words; counterfeit or substandard or poor quality and drug or medicine and Nigeria were combined in PUBMED; 10,744 articles were retrieved. However, no new relevant articles were retrieved. No new articles were retrieved when the terms pharmaceuticals, pharmaceutical products or medical products were used in PUBMED instead of drug or medicine. A repeat of the search in EMBASE by entering the same keywords as in PUBMED yielded all the articles obtained through PUBMED in addition to 2 other studies; Nnamdi et al. (2009) and Eichie et al. (2009). One article Erhun et al. (2001) was retrieved from Eichie et al. (2009). One of the studies; Shakoor et al. (1997) was reported twice (See appendix 3) as the study was carried out for Nigeria and for Thailand. Searches were unlimited for all the databases searched. A bibliographical review was done for the studies retrieved from EMBASE. Relevant articles were seen; however, most of them were already retrieved from PUBMED. A search of an article Arya (1995) which was retrieved from PUBMED, provided a link to a review; Kelesidis et al. (2007); from which the citation; Okeke et al. (1995), Newton et al. (2001), Kayumba et al. (2004), Nazerali and Hogerzeil (1998) and Kenyon et al. (1999) were obtained. One of the articles (Odeniyi et al., 2003) was retrieved from the citation of Deisingh, (2005).

The key words counterfeit and medicines were combined with names of 45 countries in Sub-Saharan Africa; Tipke et al. (2009) was retrieved when combined with Ghana. A study, Idowu et al. (2006) cited in Amin and Kokwaro, (2007) was excluded from the study, as there were no details on the analysis performed on the chloroquine samples. In all 46 articles that were relevant in

determining the extent of poor quality medicines in Nigeria and related countries were obtained (these are summarised in Appendix 3).

Further searches were conducted by combining the key words such as extent or scope and drug quality or substandard or counterfeit and drug/drug*/medicine/medicine* and Nigeria. However, this did not help to retrieve any more relevant articles. Key questions were also entered in the Google search engine in order to retrieve relevant articles. In doing this, a lot of news articles and other grey literature were obtained rather than peer reviewed studies or articles. A few of the articles that were already seen in PUBMED reoccurred when searches were conducted in the Google search engine.

A search of the term counterfeit medicines in the WHO regional library data database for the Western Pacific retrieved WHO, (1999a) and WHO, (1999b), when the same key words were entered into other regional databases such as South East Regional Office (SEARO) and African Regional Office (AFRO); no relevant article could be retrieved. A repeat of the search by entering the same key words and searching all WHO sites yielded nineteen other relevant articles; WHO, (2003) and WHO, (2010a), WHO, (2010b), WHO, (2010c), WHO, (2010d), WHO, (2010e), WHO, (2010f), WHO, (2010g), WHO, (2006a), WHO, (2006b), WHO, (2006c), WHO, (1998), WHO, (1995), WHO, (2008), WHO, (1997), WHO, (2005), World Health Organisation (2003), World Health Organisation (1999a) and World Health Organisation (1999b).

No study on the extent or impact of poor quality medicines could be retrieved from NAFDAC official website when it was visited. However, other articles related to poor quality medicines in Nigeria and current initiatives were obtained. One of the articles (Akunyili, 2006a) obtained from a Google search made reference to studies by NAFDAC at baseline in 2001 (Nnani et al., 2001) to determine the extent of unregistered and unauthorised medicine use with

repeat studies conducted in 2003 and 2004 as well as reference to another study by NAFDAC in collaboration with WHO and DFID. However, the studies referred to could not be retrieved directly from the databases searched, as the full citation details were not provided. NAFDAC and DFID were both contacted directly via e-mail in order to retrieve these studies or get more information regarding them. However, the stated studies could not be retrieved from both sources.

A further search of the following terms; anticounterfeiting and pharmaceuticals on the International Bibliography of Social Sciences (IBSS) database retrieved two relevant articles; Lybecker, (2007) and Lybecker, (2008) which focused on extent, impact and strategies in combating medicines counterfeiting. The use of the key words used in PUBMED in IBSS and the Web of Knowledge could not retrieve any more relevant article.

Due to the key strategies instituted under the leadership of Akunyili, a search was made via Google and Google scholar to retrieve any of her relevant articles; this retrieved Akunyili (2003), Akunyili (2004), Akunyili (2005a), Akunyili (2006a), Akunyili (2006b) and Akunyili (2007). When the phrase “quality of metformin tablets in Nigeria” was put into the Google search engine, one article Osadebe and Akabogu (2003) was retrieved. NAFDAC website was visited to retrieve NAFDAC (2010a) and NAFDAC (2010b). The International Pharmaceutical Students’ Federation (IPSF) site was visited and information on the Anti-counterfeit Drug Campaign organised by IPSF was retrieved (IPSF, 2007). International Pharmaceutical Federation (FIP) website was visited and this yielded FIP, (2010a), FIP (2010b) and FIP (2010c). FIP (2010b) provided link to the European Directorate for Quality of Medicines and Health Care (EDQM) website, from which EDQM, (2010) was obtained. The European Federation of Pharmaceutical Industries and Associations (EFPIA) website was visited; from which EFPIA (2010) was retrieved. The Food and Drug

Administration (FDA) website was visited; from which FDA (2009) was retrieved as it contained relevant information on strategies employed by the FDA.

Furthermore, the websites of different pharmaceutical companies were visited (Pfizer, Glaxo, GSK, AstraZeneca, Johnson and Johnson, Eli Lilly, Abbott, Merck, Aventis, Novartis, Bristol-Myers Squibb, Wyeth and Roche); most of the information available was vague rather than empirical as they lacked adequate methodology. Except for Bristol-Myers Squibb, some information were retrieved on strategies the other firms have employed in curbing medicines counterfeiting (see Appendix 3).

In order to evaluate the effectiveness of anti-counterfeiting strategies, a search on IBSS using the key words anti-counterfeiting and pharmaceuticals revealed two relevant articles; Lybecker, 2007 and Currais et al. (2008) which developed an economic model to evaluate some of the anti-counterfeiting strategies geared towards curbing medicines counterfeiting. When the question; mobile phones for detection of counterfeit or fake medicines was entered into EMBASE; an article; Abdoulaye et al. (2006a) was retrieved. Combination of keywords such as counterfeit, substandard, poor quality, medicines or drugs or pharmaceuticals and barriers or strategies in PUBMED, EMBASE and IBSS could not retrieve any more relevant articles.

Contact was made with some organisations to retrieve materials that were identified during the search and thought would be helpful. For instance African Matters Limited (AML) was contacted for the proceedings of the counterfeit medicines workshop in the East African Countries (EAC) but this could not be retrieved. Proof of concept result, one page overview of MAS, brochure and the Biofem case study report on MAS were obtained from Sproxil.

2.4 Objective 1: Extent of poor quality medicines in Nigeria

2.4.1 Size of the problem of poor quality medicines in Nigeria

Out of all the quantitative field studies retrieved from the search of the literature, Sixteen of them were conducted specifically to determine the proportion of collected samples which did not meet pharmacopeial criteria in order to ascertain the incidence of poor quality medicine in Nigeria; Taylor et al. (2001), Shakoor et al. (1997), Bate at al. (2009a), Eichie et al. (2009), Nnamdi et al. (2009), Onwujekwe et al. (2009), Odeniyi et al. (2003), Sowunmi et al. (1994), Babalola et al. (2004), Okeke and Lamikanra, (1995), Odunfa et al. (2009), Osadebe and Akabogu, (2003), Esimone at al. (2008), Ifudu, (1989), Ofonaike et al. (2007) and WHO (2011). None of the studies identified clearly distinguished between counterfeit and substandard medicines.

In trying to describe the extent of medicines counterfeiting as one category of poor quality medicines, it is important to note that the majority of the evidence available is anecdotal. This is probably due to either the limited number of peer reviewed studies conducted to estimate the scale or concealment of the problem by some legitimate manufacturers in order to avoid adversely affecting their reputation and public trust in medicines (Shakoor et al., 1997). Much of the information on the quality of medicines is published in the grey literature such as in newspapers and Internet articles instead of in the scientific literature, suggesting significant under reporting or a lack of properly designed studies.

Studies aimed at determining the extent of poor quality medicines where available are often limited to a few drug classes and test for a narrow set of problems such as antimalarials and antibiotics as can be seen from Appendix 3. Thirty-one of the studies included anti-malarials, six of the studies involved anti-bacteriaes while four involved anti-tuberculosis drugs. Only a few of the studies involved a relatively wider range of therapeutic classes; Taylor et al. (2001)

sampled anti-malarials, anti-bacteriaes, anti-tuberculosis, antifungal and anthelminthic drugs. Bate at al. (2009a) and Bate et al. (2009b) sampled anti-malarial, antibacterial, and anti-tuberculosis, Wondemagegnehu (1999) sampled antimalarials, anti-bacteriaes, anti-tuberculosis drugs, and analgesics in addition to other medicines such as diazepam, cimetidine, ranitidine, multivitamin/ vitamin B, prednisolone and salbutamol. One study; Osadebe and Akabogu (2004) assessed the quality control parameters and interchangeability of different brands of metformin hydrochloride marketed in Nigeria. Ifudu (1989) sampled purgatives, benzodiazepines, antipsychotics, multivitamin/vitamin B and some haemopoetic medicines. Eichie et al. (2009) and Ofonaike (2007) were the only two studies that involved solely analgesics.

The majority of studies conducted in developing countries in order to determine the prevalence of medicines counterfeiting show that about half of the drugs tested were substandard. In one study conducted as part of the Juniper operation by INTERPOL anti-counterfeiting taskforce, it was found that about half (195) samples out of a total of 391 samples of anti-malarial drugs collected from different regions of South East Asia (Vietnam, Cambodia, Lao PDR, Myanmar (Burma) and the Thai/Myanmar border contained no or small quantities of artesunate. Some of the medicines contained banned pharmaceuticals, such as metamizole, and Safrole, a carcinogen and raw material for the manufacture of methylenedioxymethamfetamine (ecstasy) (Newton et al., 2008). Fake Viagra tablets made by combining ingredients in a cement mixer have been found in Egypt (NST online, 2007 cited in Millisa McGinnis, 2010).

Studies conducted in selected African countries (Ghana, Kenya, Mali, Mozambique, Sudan, Zimbabwe, Rwanda, Tanzania, Uganda, Congo, Burundi, Angola, Botswana, Cameroon, and Burkinafaso) seemed to have similar findings. Previous studies in Kenya by Kibwage et al. (1992) and Roy, (1994) revealed that about 46% and 31% respectively of different drug samples

obtained from Kenya were substandard while more recent studies show that about 40% of medicines sampled from Kenya failed quality tests Amin et al. (2005).

Another study carried out to determine the prevalence of substandard drugs include the study by Atemnkeng et al. (2006), which showed that about 37.5% of antimalarials (artemisinin derivatives) randomly collected from pharmacies in Peoples' Republic of Congo and Kenya failed quality tests for active ingredients. Other studies aimed at determining the prevalence of poor quality medicines have also been conducted in other countries such as India (see Appendix 3).

These studies clearly show that poor quality medicines are prevalent in Africa; with almost half of the samples collected in this region being shown to fail the necessary tests. High failure rates were also obtained from samples from Thailand, Lao PDR, Myanmar, Viet Nam and Cambodia. While samples from India showed relatively lower failure rate compared to other parts of Asia. Pharmaceutical Security Institute (PSI) found that about 7% of the medicines marketed in the Philippines were counterfeits (Ham, 2003).

This finding is similar to the studies on the extent of poor quality medicines in Nigeria, which ranged from about 32% to 48% in the majority of the studies. The study by Bate et al. (2009a) showed a smaller proportion (18%) that failed the standard tests. Even so; 18% is unacceptable, as the dangers that may result from it cannot be under estimated. This reduction observed from Bate et al. (2009a) may have been due to the methodology used to determine the chemical constituent of the medicines or the small sample size (140 treatment packs). A repeat study by Bate and Hess (2010) showed that overall failure rates in Lagos had fallen from about 32% observed in 2007 to about 13% in 2010. However, this finding may have been due to the small sample sizes involved (22 samples in 2007 and 94 samples in 2010) and therefore may not

be conclusive without larger studies conducted to confirm such observations. A more recent study; WHO, (2011) shows that Nigeria had the highest number (63.9%) of failing antimalarial samples. Again the small sample size used in this study may have limited its findings.

A study by Taylor et al. (2001) which showed that 48% of randomly sampled drugs (antibiotics and antiparasitics) from Nigeria failed to comply with set pharmacopeia standards seemed to be the first to employ random sampling and tried to appropriately describe the methods used (Newton et al., 2006a). Other studies on drug quality determination which have employed random sampling in order to reduce bias include Amin and Snow (2005) and a study which was conducted in Laos (unpublished work cited in Newton et al., 2008).

A review; Kelesidis et al. (2007) showed that counterfeit and substandard forms of anti-malarials and antibiotics have been found in Nigeria (see table 2 below). This does not necessarily mean that counterfeit forms of other drugs not mentioned here do not exist in Nigeria, as there is a probability that they may not have been sampled for testing.

Table 2: Counterfeit and substandard form of medicines that have been found in Nigeria

Drug class	Examples
Antimalarials	artemisinin derivatives: dihydroartemisinin and artemether-lumefantrine), Others: Chloroquine, Sulfadoxine-pyrimethamine, Quinine sulphate and Halofantrine
Antibiotics	Penicillins: Ampicillin, Ampicillin-clavulanate, Ampicillin-cloxacillin, Amoxicillin, Cloxacillin) Macrolides: Erythromycin Sulphonamides (Cotrimoxazole, Sulphamethizole), Quinolones (Ciprofloxacin), Aminoglycosides: Gentamycin and Neomycin Others: Chloramphenicol, Tetracycline, Metronidazole

Adapted from Kelesidis et al. (2007)

Medicines from all therapeutic classes can be counterfeited (Cockburn et al., 2005). This is further illustrated by the recent drug seizures by INTERPOL in Asia and Egypt, which found counterfeits in almost all drug classes (WHO, 2010b). However, the majority of counterfeited medicines in developing countries such as Nigeria are life saving medicines such as antibiotics, anti-malarials and anti-infectives (Bate et al., 2009a).

Furthermore, contrary to expectations, it may not always be the most expensive drugs that are counterfeited; economies of scale may make counterfeiting even the cheapest drug attractive. This is shown from the results of Ofonaike et al. (2007) where relatively inexpensive medicines such as paracetamol and chloroquine were found to be of poor quality and Tipke et al. (2009) where chloroquine samples formed a significant proportion of samples that were of poor quality. It may also have been that failures observed in these studies were due to poor quality control on the part of genuine manufacturers.

Figure 3 shows the different therapeutic classes of counterfeit medicines that have been reported according to WHO.

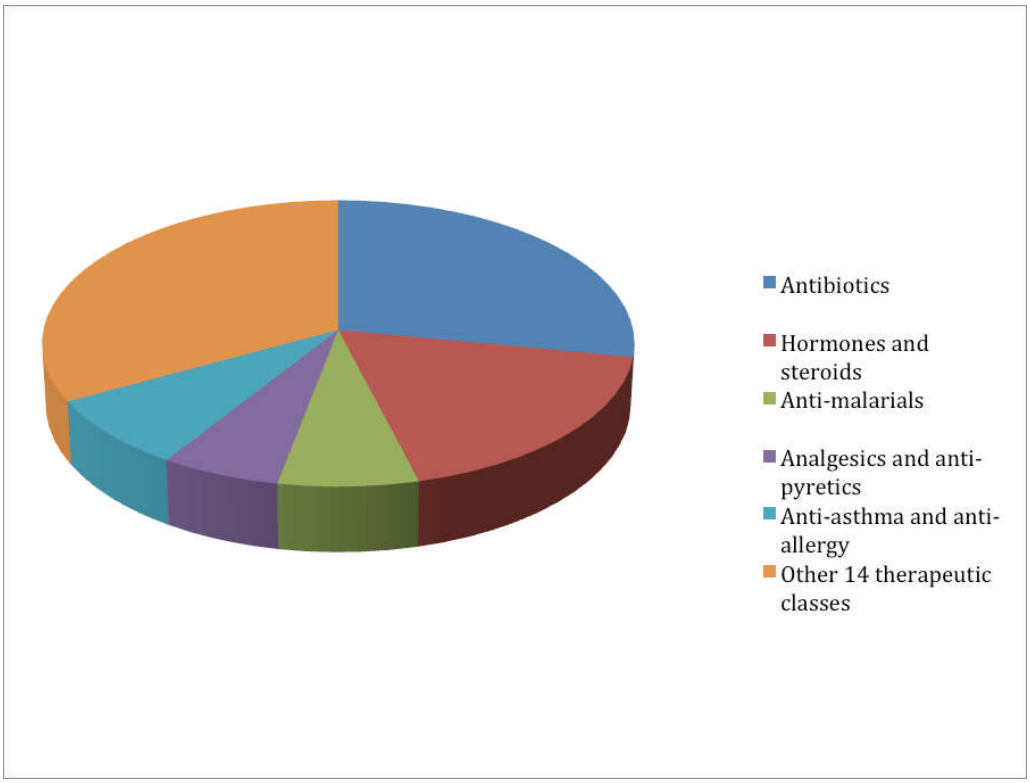


Figure 3: Therapeutic classes of counterfeit medicines that have been reported. Adapted from Harris et al. (2009).

From the results of the studies reviewed, it seems that the WHO's estimate of about 10% of the global Pharmaceutical commerce being counterfeit may be reasonable. A survey by the WHO of the quality of anti-malarials in seven African countries (Gabon, Ghana, Kenya, Mali, Mozambique, Sudan, and Zimbabwe) revealed that a significant proportion of the chloroquine and sulphadoxine-pyrimethamine tablets sampled failed quality testing (content of active ingredient and dissolution testing). About 20% to 67% of the chloroquine tablets and 5-28% of the sulphadoxine/pyrimethamine failed test for active ingredient (Maponga and Ondari, 2003).

Between 1991 and 1993, 519 samples were collected from private, public and non-governmental drug outlets and illegal markets in three African countries by the WHO; 429 of the samples were tested in independent laboratories; out of which 77 (18%) were discovered to be substandard (WHO 1995 cited in WHO, 1999b). Sixteen of the samples that failed quality tests did not contain any active ingredient, and were therefore deemed counterfeit (WHO 1995 cited in WHO, 1999b). About 20% of medicines sampled from Cameroon were found to be substandard (Taylor and Craig, 2009)

The WHO started collecting data on medicines counterfeiting in 1982; most of which were from developing countries (Forzely, 2005). Between 1984-1999, the WHO received about 771 reports of medicines counterfeiting from different countries; 78% of these were from developing countries. Figure 4 shows the geographic origin of reports of counterfeited drugs received between 1984 and 1999 by WHO region. From January 1999 to October 2002, 46 confidential reports were received from 20 different countries; 60% from developing countries and 40% from developed countries (Akunyili, 2003). Almost a third of reported counterfeited medicines did not contain active ingredients. About 20.2% had incorrect quantities of active ingredients, 21.4% included wrong ingredients, 15.6% had the correct quantities of active ingredients but with fake packaging, 1% was copy of the original and 8.5% contained high levels of impurities and contaminants (Patel, 2006). Comparing the trend in reports between 1984 and 1999 with that between 1999 and 2002 reveals that although the problem of poor quality medicines is prevalent in developing countries, there has also been an increase in counterfeiting in the developed countries (Association of International Pharmaceutical Manufacturers, 2007 cited in Lybecker, 2008). It must be noted that the information contained in the WHO database may not be completely accurate as it may contain some reports that have not been validated (Ham, 2003).

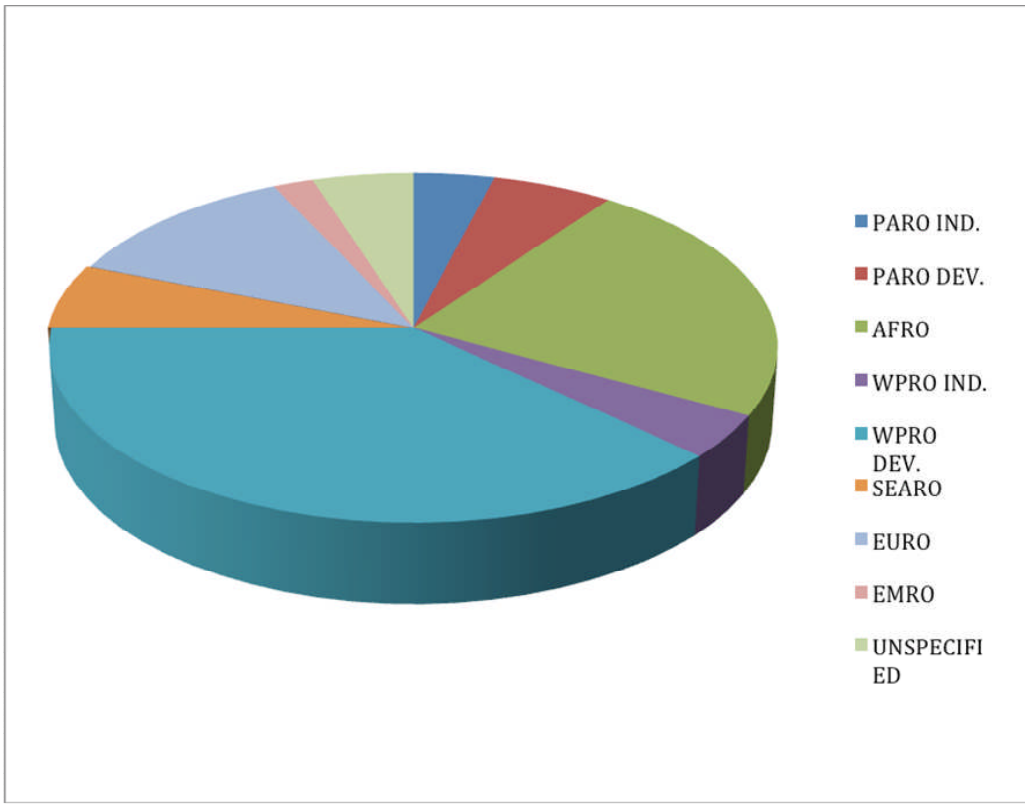


Figure 4: Geographic origin of reports of counterfeited drugs by WHO region between 1982 and 1999 adapted from Ham, (2003)
PARO: Pan American Regional Office; AFRO: African Regional Office; WPRO: West Pacific Regional Office; SEARO: South East Asian Regional Office; EURO: European Regional Office; EMRO: East Mediterranean Regional Office; Dev: Developing; Ind: Industrialised.

Nigeria has been stated to be the second largest producer of counterfeit medicines, accounting for about 23% of counterfeit medicines distributed worldwide after India, which is thought to account for about 35%; and Pakistan, 13.3% (Datta, 2003 cited in Lybecker, 2004). Medicines counterfeiting is now very similar to the worldwide narcotic trade in that in majority of the cases, the raw materials are obtained from one country, formulated into tablets or capsules in another country, packaged in a different country and then shipped through several countries before arriving at its final destination (Lybecker, 2007). An example is the report from The Partnership for Safe Medicines where Spanish Police discovered that counterfeit medicines from Mexico, Brazil and Thailand

were being exported to Spain and then sold in Italy, France and Portugal (Taylor and Craig, 2009).

Profits from medicines counterfeiting may equate to and may even supersede that of the narcotics trade, yet it is subject to lesser penalties in some countries (Lybecker, 2004). For instance, one gram of cocaine may be valued at one hundred US dollars ($100) while some counterfeited medicines may sell for up to $3,000 per gram (Kontnik, 2003). Aside from the personal monetary gains that may be obtained from medicines counterfeiting, there is some evidence that funds raised from such crime may be used to sponsor terrorism or be linked to some form of social disruption (Kontnik, 2003 and Millar, 2002, O'Mathuna and McAuley, 2005, Clark, 2008, Harper, 2008 cited in Taylor and Craig, 2009).

The WHO, the Organization for Economic Cooperation and Development (OECD) and the Pharmaceutical Security Institute (PSI) estimates that about 30% of medicines in some parts of Latin America, South East Asia and Sub-Saharan Africa are fake; it can even be as high as 50% in some of these countries while in many of the former Soviet republics it can be as high at 20%. About 10% of drugs in emerging economies may be counterfeit while in wealthy countries, it may account for less than 1% of the market value (WHO, 2010a). About half of medicines illegally sold through the Internet may be counterfeit (WHO, 2006a). These are usually a threat to people who look for cheaper, stigmatized or unauthorised treatments (WHO, 2006b).

Although these estimates and findings may not accurately represent the situation in all countries, they are indicative of an unsatisfactory and potentially hazardous situation. Figures 5 and 6 seem to show an increased incidence of medicines counterfeiting. However, this increase may have been due to

improved data collection and reporting, greater law enforcement and increased awareness (PSI, 2010). Also the increase seen in Figure 5 may have been confounded by increase in reports of cases of illegal diversion and theft. However, they show that national measures and co-operation between pharmaceutical companies and governments have not been able to tackle the growing problem of medicines counterfeiting. As a result of this failure, the need for an international framework convention in response to the problem was recognised. This led to the formation of International Medical Products Anti-Counterfeiting Taskforce (IMPACT) in 2006 (Forzley 2006).

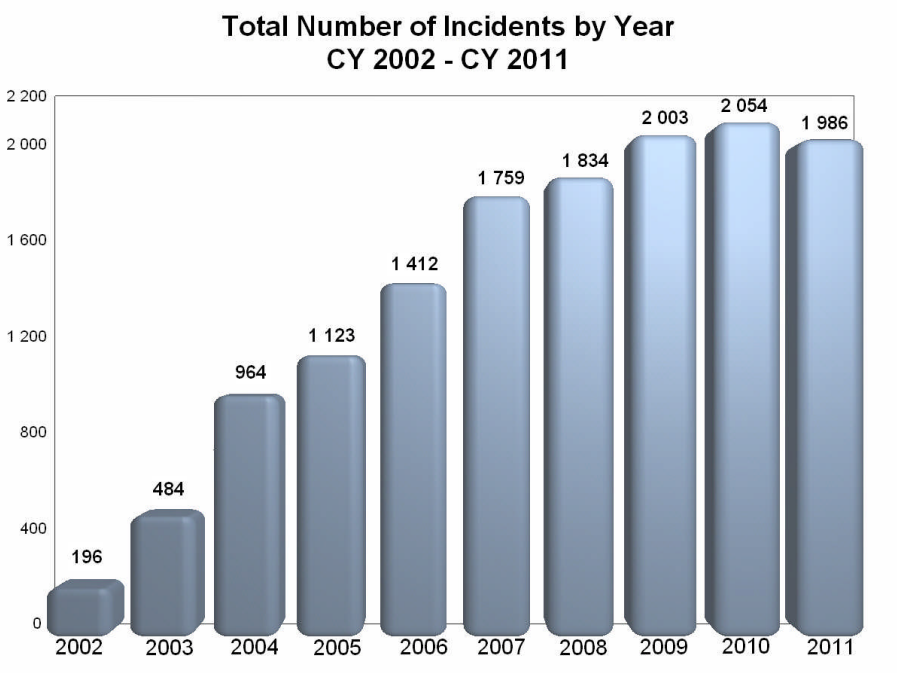


Figure 5: Annual data collected by PSI on counterfeiting, illegal diversion and theft incidents for eight consecutive years. Adapted from PSI, (2010) and PSI, (2014)

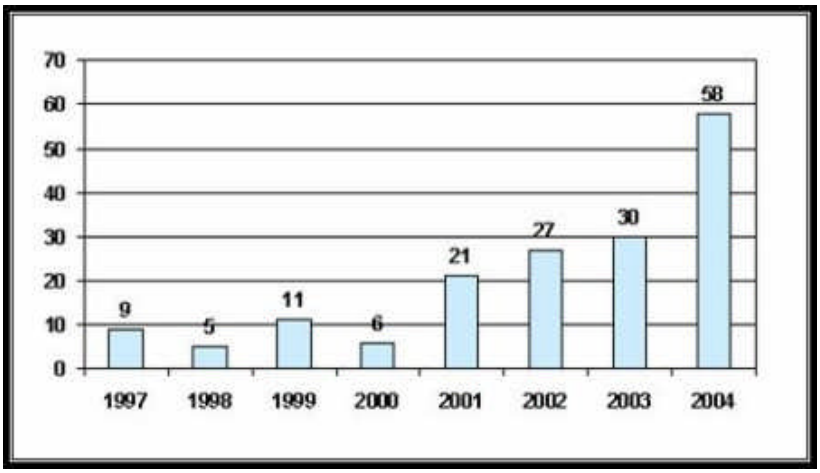


Figure 6: Counterfeit drug cases opened by the USFDA/year. Adapted from Patel, (2006)

Figure 5 shows the number of pharmaceutical crime incidents (cases of medicines counterfeiting, illegal diversion or pharmaceutical theft) from different countries in 7 regions of the world (Asia, Europe, Latin America, North America, Eurasia, Africa and Near East) documented by PSI. It shows a steady increase from 2002 to 2010. More recent data from PSI indicate that there was an increase in the documented pharmaceutical crime incidents in 2012 and more significant increase in 2013 when compared to year 2012 (PSI, 2014). Figure 6 shows the number of counterfeit drug cases opened by the United States Food and Drug Administration's (USFDA) office of criminal investigation per fiscal year. It shows a steady increase in medicines counterfeiting from 2001 to 2004. More recent data from USFDA also show that the number of counterfeit drug cases increased significantly again in 2009 (Bernstein, 2012).

2.4.2 Source of poor quality medicines

Three of the studies obtained from the literature review; Onwujekwe et al. (2009), Tipke et al. (2001) and Lon et al. (2006) discussed possible sources of poor quality medicines. These studies showed that drugs found in places such as the streets and open markets may be of lower quality since they are often

not well regulated. For instance patent medicine vendors accounted for 78% of suspect medicines in Onwujekwe et al. (2009) and 90% of medicines found to be substandard in Tipke et al. (2009) were obtained from illicit outlets (market, street vendors and shops). Similarly, a large proportion (100 out of 122) of samples that failed quality tests in Lon et al. (2006) were obtained from illegal or unlicensed outlets.

The National Agency for Food and Drug Administration and Control (NAFDAC) reported in 2006 that the incidence of counterfeit medicines had been reduced to about 16.7% from previous values of as much as 70% (Taylor and Craig, 2009). However, this figure is believed to have been made worse by the increased incidence of about 40% at the open drug market located in Onitsha, popularly known as head bridge market (Pharmaceutical Society of Nigeria (PSN), 2007, Okoye, 2007 cited in Milissa McGinnis, 2010). Other open drug markets in Nigeria which may have contributed to the high prevalence of substandard and counterfeit medicines include Ariaria market (alleged in 2002 to have about 75% of drugs in stock as fake), Sabon Gari market, Kano (survey by NAFDAC showed about 90% of drugs in this market are unregistered) and Idumota market, Lagos (PSN, 2007). This raises a question of whether Nigeria should devote more efforts in curbing counterfeiting in areas perceived to have a higher prevalence.

The trend of medicines counterfeiting seems to vary between different regions. In Europe and the United States of America as well as other developed countries, the target of the counterfeiters seems to be on the Internet due to increased access to the Internet in these countries. It is estimated that about 44% to 90% of medicines sold over the internet are counterfeit (Jackson et al., 2010). However, this is common for drugs purchased from Internet sites that conceal their physical address (IMPACT, 2008). The majority of the most commonly counterfeited medicines in these countries are lifestyle medications. It has been estimated that 2.5 million men in Europe are exposed to illicit

sildenafil; suggesting that the number of legal and illegal users of sildenafil may be equal (Jackson et al., 2010). WHO, (2010b) made mention of a Dutch study cited in the International Journal of Clinical Practice which showed that only 10 out of 370 seized Viagra® samples were genuine. Recently, it was discovered that counterfeit life saving prescription medicines such as drugs for cancer and cardiovascular diseases are also available over the Internet (WHO, 2010b).

2.5 Limitations of the studies on extent of poor quality medicines

Most of the studies had an unclear or inadequate methodology, which may have led to unreliable conclusions. The inability to distinguish between counterfeit, substandard and degraded medicines in the articles included in this review has made it difficult to ascertain the extent of either of the problems. The differences in methodology, lack of uniformity in reporting of findings as well as incompleteness or limited scope of methodologies employed in these studies make comparisons between them difficult. This calls for a standardised method of reporting of results from drug quality studies as proposed by Newton et al. (2009). Small sample size and range of products sampled may have resulted in lower or higher number of products failing quality tests in some of the studies. Most of the studies did not include paediatric formulations contrary to the WHO recommendations for field sampling (WHO, 1999a).

Most of the studies collected samples from specific regions and majority of them employed convenient sampling, which may have contributed some bias to the findings of the studies. Also, majority of the studies focused on therapeutic drug classes which they anticipated where most likely to be of poor quality for instance anti-malarials and anti-infectives.

Furthermore, the majority of the studies merely involved collection of samples and testing them without a further investigation of whether the manufacturers stated on the products were actually genuine or existing and if they were produced by genuine manufacturers; a step recommended by WHO as being important in determining which of the products were counterfeit rather than substandard (WHO, 1999b). None of the studies aimed at determining the extent of poor quality medicines determined the proportion of counterfeit or substandard medicines emanating from each outlet. This is important as it may reveal whether the problem of counterfeiting is localised or peculiar to certain outlets and help to better channel the effort in curbing the problem by ceiling up the outlets involved and further investigating where such retailers obtain their medicines.

These limitations highlight the need for more research which employing well designed random sampling technique and possibly involving pollen analysis and forensic analysis in order to determine the source of raw materials or location of drug manufacture as well as the real extent of counterfeiting (Newton et al., 2008).

2.6 Objective 2: Impact of poor quality medicines

There are no reliable data on the mortality and morbidity arising from the use of poor quality pharmaceutical products in Nigeria and other developing countries. The effects go unnoticed except when it causes easily observable tragedies (Erhun et al., 2001). When data on extent and impact of counterfeiting are available, they are often limited as only 5-15% of the 191 WHO member states report cases of counterfeiting and generalisations made from such reports may not be accurate (Newton et al., 2010).

2.6.1 Economic consequences for industries

Five articles; Morris and Stevens, (2006), Beach, (2001), Naik, (2004), Business call to action, (2012) and Lybecker, (2007) retrieved from the literature review

discussed the economic consequences of medicines counterfeiting to pharmaceutical industries. Only 2 of these; Beach (2001) and Lybecker, (2007) were journal articles. The other 3 were web articles.

Medicines counterfeiting undermines the ability of Research and Development (R&D) based companies to invest in future innovation (Morris and Stevens, 2006). It also negatively affects the R&D companies by reducing their sales; for example Beach (2001) showed that circulation of counterfeit copies of a product of an international pharmaceutical company in China caused a drop in their annual sales to $242,000. However, after the counterfeiting was controlled, sales rose to $1.2 million. In Nigeria, sales volume for Panadol® and Glaxo's antimalarial halofantrine (Halfan®) doubled in 2002 compared with 2001 when medicines counterfeiting was considered to be more prevalent (Naik, 2004). It is also believed that following the introduction of the Mobile Authentication Service (MAS) on Glucophage® which is marketed by Biofem in Nigeria, Biofem has been able to regain its market and therefore experienced increased sales resulting from the possible reduction in the counterfeiting of Glucophage® (Business call to action, 2012).

Genuine medicine suppliers are greatly affected by this menace as it has been shown that consumers have a particular preference for these counterfeited medicines because they are relatively cheaper leading to lower patronage of genuine medicines (Rozendaal, 2001 cited in Lybecker, 2007). In addition, counterfeiting also causes serious harm to the reputation of the genuine pharmaceutical manufacturers and makes them liable to any harm that may result from consumers taking such products. It also increases the expenditure of the legitimate manufacturers, as they have to constantly develop new strategies to thwart counterfeiting.

2.6.2 Economic consequences to consumers

Three articles; Seiter, (2009), Willyard, (2010) and IMPACT, (2009) retrieved from the literature review discussed the economic impact medicines counterfeiting can have on consumers.

Seiter (2009) tried to quantitatively assess the cost of ineffective anti-malarials. From previous estimates, he estimated that in a country of about 20 million people, there might be 4 million anti-malarial treatments. Among these, there may be an estimated 800,000 cases treated with poor quality anti-malarials resulting in up to 4,000 childhood deaths. From his calculations an average worker spends about half a day working to pay for these ineffective drugs. In total, about 3.2 million working days is spent working to obtain money for these illicit medicines. One can therefore imagine the indirect financial losses of fake drugs that far exceed their face monetary value.

The calculations and estimates by Seiter, (2009) may be lower than the real costs of these medicines as they do not take into consideration the possibility that one patient can be treated on multiple occasions per year for malaria and the chances of treating the individual with an ineffective medicine are the same each time treatment is received (Willyard, 2010). There is therefore no doubt that patients who buy these illicit drugs waste money which can be equated to several days' wages considering the low socio-economic status of patients in such resource poor countries as Nigeria where about 34.1% of the population live below the poverty line (Seiter, 2009 and UN Human Development Report, 2008 cited in IMPACT, (2009).

2.6.3 Economic consequences on national economies

Five articles from the literature review discussed the economic impact medicines counterfeiting may have on national economies. These were Fenoff and Wilson, (2009), Akunyili, (2005a), Lybecker (2007), Wertheimer and Norris, (2009) and Seiter, (2009).

Medicines counterfeiting can be detrimental to national economies. This is because genuine manufacturers compete with illegal manufacturers who do not pay any import duties and sales tax on the drugs they sell (Fenoff and Wilson, 2009). In addition to this, medicines counterfeiting reduces public trust in indigenous manufacturing companies and health-care providers as a whole. In developing countries, this may lead to importation of costlier branded medicines that the patients consider to be more effective (Seiter, 2009).

Also, through such avenues as parallel importation, counterfeiting may affect other markets such as the US market (Lybecker, 2007). It also hampers trade relations between countries as it may result in trade restrictions. An example is the ban of sale of 'Made in Nigeria' pharmaceutical products which were sold in neighbouring countries before 2001; a time when Nigeria seemed to be well known for medicines counterfeiting (Fenoff and Wilson, 2009). Between 2001 and 2005, 30 Indian and Chinese pharmaceutical companies and one Pakistani company that were confirmed to be manufacturing counterfeit drugs were banned from exporting drugs to Nigeria (Akunyili, 2005a). Counterfeiting therefore repels foreign investment in the countries concerned, reduces profits for developing countries by reducing incentives for further research in such countries, and diverts resources for genuine treatment (Lybecker, 2007).

2.6.4 Health Risks of poor quality medicines

Roy (1994); Abdi et al. (1995); Arya (1995); Kron (1996) focused on treatment failure as a consequence of poor quality medicines use while seven other articles; Milan (1987); Pandya (1988); Masland and Marshall (1990); Silverman et al. (1990), Okuonghae et al. (1992), OgohAlubo (1994) and Hanif et al. (1995) showed that consumption of poor quality drugs could result in serious damage to the patients health or even death. Majority of the information in this area were from grey literature or web articles.

2.6.4.1 Death as a consequence of poor quality medicines

It is a difficult task to trace illness and death to counterfeit or substandard medicines. However, evidence show that poor quality medicines pose significant threats to consumers as they cause adverse reactions, lack of successful treatment and possibly death as can be shown from previous incidents in some developing countries (Nsimba, 2008). In 1990, 100 children in Nigeria were speculated to have died following the ingestion of a cough mixture that was diluted with a poisonous solvent, diethylene glycol (DEG) (Deisingh, 2005). Eighty-four more children were said to have died in Nigeria between late 2008 and early 2009 due to the consumption of diethylene glycol-contaminated teething medicine "*My Pikin Baby Teething Mixture*", distributed by Barewa Pharmaceuticals; a company licensed by NAFDAC (Polgreen, 2009, Eboh, 2008, Harris, 2008, Mbachu, 2009 cited in Milissa McGinnis, 2010). This event is similar to the 109 cases of acute renal failure among children in Haiti, which was associated with an epidemic of severe systemic effect from DEG contaminated paracetamol syrup (O'Brien et al., 1998). In Bangladesh, Paracetamol elixirs that were found to contain DEG were associated with an outbreak of fatal renal failure between 1990 and 1992 (Hanif et al., 1995). In 2006, about 200 patients died in Panama due to the manufacture of medicines with counterfeit glycerine (Seiter, 2009).

Another catastrophic example is the death of about 2,500 people resulting from the consumption by about 60,000 people of vaccines donated by Nigeria to Niger during a meningitis epidemic which were later found not to contain any active ingredient (Fenoff and Wilson, 2009). Other incidents that have been attributed to the use of poor quality medicines include the report from three Nigerian hospitals of cases of adverse reactions from the use of infusions that were contaminated with microorganisms. Also, 147 out of the 149 water for injections analysed from these hospitals were found to be unsterile (Akunyili, 2006a). Three children in Nigeria were reported to have died as a result of fake adrenaline (Akunyili, 2007). It is also estimated that about 80,000 children may have been given fraudulent meningitis vaccines (Knox, 2003 cited in Lybecker,

2004). Other countries that have experienced similar catastrophic incidents include the United States of America, South Africa, Spain, Austria, India, Haiti, Argentina and China.

In 1998, about 200 unwanted pregnancies were reported in Brazil due to the use of counterfeit contraceptive tablets (Pecoul et al., 1999). In January, 2009, China's state run news agency; Xinhua revealed that a counterfeit diabetes drug that contained about 6 times the required amount of active ingredient (glibenclamide) was responsible for the death of 2 people in China and about 7 people were thought to be hospitalised in XinJiang as a result of this (Mooney, 2010, WHO, 2010a). It was estimated by a Chinese government controlled newspaper; Shenzhen Evening News of January 25, 2002 that about 192,000 people died in China in 2001 as a result of fake drugs (Goodman, 2002 cited in Lybecker, 2007). Although it has been argued that the figure quoted in the Chinese newspaper does not refer only to fake drugs as the sole cause of mortality rather it represents the number of deaths arising from drug-induced diseases due to irrational drug use (Cockburn et al., 2007); it still shows that there is a high risk associated with medicines.

The World Health Organisation estimates that about 20,000 malaria deaths per year occur due to substandard medicines use and that these deaths could be avoided if treatment was with only high quality medicines (Akehurst, 2005 cited in Lybecker, 2007; International Council of Nurses, 2005). Although it is unclear how WHO arrived at this number of avoidable deaths, it is obvious that using medicines which are of good quality should help stop development of complications and resistance thereby leading to better treatment outcomes. Similarly, Dora Akunyili, former head of the Nigerian's National Agency for Food and Drug Administration and Control speculates that medicines counterfeiting may be partly responsible for the doubling of malaria deaths over the last 20 years (Morris and Stevens, 2006). This is evidenced by the fact that 8 of the 12

major antimalarial drugs in use have been reported to be counterfeited (Newton et al., 2006a).

In early 2008, counterfeit medicines were thought to have caused the admission of about 150 people into hospital in Singapore for severe hypoglycaemia. Out of these, four died and a further seven suffered brain damage (WHO, 2010b). Forty-five out of these 150 patients were reported to admit ingesting illegal medicines for erectile dysfunction prior to developing hypoglycaemia. When the samples were tested; they were found to be contaminated with glyburide with some containing other dangerous chemicals (Kao et al., 2009). In 1999, at least 30 people died in Cambodia as a result of counterfeit sulphadoxine-pyrimethamine that was sold as artesunate (International Council of Nurses, 2005).

In 2005, about twelve children died after they were fed with counterfeit milk products (Feldschreiber, 2009). The effects of counterfeit cases of Lipitor®, Procrit®, Epogen®, Nutropin®, Neupogen®, Serostim®, Zyprexa®, Gamimune®, Oxycontin®, Combivir® and Viagra® are not yet known (Kontnik, 2003).

2.6.4.2 Development of drug resistance

Counterfeiting can lead to drug resistance. The Netherlands Leprosy Relief and Royal Tropical Institute states that about 305 samples of TB medicines tested in Nigeria did not pass the tests and may have largely contributed to the development of multidrug-resistant tuberculosis (MDR-TB) (Van der Grinten, 2000 cited in Peterson and Obileye, 2002). The WHO speculates that poor quality medicines may have also contributed to development of resistance to other diseases such as cholera and salmonella (Feldschreiber, 2009). The use of counterfeit and substandard artesunate and widespread monotherapy with artesunate has led to *Plasmodium falciparum* artesunate resistance on the

Thailand-Cambodia border (Newton et al., 2010). More recently, large numbers of fake Coartem® tablets have been found in Lagos, Nigeria and Launda, Angola (Faucon et al., 2013). This recent finding of counterfeit forms of artemisinin derivative in Africa is a serious cause for concern due to fear of development of resistance to artenisinin in the highly malaria endemic Africa (Newton et al., 2006a).

It therefore appears that until the distribution of poor quality medicines is tackled, the efforts of new drug discovery and development will continually be rendered futile. This also means that resistance at the population level renders legitimate drugs less effective, even amongst patients who have not used fake and/or poor quality medicines (Bate at al., 2009a) causing a switch to second or third line medicines which are usually more expensive and more toxic (Centre for Global Development, 2010).

2.6.4.3 Adverse drug reaction and treatment failure

There have been instances where the use of counterfeit medicines has been linked to treatment failure. A typical example of therapeutic failure attributable to poor quality medicines is the lack of response to miltefosine by Bangladeshi patients suffering from visceral leishmaniasis. The capsules taken by the patients were later discovered not to contain miltefosine (Senior, 2008 cited in Newton et al., 2010).

It is an obvious fact that the impact of medicines counterfeiting especially in the developing countries have been under reported because consumers may not link their non response to treatment to counterfeit drugs rather they may attribute it to other factors such as contamination of drinking water supply, disease complication, malnutrition, failure to complete the course of treatment or even a belief in curses or the supernatural (Lybecker, 2007). A study sourced from PSN, (2001) cited in Wertheimer and Norris, (2009) and Peterson

and Obileye, (2002) stated that fake and substandard drugs accounted for 12.8% of adverse drug reaction, 52.9% of drug resistance, 10% of therapeutic failure, 48.2% of increased disease severity and 34.2% of the patients taking such drugs may develop complications (see table 3)

Table 3: Impact of Fake and Substandard Drugs in Nigeria

Fake and Substandard drug impacts	Percentage (%)
Fatality rates	12.8
Resistance to drug therapy	52.9
Therapeutic failure	10.0
Increased severity	48.2
Development of complications	34.2
Proportion of Physicians that had life threatening encounters with fake drugs	29.0
Proportion of Physicians that had life threatening encounters with fake drugs, leading to death	9.1
Adverse drug reaction	23.6
Therapeutic response to adverse drug reaction when the source or brand was changed	29.7
Antibiotic counterfeiting accounting for total numbers of death	21.0

Adapted from PSN, (2001) cited in Peterson and Obileye, (2002)

The estimates quoted above are an indication that fake and substandard medicines can lead to a variety of problems. However, the methods employed by the PSN to arrive at these estimates are unclear so it is uncertain if vested interest by PSN may have influenced these estimates.

From the above discussion on the impact of poor quality medicines, it is clear that there is limited documented evidence on the actual impact of poor quality medicines in terms of their economic and health consequences. Most of the information presented is speculative, however it points to the fact that poor quality medicines have serious detrimental economic and health consequences for industries and individuals and at national levels.

2.7 Objective 3: Strategies and barriers in the fight against poor quality medicines

2.7.1 Strategies against poor quality medicines

One of the objectives of the literature review conducted was to identify different strategies that have been taken against medicines and any challenges or barriers that may be hindering the fight against poor quality medicines. The review revealed that there have been responses to medicines counterfeiting from government bodies, drug regulatory authorities, professional organisations and industries.

Different models/ frameworks have been developed identifying areas attention needs to be focused to help curb medicines counterfeiting. This includes the model by IMPACT, USFDA and the conceptual model by Bayer Schering Pharma. Most of the responses/strategies against medicines counterfeiting by government bodies, industries and other organisations are based on the framework on the formation of IMPACT involving key areas that were identified as needing action both nationally and internationally to tackle the problem of poor quality medicines. These five key areas are; Legislative and regulatory infrastructure, Regulatory implementation, Enforcement, Technology and Communication (IMPACT, 2008). Similarly, the United States Food and Drug Administration (USFDA) identified 6 critical measures to combat fake drugs (Mehta, 2006) (See Appendix 4);

1. Securing the actual medicine and its packaging:

   This includes all strategies that secure the medicines itself or its packaging from being counterfeited for instance, the use of colour shifting inks, holograms, finger prints and chemical markers.

2. Securing the movement of medicines through the distribution chain:

This includes ways medicines are prevented from being counterfeited when they are moving through the distribution chain. It includes all strategies geared towards ensuring that the drugs are handled by the right persons and not diverted or changed in any way.

3. Enhancing regulation and enforcement:

   This involves strategies in place to ensure that medicines are well regulated such as setting up of bodies that can regulate medicines and monitor them when they are within the distribution chain to ensure that they are manufactured according to the recommended procedures and meet all the requirements set out.

4. Increasing penalties for medicines counterfeiting:

   This involves putting in place penalties to ensure that those identified as culprits are adequately punished in a way that will discourage them from counterfeiting.

5. Increasing vigilance and awareness of medicines counterfeiting:

   This involves the medicines users adopting techniques to ensure that they are sourcing their medicines rightly. It involves adopting secure business practices like ensuring that medicines are sourced from legitimate outlets. It also involves educating health professionals and consumers of the risk of medicines counterfeiting, how medicines counterfeiting can be detected and what to do if they encounter medicines that they think are of poor quality.

6. Increasing international collaboration:

   This involves both national and international collaboration against medicines counterfeiting. The international collaboration can be between countries or at the regional level.

2.7.1.1 Strategies against medicines counterfeiting by industries

Lybecker, (2008) classified the avenues through which the pharmaceutical industries have tackled counterfeiting into three pathways. First are the technological changes of the products or their packaging with the aim of making medicines counterfeiting more difficult and expensive. Secondly is ensuring increased cooperation across the supply chain with the aim of increasing difficulty of counterfeits entering the supply chain and indirectly increasing the cost of counterfeit product distribution. Finally, firms can cooperate with enforcement agencies in order to improve the chances of detection of medicines counterfeiting and prosecution of the offenders.

As an example of technological changes on product and product packaging, firms like Roche have used advanced technology to make their product difficult to copy, for instance they have included an inscribed hole in their Valium® pill (Lybecker, 2008). GSK and Roche have also tried altering their packaging, for instance is the inscription of Roche and GSK logo in their vials. In order to avoid the counterfeiters re-using the vials from GSK, the company has also applied the use of shrinkable self-adhesive labels made of Vinyl and other colourful graphics (Goodman, 2002 and Kontnik, 1998 in Lybecker, 2008). Pfizer capsule making division has acquired non-exclusive rights to Nano codes containing encrypted information about their drug. This is punched to the surface of their medicine without altering its chemical constituent (Mullard, 2010). Novartis has adopted a hidden digital marker technology that allows customs officials to detect whether secondary packaging of a product is authentic by placing it under an office scanner and sending the resulting image to the security division of the company for verification (Taylor, 2010).

GSK and Pfizer have also adopted the use of Radio Frequency Identification (RFID) in some of their products (Weithermer, 2009). GlaxoWellcome has initiated a global anti-counterfeiting strategy for its products, which includes monitored destruction of waste, field monitoring for counterfeits, and security packaging (Kontnik, 2003). Abbott has a global product protection team focusing on the use of track and trace technologies to secure its supply chain (Abbott, 2010). Similarly, AstraZeneca conducts analysis of all suspect counterfeits of their brand and addresses any medicines counterfeiting related issues through its global issues management team (AstraZeneca, 2010).

Both Johnson and Johnson (J&J) and Abbot have employed supply restrictions to make wholesalers buy their products directly from the company rather than from other sources that are usually prone to counterfeiting (Lybecker, 2008). In addition, in order to facilitate customer access to their approved wholesalers, Abbot publicizes the names of the wholesalers who agreed to their terms and conditions (Abbot Laboratories, 2004 in Lybecker, 2008). Following such efforts by the industries, wholesalers have also expressed their commitment in discontinuing buying and selling drugs among the secondary wholesalers which is strongly viewed as an entry point for counterfeiters (Lybecker, 2008).

Sanofi-Aventis formed an anti-counterfeiting organisation in 2005 and a central operational coordination team. It launched a team to be in charge of the analysis of suspect products and development of a database for counterfeit drugs (Sanofi-Aventis, 2010). It has also recently opened a central anti-counterfeiting laboratory in 2008 in France to research on such techniques as the use of chemical markers in the detection of counterfeit pharmaceuticals. (Taylor and Davies, 2008).

Some of the pharmaceutical companies such as Pfizer, GSK, Merck, Abbott, AstraZeneca and Eli Lilly collaborate with enforcement agencies, regulatory bodies, trade unions, PSI and Microsoft Corp. to reduce the incidence of medicines counterfeiting. For instance Pfizer recently led an investigation in China leading to dismantling of an operation involving about 11 countries, which included Britain and Israel (Sommerville, 2005 cited in Lybecker, 2007). Due to the tremendous increase of sales in counterfeited drugs over the Internet and via mail order, it declared a joint effort with Microsoft Corp aimed at reducing Internet sales of Viagra (Tesoriero, 2005a). As a collaborative effort, Johnson and Johnson is employing security companies in countries such as China and India to investigate counterfeit cases and provide necessary evidence which may justify raids led by police officials (Goodman, 2002 cited in Lybecker, 2008). Between 2001 and 2003, it established 38 criminal cases against individuals/ bodies involved in counterfeiting their products in China (Goodman, 2002 in Lybecker, 2008). Companies such as Pfizer, GSK, Roche, Eli lilly, Astrazeneca and German Pharma Health Fund (GPHF) have also been engaged in the public enlightenment campaigns and training of stakeholders in the area of drug quality and detection of medicines counterfeiting.

The European Parliament and the Council of the European Union adopted the Falsified Medicine Directive in 2011 and should be implemented fully in 2018. Under this directive, all medicines will be required to have a unique serial number applied during their manufacture and displayed on the medicine pack through a 2D barcode. All prescription only medicines (POMs) except POMs that are exempt based on their risk assessment will be included while all over the counter medicines (OTCs) will be exempt unless they are identified to be at high risk of counterfeiting. Before the medicines are supplied to the patient, they will be scanned and the unique number verified against a database (Jones, 2014).

2.7.1.2 Government efforts against poor quality medicines

The literature review revealed that government of different countries have in several ways tried to curb medicines counterfeiting and poor quality medicines as a whole. Majority of these efforts are geared towards increasing penalties or enforcement (Lybecker, 2007). Information below show how government of different countries have tried to tackle the problem of poor quality medicines. Most of the information in this section has been published as 2 documents used as advocacy tools by the World Health Professions Alliance (WHPA) and can be retrieved from their website as Onwuka, (2010) and Onwuka, (2011).

2.7.1.2.1 Response from different African country governments and their regulatory bodies

Nigeria: In Nigeria, several strategies were identified that have been put in place to help curb the problem of poor quality medicines. Several technological innovations have been adopted by NAFDAC to help curb the problem of medicines counterfeiting. For instance, NAFDAC in collaboration with Sproxil launched the Mobile Authentication Service (MAS) also called Mobile Product Authentication (MPA). MAS was born out of a drive to empower consumers to authenticate the quality of their medicines. This requires consumers to send a unique code located on the scratch card on the package of their medicines to a short code to authenticate their medicines (Health Care Packaging, 2010). More recently other avenues of authentication such as using the Mobile Product Authentication (MPA) app on android and on Sproxil's website was commenced by Sproxil (Meliza, 2014).

Although it may be too early to ascertain if such services like MAS may not indirectly lead to increase in the cost of medicines, a 100-day pilot project aimed at determining the feasibility and cost implementation of the Mobile

Authentication Service (MAS) using Glucophage® as a case study showed that customers are utilising the service at no direct cost (Sproxil, 2010b). Following the pilot study, Sproxil expanded its activities to include other antidiabetics, antimalarials, antifungals and some antibiotics. The MAS has been adopted in other countries such as Ghana, Kenya and India. In Nigeria, other companies such as Pharmasecure and Mpedigree have implemented mobile authentication service for medicines.

There are anecdotal reports suggesting that the counterfeiters are already co-selling genuine medicines containing the unique identification code with the counterfeit versions in a bid to deceive the customers (Chu, 2010). Also there are questions of whether on expansion, all legitimate manufacturers of medicines distributed in Nigeria can be included in the program or if smaller firms producing locally-made versions or legitimate generics which may not be able to afford it be excluded from the programme (Freschi, 2010). If the latter is true, it may mean that these smaller firms manufacturing medicines affordable to the Nigerian population may be driven out of business by the larger firms and in turn lead to decreased access to some life saving medicines (Freschi, 2010). It is important that serious consideration is given to medicines and firms who would be engaged in this initiative, upon expansion and that the Federal Government of Nigeria is prepared not to forsake the public health implications of access to good quality affordable medicines at the expense of promoting the authentication of genuine drugs from larger multinational companies.

Furthermore, NAFDAC in partnership with Verification Technology Ltd has launched the use of Radio Frequency Identification (RFID) technology to identify and verify products, documents and other important items (Ogbebo, 2010a). Verayo, Skye Tech and Global PCCA are set to start supplying secure and easy to use RFID systems to Nigeria and other African countries at a relatively low cost (Taylor, 2010). Recently, it introduced the use of thermo

scientific TruScan® handheld RAMAN instrument for rapid identification of fake and substandard drugs (NAFDAC, 2010a).

In order to mop up the fake drugs already in circulation, the Nigerian government has in collaboration with registered manufacturers, confiscated and destroyed expired and counterfeit medicines thereby increasing the cost of obtaining such illicit medicines (Naik, 2004 in Lybecker, 2007, Akunyili, 2007). NAFDAC has engaged in raids leading to confiscation and destruction of a wide range of fake and substandard products; destroying over US$35,753,014 worth of drugs found to be fake or substandard between 2001 and 2004 (Akunyili, 2005b cited in Milissa McGinnis, 2010). Between 2001 and 2006; drugs worth US$109 million were destroyed (Edike and Obinwanne, 2006 cited in Milissa McGinnis, 2010). The Lagos State Taskforce on counterfeit, fake drugs and unwholesome processed foods has also engaged in confiscation and destruction of fake drugs, sealing of premises which are illegal and arresting of persons involved in the act of medicines counterfeiting (The Tide News, 2008, This Day, 2008, Nigerian Tribune, 2009, Akoni, 2009, Oladunjoye, 2010 cited in Milissa McGinnis, 2010). The Yobe state government formed a committee on fake drugs in 2002 to help tackle the problem (Daily trust, 2002).

The Nigerian government through NAFDAC has made efforts to develop collaborative networks against medicines counterfeiting. For instance, Nigeria plays an active role in IMPACT; with the Director General of NAFDAC acting as one of the chairs. Nigeria is also collaborating with medical equipment manufacturers such as Secure pharma, Sproxil and Global PCCA as well as international organisations (Turkur, 2009). NAFDAC has entered into partnership with the USFDA to provide training to delegates and signed a memorandum of understanding between India and China that should help harmonise strategies employed in curbing medicines counterfeiting (Ogbebo, 2010a). Nigeria also shares strategies with

other countries in the West African Drug Regulatory Authorities Network (WADRAN). NAFDAC initiated WADRAN in 2008 as an avenue to share strategies and experiences by member states in the fight against medicines counterfeiting (Akunyili, 2007). It is made up of 12 countries in West Africa.

The Nigerian government is collaborating with the Indian and Chinese governments in the fight against medicines counterfeiting; the Chinese government has agreed to provide advanced information on drugs exported to Nigeria (Turkur, 2009). Nigeria in collaboration with Indian authorities adopted the concept of "whistle blower" initiative where a cash reward of N200,000 is proposed to be given to anyone who discloses information leading to interception of fake drugs while individual identities remain confidential (This Day, 2010).

NAFDAC embarked on re-orientation and motivation of its staff for positive outcome (Akunyili, 2007). Other initiatives includes the introduction of public enlightenment campaign via jingles on the radio and television, alert notices about fake drugs in the supply chain for instance is an alert issued on fake Maloxine® tablets in circulation in 2009 (Ogundipe and Obinna, 2009). In addition, there are billboards and publications in national dailies on medicines counterfeiting for example; the list of counterfeited medicines as well as workshops/meetings/seminars on drug quality for stakeholders (Akunyili, 2007). A quarterly bulletin that distinguishes between counterfeit and genuine medicines as well as original and blacklisted companies is usually published by NAFDAC (Federal Ministry of Health and World Health Organisation, 2010). NAFDAC also engaged the local governments at the grassroots by organising workshops letting them know the need to join the agency in the fight as well as organising advocacy campaigns against medicines counterfeiting (Ogbebo, 2010a). NAFDAC in collaboration with Christables conducted a state-to-state drug market

sensitization that flagged off on 15th of July 2010 beginning with the Onitsha head bridge market, Anambra state (Daily Sun, 2010). It also conducted secondary school essay competition contests to help publicize the harmful effects of counterfeit drugs, established consumer safety clubs in schools, attempted to raise a NAFDAC army made up primary school children who are taught on the advantage of good quality products (Naik, 2004 in Lybecker, 2007; World Intellectual Property Organisation (WIPO), 2008). To facilitate the reporting of adverse drug reactions and other drug related problems by health professionals, NAFDAC has printed Adverse Drug Reaction (ADR) reporting forms with prepaid stamps (Akunyili, 2004).

NAFDAC has been engaged in updating of its laboratories and inspection of laboratories abroad to ensure their compliance to Current Good Manufacturing Practice (cGMP). Appointments of analysts in India, China and Egypt who re-certify drugs for importation, mandatory pre-shipment information before importation, mandatory NAFDAC clearance permit prior to financial document processing in Nigeria for all drug importers, discontinuation of importation of drugs marked "For export only" into Nigeria by insisting on an authenticated certificate of free sale, regular monitoring of Good Manufacturing Practice (GMP) of local manufacturers and enforcement of NAFDAC registration guidelines are also some of NAFDAC's key strategies in eliminating medicines counterfeiting (Akunyili, 2007). It has designation Calabar and Apapa seaports, Murtala Muhammed and Mallam Aminu Kano International Airports as the only ports of entry for the importation of drugs and pharmaceutical raw materials to avoid smuggling in illegal medicines.

Furthermore, NAFDAC has banned importation from some Indian Pharmaceutical companies, sealed some drugs from being imported (Chinyere, 2008 in Bate et al., 2010) and set up an office for its regulator in

India (The Economic Times, 2009 in Bate et al., 2010). NAFDAC has also conducted a survey and audit of all drugs on sale in Nigeria in order to build a pharmaceutical database (Bate and Hess, 2010).

The Federal government of Nigeria submitted a draft resolution at the 63rd WHA seeking for WHO's support in tackling its chaotic drug distribution system and enhancing the regional fight against counterfeiting (Ogudipe, 2010). The current Director General of NAFDAC, Dr Paul Orhii is advocating for passage of bill of life jail term and confiscation of assets upon conviction and compensation of victims where injury has been caused as punishment for counterfeiting. Similarly, the president of the Manufacturers Association of Nigeria (MAN) has recently called for a new legislation to be implemented to reduce the importation of counterfeit, adulterated and substandard medicines in Nigeria (Securing Pharma, 2010).

Senegal: The government of Senegal increased its monetary budget to tackle counterfeiting in 2006 (Milissa McGinnis, 2010). United States Pharmacopeia Drug Quality and Information Program (USP DQI) has set up medicine monitoring sentinel sites in Senegal and provided technical assistance to the National de Lutte contre le Paludisme (PNLP) in setting up a pharmacovigilance program in order to aid reporting of adverse effects of Artemisinin Combination Therapies (Hadiri, 2009). It has also provided training to members of the pharmacovigilance team on drug quality testing in order to conduct a study on the Quality of Antimalarials in Sub-Saharan Africa (QAMSA study) (Hadiri, 2009). In addition, it supports the Drug Regulatory Authority of Senegal in the registration of medicines (USP DQI, 2009). A technical committee was created in 2009 to enforce drug regulation in Senegal as well as raise the public awareness of the impact of medicines counterfeiting (Milissa McGinnis, 2010). A

campaign aimed at combating counterfeit medicines on the illicit market was conducted in July 2009 and September 2010 to raise the awareness of poor quality medicines sold by unlicensed vendors (USP/ASAID, 2010).

South Africa: Purchasing registered medicines from licensed suppliers, use of Standard Operating Procedures (SOPs) and audits by manufacturers, distributors and health care providers were the key strategies identified that were used to protect medicines quality in South Africa (Patel et al., 2009a).

Ghana: In 2008, the M-Pedigree developed a mobile drug anti-counterfeiting service in Ghana whereby consumers are required to text an 8-digit numerical code to a number for free authentication. Similar systems have been rolled out in other African countries such as Nigeria, Kenya and Rwanda as previously described (Mullard, 2010). Anti-illicit Trade Coalition at Kpone Landfill has been involved in the destruction of counterfeit products for instance counterfeit toothpaste (My Joy online, 2009 cited Milissa McGinnis, 2010). Also, sentinel sites for medicines monitoring were established as part of a drug quality program with the support of the US government in Bolatanga, Kumasi, Ho, Accra and Tarkwa to help identify counterfeit medicines (Kwei, 2006-2009; Bate, 2010). Through this program, fake Coartem® was detected in the Ghana market (U.S Pharmacopeia press release, 2009 cited in Milissa McGinnis, 2010). Ghana, Rwanda, Kenya and Tanzania have introduced a system of drug distribution whereby drug shops are franchised to improve access to cheap but high quality medicines as well as high quality dispensing services. It has also helped to ensure uniform standards among drug sellers in these countries (Centre for Global Development, 2010). Diocesan pharmacies of the National Catholic Health

and Pharmaceutical Services in Ghana have also established minilabs for the detection of counterfeit medicines.

Liberia: The Liberian Medicine Regulatory Authority in collaboration with USP DQI, the pharmacy board of Liberia, Ministry of Health, US Agency for International Development (USAID)/Liberia mission and Malaria Control Program is working on how to further strengthen the quality control laboratories of the ministry of health and finalised the drug legislation that established the Liberian Regulatory Authority (Smine et al., 2009).

Mali: A new technology involving the use of capillary electrophoresis to detect substandard medicines was rolled out in Mali in late 2009. This technology has been used in Switzerland, USA and Japan (IRIN, 2010a). Pharmacists in Mali have led a campaign against unlicensed medicines named “Street drugs kill” (IRIN, 2002). With the help of USP/USAID, training workshops on good laboratory practices have been conducted for staff members of the Official Medicine Control Laboratories (OMCLs) in Mali and Benin. Since 2008, USP/USAID through its Promoting the Quality of Medicine Programme has provided technical assistance to the OMCLs of Mali and Benin (Milissa McGinnis, 2010)

Lesotho: An Intellectual Property program; Operational Assistance, Services and Infrastructure Support (OASIS) was conducted by the Police in collaboration with International Criminal Police Organisation (INTERPOL) resulting in seizures of counterfeit medicines during the “operation fiela” (Ilston, 2009).

Sierra Leone: The National Drug Safety Monitoring Programme was commissioned by the Pharmacy Board to ensure drug safety in Sierra Leone (Koroma, 2006 cited in Milissa McGinnis, 2010). The Pharmacy Board of Sierra Leone has been conducting raids, which leads to destruction of counterfeit medicines (Massaquoi, 2007 cited in Milissa McGinnis, 2010). Its ministry of health has also increased monetary budget of the Pharmacy Board so that more inspectors can be hired (Horner and Hallam, 2009). The Pharmacy Board has deployed officials at Queen Elizabeth Quay and Lungi airport to aid inspection of medicines at its borders (Horner and Hallam, 2009)

Uganda: The German Pharma Health Fund (GPHF) has developed a minilab for field-testing of medicines in developing countries (Wertheimer and Norris, 2009). Five minilabs have been purchased to test medicines at the point of entry to Uganda (Kariuke, 2008 cited in Taylor and Craig, 2009). The Uganda National Drug Authority in collaboration with INTERPOL conducted raids that led to the discovery of counterfeit medicines (Ultimate media, 2009 cited in Milissa McGinnis, 2010). The National Drug Authority of Uganda conducts tests on samples of medicines in Uganda in order to determine the extent of poor quality medicines (Nafula, 2008 cited in Milissa McGinnis, 2010). It also issues alerts on counterfeit medicines in circulation in Uganda (Nyakairu and Nakabugo, 2005; Bogere and Nafula, 2007 cited in Milissa McGinnis, 2010).

Kenya: Established a Pharmacy and Poisons Board that helps to identify and destroy counterfeit medicines as well as ensuring that pharmacies are licensed (Maina, 2008 cited in Taylor and Craig, 2009). The Pharmacy and Poisons Board has launched a project in seven provinces geared towards closing down illegal drug distribution outlets (Maina, 2008 cited in Milissa

McGinnis, 2010). The East African Community (EAC) secretariat developed a draft policy and a bill on medicines counterfeiting. The anti-counterfeit bill was passed in Kenya and Uganda (Michael, 2010) and Kenya has enacted a law on counterfeiting (Equinet, 2010).

Tanzania: Its government seized large amounts of counterfeit medicines in Tanzania and have warned patients of the existence of fake Metakelfin® and Cotexin® tablets in its market (Rugonzibwa, 2008b cited in Milissa McGinnis, 2010). The Confederation of Tanzanian Industries (CTI) has called for an amendment in the Merchandize Act of 1963 that it deems out dated and ineffective in combating medicines counterfeiting (Milissa McGinnis, 2010). A key resolution by the Tanzania Food and Drug Authority (TFDA) in 2009 was to introduce the writing of trade names and batch numbers on all medicines purchased by or sold from wholesale pharmacy outlets (TFDA, 2009). TFDA carries out inspection of Pharmacies to help detect unapproved and low quality medicines (Shekighenda, 2009 cited in Milissa McGinnis, 2010). Tanzania Food and Drug Authority put a program in place for the accreditation of drug dispensing outlets and overseas the quality of services and products sold in these outlets (Centre for Global Development, 2010). Tanzania deployed the use of more than 20 GPHF minilabs across the country (Bate, 2009).

Angola: The Government of Angola banned the sale of medicines as well as surgery and hospital tools in municipal markets as they were discovered not to be sold under proper hygienic conditions (Agencia Angola Press, 2009 cited in Milissa McGinnis, 2010).

Egypt: Warehouse raids were conducted through which a large number of counterfeit medicines were confiscated from the supply chain (CNN Money, 2009 cited in Milissa McGinnis, 2010).

Ethiopia: In 2003, the Ethiopian health officials warned the public against purchasing counterfeit anti-retrovirals in the market that the Ethiopian's Drug Administration and Control Authority confirmed did not meet necessary quality specifications (Kaiser network, 2003). As part of capacity building of Ethiopian's Product Quality Assessment Directorate (PQAD), the USP/USAID through its Promoting the Quality of Medicines (PMQ) programme have trained laboratory analysts on methods used for testing medicines quality and have collaborated with the directorate in developing Standard Operating Procedures for gas chromatography (USP, USAID, 2010).

Zambia: The Zambia Bureau of Standards withdraws counterfeit medicines when discovered (Africa News, 2009 cited in Milissa McGinnis, 2010). The Zambian government issued an alert on counterfeit HIV/AIDS drug named Tetrasil® which was later discovered to be a pesticide (Medical News Today, 2007).

Cameroon: Its Food and Drugs Authority exposed 30 websites in May 2010 that are thought to be engaged in the sale of counterfeit medicines and disseminating false drug information (Kopp, 2010).

Sudan: The regional government of southern Sudan is utilising the mega phone to publicise the dangers of medicines counterfeiting in its main

markets. Village health committees have also been formed and hold consultations with relevant stakeholders such as the businessmen in order to help combat medicines counterfeiting in some of the counties (Sudan Tribune, 2010).

Zimbabwe: Police has been arresting persons involved in the dispensing of unregistered and expired medicines. The Medicines Control Authority of Zimbabwe (MCAZ) issues public alerts on counterfeit medicines in circulation (UN Integrated Regional Information Networks, 2007 cited in Milissa McGinnis, 2010). It recently warned the public that counterfeit antiretroviral are being imported and sold in its markets and salons (Milissa McGinnis, 2010).

Police in countries such as Senegal, Mauritania and Mauritius have also been engaged in raids resulting in seizures of counterfeit medicines some of which were thought to originate from China, Nigeria, Hong Kong and Syria (Milissa McGinnis, 2010).

Leem (a body representing French pharmaceutical companies held a meeting in January, 2010 involving government health officials from sub-Saharan Africa in order to reinforce public and private efforts against medicines counterfeiting (IRIN, 2010b).

2.7.1.3 Response from professional organisations

This section presents the efforts of different professional organisations against existence of poor quality medicines. Most of the information here has been published as part of 2 documents used as advocacy tools by the World Health Professions Alliance (WHPA) and can be retrieved from their website as Onwuka, (2010) and Onwuka, (2011).

International Pharmaceutical Federation (FIP): FIP adopted the FIP/IFPMA statement; "Ensuring the quality and safety of medicinal products to protect the patient" at the 1998 FIP congress. FIP policy statement on counterfeit medicines was adopted in Barcelona with a replacement of it adopted in 2003 at the FIP congress in Sidney (FIP, 2003). FIP has also been involved in creating specific and practical tools for pharmacists for fighting counterfeiting; examples include the tools for visual inspection and Guide for Pharmacists. Several articles have been published by FIP as a means of raising awareness of the risks of counterfeiting among pharmacists and pharmacy leaders as well as educating them. Sections at FIP congress meetings in 2006, 2007, 2008 and 2010 were dedicated to discussions on medicines quality, which included medicines counterfeiting in order to sensitize pharmacists on the dangers of medicines counterfeiting (FIP, 2010).

In collaboration with the World Health Professions Alliance (WHPA), FIP leads the IMPACT working group on communication. The WHPA tool kit "Be aware, take action" for health professionals and public health advocates was developed in 2008 to aid detection, reporting and prevention of medicines counterfeiting (Kopp, 2010). The first "Be aware, take action" workshop on medicines counterfeiting took place in October 2010 in San Jose, Costa Rica while a second workshop was held in Nigeria in November 2010 (Kopp, 2010). The WHPA (consisting of the International Council of Nurses, International Pharmaceutical Federation, World Confederation for Physical Therapy, World Dental Federation and the World Medical Association) has issued a joint statement on medicines counterfeiting.

FIP has also been collaborating with the Council of Europe ad hoc committee since 2004 in the fight against medicines counterfeiting. In 2008, this became the Committee of Experts on Minimizing Public Health

Risks Posed by Counterfeiting Medical Products and related crimes (CD-P-PH/CMED).

Other organisations such as the International Conference of French Speaking Orders (CIOPF) have produced recommendations on the issue of medicines counterfeiting (Chauve, 2008).

International Pharmaceutical Students Federation (IPSF) : The IPSF organised its first Anti-counterfeit Drug Campaign (ACDC) in 2007 with the aim of increasing the awareness of the risks posed by medicines counterfeiting among students in health professions as well as educating them on the threats of medicines counterfeiting (IPSF, 2007). Discussions with one of the executives of IPSF indicate that the organisation has a draft document on medicines counterfeiting that is yet to be published (Chittoory, 2010).

International Council of Nurses (ICN): In 2005, the focus of the International Nurses' Day (IND) was medicines counterfeiting. Its major objectives were raising the awareness of the problem, providing nurses with the tools for the detection and reporting of medicines counterfeiting as well as encouraging nurses and health professionals to lobby increased government and regulatory authorities' attention on medicines counterfeiting (International Council of Nurses, 2005). It has also issued a position statement on tackling medicines counterfeiting (International Council of Nurses, 2005). The ICN collaborates with IFPMA in fighting fake medicines. It has also published tool kits on the extent of medicines counterfeiting and strategies aimed at curbing it.

Pharmaceutical Society of Nigeria (PSN): The state branches of PSN organise seminars and public enlightenment campaign on drug quality during its pharmacy week (Erhun et al., 2001). PSN organises meetings that provide an avenue for sharing information on drug quality in order to guide importers (Orivri, 2009). The Kano state chapter of PSN sealed 5 drug company depots after concerns were raised that the companies were engaged in the manufacture of substandard medicines (Muhammad, 2009 cited in Milissa McGinnis, 2010). It has also organised workshops and seminars on medicines counterfeiting and drug quality in Nigeria (Ogbebo, 2010a). The Association of Community Pharmacists of Nigeria (ACPN), which is part of the PSN, has been engaged in the destruction of fake and expired drugs (Ogbebo, 2010b).

National Medical Association of Nigeria: It organises a monthly continuing education programme where doctors are taught on drugs/drug quality. It also collaborates with NAFDAC from which it obtains the list of banned pharmaceuticals that it disseminates to its members (Orivri, 2009).

Medical experts in Uganda: These experts collaborate with the police to conduct raids in order to confiscate poor quality medicines (The New Vision, 2008 cited in Milissa McGinnis, 2010).

Appendix 4 illustrates the strategies and interventions by government and/ regulatory and professional bodies and industries in Nigeria (which has been discussed in details within this report) as well as in other countries.

2.7.2 Evaluation of strategies against poor quality medicines

Due to the nature of counterfeiting, it is almost impossible to evaluate the effectiveness of different anti-counterfeiting strategies; also most of the strategies against counterfeiting are pursued with other goals in mind, for instance in Spain the proposal for the use of Radio Frequency Identification (RFID) in their medicines supply chain is to combat reimbursement fraud rather than counterfeiting (Taylor and Davies, 2008). This emphasises the need for cost benefit analysis of anti-counterfeiting strategies to take into consideration these additional benefits (Taylor and Davies, 2008).

An economic model was developed by Currais et al. (2008) to determine the impact of differential in perceived quality and cost of genuine and fake drugs on the prevalence of medicines counterfeiting. The model revealed that the efficacy of policies and strategies adopted in the fight against this illicit crime is highly dependent on the level of impact on both differential perceptions of quality as well as cost differential. In most cases such strategies are influenced by the conflict of interests between different stakeholders (Currais et al., 2008). A similar model by Lybecker, (2007) showed that some strategies such as those that are geared towards increasing penalties for offenders and those that increase cost of counterfeiting such as development of anti-counterfeit technologies or those that help to secure the supply chain have greater effect on tackling counterfeiting when compared to campaigns that raise consumer awareness of the dangers of counterfeit medicines such as the use of high school essay competitions to publicize the dangers of counterfeiting as it is done in Nigeria (Lybecker, 2007).

Except for campaigns that help consumers to distinguish between fake and genuine pharmaceuticals which may be beneficial, strategies or campaigns that raise awareness of consumers of dangers of counterfeiting may result in fall in the sale of medicines as well as increase in counterfeiting which consequently

leads to lack of access to good quality medicines (Lybecker, 2007). However, the conclusions from the model by Lybecker, (2007) does not mean that such initiatives as raising awareness of the dangers of medicines counterfeiting are completely unhelpful. An evaluation of a public awareness campaign on the dangers of medicines counterfeiting in Cotonou, Benin showed that it was effective in increasing awareness. About 90% understood the dangers of illicit medicines leading to a reduction in their demand for such drugs (Abdoulaye et al., 2006). However, the findings of this evaluation study may not be conclusive, as other factors may have contributed in the change in the consumer behaviour observed.

2.7.3 Barriers to curbing poor quality medicines

This section discusses barriers that have hindered the fight against poor quality medicines. Eight key issues were identified as major factors that have hindered efforts in this area. These are conflict of interest among stakeholders, globalisation and advancement in technology, product promotion, technological limitation of testing kits, inadequate legislation against medicines counterfeiting, inaccurate information on the true extent of medicines counterfeiting, slow litigation processes in many countries linked to corruption and disagreement on the definition of counterfeit medicines. Each of these barriers is discussed in details below.

2.7.3.1 Conflict of interest among stakeholders

One of the barriers in the fight against medicines counterfeiting is the conflict of interest that may exist between different bodies involved in curbing medicines counterfeiting. For instance while government agencies may be motivated by the public health burden associated with poor quality drug use, the industries may be motivated by profit and issues of intellectual property theft rather than the potential harm caused by such medicines to patients.

2.7.3.2 Globalisation and advancement in technology

Globalisation, increase in world trade, advances in desktop publishing as well as advancement in production technologies are just some of the factors that have helped the proliferation of medicines counterfeiting (Lybecker, 2007 and Schofield, 2001). The invention of newer and easier production technologies has made it easy for counterfeiters to replicate even complex safety features such as holograms. The existence of free trade zones have created ready markets for counterfeit medicines and indirectly increased the complexity of medicines counterfeiting and the difficulty in detecting counterfeits. This is because counterfeiters can operate in several countries. For instance they can source the materials in one country, produce the medicines in another country and then transport them to different countries for sale.

2.7.3.3 Product promotion

The increased importance which may be attached to medicines that are highly promoted for instance through advertisement by the pharmaceutical industries may cause an increase in their demand and consequently make such products an ideal target for counterfeiters. A typical example is Viagra® which is frequently targeted for counterfeiting due to increased demand for it. However, other factors may be responsible such as the tendency for consumers to purchase drugs for sexual dysfunction from unscrupulous channels rather than the legal distribution chain (Lybecker, 2007). Difficulties may be experienced in making firms not to advertise their products in order to avoid counterfeiters from targeting it because it may be difficult to prove the extent to which increased demand for their product as a result of their advertisements have contributed to their products being counterfeited.

2.7.3.4 Technological limitation of testing kits

The fact that technologies involving the use of simple testing kits to detect fake medicines may be limited as they may only be able to identify some few

ingredients was noted by Lybecker (2008) as a major barrier against reducing the extent of poor quality medicines. An example of such technology, which has been flawed by its limitations, is the simple and affordable field technique, the Minilab currently used for rapid screening of drug quality in resource poor countries such as Nigeria. The Minilab kits were found to detect only grossly substandard or counterfeited medicines after a pilot study was conducted by the Tanzanian Food and Drugs Authority (Kaur et al., 2010). Hence, the recommendation that Minilab be used in conjunction with medicine quality control laboratories (MQCL) (Risha et al., 2008 cited in Kaur et al., 2010).

Furthermore, the use of other techniques for detection of drug quality such as the use of HPLC have been found to be expensive and requiring a considerable amount of expertise. Although liquid chromatography- mass spectrometry (LC-MS) reveals an enormous amount of chemical information, it is relatively tedious and involves a time-consuming sample preparation. In order to overcome this challenge, the use of open-air ionisation techniques, direct analysis in real time (DART) and desorption electrospray ionisation (DESI) that are less time consuming have been developed (Kaur et al., 2010). Some field tests for combination drugs such as antimalarials that rely on colour tests may be unreliable; for instance one of the tests for artemisinin is dependent on its yellow colour but at least 2 antimalarials available are yellow and may give a false result according to Harparkash Kaur (Willyard, 2010). Also, the presence of small quantities of artesunate in samples may give false positive result to the Rapid Red dye test (Newton et al., 2006b). Bioavailability studies via dissolution tests are also expensive to carry out due to their sophisticated nature.

Due to the destructive nature of methods based on colorimetry, refractometry and chromatography, non-destructive spectroscopic methods such as Raman and Near Infrared Spectroscopy (NIR) are now increasingly accepted and used to test for quality of medicines and in the detection of counterfeits (Kaur et al.,

2010). The use of handheld Raman spectrometers such as the TruScans purchased by NAFDAC is extremely useful, however it is not left without disadvantages as they are subject to interference from inactive components of the pill (Mullard, 2010). Also, Raman spectroscopy may not be able to accurately detect content uniformity of the product tested since only the surface of the sample is usually detected unlike infrared spectroscopy that penetrates through the sample surface (Kaur et al., 2010). Both techniques (Raman and Infrared spectroscopy) require fingerprinting to match the spectra of the tested sample with those on the database. However Raman spectroscopy just like NIR requires less training unlike the use of other techniques such as the Thin Layer Chromatography (TLC). This may make it compare favourably with TLC even in terms of cost, as the cost of staff training is not incurred (Bate et al., 2009c). Raman spectroscopy provides both quantitative and qualitative information, not invasive and is less susceptible to external interference and climate change unlike NIR and TLC (Bate et al., 2009c).

Track and trace technologies such as RFID (Radio Frequency Identification) are less reliable with relatively high error rates and costly especially when it is used on individual products rather than on batches and when it is compared with the use of 2D-Encryption which has been found to be less expensive (Hemalatha, 2008). The use of simple digital camera and free downloadable software is currently under investigation for use in determination of content of active ingredient (Fernandez et al., 2008).

2.7.3.5 Inadequate legislation against medicines counterfeiting

The legislation in most countries has been shown to be inadequate in a survey performed in 50 most populous nations (Anisfeld, 2007). The survey revealed that only 16 of the 50 countries have legislation with particular reference to medicines counterfeiting; most of which are outdated. Drug counterfeiting is regarded as an Intellectual (IP) issue in most countries rather than seen from a

public health point of view and the punishment for drug counterfeiting is not always different from counterfeiting of other goods such as handbags and may even be less severe in some cases (Anisfeld, 2007). Inadequate international collaboration, inadequate number of inspectors and low renumeration for inspectors which are linked to increased bribery and corruption rate and insufficient funding for laboratories are barriers to enforcement of the existing legislation in most of the countries (Anisfeld, 2007).

2.7.3.6 Inaccurate information on the true extent of medicines counterfeiting

Publicising of deceitful information regarding the extent of counterfeiting is a serious limitation to its fight, for instance, the Indian government published an article in a local newspaper which stated that just about 0.04% of drugs sampled in a study were counterfeit (Bate, 2010). A figure which differs significantly from findings of other investigators; for instance; the WHO reported in 2002 that the Indian manufacturers estimated that 20% of drugs in the markets of major cities in India were illegal or substandard (Bate, 2010). Similarly, the Pakistan Pharmaceutical Manufacturers Association stated that the production rate of counterfeit medicines in Pakistan is 0.4%. Again, there is need to doubt this figure, bearing in mind that Pakistan is ranked among the top exporters of counterfeit medicines (Babar, 2005).

2.7.3.7 Slow litigation process linked to corruption

Another barrier to fighting counterfeiting is the nature of legal systems in most countries such as the slow litigation processes which encourages the criminals to carry on with counterfeiting since many of the cases may never really be concluded (Bate et al., 2010). In addition to this, is corruption, which is inherent in many countries that have a major problem with counterfeiting with many cases of counterfeiting, linked to top government officials. Bate et al. (2010)

cites instances of such in countries like India, China, Argentina, Sri Lanka, Uganda and Bolivia.

2.7.3.8 Disagreement on the definition of counterfeit medicines

Definitional confusions in this area as previously noted also contribute a serious barrier to the fight against counterfeiting for instance, while NAFDAC considers medicines not registered by it as counterfeit, the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) warns that medicines authorised for marketing by one regulatory authority but not by another should not be deemed counterfeit in the territory of the latter (IFPMA, 2010).

There are currently agitations from groups such as Health Action International and Equinet amongst others that the definition adopted for counterfeit medicines especially as included in the Uganda bill and Kenyan law may be too broad to include generic medicines and so may impede access to generic medicines which are usually more affordable to majority of the people in developing countries (Equinet, 2010). There are also concerns that the WHO actions via IMPACT is geared towards intellectual property protection thereby compromising its pubic health role as raised at the 63rd World Health Assembly (WHA) and contained in the draft resolution proposed by the delegations of India and Thailand (WHO, 2010e). Sequel to the concerns and other discussions from the 63rd WHA, the WHO decided to create a working group to evaluate the concerns and proposals raised by the member states as well as advocating that the Director General of WHO held consultations with member states and regional economic integration organisations on specific issues (WHO, 2010f). The working group presented its preliminary report at the 64th WHA. After which it was given more time to deliberate and present its final report. The final report of the working group that proposed a member state mechanism in tackling the problem of Substandard/spurious/falsely-labelled/falsified/counterfeit (SSFFC) medical products was presented and

adopted at the 65th World Health Assembly (WHO Regional office for South East Asia, 2012). The conflicts and controversies in the definition of counterfeit medicines and the role of WHO in tackling medicines counterfeiting have therefore been a major impediment to any progress made so far towards curbing medicines counterfeiting.

2.7.4 Limitations of the review and future areas of research

This review has several limitations, which include the inclusion of only studies published in English language. Although PUBMED, EMBASE and IBSS databases were searched, the majority of the information and articles included in the review were obtained from the grey literature such as newspaper pages and links to internet web pages from Google, Norton and Google scholar search engines.

There is paucity of information in the field of medicines counterfeiting and poor quality medicine as a whole. Although, the literature review showed that some studies have been carried out to determine the causes of medicines counterfeiting and the extent of poor quality medicines in Nigeria. It would be worthwhile to conduct qualitative research aimed at evaluating the awareness and perceptions of stakeholders; medicine sellers, consumers and the like on the problem of poor quality medicines in Nigeria (Newton et al., 2010) and to explore challenges such as non-governmental inefficiencies leading to irrational drug use for example sale of drugs by illegitimate outlets, dispensing of prescription medicines by unauthorised dealers and control of pharmacies by non-pharmacists to determine their magnitude and solutions to them. Any discrepancies between the stakeholder perceptions of the quality of medicines in Nigeria and the reality of the situation need to be identified (Garuba et al., 2009). Other areas identified from the literature that may need to be explored further include determining what government authorities are doing to stay current on trends and methods used by counterfeiters and exploring how

reported cases on medicines counterfeiting are handled by regulatory and professional bodies in Nigeria. Information arising from these will help inform areas that need to be improved upon to further reduce the problem of poor quality medicines in Nigeria.

From the literature review, very few studies made attempts to determine or assess improvements that have been made in curbing medicines counterfeiting in Nigeria; Garuba et al., (2009) which accessed the perceived level of transparency and potential vulnerability to corruption in the areas of drug registration, procurement and inspection and distribution. Bate and Hess (2010) and Bate and Mathur (2011) tried to assess if there were improvements in drug quality in Lagos and Accra between 2007-2010 and if there were improvements in drug quality following the introduction of the TruScans for counterfeit drug detection by comparing the quality of medicines before and after the introduction of the TruScans. Considering the relatively short interval between 2007 and 2010 to expect any significant changes, it would be more useful to conduct a larger sample study which would make comparisons with situation of drug quality at the beginning of 2001; a time where relatively few strategies were in place to combat medicines counterfeiting (Bate, 2010) and to determine the factors responsible for any improvements which were not shown in the Bate and Hess (2010) study.

Another important observation from the review is that despite the very many interventions in place to curb medicines counterfeiting in Nigeria, no study could be identified that validated any of these interventions. Therefore evidence on how best to address medicines counterfeiting is currently lacking. Also, the perceptions of stakeholders on such interventions and on issues relating to accessibility of good quality medicines are often neglected where in fact better outcomes could be achieved if the users' perceptions are incorporated in formulation of such interventions aimed at improving access to good quality

medicines. This is because the stakeholders are in a better position to discuss issues relating to medicines quality from their experience. Their opinions can then be integrated into interventions against medicines counterfeiting and poor quality medicines as a whole for better outcome.

In addition to these, many of the available studies aimed at determining the extent of poor quality medicines in Nigeria often employed convenient sampling of few drug classes mainly anti-infectives. There is very limited information on other drug classes that have been reported to be counterfeited and are of great significance such as medicines for chronic diseases like the anti-diabetics. Conditions such as Type 2 diabetes (like all forms of vascular disease) already are of growing prevalence in countries such as Nigeria. Hence, this is an appropriate area of study in relation to anticipated future trends in chronic disease management in Africa. Although there is a paucity of data on the exact prevalence of diabetes in Nigeria, there is evidence to show that it is increasing when compared to previous estimates. Current estimates of the prevalence rate of Type 2 diabetes in Nigeria show a prevalence rate of 6.8% in some areas of the country (Nyenwe et al., 2003). It is envisaged that by the year 2030, diabetes will rank the 7th leading cause of death (WHO, 2008b). It is therefore important to conduct a random sampling and testing of drugs used for the treatment of chronic diseases such as diabetes in order to assess their quality and determine ways to ensure better access to good quality medicines giving the impending disaster which may result from the increased prevalence of such chronic diseases and from consuming counterfeit medicines used for the management of such diseases. It is based on this observation of gaps in literature and the need to generate information on the current situation of the quality of medicines for chronic diseases in Nigeria as well as to make recommendations aimed at optimising the current strategies in place to curb medicines counterfeiting that this two-phase study was predicated.

The current research in addition to the systematic literature review conducted, assessed the perceptions of stakeholders on issues relating to the accessibility of good quality medicines in Nigeria and on the initiatives in place in Nigeria to curb medicines counterfeiting using the recently introduced Mobile Authentication Service (MAS) as an example. It also validated the MAS through determination of the quality of medicines to which the service has been introduced and comparing the results with the response to their SMS authentication. It also made comparisons between the quality of the innovator brand; Glucophage® and their generic counterparts in terms of the content of their active ingredient; metformin. Among other medicines which are MAS enabled in Nigeria, metformin was chosen because it is in the essential medicines list and the first medicine to which the service was introduced. Metformin also seems to be the most utilised anti-diabetic medicine in Nigeria from previous studies (Adibe et al., 2009). It was also important to focus on metformin given that the high cost of the innovator brand Glucophage® may make them attractive for counterfeiting. The price of the cheapest generic in the outlets visited during the preliminary fiedwork ranged from a hundred naira to a hundred and fifty naira (N100-N150) per card of about 10 tablets while the price of Glucophage® ranged from two hundred and fifty naira to four hundred naira (N250-N400) per card of 12 tablets. This means that the price of Glucophage® could be as high as four times the price of the cheapest generic metformin. The high cost of Glucophage may make it prone to counterfeting because when medicine prices are high and unaffordable, patients will more likely look for cheaper sources and may in the process purchase cheaper counterfeit mediicnes. It was therefore important to compare the quality of tagged Glucophage® and the cheapest generic metformin versions to determine if there were significant differences in quality between them and to make recommedations towards the promotion of the use of good quality and affordable medicines rather than expensive brands which are prone to counterfeiting.

2.8 Aims and Objectives

2.8.1 Aims

The two-phase study aimed at validating the Mobile Authentication Service (MAS) and exploring stakeholder experiences and perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria.

2.8.2 Objectives

In order to explore all the variables necessary to meeting the aims of this research, the systematic review of the literature (already presented) was conducted followed by a preliminary fieldwork. A 2-phase study comprising collection and analysis of metformin samples (Phase 1 or quantitative phase) and conducting and analysis of semi-structured interviews (phase 2 or qualitative phase) was then carried out.

2.8.2.1 Objectives of the quantitative phase of the study (phase 1)

1. To perform a test validation of the Mobile Authentication Service (MAS) by comparing the responses obtained from the mobile anti-counterfeit service with the actual quality of medicines received by the consumers via packaging and experimental/chemical analyses (Do these authentication tags imply good quality?)

2. To determine if there are differences in quality between the Glucophage® (metformin) with the authentication tags and the cheapest generic metformin versions without the tags (by comparing the results obtained from the packaging and chemical analyses of the tagged Glucophage® with that of generic metformin versions without the authentication tags)

2.8.2.2 Objectives of the qualitative part of the study (phase 2)

1. To examine stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria (in order to show the extent to which medicines counterfeiting is a problem in relation

to other inefficiencies which may be hindering accessibility to cheap good quality medicines)

2. To identify the successes and challenges (potential problems) which may arise in MAS implementation and determine how these problems can be mitigated in order to ensure optimum utilization and future expansion of the service

3. Explore the consequences of the use of MAS

4. To determine the perceptions of stakeholders on how best MAS can be improved in order to ensure optimum utilization and future expansion of the service

5. Make adequate feedback/recommendation based on the findings of this research towards the successful implementation of the Mobile Authentication Service in Nigeria and reduction of poor quality medicines. This will ultimately promote access to good quality medicines and translate to improved health outcomes.

Additional issues in the context of the research question that emerged during the data collection were also considered.

2.8.3 The Mobile Authentication Service and how it works

MAS enabled medicines have a scratch card on their packaging, which hides a unique one-time 12-digit pin or code. Patients are required to scratch the card and send the codes free of charge via SMS through a mobile phone to a short code 38353 and should receive a reply stating the medicine is genuine, fake or stolen. If the medicine is genuine, the first line of the message will say “OK, Original”. The response also usually contains some health tips and reminders that are targeted at specific patient groups for which the medicine authenticated

is used to treat. It also contains a phone number to call if any problems are encountered. Below is a typical message for a medicine, which was authenticated:

“Ok, original Glucophage® 500mg. NRN: 04-6233. If you are diabetic, avoid shoes with cracked sole. Problem? Call 08039012929. Nafdac and Biofem care. Sproxil SMS”.

More recently, Sproxil started offering a web app that allow patients to authenticate their medicines by sending the unique code via the web app. Customers can also call their call centre to verify the quality of a product. Figure 7 shows the picture of how MAS is used to authenticate medicines via SMS.

Figure 7: Picture of how the Mobile Authentication Service works (Okeugo, 2014)

2.8.4 Rationale and significance of the study

The current research assessed the perceptions of stakeholders on issues relating to the accessibility of good quality medicines in Nigeria and on the initiatives in place in Nigeria to curb medicines counterfeiting using the recently introduced Mobile Authentication Service (MAS) as an example. MAS was validated by comparing the results of the Short Message Authentication (SMS) with the quality of medicines to which the service has been introduced; metformin. The MAS was chosen as the focus of this study as it is the only end-user focused intervention introduced by NAFDAC. That is, it aims to confer the power of medicine authentication to the general public by allowing consumers to validate their medicines at or after purchase. Other anti-counterfeiting strategies tend to empower professionals and other agents.

Since the inception of MAS, very few studies have been carried out to evaluate it. These include the pilot study by Sproxil (the company that initiated the service in Nigeria), which determined the feasibility and cost implementation of MAS using data from pharmaceutical companies that have signed up for the service. Another study conducted by Oyetunde and Ilozumba (2013) assessed public response to MAS by comparing data from pharmaceutical companies on their monthly sales with monthly SMS responses received. Oyetunde and Ilozumba (2013) also assessed the effectiveness of MAS strictly from the perspective of company representatives. In 2011, a group of MIT students critically analysed MAS. However their assessment was based mainly on information from Sproxil's pilot study. All these studies have often left out the users. MAS is a social enterprise geared towards the users so would greatly benefit from research which would involve the perceptions of the users (the consumers and medicine sellers) and it is based on this that this research is predicated.

This research is the first to show from the perspective of stakeholders including the service users the impact of MAS on the prevention of medicines counterfeiting, and for the first time presented a holistic independent evaluation of its utility. Therefore, findings from this study may serve as a baseline for future evaluations of such strategies employed by NAFDAC in order to determine if there are deteriorations or improvements and help to determine areas of intervention. This is also in accordance to the WHO consensus on the evaluation of global e-health and m-health initiatives.

In addition to validating the MAS, this study provides an insight into the overall quality of generic metformin supply in Nigeria. As previously stated, other studies of counterfeiting and related issues in poorer developing countries have frequently focused on the integrity of conveniently sampled products such as antibiotics and anti-malarials. This study is therefore the first of its kind to employ random sampling and a relatively large sample size to show the quality of medicines used in the management of such a chronic disease as diabetes.

Finally, this research work also revealed the part that professionals such as pharmacists could play in promoting availability of good quality medicines and made recommendations relevant to further reduction of poor quality medicine supply in Nigeria. These recommendations should be useful to regulatory authorities in developing countries that may be facing similar drug quality problems as Nigeria and other countries such as Ghana and Kenya that are adopting the use of MAS.

2.8.5 Research approach

This research was conducted with the approval of the School of Pharmacy, University of London ethics committee and the Lagos University Teaching Hospital ethics committee. A systematic review of the literature in the area of

medicines' quality (already presented) and a preliminary fieldwork was conducted. These were followed by random sampling of metformin samples from different outets in Lagos, Nigeria, SMS authentication of tagged Glucophage® samples, packaging and chemical/experimental analyses of collected drug samples in the quantitative phase, also referred to as phase 1 of this research. Semi-structured interviews were the primary data collection method used in the second phase.

2.9 Conclusion

Medicines counterfeiting has previously been ignored due to perceived low profitability of markets in the developing countries, the unique nature of ethical drugs market and fear of loss of reputation. However, with advancement in technology and globalisation in recent times, it is now beginning to attract increased attention (Lybecker, 2008). The current disagreements on the definitions of counterfeit medicine and increasing reports of cases of medicines counterfeiting in developed countries have also contributed in making it a topic of interest among different local and international organisations.

The literature review presented in this chapter shows that some efforts have been made in Nigeria especially through NAFDAC in the past 14 years to combat the existence of poor quality medicines and internationally through various government bodies, regulatory authorities, professional organisations and the WHO. However, the extent to which the strategies have been effective in curbing counterfeiting still remains largely unknown and therefore calls for further better designed studies to determine the extent of the problem of poor quality medicines as well as evaluate the strategies in curbing this problem. The next chapter; chapter 3 presents the details of the preliminary field work which was conducted prior to commencing the data collection.

Chapter 3

Preliminary fieldwork

3.1 Introduction to the chapter

There was a need to meet with stakeholders in the field to obtain more insight into the area of medicines quality before commencing the study. The major aims of the preliminary fieldwork were to inform the research design and establish the feasibility of carrying out the research work in Nigeria. The preliminary fieldwork involved two visits to Nigeria and meeting researchers with similar interests.

The main purposes of the preliminary visits to Nigeria were to meet stakeholders in medicines supply in Nigeria for example NAFDAC officials and other individuals holding key positions within the Nigerian pharmaceutical sector and visit a convenient sample of community pharmacies and Patent Medicine Vendors (PMVs) in some major cities in Nigeria (Makurdi, Abuja, Port Harcourt, Lagos and Awka) in order to have an idea of what obtains in practice. Most of the stakeholders met were introduced to the researcher through her previous contacts while some were identified during the review of the literature. Others were opportunistically interviewed mostly at meetings attended by the researcher while in Nigeria. This strategy was appropriate because this was not intended to be a study but to obtain a preliminary knowledge, which will inform the design of the proposed study.

Summary notes were made during and immediately after each discussion to record and ensure later reflection of issues raised. In order to ensure confidentiality, names of all the individuals contacted and outlets visited were coded so that they cannot be identified.

3.2 Outcomes of preliminary meetings held with Nigerian stakeholders

During the preliminary visits to Nigeria, key stakeholders were met. This included two officials of the Nigerian drug regulatory agency; NAFDAC, four managers of pharmaceutical industries and one leader in academia. The meetings with NAFDAC officials revealed that NAFDAC has done a lot of quantitative field-testing of medicines and some social pharmacy research in this area. This led to an official application to NAFDAC to retrieve some of these research works. None of the articles requested could be obtained. One of the NAFDAC officials informed the principal researcher that NAFDAC uses the BP specification for assay of metformin. This led to the use of BP specification for percentage concentration being used as an indicator for pass/ fail of HPLC analysis in this research.

Several initiatives against medicines counterfeiting instituted by NAFDAC such as the use of TruScan®, RFID and MAS were discussed. These discussions further highlighted the need for research to be conducted on the adoption of MAS and further comparison with future research in order to determine changes in the extent/ trend of counterfeiting MAS enabled medicines. Other uses of MAS such as its application in tracking and tracing medicines while they are within the distribution chain and its adoption in other countries were subsequently discussed.

All the stakeholders expressed positive view about MAS and its advantage of targeting the end users and at no cost to the users. The stakeholders were of the opinion that the MAS system is highly secured and were optimistic that it would be difficult to counterfeit MAS enabled medicines since MAS works in the same manner with mobile phone scratch card production, which till date has not been counterfeited. However, concerns were raised about the possible

increase in the price of medicines as a result of the MAS service and the consequences that may have on users. Concerns were also raised about the type of medicines that should be MAS enabled; that is whether MAS should be for all or restricted to some categories of medicines such as the expensive branded medicines. These concerns raised were subsequently explored during the semi-structured interviews. Another concern raised was the disagreement on the definition of counterfeit medicines and need to clarify this in the research. This research focused on poor quality medicines as a whole rather than just medicines counterfeiting which form part of medicines that are of poor quality. The opinions from these stakeholders helped further inform the design of this research.

3.3 Observations from outlets visited

Fifteen outlets (9 community pharmacies and 6 patent medicine shops) were visited to find out the perception of community pharmacists and patent medicine vendors as regards medicines counterfeiting in Nigeria. Some of the issues explored were the awareness of community pharmacists and patent medicine vendors of the Mobile Authentication Service, their perceptions of initiatives in place in Nigeria to combat medicines counterfeiting and the different brands of metformin that they stock. Although the outlets were conveniently sampled, useful information were obtained on the perception of community pharmacists and patent medicine vendors of the situation of medicines counterfeiting in Nigeria and the initiatives against medicines counterfeiting. Other useful information obtained was the availability of different kinds of metformin in the Nigerian market. Below are some of the important issues discussed and how it informed the research.

3.3.1 How poor quality medicines can be tackled in Nigeria

One of the pharmacists stated the need for training of medicine sellers on detection of counterfeit medicines but added that such training should be done

in partnership with government agencies because Non-Governmental Organisations may face considerable barriers if they carry out such tasks independently. The need for frequent and recent updates from NAFDAC was emphasised. One of the interventions currently been proposed, the zonal drug distribution network was applauded as a good idea that can help remove the drug business from the hands of quacks even though it was acknowledged that this may take some time to accomplish.

3.3.2 Awareness about MAS

All the community pharmacists and patent medicine vendors met during the preliminary visit were aware of MAS and seemed optimistic about the service. However, there seemed to be disagreement as whether their patients were aware of and using it or not. Many of them were of the view that there is low awareness level about MAS except for the very few enlightened consumers who know about the service.

Out of the 9 pharmacies visited, only in one outlet did the pharmacist interviewed state that he encourages his patients to use the service and give them leaflets about the service. It was also observed that although the community pharmacists were aware of the service, some of their shopkeepers who sell medicines in their absence were not aware of MAS.

3.3.3 Glucophage® stocked in the outlets

All the 9 pharmacies visited stocked Glucophage® (3 out of these stocked untagged Glucophage®) while two out of six patent medicine shops visited stocked Glucophage® (1 out of these stocked untagged Glucophage®).

There seemed to be disagreement on the reason for stocking both tagged and untagged Glucophage®. In one outlet, the pharmacist stated that the untagged Glucophage® is an old stock while a shop keeper in the second pharmacy stated that the untagged one is locally produced while the tagged one is imported from UK. The exact reasons for stocking the untagged Glucophage® could not be ascertained from the third pharmacy that stocked it because the pharmacist was not around when the researcher visited the pharmacy. The

patent medicine vendor that stocked untagged Glucophage® stated that the tagged ones were only used during the trial period. No manufacturing date was seen on 3 of the untagged Glucophage® packets, raising questions about the authenticity of the untagged Glucophage®. As a result of this observation, the research was designed to include collection of both tagged and untagged Glucophage®. However untagged Glucophage® was later excluded because it was discovered that at the time of the sample collection, all the Glucophage® samples in Nigeria had been coded by Sproxil so no untagged Glucophage® could be obtained.

Sale volume of Glucophage® seemed to vary between the outlets. One pharmacist said that Glucophage® is rarely sold in his outlet and that he does not often recommend its use unless the patient specifically requests it. This is because of the frequent failures he has encountered with such high cost brand pharmaceuticals due to high level of faking. Some other reasons given for low sale volume in some of the outlets was the location of the outlets and the fact that Glucophage® is a prescription medicine that should be obtained from the hospitals and refilled in the pharmacies. This means that even though in Nigeria, most pharmacies prescribe medicines, the major source of most prescriptions medicines is the hospital. This observation led to the hospital been a target for easy recruitment of consumers of Glucophage® in this study.

The price of the cheapest generic in the outlets visited ranged from a hundred naira to a hundred and fifty naira (N100-N150) per card of about 10 tablets while the price of Glucophage® ranged from two hundred and fifty naira to four hundred naira (N250-N400) per card of 12 tablets.

3.3.4 Source of medicines sold at the outlets

Most of the community pharmacies and patent medicine vendors visited stated that they obtain their medicines from company representatives and wholesalers. However, the open market remain a major source of their medicines due to the

frequent "out of stock" syndrome in most of the wholesale outlets except in situations where the outlet is located very far away from the open drug market.

3.3.5 Recommendation on how MAS can work better

One pharmacist recommended the codes to be affixed on the medicine packs/cartons in order to encourage the pharmacists to use the service while making their own purchases. This is because if they open the individual medicine packs and authenticate, patients will doubt the genuinity of the opened packs. Also, because the authentication can only be done once, patients purchasing such open packs may no longer be able to authenticate them.

3.4 Outcomes of meetings held with researchers of similar interest

Several researchers in the field of medicines counterfeiting and medicines quality whom the researcher identified during the literature review phase were contacted and met to discuss issues relating to drug quality and the proposed research. Following meetings with these researchers, inputs were received which further informed different stages of the research. The discussions that follow contain information on how these inputs informed the different stages of the research.

3.4.1 Literature review

Meetings with 2 of the researchers (TM and HK) led to obtaining more information on medicines counterfeiting through further reading the articles they recommended, some of which were not retrieved during the literature review. Some of the articles retrieved at this stage were Kuar et al. (2010), Anisfeld, (2007), Assi et al. (2009), Willyard (2010), Dolgin (2010), Ghosn (2010), Killugudi (2010), Mooney (2010), Mullard (2010), Plancon (2010) and Torres (2010). Information from these articles were then included in the literature review.

Insight on how to better structure the literature review into different subheadings; extent of poor quality medicines, impact of poor quality medicines and strategies in place to curb medicines counterfeiting in different parts of the world was received from TM, this led to modification of the literature review into these different subheadings as shown in Appendix 4.

3.4.2 Data collection

3.4.2.1 Sample size for Phase 1

Insight was received from 2 researchers OS and PNN on the number of samples that can be obtained for analysis and testing in the first phase of the research.

The need to establish a hypothesis for the research to aid proper sample size calculation was discussed. Insight into the use of formulas in online databases and Newton et al. (2009) to calculate the sample size of metformin needed was provided. In order to determine the adequate sample size, the hypothesis was derived from the objectives of the quantitative phase of the research which were to validate MAS and determine if there were differences in quality between tagged Glucophage® samples and their generic counterparts which were not tagged. Based on this, the null hypothesis was that the quality (pass/fail quality tests) of tagged Glucophage® was not significantly different from generic metformin. The power and sample size (PS) software was used to calculate the number of samples that will be adequate to meet the study objectives, details of this are presented in chapter 4.

3.4.2.2 Sampling strategy- phase 1

Random sampling and its advantages over other sampling methods such as convenient and systematic sampling were discussed in detail with PNN. It was based on this discussion that the sampling method for the first phase of the

study was changed from systematic sampling to random sampling because it was thought that this would provide more reliable data with limited bias than other sampling methods. Insight was also received on the use of the Microsoft Excel Rand Between functions to obtain random numbers from the sampling frame. Random sampling in cases where there was no pre-existing sampling frame such as sampling from the drug market traders was also discussed. This provided insight on how metformin from the drug market traders were sampled. An independent statistician verified the sampling methods and techniques as well as the procedure taken to determine the sample size.

The need to confirm if other sources of medicine in Nigeria such as basket sellers/ drug hawkers were also a source of metformin and if metformin should be collected from hospitals were also discussed. This led to iteratively checking the basket sellers to determine if they were also a major source of metformin before commencing sample collection. This was done by asking them and then checking among their baskets. The need to obtain information on the components of the Medicine Quality Assessment Reporting Guideline (MEDQUARG) for field surveys of medicine quality as proposed in Newton et al., (2009) was discussed. This guided the kind of information obtained during the metformin sampling stage. It was decided that metformin from the hospitals would not be sampled because of the associated risks involved in sampling from the public sector (government regulated outlets) from previous research as discussed with PNN.

Limitations of the British Pharmacopoeia, which does not state a standard number, required for all screening and what to do if the sample units available are not enough to ensure accurate results was discussed. Judgement as to the number of tablets per sample to collect from each tablet was made based on input from 2 researchers, HK and HG who have carried out a lot of research involving analysis of medicine samples using HPLC. Practical guidance on how to conduct the chemical analyses of the samples was received from HG. The

total number of tablets analysed per sample were four tablets and they were analysed in duplicate using the HPLC equipment. This is because the research did not aim at ascertaining the content uniformity of the tablets in which case more of the tablets per sample would need to be analysed. Also given the number of metformin samples that needed to be analysed and the limited time to complete the PhD, it was practical and adequate to analyse only 4 tablets per sample. The average percentage concentration of the analysed tablets were obtained and used as an indication of failure/pass for HPLC quality test.

The importance of blinding to avoid introducing any bias to the study was discussed. This led to different people being involved in different aspects of the research; for instance the principal researcher was involved in collecting the samples and coding them while the samples were recoded by one of the sample collectors in order to blind the principal researcher to the results of the packaging and chemical analyses.

3.4.2.3 Transporting the medicines to the UK

Discussions with PNN informed the precautions taken to ensure that the metformin samples collected from Nigeria arrived in the United Kingdom safely. For instance the need to obtain a letter from a top person at The School of Pharmacy with authorising stamps or from the Medicines and Healthcare Products Regulatory Agency (MHRA) stating that the medicines were for analysis, not for resale or human or veterinary consumption and were not hazardous was raised and this led to obtaining a letter from School of Pharmacy, University of London to the UK customs been included in the pack of medicines when they were been transported to the UK.

Other important ideas shared which was implemented while trying to transport the medicines to the UK were; keeping half of the medicines in Nigeria as a

contingency plan in case the medicines were seized on transit and repackaging the samples to be retained in Nigeria with all the packaging information on the medicines written on the new pack. Others include exercising caution when removing the tablets from their original container to ensure that they were not contaminated if in the future they were to be analysed by some sensitive techniques such as mass spectrometry to detect why any of the medicine was counterfeit, sending the samples through reputable courier companies such as DHL or FedEx to avoid embarrassment by custom officials as well as including one of the yellow Gemini temperature loggers which was set to measure the temperature every 30 minutes from the time the medicines were collected through shipping and completion of analysis of the samples to ensure they were stored within the stipulated temperature range, sealing the containers for transporting the medicines with the name of the researcher written across the seal so as to be able to notice any opening and transporting the samples in polystyrene cool boxes to help maintain the temperature within specified limit.

3.4.2.4 Semi-structured interview

Useful input was received from some of the researchers that informed how the interview questions were structured and some of the questions asked during the semi-structured interviews. For instance when interviewing pharmacists, it was suggested that it may be better to begin with questions on their experiences of medicines counterfeiting before proceeding to ask them about policies in order to avoid any bias as previous research in this area have shown that they are more likely to talk negatively about the policies if they are asked first about them.

Some of the interview topics suggested by the researchers were included in the interview guide. These include which medicines that are easily counterfeited from participant's experience, participants' experience of medicines counterfeiting, how big the problem of poor quality medicine is in Nigeria, medicine sellers' perceptions of the medicines they offer to patients in terms of ethical considerations they make while selling medicines to patients, use of

cheap medicines based on the laws on generic substitution in Nigeria, the risk: benefit ratio of their use for instance depending on the class of medicine, socioeconomic class of the patient, reasons for selling particular brands of medicines and the training they need to authenticate counterfeit medicines, the kind of medicines commonly used (local production versus imported medicines) and how detected cases of medicines counterfeiting are handled.

3.4.3 Methods

3.4.3.1 Conceptual framework

As part of efforts by the researcher to further develop the qualitative phase, there was a need to understand the value of theoretical frameworks in qualitative research in order to determine the theoretical framework that would underpin the research. Conceptual frameworks were discussed with one of the researchers; AH. The Cornford et al. (1994) socio-technical framework and other theories in organisational behaviour such as the theory by Paul Sabatier; Advocacy Coalition Framework, Institutional theory, the Actor network theory and Rational Choice Theory were discussed. Following this discussion and further reading, the Cornford et al. (1994) socio-technical framework was adopted for this research. Further reading on theoretical frameworks expanded the researcher's knowledge on its use and provided insight into other theories used in prediction of adoption of new technologies especially in the field of Information technology. Some of these included the Technology Acceptance Model (TAM), the Innovation Diffusion Theory, the theory of perceived risk and the Switching barrier theory. Even though, this research did not aim at using these theories to predict MAS adoption. Constructs of the Technology Acceptance Model and Innovation diffusion theory gave the researcher an idea of the variables to be explored within the Socio-technical framework proposed by Cornford et al. (1994).

Table 4: The conceptual framework

	System functions	Human perspectives (the stakeholders)	Organisational context
Structure	Technical detail (in this case, the mobile phone) for instance availability of mobile phone networks	Work conditions and implied requirements for instance skills required by the stakeholders who use the service, do they have to be more patient in order to receive the text message responses? Is the system cost effective when compared to other anti-counterfeiting strategies? These encompass stakeholder attitude and opinions of MAS, that is what they think about MAS; its perceived risks and benefits, Perceived Ease of Use (PEOU) and Compatibility	Sustainability-mobile phone services, skills required for instance ability to use mobile phones, Impact of the geographical habitation of the users and questions on compatibility
Process	Information processing (correct and valid). This can be determined from the results of the quantitative aspect of this study (phase 1). The results from the packaging, NIR and HPLC analysis will be compared with the results from the SMS authentication	Human participation in tasks; social interaction. This includes questions such as how MAS has changed their mode of operation in terms of; for instance their concern about their medicines, the brand of metformin that they purchase. How has the users' experience of health care altered on using the service? How has MAS affected their work? Will they prefer to buy medicines at a costlier price just because they are of good quality or would they go for cheap ones irrespective of their quality? If the cost of medicines increases due to MAS, will they still buy Glucophage®? Do they trust the response they receive from MAS?	Altered delivery and practice. Is there an ability to implement MAS as a support for change? Can MAS support other health strategies aimed at improving patient outcomes; if so what are the future expectations. What suggestions can participants offer for implementing or maintaining the system? Does it take their time? Has it changed their health or purchasing behaviour? Do they report medicines counterfeiting cases? Has the sale of Glucophage® with the tags increased since the introduction of these tags or do medicine sellers now have to procure more Glucophage® to meet demand?
Outcome	Relevant/useful, applicable, reliable	Quality of service and outcomes such as users' satisfaction with MAS, complacency to use, Changes in healthcare delivered/ quality of care; effect of MAS on other health outcomes such as therapeutic failure. Do medicine sellers think that their clients on Glucophage® respond better to it since they started to use the ones with tags? Do consumers feel that they are better off with Glucophage® with the tags than without the tags? Is this service useful?	

Adapted from Cornford et al. (1994)

3.4.3.2 Analytical techniques

In order to inform the method of sample analysis that would be employed, discussions were held with 5 different pharmaceutical analysis experts (MZ, OS, AN, KJR and PNN) on the possible tests to carry out in order to meet the objectives of the quantitative phase of the research. During the course of these meetings, different methods of medicine analysis such as the use of NIR, IR and Raman spectroscopy, HPLC, dissolution and disintegration tests were discussed.

Following a review of the advantages and disadvantages of these methods discussed, analysis of the sample via NIR, packaging analysis and HPLC was chosen as the ideal method to analyse the samples for this research. This is because packaging analysis and NIR were noted as methods that can help rapidly detect counterfeit medicines while HPLC can yield quantitative information about the content of the medicines.

Although, complex counterfeits with no differences in packaging and content of active ingredient have been found, research shows that in most cases they can be identified through thorough checking of the packaging and other simpler techniques such as NIR in addition to methods that can give an indication of the content of their active ingredients. This study did not aim at determining bioequivalence of samples but rather sought to validate the information from MAS in order to find out if there were any counterfeits and to give an indication of the quality of the samples studied in terms of their active ingredient.

Need for package screening to be conducted was discussed in addition to NIR and HPLC, as it has shown to be a very important indicator of counterfeit medicine although many researchers in this field often neglect it. This should involve checking for differences in colours of the scanned copies of the

medicine packets using a colour meter, checking for differences in font and font size using a font checker or by using the eye, the use of two different languages on a packet, spelling mistakes, wrong language construction for instance the wrong use of apostrophes and commas as these are also quick indicators of counterfeits. All these except checking for differences in colour were done as part of the analysis. Differences in colour of the medicine packets could not be done using the colour meter because some of the medicines were not sold in their original packaging. Also most of the packets had markings with inks, which may have affected the colour meter reading.

The need for the original samples for comparisons to be collected from the manufacturers or their agents/ representatives was emphasised. Following input from PNN on the definition of counterfeit and substandard/degraded, the following was adopted as a guide to avoid definitional confusion;

1. Genuine packaging + Failed chemistry = Substandard/ degraded
2. Failed packaging + with or without failed chemistry = Counterfeit.

From the above, package screening is a very important test to conduct to help differentiate between counterfeit and substandard/degraded medicines. This is also in line with the recommendation by WHO on detection of counterfeit medicines as can be deduced from the definition of counterfeit medicines by WHO regional office for the Western Pacific presented in chapter 1 of this thesis.

Currently, it is difficult to differentiate between substandard and degraded medicines. However, PNN mentioned that there is an on-going research aimed at establishing degradation products for different medicines, which will help to differentiate between substandard and degraded medicines in the future using mass spectroscopy. It is based on this discussion and further

reading that the researcher incorporated packaging analysis as part of the tests to be carried out on the metformin samples.

3.5 Conclusion

The preliminary fieldwork was conducted to get input from experienced researchers in the field of drug quality since the information obtained from the literature seemed very limited and to inform the design of the study. Also visits were made to Nigeria to meet key stakeholders and visit drug outlets in order to have an idea of what was obtainable in practice so that the research could be better designed to be of greater value. Useful inputs were obtained on all stages of the research; data collection, data analysis and synthesis phases. The information obtained from the literature review and the preliminary fieldwork helped to define the direction of the PhD research. The following chapter discusses in detail the methodology employed for the 2 phases of this study.

Chapter 4

Methodology

4.1 Introduction to the chapter

In order to take a holistic approach in exploring all the variables necessary to meeting the aims of this research, a literature review on medicines' quality in Nigeria was conducted followed by a preliminary fieldwork, details of which are already presented in chapters 2 and 3. A 2-phase study was then conducted. The first phase involved a quantitative random sampling of metformin tablets in order to determine the extent of poor quality medicines in Nigeria and to validate the MAS while the second phase involved a qualitative social research approach using semi-structured interviews to obtain the views and perceptions of stakeholders on relevant issues needed to meet the objectives of this phase of the research. This chapter discusses in detail the theoretical framework underpinning the research, how the study was designed, the data collection and analysis methods used and justification for their use. It also describes the ethical issues that were considered in the course of this research.

4.2 Theoretical framework

4.2.1 Conceptual framework for MAS evaluation

Variables relating to MAS explored in this research work were adapted from the socio-technical framework approach proposed by Cornford et al. (1994) which is an advancement of Donabedian, (1978) structure, process, and outcome approach. As shown in table 4, this framework comprises the system's structure (in this case, it is the mobile phone, the process that it supports (in this case, it is the detection of poor quality medicines) and the outcome of its use (in this case, the consequences of MAS use). To ensure conformity to this framework, stakeholders with similar roles as proposed in the framework were included in the research (consumers, health professionals/providers; the

pharmacist and other medicine sellers and the administrator, in this case regulatory body staff members/policy makers in pharmacy). By using this framework, it is hoped that a wider range of issues beyond the technical performance of the service would be captured. The framework acted as a repository for findings for the research and was used to develop categories from the research questions. It also allowed collected data to be structured and analysed within a multi-dimensional scheme, thereby allowing a rich and more insightful view of the experience of the use of MAS.

This multi-dimensional concept that is proposed in the Cornford et al. (1994) framework has been endorsed by such theories as the Actor network theory that was proposed in the mid-1980s from the work of Bruno Latour, Michel Callon and John Law to aid exploration of socio-technical processes (Crawford, 2004). It has also been employed in several qualitative researches some of which include the evaluation of an Estripod information system (Cornford et al., 1994) and more recently in the evaluation of an electronic prescribing and administration system (Barber et al., 2007).

This framework provides a systematic way to consider the infrastructure surrounding technological achievements/innovations through consideration of both human and non-human factors and assigning the same level of importance to each of these factors in the theoretical framework. It shows that there is a need to consider all surrounding factors (including technical and non technical elements) when evaluating any service or intervention. The actors in this research include among others; the users of the service (community pharmacists, patent medicine vendors, traders and consumers), mobile phone manufacturers (the technology in question), the network providers, regulatory body staff and policy makers in pharmacy. The descriptors under the different categories in the conceptual framework were mainly from ideas obtained from the literature review conducted, the preliminary field work, the theories in the literature which were thought by the researcher to be applicable to the study

and the researchers own ideas about how people may respond to issues discussed. The conceptual framework was flexible; with deletions and additions made following data collection.

Other theories in the field of technology acceptance such as the Technology Acceptance Model (TAM), the Innovation Diffusion Theory (IDT) and the theory of perceived risk were considered in the course of this research as possible theories that may help explain the findings relating to MAS, which is also a technological innovation. While these theories gave the researcher some ideas on questions that can be asked during the interviews in order to obtain more useful information from the participants, they did not directly apply to the analysis and interpretation of the research findings, as they are mainly theories, which help predict the adoption of new innovations/technologies.

4.3 Research design

In order to achieve all the objectives of this study, the research was conducted in two phases. The first was quantitative and the second qualitative. The aim of the quantitative phase (phase 1) was to validate the MAS via a random sampling of Glucophage® packs bearing the relevant authentication tags. (Glucophage® was the first medicine distributed with MAS tags/identifiers). A comparator quantitative study involving the purchase of generic (branded and non-branded) metformin tablets was conducted. All the samples were purchased from community pharmacies and open market traders in Lagos, Nigeria.

A quantitative approach involving random selection of metformin and analysis was chosen to meet the objectives of the first phase of this research because it gives equal chances of sampling from all the outlets in the sampling frame used in this research. It also makes the results arising from this phase representative and generalisable to the population under study. In addition, the large sample size used, as it is typical with quantitative research will help to identify

statistically significant differences between groups (tagged Glucophage® and generic metformin).

The second phase of this research employed a qualitative social research approach, using semi-structured interview schedules and questionnaires (to collect the demographic details of the participants). The three groups of stakeholders included were consumers/members of the public; medicine sellers (community pharmacists, patent medicine vendors and open drug market traders); and health policy makers in pharmacy. This phase aimed at determining the perceptions and experiences of stakeholders and their attitudes towards the use of the Mobile Authentication Service and other drug quality related issues. Possible problems such as the acceptability of MAS to the public and to professional stakeholders, and logistical or allied concerns were systematically explored.

A qualitative social research approach involving the use of semi-structured interviews was employed in the second phase. This was chosen because the researcher thought that it would help generate rich descriptions and explanations from the participants on issues, as it is typical with qualitative research. Also, the researcher thought that the nature of the topic discussed (quality of medicines and counterfeiting) might make more detailed views to be obtained from individual interviews than from focus group interviews. Focus group interviews was considered but was not chosen because the researcher envisaged that it may make the participants not to say their honest views due to fear of being reported to regulatory authorities by other focus group members. In addition, the researcher believed that a higher response rate would be obtained through semi-structured interviews than through focus group interviews. This was because other issues such as lack of access to the focus group meeting venue may have hindered participants from attending the focus group meetings given the Nigerian context where there is an inefficient transportation system.

4.4 Ethical Approval

Ethical approval was obtained from the UCL School of Pharmacy and the Lagos University Teaching Hospital (LUTH) ethics committees (copies of the ethical approval documents can be seen in appendix 5).

4.5 Data collection process -Phase 1

The process of data collection for this phase required sampling medicines to validate the Mobile Authentication Service and to determine if there are differences in quality between the MAS enabled samples (tagged Glucophage®) and their generic counterparts. As previously noted, among all the interventions MAS was chosen for validation because it is the only end-user focused intervention introduced by NAFDAC. That is, it aims to confer the power of medicine authentication to the general public by allowing consumers to validate their medicines at or after purchase. Other anti-counterfeiting strategies tend to empower professionals and other agents. The MAS helps users to determine if the medicine they wish to purchase is authentic or not. Medicines which are MAS enabled have a unique number under a silver panel which can be scratched by the user and sent via text message to a short code. Response is received as to whether the medicine is "OK, Original or fake".

Since the introduction of MAS in Nigeria many medicines have become MAS enabled. Among all the medicines that are MAS enabled, metformin was chosen because it is in the essential medicines list and the first medicine to which the service was introduced. Metformin also seems to be the most utilised anti-diabetic medicine in Nigeria from previous studies (Adibe et al., 2009). Although few studies have been conducted to determine the quality of some brands of metformin distributed in Nigeria, they mainly focused on determining if the brands of metformin tested were bioequivalent. This study is the first to

determine the quality of metformin samples randomly sampled from different outlets in order to validate an anti-counterfeiting service.

4.6 Sampling strategy

4.6.1 Study setting

The metformin samples were obtained from Lagos state. Lagos was chosen as the site for the collection of the samples because it is one of the first states where the Mobile Authentication Service was commenced. Lagos is the largest city in Nigeria by population (about 17 million people). It is also the most ethnically diverse; constituting the low, middle and high-income earners as well as rural, peri-urban and urban dwellers, which is very typical of Nigeria. One of the major open drug markets in Nigeria; the Idumota market is located in Lagos. Also, Lagos has the largest number of medicine outlets in Nigeria (about 30% of pharmacy outlets) and the highest number of pharmacists (2236 out of 6713 registered pharmacists in Nigeria) (Peterson and Obileye, 2002). In addition, the preliminary fieldwork showed that all the brands of metformin available in the different cities visited where also available in Lagos.

4.6.2 Study sample and sample size

This phase involved random sampling of Glucophage® 500mg tablets to which this service was first introduced and which have the authentication tags and generic metformin 500mg tablets. The samples were randomly obtained from community pharmacies in Lagos state and outlets in the open drug market at the Idumota market in Lagos, Nigeria.

Sample size calculations were performed as shown below;

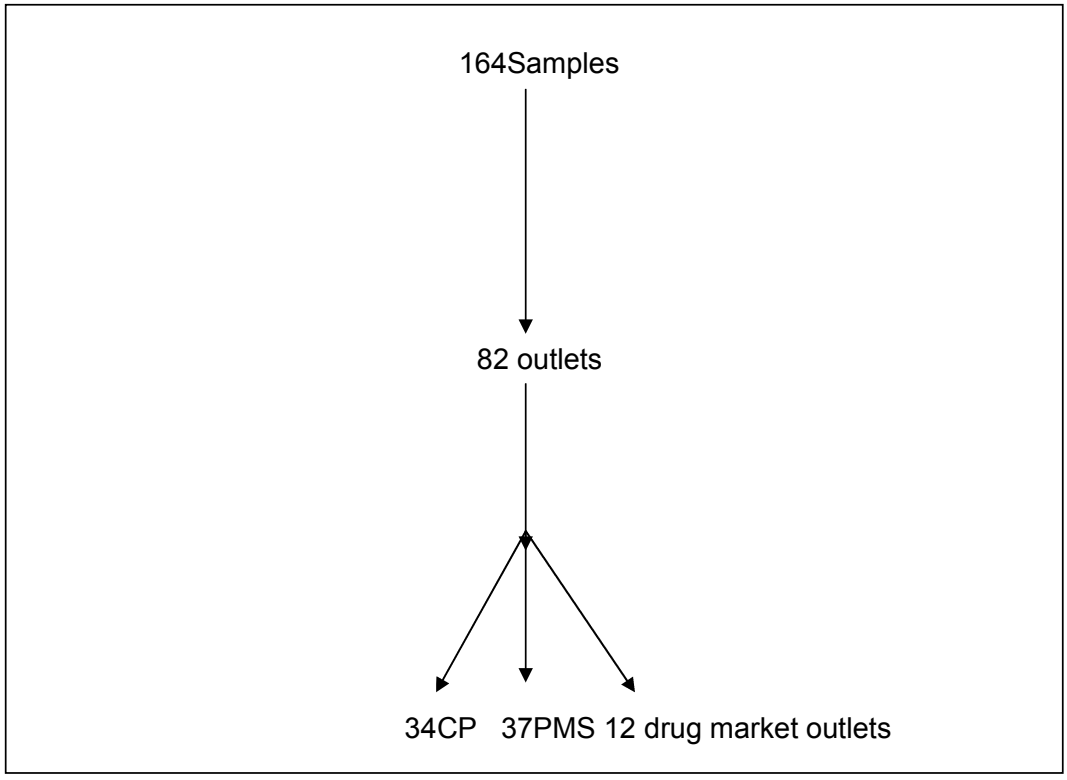
To test the null hypothesis that the quality (pass/fail quality tests) of tagged Glucophage® (experimental or comparator group) was not significantly different from generic metformin (control group). Prior data from the literature on quality of medicines in Nigeria indicated a worst-case scenario failure rate of 48%.

This worst-case failure rate is according to a report by Taylor et al. (2001). We tested whether the frequency of poor quality in the tagged Glucophage® was < 24%, Power 90% and alpha 5%. We assume that if this frequency (48%) was reduced to <24% (that is by 50%) that would be significant in terms of public health impact although no poor quality is acceptable. We also sought to compare differences in quality between the two groups (generic metformin and tagged Glucophage®).

Imputing the following variables; Power= 90%, Type 1 probability error (alpha) = 5%, Prevalence for the control group (P_0) = 48% and Prevalence for the experimental group (P_1) = 24% into the Power and Sample size (PS) software yielded a sample size of 82 samples per group (that is 82 samples of tagged Glucophage® and 82 samples of generic metformin (locally branded and non-branded) metformin tablets which in total is 164 samples) to use an uncorrected chi-squared statistic to evaluate this null hypothesis and detect any statistically significant differences between these groups.

Before commencing the sample collection, it was imperative to know if the mobile medicine sellers were also a major source of metformin in Nigeria. To determine this, 20 mobile medicine sellers (medicine sellers with no outlets) in Lagos were iteratively sampled to see if they stocked metformin. None of them stocked metformin so they were excluded from the major sources of metformin to the Nigerian public. It was therefore decided that the major sources of metformin to the Nigerian public should be the community pharmacies, the patent medicine shops (PMS) or vendors and the open drug market traders. Based on this, 164 samples (82 samples of cheapest generic and 82 samples of tagged Glucophage®) were initially set out to be collected from the community pharmacies, patent medicine shops and the open drug market traders in the proportion of their total numbers in Lagos (590:639:203) respectively. Based on this 34 community pharmacies, 37 patent medicine vendors and 12 outlets in the drug market were to be visited to collect the

samples as shown in figure 8 below assuming that all the outlets stocked both the cheapest generic version of metformin and the tagged Glucophage®.



CP: Community pharmacies; PMS: Patent Medicine Shops;
Two samples (One Glucophage® and One generic) will be sampled/outlet but at different times

Figure 8: Sample size or initial proportion of samples to obtain from different outlets

Two people were recruited and trained as sample collectors to help with the sampling phase of the data collection. These two people were recruited because they were thought to know Lagos very well so as to avoid difficulties in moving from one location to another when obtaining the samples. Also one of the sample collectors was a native Yoruba speaker, which was thought, would help to locate outlets where the samples would be purchased easily.

4.6.3 Pilot study

A pilot study was conducted to ensure that the sample collectors understood the training they were given on how to collect the samples and to ensure that the entire sample collection process went smoothly.

As a pilot study, 4 pharmacies were selected from the list of community pharmacies as at December 2010 obtained from the Pharmacists Council of Nigeria (PCN) from which samples would be purchased. For each of these 4 pharmacies, the researcher accompanied one of the sample collectors to purchase the sample. During this time the researcher acted as a close relative of the sample collector who has only accompanied him to purchase the medicines. Following this pilot study, it was clear that the sample collector who would be involved with purchasing the samples understood what to do. An agreement was therefore reached between the researcher and the sample collectors not to tell anyone the reasons why the samples were being collected to ensure the safety of the researcher and the sample collectors as well as to avoid any bias that may be introduced by the medicine sellers presenting only the medicines they felt were of good quality for sale.

4.6.4 Sampling procedure

In order to have a sampling frame, the list of Community pharmacy retail outlets as at December 2010 was obtained from the Pharmacists' Council of Nigeria (PCN). The 2011 lists were not used, as it was incomplete at the time. Attempts were made to collect the list of open drug market traders from PCN. However this was not possible, as they are not recognised by the Council despite being a major source of medicines consumed by the Nigerian public. Attempts were also made to collect the list from some of the traders through some medical representatives that supplied medicines to the drug market. This was also not possible as the traders approached were afraid of releasing their details to anyone due to the recent closure of the market by NAFDAC. In order to randomly sample from the traders in the drug market, the list was made by visiting the market and making a list of all the outlets selling medicines in each

of the streets in the drug market. In total, a list of 203 outlets in the drug market was obtained and for each outlet, a description of their location in the street was noted so as to help locate them easily when collecting the samples from the market. This was independently confirmed by one of the data collectors on a second visit.

Random numbers that represented the outlets from which medicines would be sampled were generated using the Rand function in the Microsoft Excel programme. Spare random numbers were generated to cover for repeated random numbers, outlets that may be closed at the time of visiting and outlets which for any reason may have been unable to furnish requested samples. Appendix 14 shows the audit trail of outlets visited containing the random numbers corresponding to the outlets visited.

In order to ensure the safety of the researcher and other sample collectors, the name, address and contact details of the locations being sampled per day was given to a close and responsible relative of the principal researcher in Nigeria at the beginning of each day before commencing the sample collection.

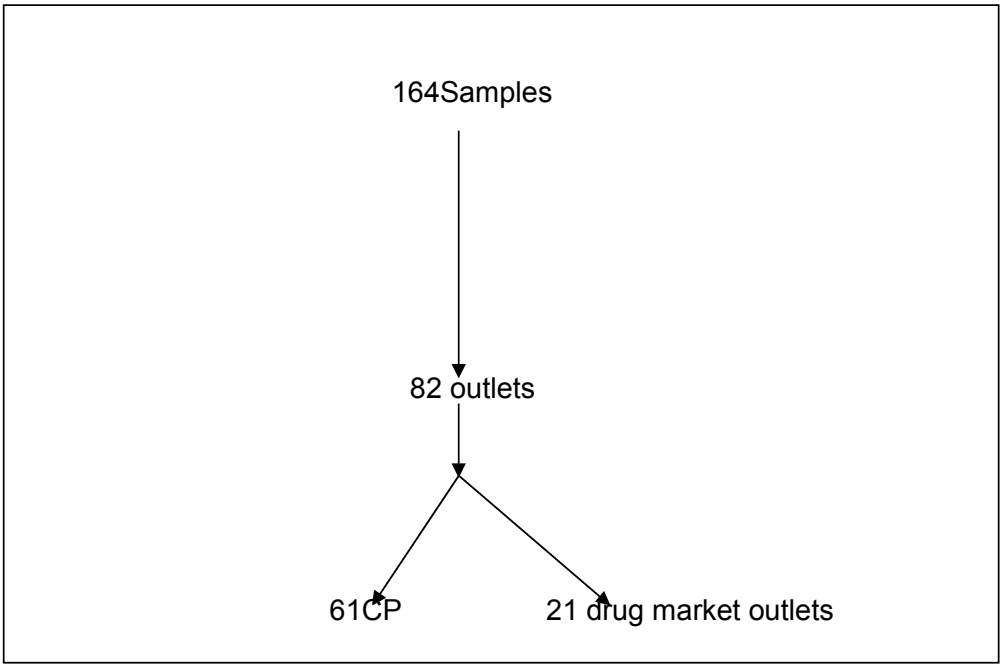
4.6.5 Collection of samples

For each of the outlets, the researcher went with one of the sample collectors to collect the medicine for easy location of the outlets. The sample collector collected the tagged Glucophage® while the researcher collected the cheapest generic metformin. These samples were collected at two different times to avoid any suspicion by the medicine sellers that their medicines were being sampled for testing. The researcher and the sample collector posed as ordinary shoppers while collecting the samples. Outlets not furnishing the samples were noted and the reasons for this were obtained in order to determine if such outlets differed systematically from those where samples were obtained. Extra

care was taken to avoid the medicine sellers knowing that their medicines were being sampled for quality testing. For instance, the sample collectors avoided asking the medicine sellers any questions aside requesting to purchase the medicines except if the medicine sellers offered to talk to them about any issues relating to medicines. The sample collectors avoided any form of note taking until they were outside the vicinity of the outlet or the drug market.

Outlets corresponding to the first 34 distinct random numbers for community pharmacies, the first 37 distinct random numbers for patent medicine shops and the first 12 distinct drug market trading outlets were to be visited. Out of the 37 patent medicine outlets randomly selected, 18 in 11 different locations were visited to purchase the samples. Out of these 18 outlets; only two tagged Glucophage® samples and one generic sample could be obtained. Among the reasons given for not furnishing samples by the patent medicine vendors included lack of knowledge by the store keepers as to whether metformin was stocked or not. This was because the owners of some of the patent medicine shops were absent for some of the outlets visited. Also some store keepers lacked knowledge of different brands of metformin available in the market and some said they stock only what people ask for except in cases of special requests for such medicines. Some of the patent medicine outlets visited stocked only particular groups of medicines such as cough syrups as patent medicine vendors are only licenced to sell over the counter (OTC) medicines, so did not stock metformin, which is a prescription medicine. Some were closed at the time the data collectors went to purchase the samples and some outlets were no longer patent medicine shops or had moved from the location. Following these observations, the patent medicine outlets were excluded as a major source of metformin. The community pharmacies and the traders were therefore included as major sources of metformin and the proportion of samples obtained relative to their total numbers (590 and 203) respectively. Based on this, 61 community pharmacies and 21 outlets at the Idumota drug market were randomly selected to be visited to collect 122 samples (61 tagged Glucophage®

and 61 cheap generic versions) and 42 samples (21 tagged Glucophage® and 21 cheap generic versions) respectively as shown in figure 9.



CP: Community pharmacies
Two samples (One Glucophage® and One generic) were sampled per outlet but at different times from each outlet

Figure 9: Sample size and proportion of samples collected from the different outlets types

All samples were collected in their original container. The minimum number of units (tablets) per sample collected was 20 (if greater quantity was not available). This was to ensure that sufficient numbers of tablets were collected for analyses. Therefore, in this context, a sample is, at minimum 20 units from the same batch number and tablet pack and collected from the same location/outlet. Apart from the innovator brand; Glucophage® with the tags, all other commercially available metformin products were regarded as generic metformin. Sample collection commenced on the 19th of October 2011 and was completed on the 17th of December 2011.

4.6.6. Selection of samples

In shops where there were two different generic metformin products of the same price, the cheapest was randomly selected by following the following procedure; the researcher asked the shopkeeper to display the available brands on the counter, pretending that she will choose which to select. She then selected a container based on the number of available generic metformin products in accordance to a list of random numbers generated prior to visiting the outlets.

4.6.6.1 Samples collected

Although the sample collectors aimed at stopping when a total of 82 samples of tagged Glucophage® and 82 samples of the cheapest generic brands were purchased, a total of 92 tagged Glucophage® and 87 cheapest Generic metformin samples were purchased. This is because both tagged Glucophage® and cheapest generic versions were requested in all shops visited including the shops covering for outlets in which one of the samples had been collected. This was done to avoid any bias being introduced in sampling differently from the outlets. In total, samples were obtained from 90 instead of the 61 initially proposed community pharmacies and 60 instead of 21 initially proposed medicine outlets in the open drug market.

4.6.7 Sample processing

All the samples were initially coded following their collection by the researcher. A sample collection form adapted from WHO, (1999) and USP/DQI (2004) was filled out and attached to each of the medicines collected. Information filled included the sample code, the International Non-proprietary Name (INN) and strength, brand name, the manufacturers name and address, the price, the batch or lot number, the manufacturing and expiry date, the NAFDAC number,

the package size (number of units), quantity purchased as well as the date and place of collection (See appendix 15). Following this, the text messages for the authentication were sent from Nigeria with 5 different mobile phone lines and on different days in order to authenticate the collected samples. This was done to avoid any suspicion that may arise from the verification centre.

Once all the samples were verified through text message they were recoded against the researcher's initial coding by one of the sample collectors so as to blind the principal researcher. The second sample collector then crosschecked this in order to avoid any bias that may be introduced since the principal researcher will be involved with the chemical analyses of the samples. The tablets in each pack (sample) were divided into two portions with each containing a minimum of 20 tablets except for samples where lower quantities were obtained; in which case it was divided into two portions in accordance to the amount obtained. One portion was transported to the United Kingdom by courier on 10th February 2012 for testing with a letter to UK Customs from UCL School of Pharmacy indicating that the samples are not for re-sale, not for human or veterinary consumption and are not hazardous (see appendix 6). They were sent to the UCL School of Pharmacy pharmaceutics laboratory for analysis. The 2nd portion was retained in Nigeria and was repackaged with all the packaging information on the original pack and its code written on the new packs. This was a contingency plan put in place to avoid losing the entire samples collected in case the first portions were seized or lost while being transported to the United Kingdom.

All samples were within their stated shelf life as at the time of collection. All samples were stored and kept according to the manufacturers' recommended storage conditions (room temperature for metformin) until analysis and authenticity investigation was completed (see appendix 7 for the temperature log of samples during transport and storage). They were retained in their original packaging and safeguarded against any conditions that may cause it to

deteriorate or degrade such as air, light, and moisture. For example each sample was sealed in an airtight plastic with their initial codes stuck on them.

Additional efforts were made to prevent the tablets from any physical damage while they were being transported from their site of collection (Nigeria) to where they would be tested (London, United Kingdom). For instance the samples were transported in a polystyrene cool box with a temperature logger inserted into it so as to monitor temperatures the samples were exposed to during their transit to the United Kingdom. The temperature logger was set to measure the temperature every thirty minutes and the data generated were downloaded unto a computer (see appendix 7). Temperature monitoring continued until analyses were complete. In addition, the box in which the samples were transported was sealed with the researcher's name written across the seal so as to help easily identify any opening of the boxes.

Following arrival of the medicines in the UK, relevant tests (packaging, NIR and HPLC) analyses commenced. Medicines collected were analysed before their stated expiry dates in order to prevent the results of the analysis from being confounded by failures resulting from degradation. Analyses of the samples were completed on the 22nd August 2012.

Although, complex counterfeits with no differences in packaging and content of active ingredient have been found, research shows that in most cases counterfeits can be identified through thorough checking of the packaging and other simpler techniques such as NIR conducted in addition to methods that can give an indication of the content of their active ingredients. This study did not aim at determining bioequivalence of samples but rather sought to validate the information from MAS in order to find out if there were any counterfeits and to give an indication of the quality of the samples studied in terms of their active ingredient. Given the time available to complete this PhD, the choice of the

analytical methods (packaging, NIR and HPLC) used in this study to meet the research objectives is justifiable.

4.6.8 Packaging analysis

Packaging analysis involved visually checking the packaging for obvious differences in the colour of the packaging, differences in font and font size and checking for spelling mistakes and wrong language construction. The WHO visual inspection tool kit was employed in conducting the packaging analysis (See appendix 8). The analysis was performed in comparision to genuine products from the manufacturers. Any differences in appearance meant that the sample failed the packaging analysis.

4.6.9 Short Message Service (SMS) authentication of the samples

Following collection of all the samples, the tagged Glucophage® samples were initially coded and then authenticated. Random numbers corresponding to the number of sachets in each pack of Glucophage® were generated. The sachet corresponding to the first random number generated when the pack was opened from the right side was collected for authentication. Authentication was done via SMS by scratching off the panel on the back of the card of medicine and sending the unique PIN number to a five digit short code, 38353 to check if the medicine was genuine ("OK, Original") or fake. The Glucophage® samples were authenticated via the four network providers enrolled in the scheme (GLO, MTN, Etisalat and Airtel) on five different days using 5 different mobile phones. This was done to ensure that there was no suspicion that medicines were being authenticated as part of a research project.

4.7 Near Infrared Spectroscopy (NIRS) analysis

NIR involves exciting molecules in a compound in order to generate a unique fingerprint (Kaur et al., 2010). It uses the Near Infrared region of the electromagnetic spectrum, which is approximately between 800-2500nm. The

fingerprint obtained from NIR shows if the compounds in a sample are not in correct proportion, which indicates that it may be counterfeit. This method is non-destructive in that the samples remain intact after analysis and less time consuming. It is often utilised in the measurement of homogeneity and particle size of tablet components. In addition to this, NIR can yield both qualitative and quantitative information about medicines (Deisingh, 2005). This means that it can detect medicines that are counterfeit and also determine the concentration of active ingredients of the samples. However, its major disadvantages are that it is affected by humidity, position of the sample relative to the probe and the type of tablet surface (Deisingh, 2005).

4.7.1 Procedure for NIR analysis

The Foss NIRSystems 6500 spectrometer was used. A tablet sample was placed in the machine and the NIR spectrum was obtained. The surface of the tablet sample was scraped and the same process repeated in order to find out if the film coating on the tablets had any effect on the NIR spectrum. The two spectra (with and without the film coating) obtained were the same, so it was concluded that the presence of the film coating on the metformin tablets had no effect on the NIR analysis. The tablets were therefore tested without scrapping off the surface.

In order to ensure that the resulting spectrum was representative of the sample being tested and that the results were accurate, ten intact tablets from each of the authentic samples of metformin products from the manufacturers were measured once on each side. The mean Standard Normal Variate (SNV) second derivative (D2) spectrum was then taken from the 20 spectra per sample in the portable Unscrambler software version 9.7. This was done to help remove the effect of particle size and scatter that may be caused by the different orientations and sides of the tablets in the NIR spectrometer. The randomly selected samples from the outlets were measured in the same way as

the authentic samples to get the mean SNV-D2 spectrum for each metformin sample collected. The spectra of the authentic samples from the manufacturers and those from the corresponding samples from the outlets were then compared using correlation in wavelength space (CWS) method. The correlation coefficient (r) of the samples analysed were obtained using the Microsoft Excel 2013 software. This method of spectra comparison was used because it has been shown in previous studies to be easy and fast (Moffat et al., 2010). It enabled comparison to be made between the correlation coefficient (r) of the SNV-D2 mean spectra of the samples from the outlets and that of the authentic sample. The closer the r is to 1, the greater the similarity between the tested sample and the authentic sample.

Previous research in this area has shown that the spectra of counterfeit medicines always fall below a correlation coefficient of 0.95 (Moffat et al., 2010). Therefore, for the present research, a threshold of $r < 0.95$ was used to identify if the samples from the outlets (the test samples) were counterfeit. Test samples were said to be authentic if their correlation coefficient (r) was ≥ 0.95.

4.8 Analysis by High Performance Liquid Chromatography (HPLC)

HPLC is used to separate, identify and quantify compounds present in a sample. While the retention times are used to identify the compounds, the area under the curve helps to quantify the compounds (Clark, 2007). In order to determine the quantities of active ingredient present, pure samples are often used as reference (Kaur et al., 2010). Its major advantages are its accuracy, specificity and precision while some of its disadvantages include that it is expensive to conduct, requires some degree of expertise and destructive as the samples analysed cannot be re-used.

4.8.1 Materials

The High Performance Liquid Chromatographic system was made up of Agilent HPLC model (1200 series) with a quaternary pump, sample thermostat, column thermostat, thermostatic auto sampler and variable wavelength programmable detector. Analysis was carried out with a C_{18} column (Discovery® HS F5 HPLC Column). The Metter Telledo electronic balance (AX 105) was used for weighing. Analytically pure metformin, acetonitrile, methanol, trifluorocacetic acid used were purchased from Sigma-Aldrich. The acetonitrile, methanol, trifluorocacetic acid and water (TKA water purification system) used were of HPLC grade.

4.8.2 Chromatographic parameters

For the HPLC analysis, a flow rate of 1.0 mL/minute and detection wavelength of 210nm was used. The sample injection volume was 10µL and the column was maintained at a temperature of 40^{o}C. The run time for each injection was 7 minutes.

4.8.3 Method development and sample preparation

Metformin hydrochloride is an oral anti-diabetic medicine that belongs to the biguanide class. Its chemical name is 1,1-dimethylbiguanide hydrochloride. C_{18} column (Discovery® HS F5 HPLC Column) was used for the analysis of the metformin samples at the chromatographic parameters stated above. The buffer used was 0.1% trifluoroacetic acid (PH: 2-3) while the mobile phase was acetonitrile. After the chromatographic conditions were set and the instrument was stabilised to obtain a steady baseline, the calibration curve was obtained using the pure metformin. 0.01218g of pure metformin was weighed and put into a 100ml volumetric flask. 10mls of methanol was added, shaken and sonicated to dissolve the metformin. This was then diluted with 0.1% trifluoroacetic acid (1ml trifluoroacetic acid in 1000mls of water) to get a stock

solution of concentration of 120µg/ml. 9ml, 8ml, 7ml, 6ml, 5ml, 4ml, 3ml were respectively obtained from the stock solution and put in 10mls volumetric flasks. These were then made up to 10ml respectively using 0.1%trifluoroacetic acid. The solutions were then analysed in HPLC instrument and the chromatograms were recorded. The readings (the area under the curve for the different concentrations) obtained were used to plot the calibration curve. The mean retention time for metformin was 4.5 minutes.

After obtaining the calibration curve, analysis of the individual tablet samples commenced. The tablet samples equivalent to 500mg metformin were prepared by crushing and dissolving in 0.1% trifluoroacetic acid using the ultrasonic cleaner, shaken and made up to 100ml using 0.1% TFA (5000µg/ml solution). The solution was well shaken and allowed to settle for about 10 minutes to eliminate any bubbles generated by shaking the conical flask. It was then diluted further by withdrawing 2ml and making it up to 100ml (100µg/ml). A 2ml syringe was used to withdraw the solution and each sample solution was filtered with the 0.45µm sterile Millex filter. The filtered solution was then put into the HPLC vials and screwed with the cap. Each sample was prepared in duplicate. After the chromatographic conditions were set and the instrument was stabilised to obtain a steady baseline, the prepared sample solutions were then loaded in the instrument according to the sequence template. The sample solutions were run/injected in duplicates and the chromatograms recorded.

4.8.4 Method validation

The method developed for the HPLC analysis was validated for linearity and range, precision, and system suitability according to the International Conference on Harmonisation (ICH) guidelines.

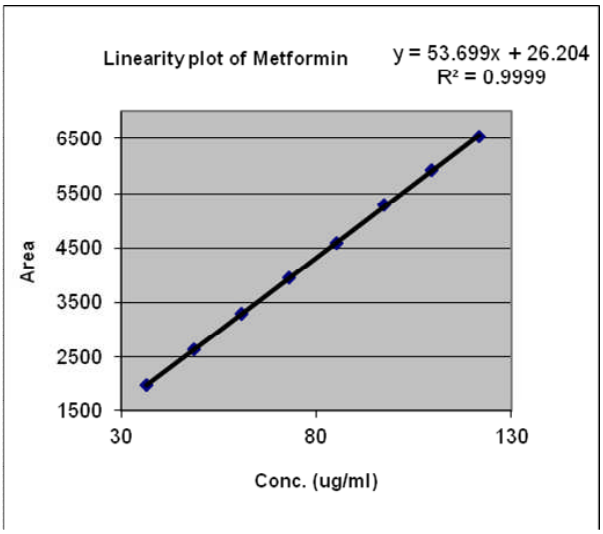
4.8.4.1 Linearity and Range

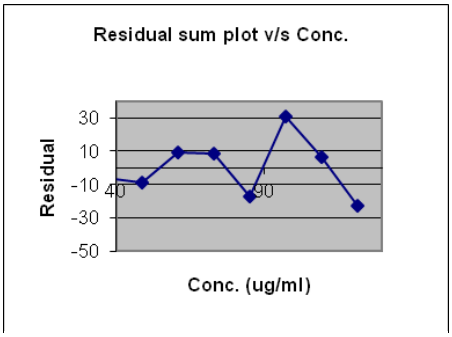
The linearity and range of the method was determined by recording the response of a standard metformin preparation at 8 different concentrations

prepared in the range of 40 to 120% (although the range for linearity is between 80-120%) of nominal concentration injected three times each. The linear regression analysis of the data was done by method of least squares to obtain the correlation coefficient as reported in table 5.

Table 5: Linearity of metformin

Area of Metformin			Concentration	Average	Predicted	Residual
inj 1	inj 2	inj 3	(µg/ml)	Area	Response	
			0		26.20	
1961.20	2002.80	1982.00	36.54	1982.000	1988.38	-6.38
2645.60	2621.50	2633.55	48.72	2633.550	2642.43	-8.88
3312.90	3298.80	3305.85	60.90	3305.850	3296.49	9.36
3965.50	3952.90	3959.20	73.08	3959.200	3950.55	8.65
4600.40	4574.30	4587.35	85.26	4587.350	4604.60	-17.25
5283.80	5295.50	5289.65	97.44	5289.650	5258.66	30.99
5917.30	5920.70	5919.00	109.62	5919.000	5912.72	6.28
6544.30	6543.70	6544.00	121.80	6544.000	6566.78	-22.77
	Slope		53.699		Mean conc.	79.17
	Intercept		26.204			
	Correlation Coefficient		0.9999			
	Residual Sum Of Squares		2098.228			
	Theoretical 100% conc.		100.000			
	Intercept/(slope x nominal conc.)		0.488	←Ratio		
	95% CI of intercept		106.573	to	-54.165	





Slope	**53.70**
Intercept	**26.20**
Correlation Coefficient	**0.9999**

Correlation coefficient is more than 0.995
The residual plots does not have a systematic trend

The results from the linearity of metformin meet the acceptance criteria as specified (correlation coefficient greater than 0.995 and no systematic trend in the residuals) and confirms that the method is linear over the concentration range of 40 to 120 mcg/ml of metformin.

4.8.4.2 Precision

The precision of the method was determined by measuring the system repeatability and the intermediate precision.

4.8.4.2.1 System precision

Six injections of a solution containing 100µg/ml of metformin were injected and the coefficient of variation calculated. Below are the results.

Table 6: Percentage Relative Standard Deviation (%RSD) for system precision

Sample injections	Area
GLUCO for Preci inj 1	5390.2
GLUCO for Preci inj 2	5389.6
GLUCO for Preci inj 3	5412.7
GLUCO for Preci inj 4	5391.4
GLUCO for Preci inj 5	5407.0
GLUCO for Preci inj 6	5422.3
Mean	**5402.2**
SD	**13.83**
%RSD	**0.26**

The %(RSD) of the areas of the standard metformin is less than 0.85, thus the system precision is acceptable.

4.8.4.2.2 Method precision

At least 6 tablets were analysed to check the method precision. The product samples were the same as were used for establishing system precision with the assays being performed on a different day. The time interval between the two occasions was ≤ 7 days. Table 7 below shows the relative %RSD for the method precision.

Table 7: Percentage Relative Standard Deviation (%RSD) for method precision

Test Samples at 100% API level		Area	Amount of Metformin found (mg)	% of Metformin (%)
	inj 1	5304.60	491.50	98.30
OGL NOV 3 SAMP 1	inj 2	5350.50	495.80	99.15
	inj 1	5326.40	493.50	98.70
OGL NOV 3 SAMP 2	inj 2	5350.30	495.70	99.15
	inj 1	5362.40	496.90	99.37
OGL NOV 3 SAMP 3	inj 2	5413.60	501.60	100.33
	inj 1	5376.30	498.20	99.63
OGL NOV 3 SAMP 4	inj 2	5399.70	500.30	100.07
	inj 1	5367.40	497.30	99.47
OGL NOV 3 SAMP 5	inj 2	5365.40	497.10	99.43
	inj 1	5320.30	492.90	98.59
OGL NOV 3 SAMP 6	inj 2	5324.70	493.40	98.67
			Mean	**99.24**
			overall %RSD	**0.61**

The % RSD is 0.61. This is less than 2, thus the method precision is acceptable

4.8.4.3 System suitability and supplement tests

4.8.4.3.1 Stability of standard solution

Stability of metformin standard solution was checked by injecting duplicate injections of standard solution of metformin over 96 Hours for solutions kept at room temperature (20-25°C), as well as solutions kept in a fridge at around 4°C. The stability data are shown in tables 8 and 9 and figures 10 and 11.

Table 8: Percentage concentration of pure metformin (Standard) at room temperature at different time intervals (0-96 hours

Time (Hours)	% Amount of metformin
0	100.10
24	99.68
48	97.96
72	98.46
96	99.06

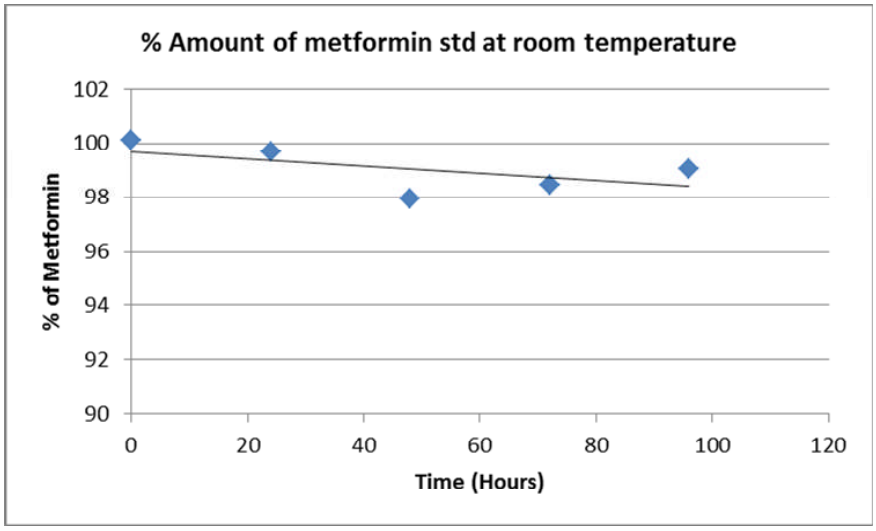


Figure 10: Graph of percentage concentration of pure metformin over 96 hours at room temperature

Table 9: Percentage concentration of pure metformin (Standard) in the fridge at different time intervals (0-96 hours)

Time (Hours)	% Amount of metformin
0	100.36
24	100.06
48	99.87
72	99.73
96	99.04

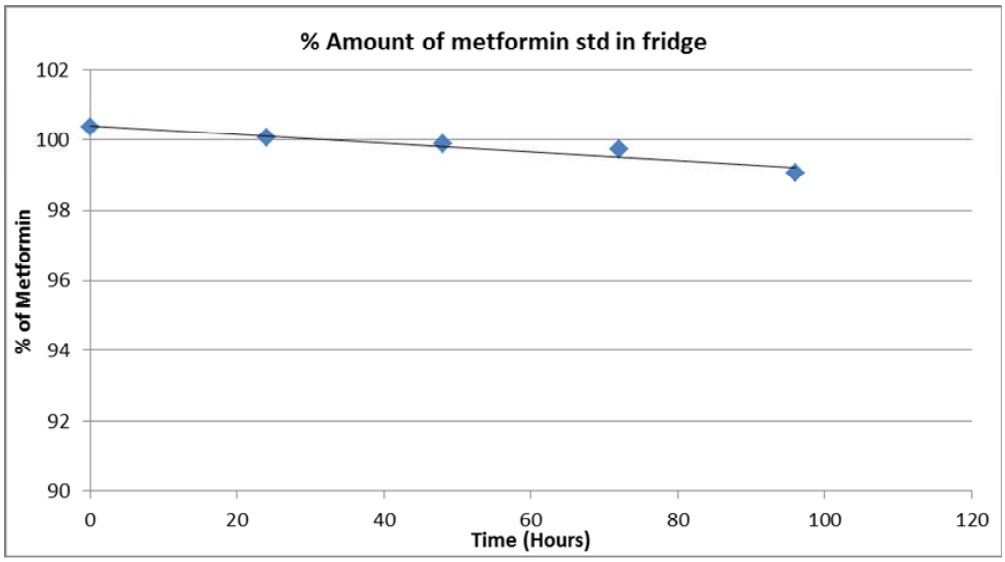


Figure 11: Graph of percentage concentration of pure metformin over 96 hours in the fridge

For stability the percentage of standard in the solution should not be less than 98%. The above results confirm that the standard solution of metformin is stable for 96 hours at room temperature and in the refrigerator.

4.8.4.3.2 System suitability

System suitability tests were performed in order to verify that the resolution and reproducibility of the system were adequate for the analysis to be performed. These tests are based on the concept that the equipment, electronics, analytical operations, and samples constitute an integral system that can be evaluated as a whole.

Table 10: System Suitability for Metformin Standard

System suitability parameters	System suitability values
Rt	4.4
Capacity factor (k')	2.0
USP Tailing	**1.7**
Symmetry	0.49

Rt= Retention time, k'= Capacity factor

The capacity factor (K')= $(R_t-T_0)/T_0$

$=(4.360-1.45)/1.45$

$= 2.0$

K' should not be less than 2. The USP tailing should not be more than 2, so the system is suitable for the analysis performed.

4.9 Data analysis for phase 1

The concentration of metformin, % RSD values, correlation coefficient, and linear regression analysis by method of least squares were calculated using Microsoft Excel 2013. Descriptive statistics in the Statistical Package for the Social Sciences (SPSS) software version 22.0 were used to analyse the results of the quantitative tests of the drug samples. Every component of the Medicine Quality Assessment Reporting Guideline (MEDQUARG) for field surveys of medicine quality as proposed by Newton et al. (2009) was reported on.

4.9.1 Descriptive statistics

Nominal variables (metformin products/brands, adherence to packaging, HPLC and NIR requirement, outlet type and the SMS authentication result) were described with numbers and percentages.

4.9.2 Inferential statistics

Dichotomous variables were compared using the Chi-square (χ^2-test) to test differences in frequencies. The results of the cross tabulation analysis were also stated. P-values of < 0.05 were considered to be significant. Association between metformin products and quality (pass/fail of packaging, NIR and HPLC analysis) were determined with the Chi-square test in order to assess whether there were differences in these variables between tagged metformin; Glucophage® and their untagged generic counterparts as this involved comparing the proportions in categories of two nominal variables. The Chi-square (χ^2) was used if no cell had an expected count of less than 5 for a 2 by 2 table while the Fisher's exact test was used instead if any of the cells had an expected count of less than 5.

4.9.3 Data collection process-phase 2

The data collection for the second phase was not commenced until the data collection for the first phase was completed. This was to help exclude outlets from which samples were obtained from the qualitative phase to avoid any bias from the medicine sellers that the researchers had sampled their medicines for quality testing.

4.9.3.1 Study setting

Data collection for the second phase was conducted in Lagos. As previously mentioned, Lagos is the most ethnically diverse state in Nigeria; constituting the low, middle and high-income earners as well as rural, peri-urban and urban dwellers, which is very typical of Nigeria. It is also home of one of the major drug markets in Nigeria; the Idumota market. It was thought that this would make it easier to locate traders that will be willing to participate in the study. Also, the researcher needed to include both users of the MAS service and non-users to meet the objectives of the research, sampling participants from Lagos which is the largest city in which the service was first rolled out was considered ideal as it was thought that that will aid easy recruitment of MAS users. Lagos is home to many agencies in Nigeria including NAFDAC; hence this made recruitment of policy makers easier.

4.9.3.2 Development of interview topic guide

The semi-structured interview topic guide was developed for each category of stakeholders (consumers, medicine sellers and policy makers in pharmacy) to meet the aims and objectives of this research (copies of the interview guide for the stakeholders are presented in appendix 9). Topics explored were mainly from the literature review conducted prior to commencing the study. The interview included mainly open-ended questions and some closed ended questions. The open ended questions were used to allow the participants to describe their views and experiences in their own words as recommended by Smith, (2010) for example consumers were asked to describe what they thought were the potential or actual benefits of the Mobile Authentication Service.

Closed ended questions were used to get factual data (for instance, have you used the Mobile Authentication Service?) and to get a summary of a participant's view on an issue discussed (for instance, "Overall how satisfied are you with the Mobile Authentication Service?"). Probing questions and prompts were used to get more detailed information on the views and experiences of the participants. Leading questions were avoided to prevent any bias that may have arisen from participants giving anticipated responses or responses, which they think were the interviewers' opinion.

Questions in the interview guide were aimed at helping to get detailed views and experiences of participants on the current situation of poor quality medicines in Nigeria and also the recently introduced Mobile Authentication Service. For instance, some of the topics explored for the consumers and medicines sellers included their perceptions of the quality of medicines distributed in Nigeria, experiences with poor quality medicines, their perception of branded and generic medicines, initiatives against poor quality medicines and challenges to fighting poor quality medicines, their awareness of MAS and factors that may hinder or promote its use, their perceived benefits of MAS and how MAS can be improved. The interview questions for the policy makers included their perception of the quality of medicines distributed in Nigeria, initiatives against poor quality medicines and challenges to fighting poor quality medicines in Nigeria, their perceived benefits of MAS, factors that may affect the use of MAS and how MAS can best be improved.

Interview sessions were held with 3 students in London to develop and check the interviewing technique. Following the pilot interviews, the interview schedule was modified by re-organising the order of the questions to ensure an easy flow and that questions that fell into more than one topic were not repeated. The recordings using the cassette recorder were unclear so it was decided that instead of using one digital recorder and one cassette recorder, two digital recorders would be used in the main study. The interview schedule

was further modified during the course of the main interview sessions to incorporate new emerging issues that were considered necessary to be explored in greater detail. The participants were free to talk as long as they wished and in no particular order.

4.9.3.3 Sampling strategy

4.9.3.3.1 Study sample

In order to meet the study objectives, it was necessary to include stakeholders in the field of medicines quality/ regulation. This includes the consumers (that is the Nigerian public) because they are the medicine users and they also form part of the users of MAS. Medicine sellers (Community pharmacists, patent medicine vendors and drug market traders) are also major stakeholders included in this research because they form users of the MAS. Even though they may not be direct users of the medicines, they are involved in purchasing and selling of medicines. The third group of stakeholders included in this study were the policy makers in pharmacy. This is because they are involved in implementation of policies and interventions aimed at tackling poor quality medicines such as MAS.

4.9.3.3.2 Inclusion and exclusion criteria

4.9.3.3.2.1 The inclusion criteria (consumers)

1) Persons who can communicate in English

2) Persons who are aware and/ have used the MAS service

3) Persons who consented verbally because they cannot write or those who provided a written consent

4.9.3.3.2.2 Exclusion criteria (consumers)

1. Persons who cannot communicate in English

2. Persons who are unaware and/ have not used MAS

3. Persons who have not given their consent to participate in the study

4.9.3.3.2.3 Inclusion criteria (community pharmacists, patent medicine vendors and traders)

1. Those who are involved in selling medicines to the Nigerian public

2. Have given a written or verbal consent to participate in the study (because they wish to be anonymous)

4.9.3.3.2.4 Exclusion criteria (community pharmacists, patent medicine vendors and traders)

1. Those who are not involved in selling medicines to the Nigerian public

2. Those who have not given any consent to participate in the study

4.9.3.3.2.5 Inclusion criteria for regulatory body staff/ relevant policy makers in pharmacy

1. Persons who were deemed by the researcher as knowledgeable in the medicine policy making process in Nigeria either because they have been introduced to the researcher as been involved with policy making or individuals who have been delegated to talk on the views of the regulatory body and are willing to participate in the study

2. They must have held or currently hold a post with the drug regulatory authority in Nigeria, a medical professional organisation or regulatory authority or the Ministry of Health to be considered knowledgeable

3. Those who have given a written consent to participate in the study

4.9.3.3.2.6 Exclusion criteria for regulatory body staff/ relevant policy makers in pharmacy

1. Persons who were neither introduced to the researcher as being knowledgeable in the medicine policy making process in Nigeria nor were delegated to talk on the views of the regulatory body

2. Persons who have not held or are not currently holding a post with the drug regulatory authority in Nigeria, a medical professional organisation or regulatory authority or the Ministry of Health to be considered knowledgeable in policy making in Nigeria

3. Persons who did not consent to participate in the study or those who are unwilling to participate in the study

Persons who can communicate in English were chosen as English is the most widely used and official language in Nigeria. The researcher envisaged that people of diverse ethnic groups and different native languages are most likely to be included in the study and therefore decided to include only those who can communicate in English. There are presently more than 250 ethnic groups in Nigeria and with one ethnic group speaking more than one language; the total number of languages in Nigeria is about 527 (Ethnologue, 2011). The total number of dialects numbers even higher.

4.9.3.4 Recruitment procedure for the phase 2

Purposive sampling was used to sample the stakeholders (consumers, medicine sellers and regulatory body staff/policy makers) included in the study. This means that the researcher sampled with a purpose of targeting those who met the inclusion criteria of this research. Purposive sampling is a non-random method of sampling where a group of people or setting with a particular characteristic is deliberately sampled (Bowling, 1997). This method of sampling

has been shown to be useful when there is need to reach the targeted sample quickly (Trochim, 2006).

4.9.3.4.1 Recruitment of the consumers

The consumers were recruited from the diabetic/endocrinology clinics of the federal teaching hospital in Lagos (Lagos University Teaching Hospital, Idi Araba, Lagos). This was chosen as the best method to recruit consumers who have used MAS following the findings from the preliminary fieldwork conducted which showed that most diabetic patients obtain their prescriptions from the hospital while subsequent refills may be obtained from the private oulets such as the community pharmacies.

4.9.3.4.2 Recruitment of the medicine sellers

The community pharmacists and the patent medicines vendors interviewed were selected from different places in Lagos. Traders in the drug market interviewed were key informants that were introduced to the researcher by a pharmacist that was well known to the drug market traders.

4.9.3.4.3 Recruitment of the policy makers

Five policy makers previously known to the researcher were contacted by telephone and/ e-mails because they have a present role or have held a key position at the Pharmacists' Council of Nigeria, Pharmaceutical Society of Nigeria or NAFDAC and met the other inclusion criteria. Appointment for interview was scheduled on the dates and times that were suitable for them. All the interviews took place in their respective offices.

For each category of stakeholders, there was no further recruitment once similar themes began to emerge or when there were no new emerging themes (point of saturation).

4.9.3.5 Data collection instruments

All the participants were approached by the researcher who told them about the research and sought their consent to participate. Leaflets containing a detailed description of the research as well as consent forms were given to all the participants except the traders (See appendices 10, 11 and 12). There was opportunity for them to ask any questions they may have concerning the research and clear any concerns they may have. Their permission to tape record the interviews was sought. Following this, semi-structured interviews were conducted for participants who met the inclusion criteria, were willing to participate and gave their consent (written or verbal for those who cannot read or write or those who preferred not to write) to participate in the study using the appropriate interview guide.

As previously noted, the consumers were sampled from the Lagos University Teaching Hospital (LUTH). The hospital was visited on the diabetic clinic days (Tuesdays and Thursdays) in order to easily reach the target population, which were consumers that have used MAS. Consumers/patients were approached and given the information leaflet and verbal explanation of what the research was about and what the interviews involved as well as consent forms. If consent was granted (either written or oral in the case the patient preferred not to write or cannot read or write) they were asked for their preferred convenient place and time to be interviewed. All the patients approached preferred to be interviewed while they were still in the hospital waiting to see their doctor at the consultation section of the diabetic clinic or while they were waiting to collect their medicines from the pharmacy unit. Even though the interviews were conducted in the quietest area in order to minimise interruptions during the

interview, they were told they could excuse themselves at anytime to see their doctor or nurse or pharmacist.

All the traders preferred to be interviewed immediately they were approached. Written information leaflets and consent forms were not given to the traders due to the nature of the market and to avoid any suspicion. Therefore only verbal explanation of the research objectives was given to them and any clarifications they needed were provided. Traders who verbally consented to participate in the study were interviewed. This method of obtaining consent was justifiable in this circumstance as the researcher envisaged that there were no risks to the participants and no potential invasion of their privacy. Their rights of voluntary participation and withdrawal at any time during the interview were respected.

The pharmacists and patent medicine vendors were approached and given the information leaflets and consent forms. Semi-structured interviews were conducted for those who met the inclusion criteria and gave their consent to participate. Apart from one pharmacist who preferred to be interviewed at her home, all the other community pharmacists and patent medicine vendors preferred to be interviewed at their outlets immediately they were approached or on subsequent appointment with the researcher. They were therefore told they could excuse themselves at anytime to attend to their clients. One pharmacist approached declined to take part due to time constraint and one other pharmacist could not take part as no convenient time could be arranged. All the pharmacists and patent medicine vendors who took part in the study gave their written consent.

The policy makers were contacted by telephone or e-mail and appointment for the semi-structured interview was booked with each of them on the day and times they considered was most convenient. No response was received from one out the five policy makers contacted. The interviews with the 4 policy

makers took place at their respective offices on the day agreed. They were also given the information leaflets and consent forms and the interviews were conducted if written consent was provided. Their rights of voluntary participation and withdrawal at any time during the interview were respected.

All participants were given a demographic data sheet after the interview (See appendix 13). Variables explored from the demographic data sheet were their age, gender, educational background, place of residence and work status (for consumers), position (for policy maker), location of outlet (for community pharmacies and patent pedicine vendors) and years of practie or work in the field of pharmacy/medicines regulation. Although it was anticipated that each interview would take about 20 to 30 minutes, participants were given the opportunity to talk for a longer time if they wished so that greater details could be obtained. Two digital recorders were used to record the interviews to avoid any disappointment of one of the recorders not working, to ensure that nothing was missed out and to ensure validity.

A reflective diary was kept by the researcher and all observatory notes and interview summary were written immediately after the interviews. This included details about the time and place of the interview, the participant, duration of the interview, and details about the content and emerging themes. The summary notes were attached to the transcripts in order to facilitate the data analysis stage. Figure 12 shows the different stages of the data collection in the 2 phases of this study.

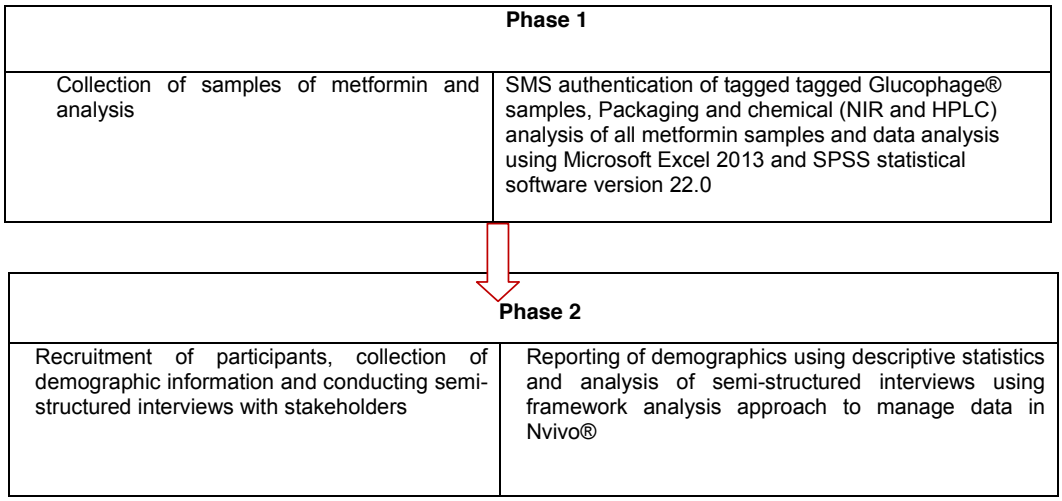


Figure 12: Data collection stages

4.9.4 Data analysis for phase 2

The semi-structured interviews were transcribed verbatim and any confusing information was confirmed with the participants. Various techniques were employed to make appropriate sense of the data collected. Deductive (theory driven) approach to data analysis was combined with inductive (finding driven) approach while analysing the data. The deductive approach formed a major part of the analysis as data collected were coded into various themes, which the researcher had identified as important to interpretation based on the variables identified from the literature, which formed part of the conceptual framework of the research. However, the researcher employed some element of induction by being open to new and relevant findings that were not in the framework.

Comments and thoughts on incidents and linkages between variables were kept as the analysis progressed in order to build an in-depth understanding of all the issues explored. By employing a deductive approach to analysing the data obtained, it was easier to explain patterns of relationships better since data were grouped by clearly defined variables obtained from the pre-conceived conceptual framework.

The methodology employed in analysing the data obtained from the qualitative aspect of this research was the framework analysis (a form of deductive data analysis approach). In framework analysis, data are gathered, sifted, charted and sorted in line with key issues and themes (Srivastata and Thomson, 2009). Framework analysis is used when the aim of the research is to generate recommendations within a specific period on a given issue with specific a priori issues that may inform the research question and with a predetermined sample population as is the case with the present study (Srivastata and Thomson, 2009).

Framework analysis allows for generation of rich data from interviews to be complemented with observational notes. The process involves 5 distinct stages; familiarisation (this is done by listening to the tapes arising from the interviews, reading the entire transcripts severally, reading the observatory notes taken during the interview and summary notes written shortly after the interview so as to get the researcher acquainted with the details to make a holistic sense of the interview before fragmenting them into parts). It is during the familiarisation stage that themes start to emerge (Rabiee, 2004). This stage is followed by identification of a thematic framework (this is done by writing memos, for example short phrases and ideas by the margin of the text).

The third stage is indexing. This involves sifting data, highlighting and sorting quotes and making comparisons within and between cases. This stage leads to charting where the quotes are lifted from the original text and are re-arranged under the developed thematic contents. The final stage is mapping and interpretation of the data.

In a bid to make the analytical process more reliable or dependable, an audit trail of how the data were collected and analysed was maintained. In addition, all the procedures involved in the data analysis were counterchecked by another researcher, for instance the first two interviews were recoded by another researcher so as to establish inter-rater reliability.

Framework analysis has the advantages of being dynamic (in that it allows for change such as additions and amendments throughout the analytical process). It is systematic and comprehensive (in that it allows a full review of all the materials used in the data collection phase) and transparent (in that it allows easy access to the original textual data making it easier for others other than the primary researcher to view and judge the analytical process and interpretation. Framework analysis also allows within case and between case analysis thereby making it easy for comparisons and associations to be made (Srivastata and Thomson, 2009). It is also flexible as it allows the researchers to either collect all the data before analysing them or to analyse the data while data collection is still on-going (Rabiee, 2004). For the present research, data analysis commenced while the data collection was still on-going so as to explore evolving issues from the analysis.

In order to facilitate the data analysis process, the transcripts from the semi-structured interviews were analysed using the Nvivio 10® Software programme which is a Computer Assisted Qualitative Data Analysis Software (CAQDAS). This has the capacity to facilitate the efficient organisation and analysis of this type of data and has a friendly outlook interface, allowing the use of colours to differentiate between themes. This qualitative data analysis software package also supports the framework methodological approach employed in this study. This software enabled the data obtained from the interviews to be organised into nodes, making case based and thematic analysis easier.

4.9.5 Ethical considerations

It is the researcher's responsibility to ensure that informed consent is obtained from the participants, that the participants are protected from harm and that their privacy is ensured (Bloomberg and Volpe, 2008). Other ethical issues in quantitative research such as the objectivity and generalisability of the study and in qualitative research such as the issues of trustworthiness (reliability and validity of the research, reflexivity and transferability) were critically considered.

Although there were no significant ethical threats to the participants anticipated by the researcher, steps were taking to ensure that all the necessary ethical issues were appropriately considered. Details of how they were considered are shown below.

4.9.5.1 Informed consent and confidentiality

Participants were given the information leaflet that contained details of the aims of the research, the methods to be used, the possible outcomes and their role if they choose to take part. Verbal explanation of the study was also given to participants and they were given the chance to ask questions. Participants were included in the research if they agreed to take part either through written or in some cases through a verbal consent, for instance if the participant cannot read or write or if they preferred not to write. Data collected were kept securely in a password-protected computer throughout the research, with access granted only to the researcher. The filled consent forms were kept secured in a locked cabinet. In order to ensure confidentiality and anonymity, codes were assigned to all participants included in the preliminary fieldwork and during the qualitative phase of the research. All outlets visited during the preliminary fieldwork and the quantitative phases of the study were coded. These codes were also used during the analysis of the data and cannot be linked to the participants or the outlets in anyway. The researcher removed all identifying information such as names of the participants noted on digital recordings immediately after they

were transcribed. The names of the participants or their identifiers have not and will not be used in any publication or reports from this study.

In accordance to the Data Protection Act of 1998, data collected were used strictly for the purpose of this research and was not transferable to other parties. As previously noted, data collected were kept securely throughout the research, with access granted only to the researcher and other members of the research team. This will be kept securely up to 5 years after the research is completed and would then be appropriately destroyed afterwards.

4.9.5.2 Beneficence

Participants were informed that their contributions would help to achieve the aims and objectives of the research and contribute to existing literature and research on medicines' quality as well as aid formulation of adequate interventions aimed at curbing the problem of poor quality medicines in Nigeria.

4.9.5.3 Non-malfeasance

To the best of the researcher's ability, appropriate measures were taken to protect the interests of all participants in this research. For example, interviews were halted if participants became uncomfortable to continue with the interview or if they needed to attend to other more crucial issues such as seeing their doctor (for consumers) and attending to clients (for medicine sellers). Also, participation in the study was voluntary, so participants were given the opportunity to withdraw from the study at any time if they wished to do so.

4.9.5.4 Issues of trustworthiness

4.9.5.4.1 Validity and reliability

Efforts were made to ensure the validity and reliability of the study. Validity refers to the extent to which the research measures what it aims to measure while reliability refers to the consistency with which it measures it over time (Bloomberg and Volpe, 2008).

In order to ensure the reliability of the study, unclear responses were verified from the participants before moving on to the next question. Inconsistencies observed were also followed up and clarified from the participants. Also, another researcher counter checked the initial codes generated from the interview transcripts. In addition, two digital recorders were used to record the interviews to avoid any disappointment of one of the recorders not working, to ensure that nothing was missed out and to ensure validity. An audit trail of the evolution of the researcher's thinking as well as rationale for the decisions and choices made during the research process was documented in order to ensure 'transparency of method' as advocated by Bloomberg and Volpe (2008).

In order to ensure the validity, the inter-relationship between the aims and objectives of the research, the conceptual framework, and methods used for collecting and analysing the data were critically examined. Also appropriate interviewing techniques were employed during the semi-structured interview sessions, for instance the use of leading questions were as much as possible avoided in order to be sure that data obtained reflected the views and experiences of the participants and not that of the researcher. Also, in order to avoid influencing the views of the participants, the researcher avoided interrupting participants when they were answering questions. The use of neutral comments such as 'I see' and 'hmmm' instead of evaluative comments like 'good' were employed whenever the participants sought to confirm their

own views and at such points, they were reminded that there were no right or wrong answers to the questions they were asked, instead their honest opinions on the topics discussed was what was needed.

Furthermore, the findings of the research were compared with existing literature and some of the participants were asked to comment on the extent to which the findings reflected their views and experiences as recommended by Smith (2010).

4.9.5.5 Reflexivity

Reflexivity includes a process of demonstrating how the research can be traced back to its origins (Bloomberg and Volpe, 2008). The researcher acknowledges that there may be some bias in the methodology, analyses and interpretation of the findings of this research because she is a pharmacist from Nigeria where the study was conducted. This means that prior knowledge of medicines distribution and regulation in Nigeria may have influenced the claims made concerning the data obtained from this study. To minimise this kind of bias, the researcher engaged in on-going critical reflection by journaling and discussing with colleagues. The researcher also remained open and believed that it is possible for others to have a different perception of issues.

An audit trail of the evolution of the researcher's thinking as well as rationale for the decisions and choices made during the research process was documented and presented in detail in section 7.5 of this thesis. In addition, all the procedures involved in the data collection analysis were counterchecked. For instance, as previously noted the first two interviews were recoded by another researcher. Also the list of outlets in the drug market made by the researcher was counterchecked by one of the sample collectors.

The audit trail and memos kept throughout the research as well as the field notes and transcripts offer an opportunity to assess the findings of the research.

4.9.5.6 Transferability and generalisability

Both concepts of transferability and generalisability were considered in this research because it consisted of both quantitative and qualitative research methods. Transferability is a term used in qualitative research to refer to the "applicability of findings to other situations under similar, but not identical, conditions" (Patton, 1990 cited in Bloomberg and Volpe, 2008). Through the in-depth and detailed descriptions obtained from the participants who took part in the semi-structured interviews, the researcher believes that the findings of the qualitative phase of this research may be of relevance in some broader contexts. This means that the findings arising from this research may not be applicable to only Lagos where the research was conducted but may be applicable to other similar areas. Also the recommendations arising from this research may also be beneficial in other contexts such as other African countries facing similar drug quality problems as Nigeria and countries that are adopting the use of MAS.

Generalisablity in quantitative research refers to the extent to which conclusions from a study on a sample population can be extended to the population at large (Writing@CSU, 1993-2012). The large sample size of medicines analysed in this study, the study site (Lagos) which has the largest number of medicine outlets in Nigeria with urban, peri-urban and rural areas as well as the random sampling method used in this study are necessary attributes which may make the results and conclusions from the quantitative phase generalisable. Although metformin was anaysed in this study, the findings arising from it such as the low failure rate may be similar to other medicines for the management of other chronic diseases such as the antihypertensives, which have not been predominantly counterfeited in the past. This situation may be different for other

medicines that have been commonly counterfeited such as antibiotics and antimalarials. Therefore it may be necessary for a repeat study of this kind involving large sample size of a medicine such as the antibiotics to be conducted to know if similar findings to this research will be obtained and how the findings of this research may be applicable to other categories of medicines. Although it was thought that conducting this research in Lagos should represent the Nigeria situation and make the findings generalizable to other parts of Nigeria because of the perculiar attributes of Lagos previously mentioned, the findings may not have been entirely the same if this study was conducted in the Northern parts of Nigeria given the socio-economic and cultural differences between the North and South of Nigeria (where this study was counducted). However, this can only be confirmed through a repeat study in other settings such as the Northern Nigeria.

4.9.6 Methodological limitations

4.9.6.1 Collection of drug samples

One of the challenges faced while compiling the list of outlets in the drug market is the lack of names and adequate numbering system for the outlets. In addition to this, the streets could not be easily located through the Global Positioning System (GPS). Some of the shops were closed at the time the market was visited to compile the number of the outlets and as such were excluded, as the reason for their closure could not be easily ascertained. This is because the data collectors thought that any further enquiries about shop closures might raise some suspicion that they were sampling medicines for some official purposes. In addition to these, the criteria for inclusion of the outlets in the list was if medicines were being stocked and sold in the shops which made it difficult to differentiate the retail outlets where medicines should be sampled from the wholesale outlets which only sell medicines in large quantity. This caused some delay during the sample collection as more outlets had to be visited to be able to obtain the number of samples needed for the study.

Furthermore, the disorganised nature of the drug market may have affected the random sampling technique as some furnished samples even after they said they did not have the medicines asked for. Out of the quest to sell, they often obtained the medicines from elsewhere to sell to the data collectors. Although such samples were purchased, as that is what is obtainable in practice, they may have obtained it from a previously sampled outlet or outlets not in the sampling frame.

In addition, some of the shopkeepers at the drug market and the community pharmacists may not have supplied the cheapest available brand as the data collectors observed that some of them were sceptical of furnishing their cheapest available brand especially when it was requested against their advice. This may be because they are not confident of the quality of the cheapest brands as explained by some of the shop keepers, in which case they may have supplied what they felt was of good quality and at a reasonable price and not necessarily their cheapest available brand.

The rainy season and the early closure of the market on some of the days disrupted the sample collection from the drug market. The Salah public holiday also disrupted sample collection from the community pharmacies as most of them were closed during the holiday period. The sample collection was also delayed by the on-going local government elections at the time, which meant that some areas could not be visited on some days due to safety concerns by the researcher and the other sample collectors.

4.9.6.2 Analyses of drug samples

Differences in colour between packets could not be ascertained as part of the packaging analysis that was conducted because some of the medicines were

sold without the original packaging even though the sample collectors requested that the medicines should be in its original packaging. The use of handheld portable counterfeit detection device 3 (CD-3) which uses an alternate light source with multiple wavelengths in the visible (350-700nm) and non-visible (>700nm) electromagnetic spectrum (Ranieri et al, 2014) may have provided more accurate information on any differences between the samples and the genuine products.

The chemical analyses of the samples were by Near Infrared (NIR) spectroscopy and High Performance Liquid Chromatography (HPLC). Both NIR and HPLC techniques yield useful information. However, they are also limited in various ways. For instance, the sample preparation stage of the HPLC analysis is time consuming. Also, the technique is expensive and requires some degree of expertise. This method of analysis is also destructive which means that the tablets used were destroyed in the process of the analysis, so would not be available for subsequent analysis. Analysis of the samples via NIR is also subject to some limitations. NIR is susceptible to external interference and climate change, which means that the results obtained through this method may be confounded by some of these factors.

4.9.6.3 Sampling and recruitment of participants

Consumers were recruited from the hospital. This may not be representative of the views of the other consumers. This is because patients who visit the hospital may be more concerned about their health as previous studies have shown. This may mean that only consumers who are more cautious of the kind and source of medicines they take have been recruited and may have held a different opinion when compared to other patients who obtain their medicines from elsewhere such as the community pharmacies, patent medicine shops and the drug market. Furthermore, it may have been better to distribute questionnaires as a first step towards recruiting the consumers to participate in

the qualitative phase so that those who have used the service can easily be identified and to triangulate the data obtained. Also some particular group of people may have been excluded from the interviews since it was conducted in English. This means that the views of those who cannot speak and understand English may have been excluded.

4.9.6.4 Information leaflet and consent forms

Some consumers and patent medicine vendors did not want to read the information leaflet or complete the consent forms either because they were not literate enough to read and write or because they considered it too formal. Most of them preferred that the research be explained to them and if they wished to participate gave a verbal consent. The traders in the drug market were not given any paperwork (information leaflet and consent forms) because the researcher was informed by an informant that presentation of any paper work to this group would make them reluctant to participate in the study as they were more likely to view the process as an official activity linked to the government from their previous experience. An informal forum was therefore created by the researcher whereby each trader was told what the research is about and what participating in the study would involve. They were also informed of how the information from the research would be used or disseminated and how their confidentiality would be maintained. Any questions they had concerning the research was answered by the researcher. Their rights not to participate or to withdraw at any point were respected. Although this technique used for the traders was considered the most appropriate way to obtain information from them, it may have affected the findings from this research as they may have responded differently if they were given the information leaflets and consent forms.

4.9.6.5 During the interviews

Some of the interview sessions with the patients were often interrupted by the doctors/nurses/pharmacists because most of them preferred to be interviewed while they were waiting to see their doctor or while awaiting collection of their medicines from the hospital pharmacy. This also happened with the medicine sellers who in most cases preferred that interviews be conducted at their place of work and were often interrupted if they needed to attend to patients and by noise as most of the outlets were located close to the roads. These interruptions may have disrupted the flow of the interviews in these stakeholder categories.

Due to the sensitive nature of the topic addressed, most of the participants exercised some caution in giving information especially participants in the policy making group. This also seemed common with majority of the medicine sellers (community pharmacists, patent medicine vendors and traders) and few of the consumers. For instance, one consumer refused to be tape recorded stating that he has held a key position with the Lagos state government, most of the traders did not want to talk in details on issues raised and were not ready to mention names or give instances when and where necessary. The policy makers were cautious by avoiding giving instances or going in depth on issues raised or questions asked rather they spoke more generally. Also, the use of tape recorders as previously mentioned may also have limited the amount of information given by the participants as it was observed that important information were often given once the tape recorders were switched off. As a result of this, the interviewer took notes of major points raised by the participants when the recorders were switched off.

Furthermore there may have been increased willingness to give information to the researcher by some of the participants because of her being a fellow Nigerian as expressed by some of the participants, this may have also

contributed some bias to the study. For instance the researcher may have introduced some preconceived ideas from her experience of being Nigerian into the study especially during the interviews in a bid to impress the participants in return.

4.9.7 Conclusion

This chapter provided a detailed description of the conceptual framework from which variables relating to MAS explored in the study were derived. It also discussed the research methodology used and the justification for methods chosen to collect the drug samples for the first phase, recruit the participants that were included in the second phase and methods used to analyse the data obtained. It showed how the different ethical issues in quantitative and qualitative research were critically considered throughout the research process and possible methodological limitations of this study. The results of the first and second phases of this research are presented in the next 2 chapters, Chapter 5 and Chapter 6.

Chapter 5

Presentation of results- Phase 1

5.1 Introduction to chapter

This chapter of my thesis presents and discusses the results of the first phase of this study. It starts by discussing the samples collected, then the results of the verification of tagged drug samples via text messaging. The results obtained from the packaging and chemical (HPLC and NIR) analyses conducted are also presented in this section.

5.2 MAS valiation and quality of medicines collected

A test validation of the Mobile Authentication Service (MAS) was conducted by comparing the responses obtained from the MAS with the actual quality of medicines received by the consumers via packaging and chemical analyses. Following this, differences in quality between the tagged Glucophage® samples and the cheapest generic versions without the tags were determined. The samples of tagged Glucophage® and other cheaper generic versions were obtained from different outlets in Lagos, Nigeria as previously noted.

5.2.1 Plan for sample collection

5.2.1.1 Sample size and collection of samples for analysis

Following the sample size calculation performed to determine the number of samples that would be adequate, details of which are presented in chapter 4 of this thesis, the sample collectors aimed at stopping when a total of 82 samples of tagged Glucophage® and 82 samples of the cheapest generic brands were

purchased. However, a total of 92 tagged Glucophage® and 87 cheapest Generic versions were purchased. This was because both tagged Glucophage® and cheapest generic versions were requested in all shops visited including the shops covering for outlets in which one of the samples had been collected. This was done to avoid any bias that may have been introduced by sampling differently from the outlets.

5.2.2 Samples collected

None of the outlets visited stocked untagged Glucophage® contrary to observations in the preliminary fieldwork. This may be because all the Glucophage® without the tags which were in stock during the preliminary field work when the service was newly introduced had been used up. This may be a confirmation of some of the reasons given by medicine sellers for stocking untagged Glucophage® during the preliminary fieldwork; that the untagged Glucophage® was from the old stock obtained before MAS was commenced.

Tagged Glucophage® in addition to 21 other cheaper metformin products (branded and unbranded generics) from different manufacturers were obtained as shown in the table 11.

Table 11: Metformin products collected

S/no	Codes of metformin products collected	Names of metformin products collected	Name of manufacturer stated on the packaging	Name of distributor in Nigeria
1	Z	Glucophage®	Merck Sante sas, France	Biofem pharmaceuticals
2	A	Diabetmin®	Hovid Bhd, Malaysia	Pharmatex Nig. Ltd
3	B	Diabex®	Medopharm, India	Solidium Pharmaceuticals Limited
4	C	Glumin®	Rajat Pharm Chem Ltd., India	Seagreen Pharmaceuticals Ltd.
5	D	Ionophage®	MBL Pharma, Pakistan	Innobest Pharmaceutical Company (Nig) Ltd.
6	E	Glucopac®	Zhejiang DND Pharmaceuticals Co Ltd., China	Pacmai International Ltd.
7	F	Diamet®	May and Baker Nigeria Plc., Nigeria	May and Baker Nigeria Plc., Nigeria
8	G	VPL® Metformin	Jiangsu Ruinian Qianjin Pharmaceutical Co. Ltd.	Vixa Pharmaceutical Co. Ltd.
9	H	Askaphage®	Endolabs Limited, India	Tenderwell limited
10	I	Formet®	Strides Arcolab Ltd., India	Strides vital (Nig) Ltd.
11	J	Sanformin®	Micro Labs Limited, India	Sanpharm Nigeria Limited
12	K	Lifeback® metformin	Rhydburg Pharmaceuticals Ltd., India	Lifeback pharmacy and stores limited
13	L	Trippleace® metformin	Healthy life Pharma PVT Ltd., India	Trippleace pharmaceuticals Ltd.
14	M	Betaphage®	Shine Pharmaceuticals Limited, India	Eurosource Pharm and Chem Inds. (WA) Ltd.
15	N	Metformin by Bristol Laboratories	Bristol Laboratories Ltd., United Kingdom	-
16	O	Juformin®	Juhel Nigeria Ltd., Nigeria	Juhel Nigeria Ltd.
17	P	Diamin®	Henan Topfond Pharmaceuticals Co. Ltd., China	Korlyns Pharmaceuticals
18	Q	Gluformin®	Nigerian German Chemicals Plc, Nigeria	Nigerian German Chemicals
19	R	Miformin®	Mano Greater Pharma Ltd., Thailand	Didachons Pharm. Ltd.
20	S	Glucophage® by Merck (Private)	Merck (private) limited, Pakistan	-
21	T	BG Lophage®	Stallion Laboratories PVT. Ltd., India	BG Pharmacy and stores Limited
22	U	Climax® metformin	Mancare Pharmaceuticals PVT. Ltd., India	Royal Pharmacy

In total, 22 different metformin products were collected from the community pharmacies and the drug market as shown in table 11. This included the innovator brand; Glucophage® and 21 generic metformin products. Only one of the generic versions (N) is unbranded while the rest are branded. Three of the metformin products collected (F, O and Q) are locally produced while the 19 others are imported. Ten of the generic sample brands were claimed to be manufactured in India, three in Nigeria, three in China, two in Pakistan, one in France, one in Thailand, one in the United Kingdom and one in Malaysia. Four of the cheapest generic brands (S, T, N and U) did not have a NAFDAC number.

5.2.3 Collection of original samples from manufacturers

Original samples from the pharmaceutical companies/ manufacturers stated on the pack of the medicines were collected in order to compare their quality against the other samples obtained using packaging analysis and Near Infrared spectroscopy. This was done to help detect any differences that may show samples that may be counterfeit. All the manufacturers stated on the packet of the medicines were initially contacted via the telephone numbers and e-mail addresses provided but no response was received. Manufacturer's samples were later obtained for 20 of the samples. With the exception of N which was obtained from the UK and Q which was obtained from a wholesaler recommended by its manufacturer; Nigerian German Chemicals (NGC) because they had no samples in stock as at the time of visit as production of Q was on hold at the time, the rest were obtained mainly through the medical representatives of the company or their distributor in Nigeria. This is because efforts to obtain them directly from the companies in their countries of manufacture proved abortive.

Manufacturers' sample of S and U could not be obtained, as neither their medical representatives nor their distributors in Nigeria could be identified. The manufacturers stated on their packaging were repeatedly contacted for a sample through e-mail but no response was received.

5.2.4 Quantity of each metformin product collected

Over half of the samples collected 92 (51.4%) where tagged Glucophage® while the rest 87 (48.6%) were generic (branded and unbranded) metformin as shown in the figure 13 below. Table 12 shows the individual quantities of the different metformin products collected. For the purpose of this thesis all the metformin products with the exclusion of the tagged Glucophage® samples are regarded as generic metformin. This is because comparisons of the quality of metformin samples collected were between the tagged Glucophage® samples and the generic versions.

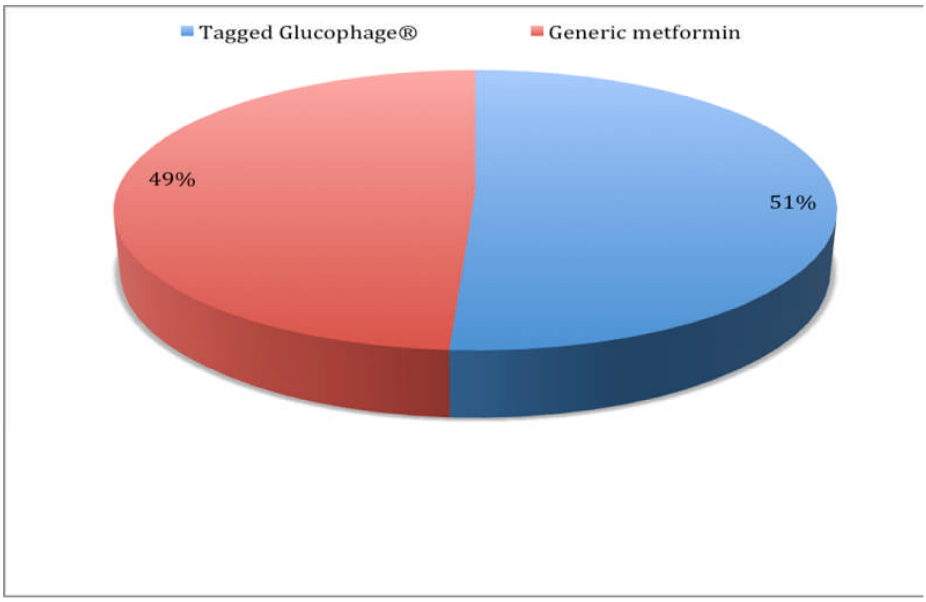


Figure 13: Quantity of tagged Glucophage® and generic metformin samples collected

Table 12: Total number of each metformin product collected

Group	Metformin products collected	Number collected	Percentage (%)
Tagged Glucophage®	Z	92	51.4
Generic versions	A	35	19.6
	B	7	3.9
	C	1	0.6
	D	2	1.1
	E	6	3.4
	F	7	3.9
	G	2	1.1
	H	1	0.6
	I	1	0.6
	J	1	0.6
	K	2	1.1
	L	1	0.6
	M	1	0.6
	N	1	0.6
	O	1	0.6
	P	1	0.6
	Q	10	5.6
	R	2	1.1
	S	3	1.7
	T	1	0.6
	U	1	0.6

5.2.5 Outlets/Sources of samples collected

The community pharmacies and the drug market were included as major sources of metformin and the proportion of samples obtained from them was relative to their total number in Lagos; 590 and 203 respectively. 61 community pharmacies and 21 outlets at the Idumota drug market were randomly selected to be visited to collect 122 samples (61 tagged Glucophage® and 61 cheap generic versions) and 42 samples (21 tagged Glucophage® and 21 cheap generic versions) respectively based on the sample size calculation performed details of which are presented in chapter 4.

In total, 90 community pharmacies (the first 61 distinct community pharmacies and the following distinct 29 community pharmacies corresponding to the extra random numbers) were visited. Five pharmacies were repeats of previously generated random numbers. 59 outlets furnished both tagged Glucophage® and cheapest available generic metformin, 5 outlets furnished only the cheapest available generic metformin, 12 outlets furnished only Glucophage®, 2 outlets did not have any metformin product, 3 outlets were no longer pharmacies at the time of visit, 2 outlets were still pharmacies but had changed their name, one outlet was closed at the time of visit and 3 outlets could not be located. For some of the pharmacies not furnishing the requested samples, the exact reason could not be ascertained probably because for most of the outlets visited, the pharmacists were not around to explain why the sample was unavailable and the shopkeepers seemed not to know why the medicines were not available. Sometimes the shopkeepers were completely unaware of the existence of any other metformin product aside Glucophage®. Some of the reasons given for not furnishing the sample included either that the medicines had finished or that they stocked medicines based on demand. Some pharmacists stated they only stock Glucophage® as that is the only metformin with a “guaranteed” quality.

In the drug market, the first 60 distinct medicine outlets from the list of randomly generated numbers were visited (samples were obtained from only 29 out of the 60 outlets visisted; 16 supplied both Glucophage® and the cheapest available generic metformin, 6 supplied only Glucophage® and 7 supplied only the cheapest available generic). 31 outlets did not supply any sample. The reason given for inability to supply samples included being solely wholesale outlets, not selling diabetic medicines but instead dealing on specific medicine categories, stocking only specific company products or that metformin was finished at the time of visit. For outlets stocking only one version (Glucophage® or cheapest generic metformin), the most common reasons given were that they stocked medicines based on demand or based on the medicines they trust their quality.

In total 135 (71 tagged Glucophage® samples and 64 untagged generic versions) samples of metformin from the community pharmacies and 44 (21 tagged Glucophage® samples and 23 untagged generic versions) samples from the drug market were obtained as shown in table 13 below. As previously noted, the number of samples collected were more than the 122 samples and 42 samples aimed at been collected from the sample size calculation. This is because both tagged Glucophage® and generic versions were requested from all outlets visited including the outlets corresponding to the extra random numbers.

Table 13: Quantity of samples collected from the outlets

Outlet type	Quantity collected	Percentage collected
Community pharmacy	**135**	**75.4%**
Drug market	**44**	**24.6%**

5.2.6 Objective 1: To perform a test validation of the Mobile Authentication Service (MAS)

A test validation of the Mobile Authentication Service was done by comparing the responses obtained from the mobile anti-counterfeit service with the actual quality of medicines received by the consumers via packaging and experimental/chemical analyses. This was done in order to compare the results of responses obtained about the quality of the samples with the actual quality of the samples determined via packaging and experimental/chemical analyses. The tagged Glucophage® samples were initially coded and authenticated via SMS/text message. Following this, the authenticated samples were recoded and analysed via packaging analysis, NIR and HPLC. The results of the text message authentication and the packaging and chemical analyses were then compared. The results of the SMS/text message authentication, packaging and chemical analyses (NIR and HPLC) are presented below;

5.2.6.1 Short Messaging Service (SMS) sample authentication

The tagged Glucophage® samples were authenticated via the four network providers that were enrolled in the scheme (GLO, MTN, ETISALAT and AIRTEL) on five different days. All the 92 samples of tagged Glucophage were authenticated (23 samples with GLO network, 23 samples with MTN network, 23 samples with Etisalat network and 23 samples with Airtel network). Aside 2 samples (TGIBPM and TGIEMAU), almost an immediate response were received for all the other samples. The average time of response for each network was 58.58 seconds for GLO, 12.07 seconds for MTN, 6.41 seconds for ETISALAT and 50.7 seconds for AIRTEL. Responses received from the text message authentication showed that all the 92 samples were "OK, ORIGINAL". This means that all the 92 samples of tagged Glucophage® passed the text message authentication as the response meant they were genuine samples. Table 14 and Appendix 16 show the result of the responses received from the text message authentication for the tagged Glucophage® samples.

Table 14: Short Message Service (SMS) authentication of tagged Glucophage samples

	No. (percentage) that were confirmed as genuine	No. (percentage) that were confirmed as fake
Tagged Glucophage® samples (N=92)	92 (100%)	0 (0%)

Following the SMS authentication of the tagged Glucophage® samples, they were recoded before other (packaging, NIR, HPLC) analyses were conducted to avoid introduction of bias to the results from the researcher who was involved with the SMS authentication.

5.2.6.2 Packaging analysis

Packaging analysis performed involved checking all the medicine packets of the samples for any differences in font or font size when compared to the original versions from the manufacturers, checking for spelling mistakes and wrong language construction in addition to other parameters in the visual inspection tool in Appendic 8. Samples passed the packaging analysis test if there were no differences in these parameters when compared to the original samples from the manufacturers. The results of the packaging analysis conducted for tagged Glucophage® samples can be seen in table 15 below and appendix 17. All (100%) the samples of 92 samples of tagged Glucophage® passed the packaging analysis.

Table 15: packaging analysis of tagged Glucophage® samples

	No (percentage) that passed packaging analysis	No (percentage) that failed packaging analysis
Tagged Glucophage® samples (N=92)	92 (100%)	0 (0%)

5.2.6.3 Near infrared (NIR) analysis of the tagged Glucophage® samples

The spectrum of the authentic Glucophage® from the manufacturer was obtained by individually placing 10 tablets of it and measuring once on both sides in the NIR spectrometer. The mean Standard Normal Variate (SNV) second derivative (D2) spectrum was then taken from the 20 spectra. Each of the Glucophage samples from the outlets were analysed in the same manner as the authentic sample. The mean Standard Normal Variate (SNV) 2^{nd} derivative spectra of the Glucophage® samples obtained from the outlets were individually compared with that of the manufacturer's sample for any differences that may suggest that the samples may not be original or genuine using the correlation in wavelength space (CWS) method to obtain their correlation coefficient (r). The sample tested was regarded as failing the NIR analysis/ counterfeit if the correlation coefficient was less than 0.95 while samples with correlation

coefficient of ≥0.95 were regarded as passing the test/authentic. All the Glucophage® samples analysed passed the NIR analysis because they had a correlation coefficient of > 0.95 (see appendix 18) and the SNV-D2 NIR mean spectra of all the Glucophage® samples from the outlets and the authentic sample from the manufacturer showed that they are practically super-imposable when individually compared. Therefore, none of the tagged Glucophage® samples analysed was identified as counterfeit using NIR (see table 16). Figure 14 shows the comparison of the SNV-D2 NIR mean spectra of the authentic/ manufacturer's sample of Glucophage® (OGL GLUCO) and a sample from the outlet (GL27) as an example.

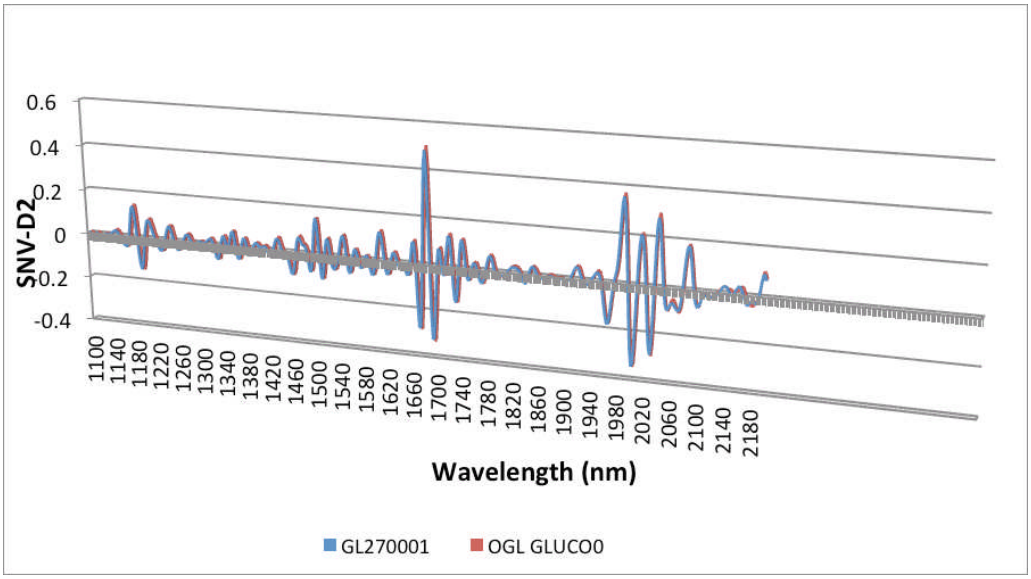


Figure 14: SNV-D2 NIR mean spectra of authentic Glucophage® (red) and Glucophage from outlet (blue, r=0.9996 compared to the authentic Glucophage®)

Table 16: NIR analysis of tagged Glucophage® samples

	No (percentage) that passed NIR analysis	No (percentage) that failed NIR analysis
Tagged Glucophage® samples (N=92)	92 (100%)	0 (0%)

The results of the NIR analysis presented in table 16 above are in agreement with the responses obtained from the text message authentication of the samples which identified all the collected tagged Glucophage® samples as "Original" and the packaging analysis which showed that all the samples were the same with the original sample from the manufacturers.

5.2.6.4 HPLC analysis of tagged Glucophage® samples

The concentration of metformin for each Glucophage® sample was obtained using the calibration curve method (See appendix 19). The mean concentration of metformin for each sample was calculated in the Microsoft Excel 2013 software. Samples with metformin concentration within the specified British Pharmacopoeia standard of 95-105% were regarded as meeting the standard or passed the HPLC analysis. While samples with metformin concentration outside this range were regarded as not meeting specified standard or failed the HPLC analysis. The specification for percentage concentration of metfmorin is the same for the British Pharmacopoeia, International Pharmacopeia and the European Pharmacopoeia. However, throughout this thesis compliance to the British Pharmacopoeia was used to judge if medicines passed or failed HPLC analysis as that is the standard for metformin used by NAFDAC according to the information obtained from one of the NAFDAC officials during the preliminary fieldwork.

Appendix 19 and table 17 show the results obtained from the HPLC analysis of the Glucophage® samples. They show that all the 92 samples of tagged

Glucophage® passed the HPLC analysis since the concentration of metformin in all the samples were within the stated range 95-105%.

Table 17: HPLC analysis of tagged Glucophage® samples

Tagged Glucophage® samples (N=92)	No (percentage) that passed HPLC analysis (%Concentration of metformin within 95-105%)	No (percentage) that failed HPLC analysis (%Concentration of metformin outside 95-105%)
	92 (100%)	0 (0%)

The results from the Short Message Service (MAS) authentication of the tagged Glucophage® samples show that all the 92 samples are "authentic" or "original". This means they should be of good quality. This result agrees with that of the packaging and chemical analyses (NIR and HPLC) analyses, which showed that none of the tagged Glucophage was counterfeit and that the percentage concentration of metformin in them were within the specified limits. This is because all the samples passed the packaging analysis, NIR and HPLC analysis.

From results presented above, it seems that the Glucophage® samples are original (from genuine manufacturers) as stated in the MAS SMS response and of acceptable quality in terms of their active ingredient with percentage metformin concentration in all the tagged Glucophage® samples falling between 95-105% recommended by the British Pharmacopoeia.

5.2.7 Objective 2: To determine if there are differences in quality between tagged Glucophage® samples and the generic metformin samples without tags

In order to determine if there were differences between the tagged Glucophage® samples and the generic versions, the generic metformin samples were recoded and then analysed using packaging analysis, NIR and

HPLC. The quality of the generic metformin samples were then compared with that of the tagged Glucophage® samples presented above.

5.2.7.1 Packaging analysis of the generic metformin samples

Packaging analysis performed involved checking all the medicine packets of the 87 generic samples of metformin for any differences in font or font size when compared to the original versions from the manufacturers, checking for spelling mistakes and wrong language construction in addition to the parameters in the visial inspection tool in Appendix 8. Samples passed the packaging analysis test if there were no differences in these parameters when compared to the original samples from the manufacturers. The results of the packaging analysis conducted for the generic metformin samples are presented in appendix 20 and table 18 below. All but 4 of the samples of generic metformin samples passed the packaging analysis test. The four (Ge38, Ge60, Ge67 and Ge83) samples were not analysed because there were no manufacturers' samples to which comparisons could be made.

Table 18: packaging analysis of generic metformin samples

	No (percentage) that passed packaging analysis	No (percentage) that failed packaging analysis	No (percentage) that could not be analysed
Generic metformin samples (N=87)	83 (95.4%)	0 (0%)	4 (4.6%)

From the results of the packaging analysis, no differences could be established between the tagged Glucophage® and generic metformin because all the samples analysed (both tagged Glucophage® and generic metformin) passed the packaging analysis.

5.2.7.2 NIR analysis of the generic samples

The spectra of the authentic/manufacturer's sample of each generic metformin product (A- U) were obtained by individually placing 10 tablets each of authentic generic metformin products (A-U) obtained from the manufacturers and measuring once on both sides in the NIR spectrometer with the probe. Each of the generic metformin samples from the outlets were analysed in the same manner as the authentic samples. The mean Standard Normal Variate (SNV) 2^{nd} derivative spectra of the samples obtained from the outlets were then compared with that of their corresponding manufacturer's sample for any differences that may suggest that the samples may not be original or genuine using the correlation in wavelength space (CWS) method to obtain their correlation coefficient (r). The sample tested was regarded as failing the NIR analysis/ counterfeit if the correlation coefficient was less than 0.95 while samples with correlation coefficient of $\geq$0.95 were regarded as passing the test/authentic.

The SNV-D2 NIR mean spectra of all the generic metformin samples from the outlets analysed and the corresponding authentic sample from the manufacturer were all practically superimposable when they were individually compared. Therefore, none of the tagged generic metformin samples analysed was identified as counterfeit using NIR. Figure 15 shows the comparison of the SNV-D2 NIR mean spectra of the authentic/manufacturer's sample of a generic brand of metformin, Gluformin® (OGE GLUFOR) and a sample of Gluformin® from the outlet (GE40) as an example.

As Illustrated in appendices 21 and 22 and Table 19, 83 out of the 87 generic samples passed the NIR analysis because they had a correlation coefficient of >0.95. Four of the generic samples (Ge38, Ge60, Ge67 and Ge83) could not be analysed because their manufacturers' sample could not be obtained. Table 20 compares the result of the NIR analysis of tagged Glucophage® samples with the generic metformin and it shows that all the samples of both tagged Glucophage® samples and generic metformin samples that were analysed passed the NIR test.

Table 19: NIR analysis of generic metformin samples

	No (percentage) that passed NIR analysis	No (percentage) that failed NIR analysis	No (percentage) that could not be analysed
Generic metformin samples (N=87)	83 (95.4%)	0 (0%)	4 (4.6%)

Table 20: Comparison of the results of NIR analysis of tagged Glucophage® with generic metformin samples

Metformin	**No. (Percentage) that passed NIR analysis**	**No. (Percentage) analysed that did not pass NIR analysis**	**No. (Percentage) that was not analysed via NIR**
Tagged Glucophage®	**92 (100%)**	**0 (0%)**	**0 (0%)**
Generic metformin	**83 (95.4%)**	**0 (0%)**	**4(4.6%)**

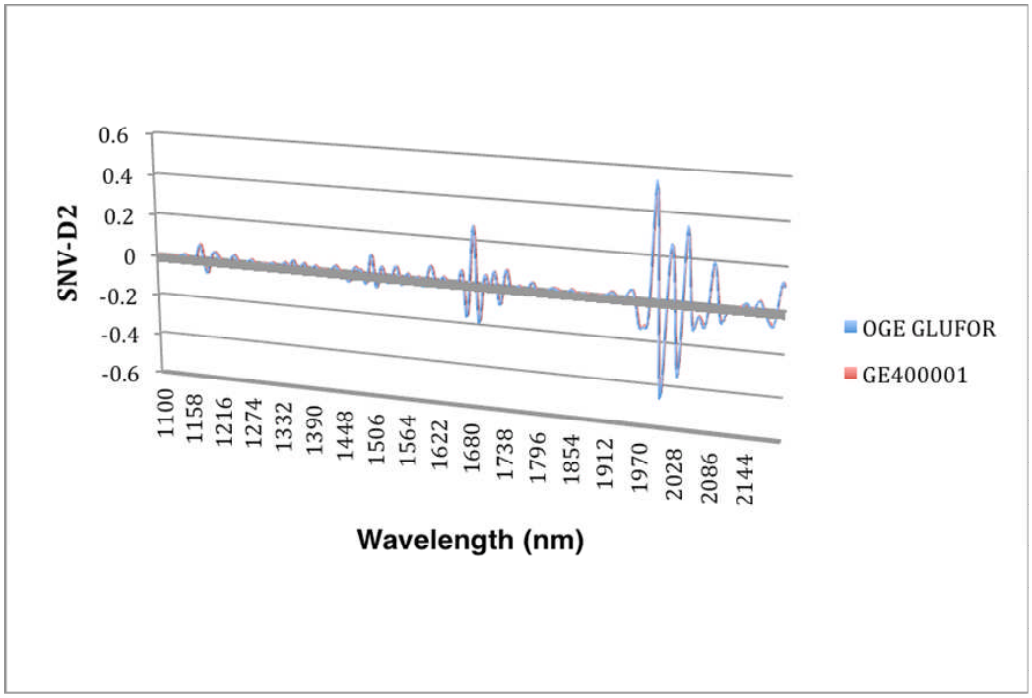


Figure 15: SNV-D2 NIR mean spectra of authentic metformin product; Gluformin® (blue) and Gluformin® from outlet (red, r= 0.9998 compared to the authentic Gluformin®)

From the results of the NIR analysis, no differences in quality could be established between the tagged Glucophage® and generic metformin samples because all the samples analysed (both tagged Glucophage® and generic metformin) passed the NIR analysis.

5.2.7.3 HPLC analysis of the generic metformin samples

The concentration of metformin for each sample was obtained using the calibration curve method (See appendix 19). The mean concentration of metformin for each sample was calculated in the Microsoft Excel 2013 software. The quality of the samples was evaluated in terms of the percentage of active ingredient (metformin) present. Samples with percentage of metformin between 95-105% as specified by the British Pharmacopoeia (BP) passed the test while samples with percentage of metformin outside this range failed the test. 87

samples of generic metformin were analysed; results of HPLC analysis of tagged Glucophage® samples are already presented above in section 5.2.6.4.

Following the HPLC analysis of the generic metformin samples, the quality of tagged Glucophage® samples were compared to the quality of the generic metformin samples and any differences were noted. Table 21 shows the results of the HPLC analysis of generic metformin samples and appendix 23 shows the concentration of metformin obtained from the HPLC analysis conducted for each sample of generic metformin.

Table 21: HPLC analysis of generic metformin samples

a) Overall result of HPLC analysis of Generic metformin samples

Generic metformin samples (N=87)	No (percentage) that passed HPLC analysis (%Concentration of metformin within 95-105%)	No (percentage) that failed HPLC analysis (%Concentration of metformin outside 95-105%)
	80 (91.95%)	7 (8.05%)

b) Percentage concentration of metformin in the genetic metformin samples that failed HPLC analysis

Sample code	Percentage (%) concentration of metformin
Ge1	94.06
Ge7	93.80
Ge10	93.03
Ge31	94.02
Ge32	92.85
Ge60	86.68
Ge69	83.11

5.2.7.4 Compliance of samples to HPLC standard for metformin

Seven (3.9%) out of the 179 samples did not meet standard for concentration of metformin recommended by the British Pharmacopoeia. That means they had

percentage metformin concentration outside the range of 95-105%. The seven samples that failed were all from the generic sample group. This means that 7 (8.05%) of the 87 generic metformin samples failed quality test for concentration of active ingredient. The seven samples that failed were; three samples of F (Ge1, Ge31 and Ge69), one sample of D (Ge7), O (Ge10), Q (Ge32) and U (Ge60) respectively. Only one (Ge60) of the samples that failed was not registered by NAFADC while 4 out of the 7 samples that failed were locally produced. As previously noted, all the tagged Glucophage® samples were within the specified range (95%-105%) of active ingredient as shown in table 22 below.

Table 22: Compliance of tagged Glucophage® and generic metformin to standard specification for percentage of metformin

Metformin	Number (Percentage that met HPLC standard)	Number (Percentage that did not meet standard per group)	Number (Percentage that did not meet standard overall)
Tagged Glucophage®	92 (100%)	0 (0%)	7 (3.9%)
Generic metformin	80 (91.95%)	7 (8.05%)	

In order to determine if there was any significant difference between the two-level categorical variables: metformin product (tagged Glucophage® and generic metformin) and adherence/non adherence to the BP standard for metformin (pass or fail of HPLC analysis), the Chi-square analysis was conducted in SPSS statistical software version 22.0. Following the analysis conducted in SPSS, some (>20%) of the cells had an expected count of less than (<) 5, therefore the Fisher's exact test was used instead of the Chi-square analysis to test whether there was any significant difference in quality between them (tagged Glucophage® and generic metformin), this resulted in a P value of 0.006 as shown in Table 23. A P-value of less than 0.05 shows that there is a significant difference between the quality of the tagged Glucophage® in terms of the concentration of active ingredient when compared to their generic

counterparts for the samples included in this research. Although there seems to be a significant difference in quality between the tagged Glucophage® samples and generic metformin, it is important to note that this result/finding may have been limited by the small sample size in each generic product/ brand collected. It is also important to note that as shown in Table 21b, the percentage concentration of metformin in the lowest failing sample is 83.11% and more than half (4) of the samples that failed had a percentage concentration of metformin of >92%. Considering that metformin is an oral anti-diabetic with a wide therapeutic window and that it may not be possible to develop resistance from the use of subtherapeutic doses, it may be concluded that although the 7 generic medicines that falied the HPLC analysis did not meet the BP specification for concentration of active ingredient, this failure may not be clinically significant and may be considered acceptable because of the reduced associated risk from their use. This kind of flexibility can be considered acceptable according to UN Millennium Project, (2005).

Table 23: Result of the Chi-Square analysis conducted to determine difference in quality between Tagged Glucophage® and generic metformin samples

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.704[a]	1	.006		
Continuity Correction[b]	5.711	1	.017		
Likelihood Ratio	10.402	1	.001		
Fisher's Exact Test				.006	.006
Linear-by-Linear Association	7.661	1	.006		
N of Valid Cases	179				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.40.

b. Computed only for a 2x2 table

5.2.7.5 Major findings- phase 1

From the results presented above, the key findings for the first phase of the study are therefore as follows;

1) The results of the MAS authentication agree with the packaging and chemical analyses conducted. The Glucophage® samples seem to be original as stated in response to the SMS authentication and of good quality in terms of their packaging and content of active ingredient from the results of the packaging analysis, NIR and HPLC conducted.

2) No differences in quality in terms of the percentage concentration of active ingredient; metformin between the tagged Glucophage® samples and generic metformin was detected via packaging and NIR analysis. However, there seems to be a significant difference between the tagged Glucophage® samples and their cheaper generic counterpart with a p value of 0.006. The tagged Glucophage® samples seem to be of better quality than their generic counterparts.

5.3 Conclusion

This chapter of my thesis presented the results of the SMS/text message authentication, packaging, HPLC and NIR analysis of metformin samples randomly selected from different outlets (community pharmacies and open drug market) across Lagos, Nigeria. All the tagged Glucophage® samples were certified as original via SMS and seemed to be of acceptable quality in terms their percentage of active ingredient; metformin with values falling between 95%-105% as recommended by the British Pharmacopoeia. No counterfeit samples were detected from the packaging and NIR analysis conducted. However there seems to be a significant difference in quality between the tagged Glucophage samples and their cheaper generic versions (P-value= 0.006) as 7 (8.05%) of the generic versions failed to meet standard for percentage concentration of active ingredient

Having presented the result of the SMS authentication and analyses of collected samples, the next chapter will focus on presenting the results arising from the exploration of the perceptions and experiences of stakeholders of MAS and issues relating to the quality of medicines distributed in Nigeria.

Chapter 6

Presentation of results-Phase 2

6.1 Introduction to chapter

This chapter presents the key findings obtained from 37 semi-structured interviews conducted in the second phase of this study. It starts by discussing the profile of the qualitative data including the demographic profile of the participants. Stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria were presented. Finally, findings arising from exploring stakeholder perceptions of the successes and challenges that may arise in the implementation of MAS, the impact of MAS and how MAS may be improved are presented.

6.2 Profile of the qualitative data

Eleven pharmacists, five patent medicine vendors, twenty patients, five policy makers and seven traders were approached to participate in the research. Out of these, 3 pharmacists, 6 patients, 1 policy maker and 1 trader could not participate mainly due to time constraints. In total, 37 interviews were conducted; 8 community pharmacists, 5 patent medicine vendors, 6 traders, 4 policy makers and 14 consumers were interviewed. Only 3 out of the 14 consumers interviewed had used the MAS. Out of these, comprehensive interviews were conducted for 2 of the consumers while the 3rd (patient 14) could not be interviewed comprehensively because the interview session was interrupted by his doctor who requested to see him and the researcher could not locate him afterwards to complete the interview. The duration of the interviews ranged from about 10 minutes to 1 hour. The mean time duration for the interview was 35 minutes. One participant in the consumer category preferred not to be tape-recorded as he said he previously held a key government position with the Lagos state government. Therefore notes were taken instead. The interview topic guide for the different stakeholder categories

were used to interview the participants. The questions asked were based on the interview topic guide and where new issues were raised, they were explored in subsequent interviews in order to triangulate and confirm findings.

6.3 Demographic profile of participants

One of the policy makers interviewed was a senior official of the National Agency for Food and Drug (NAFDAC), 2 were past senior officials of the Pharmaceutical Society of Nigeria (PSN) while one was a senior official of PSN. All the community pharmacies and policy makers were aware of MAS while all but one of the patent medicine vendors were aware of MAS. The patent medicine vendor who was unaware of the MAS stated that it is because she has been sick and has been away from Nigeria for a long time. Only 3 out of the 15 consumers interviewed had used MAS.

Table 24: Demographics of participants (N=37)

Gender Male: 65% Female: 35%	**Education (maximum achieved)** University: 62% Secondary school: 35% Primary school: 3% Uneducated: Nil	**Stakeholder group** Community pharmacists: 22% Patent medicine vendors: 13% Traders: 16% Consumers: 38% Policy makers: 11%
Age (Years) 20-39: 32% 40-60: 46% >60: 22%	**Employment** Retired: 16% Working: 81% Unemployed: 3%	

Table 25: Number of years of practice for the medicine sellers

Community pharmacists (N=8)	Patent Medicine Vendors (N=5)	Traders (N=6)
< 2 Years: 13% 2 to 5 Years: 25% 5+ to 10 Years: 25% >10 Years: 37%	< 2 Years: Nil 2 to 5 Years: 20% 5+ to 10 Years: 60% >10 Years: 20%	< 2 Years: Nil 2 to 5 Years: 17% 5+ to 10 Years: 33% >10 Years: 50%

The 37 interviews were transcribed verbatim. Out of these, 24 participants discussed issues relating to MAS while all the participants discussed issues relating to the current situation of medicines counterfeiting in Nigeria. The statements were carefully examined and analysed using the framework analysis approach in Nvivo 10® software.

To help organise the information arising from the interviews; 2 coding frames were developed (see tables 26 and 27). The first coding frame consisted of all the themes relating to the perceptions of stakeholders of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria while the second coding frame consisted of all the themes relating to the perceptions, experiences and attitudes of the stakeholders towards the MAS (See appendices 24-29). The coding frames were first deductively generated from the interview topic guide, which was based on the conceptual framework underpinning the research. Additions were made inductively as the researcher read the interviews.

The coding frames remained flexible throughout the analysis as new themes were added. Previous interviews were re-read to identify any comments relating to the newly added themes. Matrices were created and themes arising from the participants were placed accordingly in the matrices they belonged. In order to ensure rigour, another experienced researcher reviewed the coding matrix and the interview transcripts. A research journal of changes made to the coding matrix was kept. The initial codes were further grouped as categories with subthemes. The categories/themes and subthemes formed the coding index that was used to organise the entire qualitative data. The coding index remained flexible and was refined as new insights developed. The researcher remained true to the participants' descriptions by constantly referring to the original transcript to check meanings across the interviews using the text search

and word frequency search query functions in Nvivo®. Also, at every stage of the analysis, the researcher tried to reflect on what the participants were really trying to describe and the participants' words were used as much as possible to ensure that their views were accurately reflected. Quotations were taken from the interview transcripts to show the perspectives of multiple participants.

The objectives of this phase were to;

1) Examine stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria

2) Identify the successes and challenges (potential problems) which may arise in the implementation of MAS and determine how these problems can be mitigated in order to ensure optimum utilization and future expansion of the service

3) Explore the consequences of MAS use (what are their actions after using MAS? does this increase their confidence on the medicines they buy? do they report cases of medicines counterfeiting through the use of MAS?); this will inform areas that consumers may be educated in order to achieve better outcomes

4) To determine the perceptions of stakeholders on how best MAS can be improved in order to ensure optimum utilization and future expansion of the service

Table 26 shows the categories that were developed to meet the objectives of this phase and the subthemes identified

Table 26: Categories and final themes developed based on research objective 1 of phase 2

Current situation of medicines counterfeiting and quality of medicines in Nigeria Objective 1: To examine stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria	
Categories	Subthemes
Size of the problem of poor quality medicine in Nigeria	Trend in the size of poor quality medicine in Nigeria Encounter with poor quality medicines Medicines most likely to be faked
Factors that encourage or discourage existence of poor quality medicines in Nigeria	Reasons for the existence of poor quality medicines Reasons for perceived reduction in the incidence of poor quality medicines in Nigeria Awareness as an initiative against existence of poor quality medicine in Nigeria How medicine sellers can help reduce existence of poor quality medicines
Generic and branded medicines	Choice between generic and branded medicines Perceived quality of locally made medicines Perception of drug quality in relation to the cost of medicines Educating consumers about generic medicines

Table 27: Categories and final themes developed based on research objective 2-4

Barriers/facilitators to MAS use Objective 2-To identify the successes and challenges (potential problems) which may arise in the implementation of MAS	Barriers Cost issues MAS awareness Time issues and MAS Educating consumers about MAS Trust in source of medicine Confidentiality Dispensing practices in rural areas and hospitals Poor phone network service Facilitators Compatibility of MAS Ease of use Time taken to respond to text message authentication
Impact of MAS Objective 3- Explore the consequences of MAS on the health and purchasing behaviour of the users (what are the actions after using MAS?, does this increase peoples' confidence in the medicines they buy? do they report cases of medicines counterfeiting through the use of MAS?); this will inform areas that consumers may be educated in order to achieve better outcomes	Change in purchasing behaviour of consumers Other usefulness of MAS Detection of medicines counterfeiting, increased confidence in medicines purchased, increased knowledge about state of health through the tips from the response sent to consumers, increased trust in medicine sellers
How to improve MAS Objective 4-To determine the perceptions of stakeholders on how best MAS can be improved in order to ensure optimum utilization and future expansion of the service	How to improve MAS Authentication by the medicine sellers for instance pharmacists Choice of medicines that will be MAS enabled Network service improvement Assistance by government and its agencies Improved awareness creation

6.4 The major findings of Phase 2

Below is a presentation of the findings based on the objectives of the second phase of this research with details that support and explain these findings using quotations from the semi-structured interviews. This was done to better understand the reality of the research participants and their experiences. These quotations help to show perspectives of multiple participants. Attempts were made not to over quote participants; rather quotations were taken from different stakeholder groups where possible to illustrate findings.

This section starts by presenting the findings relating to the perceptions and experiences of stakeholders of the situation of poor quality medicines in Nigeria. The findings relating to the perceived size of the problem of poor quality medicines in Nigeria and the reasons for the existence of poor quality medicines were first presented. It then goes ahead to present reasons for the perceived reduction in the incidence of poor quality medicines. Findings from other issues which arose during the semi-structured interviews such as stakeholder perception of generic medicines compared to the innovator brands and locally manufactured medicines as well as the role of medicine sellers in tackling poor quality medicines in Nigeria are also presented.

This is followed by the presentation of findings relating to the successes and challenges that may arise in the implementation of MAS in the form of perceived barriers and facilitators to its use by stakeholders. Furthermore, findings relating to the perceived impact of MAS and how MAS could be improved were presented.

6.5 Stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria

6.5.1 Size of the problem of poor quality medicines in Nigeria

6.5.1.1 Trend in the size of the problem of poor quality medicines in Nigeria

As part of the interviews, participants were asked what they perceived was the current situation of the existence of poor quality medicines in Nigeria. This section describes the subthemes relating to the perceived size of the problem of poor quality medicines in Nigeria.

All the participants in the entire stakeholder groups interviewed were of the view that existence of poor quality medicine is a problem in Nigeria. However there was disagreement among the participants as to whether the problem is increasing or decreasing. All the consumers, traders and policy makers were of the view that the problem is decreasing while few of the participants from the community pharmacists and patent medicine vendor groups thought that the problem is on the increase as illustrated below. This perceived increased level of poor quality medicines by these participants might be linked with their observation of increase in activities such as illegal hawking of medicines; an activity that they think promote the existence of poor quality medicines as illustrated below;

"It is increasing. It is increasing. Have you entered public transport? They will be selling medicines. They will be saying this medicine cures syphilis, it cures heart disease, it cures gonorrhoea. They will be talking rubbish"

Patent medicine vendor 3, female, line 208-210

Majority of the participants thought that the problem is decreasing mainly due to interventions in place by regulatory agencies such as NAFDAC and the Pharmacists' Council of Nigeria as illustrated below. This view was shared across all the stakeholder groups interviewed.

"It has reduced drastically. There is no doubt about that. It has reduced. Both NAFDAC, the Pharmacists' Council and so on and so forth have done a lot in that direction and there are so many things they have done to reduce the incidence, even some of these people who even hawk, who sell drugs on the road side, the incidence have gone down"

Community pharmacist 7, male, line 87-91

"Sometime ago it was a problem but as far as NAFDAC came into the drug industry it is now reduced, so it's not as rampant as it used to be let us say as at 5 or 7 years ago"

Patent medicine vendor 1, female, line 23-25

"It is decreasing because since the establishment of NAFDAC at least there has been quality control to check on fake drugs, arrest fake drug traffickers and manufacturers and there have been stern measures taken by the government that has checked fake drugs"

Patient 1, male, line 48-50

Although, all the participants interviewed stated that poor quality medicine is a problem in Nigeria, only few of the participants seemed to have encountered medicines of poor quality. Only few of the participants in the medicine seller and consumer groups stated that they have encountered medicines they thought were of poor quality. Therapeutic failure, death and adverse drug reaction were

the major consequences of such encounters noted by the participants as shown below.

"A case was that of somebody who took Flagyl® 400mg and there was no response, the diarrhoea was still there so the people complained that it is not working, so on a second visit, Flagyl® from another place but from the same company; that is the same make from another source was administered and the person got well so there is nothing to query again other than the quality of the original medicine that was administered to the patient initially"

Community pharmacist 6, male, line 148-152

"It (my sugar level) was just not coming down. It gave me heartache and headache as I was thinking that I was dying. So I had anxiety that I was dying"

Patient 1, male, line 200-202

These two instances above illustrate a case of therapeutic failure as a consequence of poor quality medicines.

"They were putting the drip for the mother not knowing that the drip was fake one that they were putting on the mother so before you know it, the mother died and later the doctor now confirmed that the drip was not the original one. So it is a problem"

Patent medicine vendor 2, male, line 48-50

The case directly above illustrates death as a consequence of the use of poor quality medicines. Another instance illustrated below indicate development of adverse drug reaction after the use of a medicine, which was thought to be of poor quality.

"For instance where I'm living now, there was a day this girl was coughing. Her mother went to chemist to buy her drugs and later they found that the drugs did

not have NAFDAC number and the drug reacted so badly to that girl. The thing became worse and something started to come out of her body which she was not seeing before she started taking that medicine"

Patient 2, female, line 55-63

In all the encounters stated by the participants above, it seems that cases of poor quality medicines are discovered when they have caused harm rather than before the harm is done. This may be because of the complex nature of medicines counterfeiting where they are produced in such a way that they look almost exactly like the original so cannot be overtly noticed at the time of purchase. It may also be that the medicines in these cases were substandard rather than outright counterfeits.

The reason why some of the participants may not have had encounter with medicines of poor quality may be due to precautions taken by some of them such as sourcing their medicines from reputable outlets or maintaining a particular source for their medicines so as to aid easy rectification of any issues that may arise as described below. These precautionary steps taken were stated by the community pharmacists, patent medicine vendors and the consumers.

"I have not come in contact with any because I make sure that I get my own drugs from the manufacturers. Most of the drugs are gotten from the manufacturers or registered distributors because we tend to get all these adulterated or counterfeit products through marketers let me just put it that way"

Community pharmacist 1, female, line 55-57

"I don't just walk up to any place and say I want to buy medicine, both for personal use or for corporate use. My boss is very particular about it because if anything happens I would phone that place, honestly I will phone that place and say I got this drug from you people, what happened? So we can start right there to trace whatever it is that has happened"

Community pharmacist 3, male, 539-542

"You see I don't normally buy drugs just anywhere because there are too many fake drugs in the market so what I normally do is either buy my drugs here or go to a licensed pharmacist that I know like "Tabade"; they do not sell fake drugs, they have not been accused of selling fake drugs as far as I know so there are pharmacists that sell quality drugs and we know them and once you know them, you buy your drugs from them"

Patient 1, male, line 23-27

Other precautionary steps noted by the consumers which may have protected them from encountering medicines of poor quality include relying on their doctor to tell them where to purchase their medicine and/ getting a confirmation about medicines purchased from their doctors as described below;

"My doctor tells me the place to buy from. He says buy from so and so company. I go there and I see the exact one he prescribed for me. I will be convinced. And another thing, if I buy it I will get it, go back to him so that he can certify it ok"

Patient 4, male, line 97-99

Furthermore, other precautionary steps taken by some of the participants such as visually inspecting the packaging may also have contributed to their not having encountered medicines of poor quality as shown below;

"From the pack, I'm very particular about those very small details they say watch out for; expiry date, validity of your medicines. All these things they say I check unless where they don't write it"

Patient 9, male, line 33-34

"Yea, I look at of course like I said packaging, that's the first thing, the physical appearance because people who fake medicines are not so interested in quality so sometimes the physical appearance can tell you"

Community pharmacist 3, male, line 548-550

As can be seen from the illustrations above, there seems to be some level of caution exercised by the consumers and medicine sellers to guard against purchasing medicines of poor quality. Most of the consumers and medicine sellers rely on visual examination of the packaging and obtaining their medicines from reputable sources. Some of the consumers also go further to verify the authenticity of their medicines from their doctors.

None of the medicine sellers commented on the actions they took after an encounter with medicine they perceived to be of poor quality. However, among the consumers who have encountered poor quality medicine, the immediate reaction was to discard or stop the medicine in question and/ return it to where they purchased it rather than reporting the incident as noted by some of the participants below;

"So what I did was to dump the drugs given to me that time, then I went to a pharmacy shop in Ebutte metta and I told them that I wanted good drugs not fake and they gave me and I started taking them, within few days it (my sugar level) came down"

Patient 1, male, line 202-204

"I will not just take the drug. I will just discard and go to doctor to tell me what to get and where to get it. That is what I have been doing whenever I notice anything"

Patient 4, male, line 68-69

"I haven't reported that to anybody now because if I experience that I will stop using the drug, that is it"

Patient 5, male, line 32-33

One of the reasons for this low reporting rate observed in this study may include fear of the reporter being harassed by enforcement officials or lack of trust in how such cases will be handled based on participants' experience for instance whether the culprits will be adequately punished as noted by some of the participants below;

"You see it has been happening in other areas before. You know at times may be you notice a robbery case in some areas, then you phone police. They will tell you that they are coming. They may not come. You see what they are doing there can be extended to other areas. That is why people will not even bother to report. If you give the information they won't work on that information, you understand? That is why I said it would be a wasteful effort. That is it"

Patient 5, male, line 215-219

Interestingly this view was also shared by one of the policy makers as a reason why people may not report incidents of medicines of poor quality as described below.

"But are they (the laws) applied? As small as those laws are, they are not even applied. Somebody comes with fake container of antibiotics, when you report to the agency they cover it up"

Policy maker 2, male, line 213-215

6.5.1.2 Reasons for existence of poor quality medicines

High cost of medicines, poverty, corruption, high cost of product registration, low level of local drug manufacturing, ignorance and lack of awareness on how to detect medicines counterfeiting or sourcing medicines, demand surpassing supply, lack of stringent laws, inadequate law enforcement, difficulty tracing counterfeiters, inadequate knowledge of pharmacy graduates, poor availability of/ shortage pharmacists, greed, existence of open drug markets, lack of commitment by the industries, porous borders, poor government financing, lack of co-operation among stakeholders and global warming were the major factors identified that may be responsible for the existence of poor quality medicines in Nigeria as described by some of the participants below. Table 28 shows the reasons given for the existence of poor quality medicines in Nigeria. The table shows that that corruption (with the largest number of respondents) within the medicines regulation and distribution in Nigeria ranks highest as a cause of the continued existence of poor quality medicines. This is followed by ignorance and lack of awareness, poverty and greed.

Table 28: Reasons for existence of poor quality medicines in Nigeria

Reason	Number of Respondents (N=37)
High cost of medicines	4
Poverty	6
Corruption	12
High cost of product registeration	1
Low level of local drug manufacturing	3
Advancement in technology	1
Ignorance and lack of awareness	8
Demand surpassing supply	3
Lack of stringent laws and inadequate enforcement of existing laws	5
Difficulty tracing counterfeiters	2
Inadequate knowledge of pharmacy graduates	2
Shortage of pharmacists	2
Greed	6
Existence of open drug markets	4
Lack of commitment by the pharmaceutical industries	2
Porous borders	4
Global warming	2
Poor government financing	3
Lack of co-operation among stakeholders	2

6.5.1.2.1 High cost of medicines

High cost of medicines have been a major barrier to access to good quality medicines in Nigeria as about 70% of the population live below poverty line (CIA, 2011) and therefore may not afford expensive medicines. Some (11%) of the participants of the participants stated that high cost of medicines will make such medicines attractive to counterfeiters who may want to counterfeit the medicine to sell at a more affordable rate as described below.

"Most of the prescription drugs are expensive and why people fake is that they feel they can go to China, fake it, bring it down and sell it at a very cheap price and give it to the people so that is just that"

Trader 6, male, line 73-75

Another point raised by some of the participants described below is the belief that medicines priced highly may be of better quality. As such they always prefer the expensive brands to the cheaper generics. Due to the high demand for such expensive brands, counterfeiters may want to counterfeit them to sell at cheaper rates so that people will be lured to buy them just because it bears the popular brand name;

"The costly ones may be more preferable to me that those cheaper ones. If it is a cheap one, it may not be good. It may not work"

Patient 12, male, line 79-80

6.5.1.2.2 Poverty

Another reason echoed by majority of the participants is poverty. Some of the participants in all the stakeholder groups were of the view that not having enough money for instance not been adequately remunerated may lure even the professionals like pharmacists to go into the business of counterfeiting as described below;

"That is what I am saying, Poverty! The economy is not friendly to even the professionals. Is it friendly to me and I am here? How can you ask that kind of question now? It is not easy my sister"

Community pharmacist 3, male, line 155-157

Also, not having enough money by consumers was seen as a major reason why such consumers demand cheap medicines which makes them prone to purchasing counterfeit medicines as described below. This view was expressed by the medicine sellers rather than the consumers.

"Nobody wants to spend money to buy medicine. If somebody comes now and complain of fever, loss of appetite and you say take a better drug like Dart®, Farinex® or lonart DS®, he will say mummy how much and you say seven hundred and fifty naira, he will say no, you don't have the one of hundred naira? Or mix the one of twenty naira for me. Me, it is twenty naira I have. So which twenty naira medicine will cure malaria? If it is people who are not well trained they give them anything to take"

Patent medicine vendor 3, female, line 88-93

6.5.1.2.3 Corruption

Participants in all the stakeholder groups stated that corruption inherent in Nigeria is a major cause of the existence of poor quality medicines as counterfeiters may bribe regulatory officials or custom officials at the ports so that their medicines can be released as described below.

"It is bribery and corruption. You understand? If they want to bring in fake drugs, drugs that are substandard; if they bribe them at the ports, they will release their drugs. You understand what I am saying?"

Community pharmacist 2, Female, line 126-127

"Some of them, that is the security agents still go into partnership with these people to bring in these fake drugs. Afterall they should pass through the customs and they do and some people they drove past cleared them. Drugs don't have wings. So disgruntled elements in the society have been working against government efforts"

Patent 1, male, line 108-111

6.5.1.2.4 High cost of product registration

When medicines are imported into Nigeria or locally manufactured, it is required that the medicines are registered with NAFDAC before they are distributed and sold. Therefore companies are required to send samples to NAFDAC and pay some registration fees as part of the registration process. Majority of the community pharmacists interviewed felt that the fees are exorbitant and discouraging to the professionals who may not have the money for the registration. This situation creates room for non-professionals with inadequate knowledge of medicines for instance businessmen who have enough money to go into production and importation of medicines. This also creates a scenario where manufacturers and importers are lured into distributing their medicines prior to registering them in a bid to raise funds to register them.

"One of the ways it is also discouraging is the cost of product registration. If you have to import a drug you have to pay a huge amount to register it which you and I even as professionals cannot afford but the people who are into business that have enough capital you just see them saying let me give you the capital and before you know it, they will gain access into selling of medicines and they will just think it is all about business but medicine is not like any other product"

Community pharmacist 3, male, line 188-192

"And even when they bring them in. The charges NAFDAC is asking for, most of them don't have it, so they tell them let us go and sell a bit and then come and register but by then the product has entered the distribution chain even if they retrieve it after, whatever harm it would do is already done"

Community pharmacist 5, female, line 161-170

6.5.1.2.5 Low level of local drug manufacturing

Some participants in all the stakeholder groups stated that the poor state of local infrastructure discourages local drug manufacturing. It also increases the cost of local manufacturing which may indirectly lead to reduction in the quality of locally manufactured medicines as the manufacturers may be tempted to reduce the quality of their medicines in order to cover for the cost of manufacturing as stated below;

"We don't have a lot of manufacturing plants here because of bad roads, no electricity, because like now if I am manufacturing something, I have to be putting on generator day and night because NEPA is not reliable. Also getting the finished products from the ports to where they are going to be used because of the bad roads takes a longer time"

Community pharmacist 5, female, line 148-151

"For instance the manufacturers if they want to manufacture anything in Nigeria, the light will not be there, the roads might not be there. So for you to manufacture assuming you are manufacturing it here, it will cost you almost ten times what it will cost may be in China or any of these developed countries so definitely they will try to bring down the quality?"

Trader 6, male, line 113-116

6.5.1.2.6 Advancement in technology

Some medicine sellers felt that advancement in technology has helped to make counterfeiting easier as described below. This is because counterfeiters can easily package their medicines with the technologies available in any way that it will be difficult to detect them.

"People now can copy conveniently making use of machines that are available now and you know, packaging and printing all of them are more convenient and easier done now than before. So if you think of faking it is very easy because you can always clone what you want based on the level of technology now"

Community pharmacist 6, male, line 78-81

6.5.1.2.7 Ignorance and lack of awareness

Almost all the participants in all the stakeholder groups interviewed stated that ignorance on the part of the medicine sellers and consumers may contribute to the continued existence of poor quality medicines. If medicine sellers are not aware of how to differentiate between good and poor quality products, they may unknowingly sell fake medicines to the consumers as described below.

"People don't know the difference between good and bad if it is drug. Ignorance and lack of updates on the part of medicine sellers who sell medicines make them stock and sell fake because they cannot differentiate the original from the fakes especially in the eastern part of the country such as Onitsha drug market, Enugu and Ariara market in Aba"

Community pharmacist 6, male, line 258-261

Similarly, the low literacy rate of the Nigerian populace may make some consumers to source their medicines mainly from the quacks that they think sell medicines at cheaper rates.

"People are naive so whatever they advertise for them in the buses, they convince them then you see them buying it, they tell you that it can work wonders, within a day or two you will get the results of the drugs and since people are very gullible they cash in on it and buy it"

Patient 13, male, line 87-89

6.5.1.2.8 Demand surpassing supply

Another reason for the existence of poor quality medicine stated by some of the policy makers and medicine sellers is increased demand for medicines with limited supply as described by some of the participants below. This may occur when products are banned but consumers still continue to demand them or in cases where the companies amidst increased demand for such medicines create an artificial scarcity in order to increase the price of such drugs. This creates opportunity for counterfeiting of those medicines in order meet the existing demand as described by the participants below;

"You know United States bans products occasionally. They have banned several and when they ban such products, the reputable manufacturers or importers in Nigeria will stop, they will stop and when they stop they create scarcity here. That is when people go and bring them illegally on demand because people are still asking for them. You explain to them that this product has been banned because they have found that it has some bad effects on the body but they say no I want it"

Policy maker 3, male, line 142-147

"Yes, at times they create something like artificial scarcity that is artificial out of stock. May be because they want to increase the price. They artificially withdraw or stop selling. You see the people demanding it and it is no longer available and because the demand is there, those ones who have that sense of going to China and other countries. They fly to China, bring it down. I mean faking it. That has been the issue"

Trader 6, male, line 29-33

6.5.1.2.9 Lack of stringent laws and inadequate enforcement of existing laws

Majority of the stakeholders in the policy makers' group felt that the laws against counterfeiting is not deterrent enough to discourage counterfeiting, rather some of the laws may be an incentive for the counterfeiters. This means that people may decide to go into medicines counterfeiting because they know they have little to lose if they are discovered as stated below. None of the other members of the other stakeholder groups interviewed commented on this.

"Somebody who has made millions and millions or who has been making millions and is caught once and you ask the person to pay 500,000 naira fine. It is even an incentive for him to carry on. Nobody will want to be killed but many people will like to pay 500,000 naira which is nothing out of their profit"

Policy maker 3, male, line 333-336

"You know the laws are not stringent enough. They are not deterrent enough; anybody can do anything, he knows he will just pay his way and continue"

Policy maker 4, male, line 46-47

Aside lack of stringent laws that will deter people from going into medicine counterfeiting, concerns were also expressed by some of the policy makers on the lack of enforcement of the existing laws as described below;

"We have some beautiful laws against faking and adulteration of drugs. We have the NAFDAC decree 25 of 1999 which is now an act of Parliament that talks about if you give a drug of questionable quality what should happen to you, how your things will be confiscated, how you will be jailed. You also have the Pharmacists' Council law amended now that talks about if you handle fake drugs what should happen. We also have the NDLEA law that talks about if you are found with a fake drug or narcotic drug what will happen to you. But are they applied? As serious as those laws are, they are not even applied".

Policy maker 2, male, line 207-213

6.5.1.3 Difficulty tracing counterfeiters

Another issue perceived as contributory to the existence of poor quality medicines and as a hindrance to curbing the problem of counterfeiting is difficulty locating or tracing counterfeiters as pointed out by some of the medicine sellers. This is because most of them do not have a physical address as described by some of the participants below. In most cases where medicines counterfeiting have been uncovered, it is usually discovered that they were produced in people's houses or where other products are manufactured.

"Some of them they are still in the field of producing fake but they are hidden somehow, they don't have address so because of that they can hardly trace them"

Patent medicine vendor 1, female, line 43-44

"The hindrances may be that most of these people they have no shops. They just have packing shop where they keep them so it is not all the time they will detect them. They are not in the open places like this"

Patent medicine vendor 5, male, line 68-70

6.5.1.3.1 Inadequate knowledge of pharmacy graduates

Concerns were raised about the quality of pharmacists been graduated from the schools of pharmacy in the country. Some of the participants; mainly the patients and drug market traders felt that recent pharmacy graduates are not prepared enough to handle cases in the real world as described by some of the participants below.

"There are too many schools of pharmacy in this country where half baked pharmacists are turned out. National University Commission should not accredit universities that do not have good teachers, good laboratories, good

research laboratories and researchers and there must be constant check of those institutions"

Patent 1, male, line 126-130

"You say you are a pharmacy student and the situation in Nigeria is that there are so many pharmacists today that do not even know much about the drugs themselves and yet they are in pharmacy school. Many of them will graduate and they bring them to pharmacy stores and they will not even know the drugs"

Trader 6, male, line 94-97

6.5.1.3.2 Shortage of pharmacists

Another issue raised by some of the participants (the patients and traders) is the lack of pharmacists to cater for the drug needs of the Nigerian population. Pharmacists are still limited in number and are often more in the urban areas than the rural areas. This leads to people seeking other ways of meeting their drug needs and in the process may be exposed to the dangers of medicines counterfeiting as described below;

"So that is another thing. These chemist operators are now plenty but what we call pharmacies, pharmacy shops is where we go and get drugs and before you can get a well certified pharmacy around, you have to transport yourself a distance so you just go anywhere you see around to get the drugs"

Patient 4, male, line 122-124

"When University of Nigeria is the only University in the whole south-east that is producing pharmacists, the question is how far can such a kind of thing go? So you can see that the shortage of the pharmacists is so much that it will require the proper organisation, proper planning for them to fight away fakes"

Trader 6, male, line 188-192

Another reason given by some of the patent medicine vendors is that pharmacists engage in “register and go” where they give their certificates for registration but are not always present in the outlets to oversee what goes on as described below. No pharmacist commented on this.

“In fact what they do in Nigeria is that they give their certificates and register the shops. When you come you think it is a registered pharmacist that is there but it is not. Most people go there for treatment but they really don’t know the combination to give. That is the problem. They think anybody there is a pharmacist, a doctor or a nurse”

Patent medicine vendor 3, female, line 136-140

6.5.1.3.3 Greed

Greediness is also a major cause of poor quality medicines noted by participants in all the stakeholders groups as exemplified by the comments below. This is because greed can make manufacturers to reduce the quality of medicines in order to make more money.

“Some are greedy of money. Some will have that money to produce a genuine drug but because they want to make more money, they go to China they go there tell them to do Paracetamol or Gresolvin. They say the one that is normal 250mg, they say do it 125mg and they will write it 250mg. That is greediness in order to make money.

Trader 4, male, line 46-49

6.5.1.3.4 Existence of open drug markets

Most of the stakeholders in the policy makers' and community pharmacists' groups stated that the conditions in the open drug market, which presently is a major source of medicines is not adequate for storage of medicines. Storage and marketing of medicines in these open drug market may therefore lead to degradation of such medicines as described below;

" The market system essentially does not provide the right condition for storage of medicines anywhere they are because they are shanties. They are not made for medicines' storage"

Policy maker, male, line 82-83

Some of the community pharmacists expressed concern that the existence of the open drug market is a major contributor to the existence of poor quality medicines and suggested that they should be closed down or at best be restructured and controlled by pharmacists as shown by some of the comments below;

"There is nothing anybody can do to stop faking. So clean up the system; close the markets and then set up monitoring and control systems. That is all"

Community pharmacist 6, male, line 373-374

"Why must we have drug markets and if at all we should have something of such, it supposed to be controlled by pharmacists"

Community pharmacist 8, male, line 68-69

None of the patent medicine vendors and the traders discussed any issues relating to the closure or restructuring of the open drug market.

6.5.1.3.5 Lack of commitment by the pharmaceutical industries

Another point raised is the lack of commitment by the pharmaceutical companies in terms of monitoring their medicines when it is in the distribution chain to ensure that it passes through the right channels. With the exception of the patent medicine vendors, the majority of the stakeholders (community pharmacists, policy makers and the traders) interviewed expressed the view that the pharmaceutical industries are mainly motivated by the profit they will make rather than ensuring the health of the public through ensuring their

medicines are not exposed to counterfeiting as described below. This means that majority of the companies may prefer to sell their medicines to whoever can afford to pay them the huge amount of money they need irrespective of whether they are knowledgeable enough to handle medicines, resulting in most of medicines been channelled through the open drug market where business men with enough capital can buy them.

"Even the industry must show concern to what happens to their product when it is out of the factory. In Nigeria, it is not their business. Once it leaves the factory, somebody comes and pays 10 million to them, it can go to Idumota. It can go to under the sun. It is not their business but it should be their business"

Policy maker 2, male, line 219-223

"The companies can't depend on pharmacies that are 30 sq. meter apart in Victoria Island. What quantity of drug can you sell for them? A distributor can afford to spend twenty million naira, thirty million naira buying up one drug and controlling market price. They are those controlling market price"

Trader 1, female, line 227-230

6.5.1.3.6 Porous borders

Porous borders were viewed by participants in the policymaking group as one of the main reasons for the existence of poor quality medicines as described below. A problem noted is lack of adherence of importers of medicines to designated ports through which medicines can be brought into the country.

" There are certain ports that were designated for certain drugs in this country. I think Kano and Lagos and one other one but today what of Warri? People can bring in anything through anywhere. All you need to do is to bribe the custom. The ship goes there and offloads everything in the night. Is head of state there? Is Akunyili there? Is NAFDAC DG there?"

Policy maker 2, male, line 243-247

In addition to this, the volume of the goods that pass through the ports coupled with inadequate staffing of the regulatory agencies, which are tasked with verifying the authenticity of all medicines coming into Nigeria, may make co-ordination of quality verification difficult. This creates a situation where medicines of poor quality can pass through without being noticed as stated below.

" The manifest will tell you it contains this, how can you be opening every carton? Where do you mobilise staff to do that. So they can come under different framed labels and packages and it happens. It is not easy to get them"

Policy maker 3, male, line 172-174

6.5.1.3.7 Global warming

Global warming was noted by one of the policy makers as a cause of medicine deterioration, resulting in substandard medicines as described below. This is because global warming will make medicines to be stored at temperatures usually higher than their recommended storage temperature.

"Then with the substandard products the biggest natural thing is global warming. Most of these medicines were produced to be stable at room temperature of 25 degrees, now the room temperature has risen to 30-35 degrees around here, so you find there are many products that get deteriorated easily because of increase in temperature"

Policy maker 4, male, line 51-54

6.5.1.3.8 Poor government financing

Most of the participants across all the stakeholder groups attributed the continued existence of poor quality medicines to lack of adequate capacity by NAFDAC to handle the enormous task of monitoring the quality of medicines as

described below. This lack of capacity is in terms of poor staffing and lack of funds to carry out its tasks.

"You know government funding is dwindling instead of increasing because costs are rising and we don't have much in grants to meet these costs and you know for regulation to do anything you have to pay 100%. Yes, but if there is more money there are some things we can do. A big challenge is financing"

Policy maker 4, male, line 261-269

"*Yes, I know that NAFDAC have been doing their best. The only thing is that they don't have enough manpower. They don't have enough hands that to go round and check. They don't have enough hands and money to do those things"*

Trader 6, male, line 200-202

6.5.1.3.9 Lack of co-operation among stakeholders

Almost all the traders in the open drug market that were interviewed expressed concern about the lack of co-operation by other stakeholders especially the pharmacists as described below. They (the traders) felt that this lack of co-operation has resulted in only little success being made in curbing the problem of poor quality medicines. They felt that there is need for the community pharmacists to co-operate with them (the traders) as they are also major stakeholders in medicines distribution. By doing so, better ways of curbing medicines counterfeiting can be explored.

"They (pharmacists) are not cooperative; the people are not cooperative but whether you like or not Idumota has come to stay. If they don't like Idumota they should go to hell. We have extended our hands of friendship to them many times but they are treating us like bunch of moneybags that don't know

anything. I think these pharmacists should think very well. They have to swallow their pride, let us discuss and see how these things can be tackled"

Trader 3, male, line 227-231

"But instead of that they (the Pharmacists' Council) will like us to get out from the place (the drug market) just because we are not pharmacists and because of that they are not just winning the battle. We don't have enough pharmacists and people must continue to buy drugs so in a situation like that, what do you do?"

Trader 6, male, line 163-168

This view is contrary to the views of most of the community pharmacists who stated that the existence of the open drug market was a major impediment to tackling poor quality medicines and as such advocated that such markets should be closed down.

6.5.1.4 Reasons for the perceived reduction in the prevalence of poor quality medicines in Nigeria

Some of the reasons noted for the perceived reduction of the incidence of poor quality medicines in Nigeria by the majority of the participants are adoption of technological solutions, increased involvement of pharmacists in medicines distribution, establishment of NAFDAC, routine inspection of the outlets by NAFDAC, effective stakeholder collaboration and awareness creation by NAFDAC**.** Table 29 below shows that awareness creation was a major reason stated by majority of the participants for the perceived reduction in the prevalence of poor quality medicines. Awareness creation stated by the participants included mainly awareness by NAFDAC. Few of the participants also applauded awareness creation by the Pharmaceutical Society of Nigeria and the pharmaceutical industries. Establishment of NAFDAC and its active role in monitioring and inspection of medicines and/ outlets and the industries

were also largely recognised by the participants as a major reason for the possible reduction in the prevalence of poor quality medicines.

Table 29: Reasons for the perceived reduction in the prevalence of poor quality medicines in Nigeria

Reason	Number of respondents
Adoption of technological solutions	6
Increased involvement of pharmacists	4
Establishment of NAFDAC	29
Inspections by the drug regulatory agencies	29
Effective stakeholder collaboration	4
Awareness creation	35

6.5.1.4.1 Adoption of technological solutions

One of the reasons for the perceived reduction in the incidence of poor quality medicines in Nigeria is adoption of technological solutions such as MAS as described below. This is because such technological solutions may make it difficult for counterfeiters to copy medicines. Participants in all the stakeholder groups expressed this view.

"Now it is this scratch card. So these are things that you know made it a little more difficult for those who go to copy. I know that they may come with something later but at least for now, this scratch card something has put so many of them at bay"

Community pharmacist 7, male, line 136-138

6.5.1.4.2 Increased involvement of pharmacists

Some (4) of the participants in the medicine seller group stated that the perceived reduction in the incidence of poor quality medicines may be due to increased involvement of pharmacists both at the individual and at organisational levels when compared to previous years when counterfeiting was very high. They felt that many pharmacists now go into retailing and distribution of medicines unlike before when mainly non-pharmacists controlled the drug business in Nigeria. At the organisational level, majority of the participants also noted the increased involvement of pharmacy associations such as the Pharmaceutical Society of Nigeria and the Association of Community Pharmacists of Nigeria (ACPN) in activities geared towards reduction of the incidence of poor quality medicines. Interestingly, the open drug market traders shared this view as well. This shows the important role pharmacists can play in tackling the problem of poor quality medicines.

"It is decreasing because before we didn't really have pharmacists opening premises or having premises. It was just all these Igbo boys that trade. They train their boys to know medicines even those that don't know about the drugs but now we have pharmacists, more pharmacists opening their own premises and it is being registered so they won't want to spoil their name. So they have to get good quality drugs so I think that one is trying to push out fake drugs"

Community pharmacist 2, female, line 91-96

"If you look at years back we didn't have so many retail shops. Really the non-pharmacists were those controlling drug business but now that you have more of the pharmacists. Right now in Lagos you can boast of 3, 4 pharmacists that are distributors."

Trader 1, female, line 446-449

"And then the Association of Community Pharmacists of Nigeria (ACPN) is now more active. They do monthly meetings. Pharmacists are beginning to meet regularly. It is like pharmacists woke up and said that this profession will not be taken up by people that will be abusing it, so they are now more involved"

Trader 1, female, line 210-213

6.5.1.4.3 Establishment of NAFDAC

Most of the participants in all the stakeholder groups stated that the establishment of NAFDAC might have contributed positively towards the reduction of the incidence of poor quality medicines in Nigeria as described below. This is because establishing a regulatory body like NAFDAC helps to ensure monitoring of drug quality. It also gives the body opportunity to raise funds to help tackle the problem of poor quality medicines as stated by some of the participants below;

"Well, first of all is the establishment of NAFDAC in itself because before there was no NAFDAC at all so the establishment of NAFDAC itself removes bureaucracy, creates autonomy and makes it more open to better financing because they can now raise some funds for themselves and they can use it to build the capacity "

Policy maker 4, male, line 68-71

6.5.1.4.4 Inspections by the drug regulatory agencies

Another reason why the incidence of poor quality medicines in Nigeria may have reduced according to some of the medicine sellers and policy makers is the routine inspection of outlets and pharmaceutical companies by NAFDAC as part of post-market surveillance. This is described below by some of the participants.

"Then I think another thing is this regular routine check that they (NAFDAC) does yearly or quarterly. They visit shops unannounced and close them up when they see things that they feel are not proper"

Trader 1, female, line 186-189

6.5.1.4.5 Effective stakeholder collaboration

Collaboration among stakeholders in medicines distribution in Nigeria may have contributed in reducing the problem of poor quality medicines in Nigeria. This includes inter-agency collaboration for instance NAFDAC collaborating with Pharmacists' Council of Nigeria, the trade unions, customs, National Drug Law Enforcement Agency and the police.

The policy makers stated that collaboration of NAFDAC with bodies such as the Pharmacists' Council of Nigeria, customs, police and the Consumer Protection Council through the federal taskforce may have helped curb the problem of poor quality medicines better as illustrated below. Such collaboration should help pool expertise against poor quality medicines.

"One thing that we (NAFDAC) have done is to try to build an effective collaboration and we have really worked with all the other agencies that are related in this, we brought customs, we brought police. We brought the Pharmacists Council of Nigeria, we brought the Consumer Protection Council, we brought all others together into the Federal task force"

Policy maker 4, male, line 79-92

Similarly, the market traders also felt that the formation of a taskforce, which collaborates with the police and NAFDAC within the market, has helped reduce the problem. This is because through the taskforce, anyone involved in the manufacture and sale of poor quality medicines within the drug market can be reported as stated below;

"Inside our market, we have a task force that connects with police and NAFDAC. If they catch you with fake drug and may be you are powerful, it is their work now to hand you over to the police. Police together with the association will then transfer you to NAFDAC or they will even give you a day on which they will call NAFDAC. NAFDAC will come with police and pick you up"

Trader 4, male, line 83, 86-90

6.5.1.4.6 Awareness creation

Almost all the participants stated that creation of awareness by NAFDAC and other agencies might have contributed positively in reducing the incidence of poor quality medicines in Nigeria. The majority of the participants applauded enlightenment campaigns that help them differentiate between good quality medicines and medicines of poor quality as described below.

"Before I don't know which one is fake and which one is original but since the enlightenment by NAFDAC has come I know the counterfeit. That is the impact of the enlightenment campaign"

Patient 9, male, line 56-58

"Every year they enlighten us. They have something like conference. We had it again I think 3 weeks ago. At times it will be NAFDAC, at times it will be National Drug Law Enforcement Agency. So because of that a lot of people now started to know what fake drug is and the implications of fake drug. All these things make me say that it is coming down"

Trader 4, male, line 69-75

"Awareness is created by NAFDAC. For instance, may be if there is a fake they will televise it, they will publicise that this one is fake drug, don't use it, and don't buy it because it's fake. They will show you what will make you to know that those drugs are fake. The criteria may be on the pack, the fake is like this, the original is like this. At least it is an awareness to know that so and so has fake now. So when you are going to buy it, you will be at an alert"

Patient 11, female, line 124-129

6.5.1.5 Perception of generic and innovator/branded medicines

Eighty percent of the pharmacists interviewed perceived the generic medicines as being inferior or of lower quality when compared to the innovator brands. As such this may have contributed in making some of them have a preference for innovator branded medicines when making recommendations to patients unless in situations where the patient specifically requested for a generic or cheaper

version when he cannot afford the more expensive innovator. This is described below by some of the participants;

"If the innovator branded ones are may be 90% efficacious the generics may be in the range of 80%. So if a disease is severe, you don't encourage the use of generics rather you go for the branded one. You can use generics for all these other minor issues"

Community pharmacist 3, male, 319-321

"A number of them (the generics) fall short of the label potency and standard qualities that the particular product should have. You see a lot of impurities that measures sometimes up to 20-40% and that is why the innovator branded ones are more expensive than the other ones (the generics), which don't spend anything on details. They just cut the product; go straight to active ingredient not minding the other products that should stabilise the product and market as well. So it is cheaper but the branded ones in many cases work better"

Community pharmacist 6, male, line 104-111

This view expressed by the community pharmacists was very similar to the perception of some of the consumers who stated explicitly that they will prefer to buy well known brands as shown from the comment below;

"I think about the company, the brand name of the medicine. If it is a well known brand, I can go for it"

Patient 11, female, 87-88

Consumers tended to trust advice they received from their doctors more than that of other health care providers such as the pharmacists. They seemed to be influenced more by their doctor rather than their pharmacist or medicine seller when choosing between generic and innovator branded medicines. Most consumers/patients in this study stated that they will only accept that their pharmacist should change their medicines to generic versions at the point of

sale if it was recommended by their doctor as shown below;

“I will not buy it at that time. I will go back to my doctor and say this is what I saw. I stick to their guideline because I think they know best”

Patient 4, male, line 17-18

“For me, personally anyone the doctor prescribes for me, if I can afford it, I go for that particular one. I don’t like changing prescription”

Patient 12, male, line 77-78

“I cannot agree for a pharmacist to change it. I have to see my doctor”

Patient 7, male, not tape-recorded

6.5.1.6 Perceived quality of locally manufactured medicines

An overwhelming majority (85%) of the participants seemed to see locally manufactured medicines as good quality and comparable to imported medicines in terms of their potency and in some cases may even be better. This view was shared across all the stakeholder groups as described below;

"Alabukun, though a local drug, is highly potent. It is the best analgesic after a hectic day especially for those of us that work in the sun. You might just use one sachet like this and you will be ok. I’m just telling you. You know I just told you that London panadol is very efficient so I’m now saying on the converse that there are some local drugs here that are equally good"

Patient 10, male, line 125-129

"If you look through my stock very well, 90% of what I stock are the ones produced locally. Yes, they are good. I mean definitely they will be good now"

Community pharmacist 8, male, line 389-390

However, many of the participants stated that despite their perceiving locally made medicines as being of good quality, their poor packing and aesthetics is a challenge and may contribute in make them prone to counterfeiting as noted below.

"It works just that they can easily fake it even though it works"

"There is nothing special about the packaging. You don't have to go an extra mile to do the drug. I don't know about the ingredients or the constituents but you can do it anyhow, print it out, and pack it. So there is no special packing"

Community pharmacist 2, female, line 377, 378-380

"Honestly they (locally manufactured medicines) are good but I think that their challenge has been that of poor packaging. Their poor packaging has been a challenge. They've not been able to take care of the drug. At times you have them capping stuff but in terms of potency, our local manufacturers are not doing bad"

Community pharmacist 3, male, 268-271

One of the reasons why some of the participants thought that locally manufactured medicines may be better in quality when compared to imported medicines was because they believe that most of the medicines of poor quality may be more common among imported medicines which may not be properly monitored during manufacture due to the distance barrier (that is the distance between Nigeria and their place of manufacture). This may make NAFDAC not to send representatives to where they are manufactured to monitor how they are produced unlike the local drug manufacturers whose activities are closely monitored by NAFDAC as described below;

"It (locally manufactured medicines) is good because they know that if they don't produce standard quality then their company will be closed immediately. Everybody knows where it is, both NAFDAC and Police"

Trader 4, male, line 191, 193-195

Another reason could be due to the fact that the local manufacturers can easily be contacted if any quality issues are discovered as stated by some of the participants below;

"The quality of the ones produced in Nigeria is still the best. Why I said it is the best is that if anything happens we go to them and they are closer to us.

Trader 2, male, line 161-162

Another reason could be that the imported medicines are more likely to deteriorate due to the impact of high temperatures and shipping conditions when compared to medicines that are locally manufactured as described by some of the participants illustrated below;

"It (imported medicines) can stay 2 to 3 months due to the distance from say China or India where most of them come from and you don't know how it is packaged along the way and you don't know if it is under pressure. So it is expected that the quality will be dropping unlike the one made in Nigeria here"

Trader 3, male, 240-243

6.5.1.7 What medicine sellers should do to reduce the existence of poor quality medicines

Getting medicines from reliable sources such as from the manufacturers, proper education and training and formation of task force against poor quality medicines were identified as key ways medicine sellers can tackle poor quality medicines as described by some of the participants.

6.5.1.7.1 Getting medicines from a reliable source

Most of the participants from the medicine seller group felt that poor quality medicines can be reduced if those that sell medicines get their medicines from reputable channels such as getting the medicines directly from the pharmaceutical companies or through their medical representatives as described below. This will help to ensure that any counterfeit medicines encountered are easily traced.

"Like I said, I don't just buy from anybody. Why not get it directly from the company that is importing or manufacturing the drug. By so doing, at least you can be sure if the medicine is a genuine product"

Community pharmacist 1, female, line 265-267

"They (medicine sellers) should be getting their drugs from the company directly or from their medical representatives. That will help. By the time 2 or 3 people have complained about a particular drug, you trace the invoice or get the medical representative and complain"

Community pharmacist 2, female, line 164-166

6.5.1.7.2 Education/training

All the stakeholders expressed the need for medicine sellers to be educated on drug quality so that they can be able to distinguish between good and poor quality medicine. Those involved in selling medicines such as the patent medicine vendors and the traders should have some basic knowledge about drugs. This knowledge can be obtained through undergoing training and also getting some practice experience from hospitals as described below.

"So those people (medicine sellers) should go for training or if such people that they cannot handle come they should refer them to the general hospital or to a professional who knows how to handle such"

Patent medicine vendor 3, female, line 148-150

"So if they (medicine sellers that are not professionals) can to a certain extent go to have some knowledge. May be not to come and study medicine in the university if they think it will take a longer time for them, but at least they should try to practice. Sometimes they should go to hospital to practice for a number of years and then they would know medicines better"

Patient 4, male, line 126-134

6.6 The successes and challenges that may arise in the implementation of the Mobile Authentication Service (MAS)

This section of my thesis presents the results looking at the successes and challenges that may arise during the implementation of MAS. In order to identify the successes and challenges which may arise in the implementation of MAS, it is important to understand factors which the participants perceived may be a barrier to the use of MAS and what factors they thought may encourage them to use MAS.

6.6.1 Barriers/facilitators to MAS use

As part of the interviews, participants were asked factors that they perceive may be a barrier or potential barrier in the implementation and expansion of MAS and what they thought may encourage them to use MAS. Several themes relating to the barriers/facilitators to the use of the Mobile Authentication Service emerged. This section describes the subthemes relating to the barriers and facilitators to the use of MAS as described by the participants.

6.6.1.1 Perceived barriers to MAS use

Constructs which arose from the interview and were perceived as possible barrier to the use of MAS include issues relating to cost, low level of awareness about MAS, time related issues, lack of consumer education by medicine sellers, trust in source of medicine, complacency to MAS use, confidentiality of product use data/information arising from MAS, dispensing practices in the rural areas and in the hospital and poor phone netwrok. These are presented below.

6.6.1.1.1 Cost issues

Cost was one of the issues explored, as increase in cost of medicines may present a barrier to MAS use. Cost is one of the constructs of the theory of perceived risk; a model which can be used in the prediction of new technologies. Issues relating to cost explored encompassed participants' perception of the impact of the perceived cost of the service. The scenarios below illustrate participants' perception of the impact of the cost irrespective of whether they were right or wrong.

There was disagreement among the participants as to the impact increase in cost of medicines as a result of MAS may have on the use of the service. Some of the community pharmacists were of the view that if there is significant increase in cost of medicines as a result of MAS introduction, consumers may no more purchase such medicines as described below;

"It is basically the cost that I can think of right now. Because if it is too much on the high side, people may even frown at it that why? How much are we earning that I will be spending so much on medicines. You know the way Nigerians think now"

Community pharmacist 1, female, line 360-363

One participant described the impact cost may have on the use of MAS and was of the view that MAS seems to be for the "middle and high class" as described below. This portrays the fact that most of the MAS enabled medicines are high cost brands from multinationals rather than cheaper versions such as generics or locally manufactured medicines that may be more affordable to majority of Nigerians especially those on low income.

"If the cost of medicines increase as a result of this MAS, they won't even buy that drug again. It will just be the rich that are using it. Even the drugs we are talking about, it is the people of high class or let us say average and high class that are using it. No low class patient will come and use Ampiclox®"

Community pharmacist 2, female, line 237-239

The views expressed by these participants on the impact cost may have on the use of MAS show that any increase in cost of medicines as a result of the implementation of MAS may not only hinder consumers from using the service but may also affect their decision to use or not to use the service. This is in line with the impact of perceived risk of an innovation on the behavioural intention to use the innovation. In this case, cost may be perceived as a risk by the users and therefore, as a possible barrier to their use of the service. It is also important that careful attention should be paid to the medicines enrolled in the service so that all categories of persons (both the low and high income earners) can benefit from the service. This means that systems should be put in place to encourage and ensure that generic medicines which are mostly patronised by the relatively low-income earners (or "low class patient" as mentioned by community pharmacist 2 above) in the society are enrolled in the service.

Contrary to the views already described above, some community pharmacists were of the view that despite increase in cost, people will still buy the MAS-enabled medicines as described below;

"If you are receiving a service then you should be ready to pay. Nothing is free more or less. So if it is a service that is rendered to improve quality of a drug and avoiding unnecessary faking, why not? People would not mind to pay so I will still encourage people to buy it"

Community pharmacist 3, male, line 396-399

"Of course they will buy. What matters is if it is original not just the money. You should be sure of what you are taking. Do you understand? When you are sure of what you are selling, if it is original they will buy"

Community pharmacist 4, female, line 125-127

"It is a bit more expensive, but many people feel they are safe with it. They don't mind the extra cost, so I don't think it (cost) is a hindrance to them. They will rather have that than buy substandard"

Community pharmacist 5, female, line 128-129

The community pharmacists above who expressed the view that despite any increase in cost of medicines as a result of MAS that consumers will still buy the MAS enabled medicines seemed to think of the increase in cost in comparison to any possible harmful effect the consumers may be exposed to as a result of purchasing medicines that are of poor quality. In which case they felt that consumers would still prefer to get medicines at a higher cost provided they are safe to use.

All the patients who were interviewed about MAS felt that they will still buy MAS enabled medicines despite any increase in cost due to MAS. One of the participants stated that he will still buy them as there are no other options for him as described below;

"You have no choice. Like some of the medicines we are now taking, we have been told unless you have miracle healing that you will continue drinking it for

as long as you live. If your life is dependent on a drug; you don't have a choice no matter the price, you have no choice. I was looking for option. I prefer to diet than to drink medicine but then I found out there is nothing you can do, you must drink your medicine"

Patient 9, male, line 111-115

This view expressed by most patients may have been due to the fact that most of the patients interviewed were those who came to the hospital and as such they may constitute a group of patients who are more careful about their health, financially more buoyant and ready to spend more on their health than an average Nigerian just as one of them noted below;

"As for me, I don't really care, even if they increase the price, so far as it is good for my health and the doctor tells me to buy, I will buy it. May be because I have the money. Anyway, I don't know of others but I will still buy it"

Patient 14, male, line 44-46

It may also have been affected by the fact that participants were recruited from Lagos, so may be more enlightened when compared to those in the rural areas of Nigeria or other regions like the northen Nigeria who may hold a different opinion.

Irrespective of participants' perception of the impact cost may have on the use of the service, satisfactory views were expressed by some of the medicine sellers on how they felt about the service being free as shown below;

"it is free, such information you won't be charged; that's the good thing about it. They won't remove a kobo from your handset. That is for you to really know how convenient they have really made it for the end users of those products. It is text free. Infact, I think it's ok"

Community pharmacist 3, male, line 456-458

"They (the patients) are all excited especially as they are not removing money because it is free, so there is no need for them to complain"

Patent Medicine 2, male, line 439-440

From the statements above, you can deduce that these participants seemed to be satisfied with the service since it is provided free of charge to the users. This may help promote the use of the service. Sproxil (the innovator of this service provides it free to the consumers while the pharmaceutical companies bear the cost of the text message). Participants expressed divided views at to whether the introduction of MAS has caused increase in the cost of MAS enabled medicines even though MAS users are not charged for using the service. Those who perceived that there is an increase in cost as a result of MAS seemed to perceive it as an indirect cost added to the cost of the medicines rather than a direct cost to the consumers for specifically using the service.

6.6.1.1.2 MAS awareness

17 out of the 38 participants (6 community pharmacists, 2 patent medicine vendors, 3 policy makers and 6 traders) perceived the awareness level to be low and a possible barrier to the use of MAS as described in some of the scenarios below;

"They (the consumers) are not really aware of it. So most of them will ask you if it is recharge card. Yes someone has asked me if it is real recharge card, so I think that may be they should just enlighten people about it especially those that have it on their product. They should let them know what it is".

Community pharmacist 4, female, line 186-188

"Yes, it is there but they have not actually done a lot of awareness creaton. They have not let the people know what it is all about. About 80-90% of Nigerians do not even know that it exists"

Trader 6, male, line 37-38

On the contrary, only few (three) participants felt that people are aware of the service for the medicines that have the scratch card as stated below. The other participants did not comment on the awareness of MAS.

"Yes a lot of people are aware of it, for those drugs that have it"

Community pharmacist 5, female, line 92

"Many people are aware of it now because everybody that uses Ampiclox®, everybody that buys Ampiclox® know that it is there"

Patent medicine vendor, male, line 479-480

"They always see it now. It is on the pack they are buying so naturally they will know that that particular product has scratch card so whenever they come to buy they always ask for that one".

Trader 3, male, line 124-125

From the views of these participants above, it seems that a major setback to the introduction of MAS is the low level of awareness of the public on the existence and use of MAS. Therefore, the pharmaceutical companies, medicine sellers and NAFDAC should adopt more efficient systems of awareness creation so as to the make the public aware of the service and the need to verify the authenticity of the medicines they purchase.

6.6.1.1.3 Time issues and MAS

Time was another construct that was explored as a possible barrier to MAS use. This is because if participants feel that they need to commit some of their time to be able to use the service, this may make them not to use the service.

Time constraints were perceived by some of the participants as a barrier to the use of MAS. Most of the medicine sellers stated that people might not have the time to use MAS as described below;

"*People don't have time to do that, you understand what I am saying? Many people just rush in and say I want to buy Ampiclox® and they rush out"*

Community pharmacist 2, female, line 208-209

"There are people who don't even have the time, many people are not even having the time. That is the issue. They say look at just scratching, scratching"

Community pharmacist 7, male, line 419-421

"You see people may want to text but they may not have all that time. They should be encouraging people to use it and to know about it because some of our people don't have that time that when they buy medicine they begin to scratch"

Trader 5, male, 169-171

Similarly, one of the policy makers expressed concerns that the medicine sellers may not have the time to wait for the consumers to confirm the authenticity of their medicines due to large number of people they may have waiting to be attended to as described below;

"Even the Mobile Authentication Service has problems that we have identified. A patient has about 5 medicines in his prescription list and you've told the person to go to the pharmacy, buy the drugs and stand in one corner and begin to send text messages through to someone else. Then the person selling medicine will wait for him. Will he pay before he begins to scratch or the seller will wait for him to text or call? Will he certify his medicine is genuine before he pays? He has 3 items on that prescription and he has four other people waiting for him. So those are challenges I shared with the group that came here and I think the pharmacists should be able to authenticate the medicines themselves"

Also time wasted due to delay in getting responses to the text message authentication may discourage people from using the service. Few of the medicine sellers stated that they have experienced delays in getting responses when they tried authenticating their medicines as described below. This delay may be linked to poor phone network rather than inefficiency of the MAS provider; Sproxil. However, this experience may discourage them from using the service even if they have the time to authenticate their medicines.

"I have tried but actually the response from those manufacturers have not always been immediate. I scratch, try to call but the response have not always been immediate".

Trader 6, male, line 16-17

"It's ok but you know at times even network problem. I have an experience with it, I think I texted up to 3 or 4 times before I heard from them so that is the challenge.

Trader 3, male, line 71-72

None of the consumers interviewed stated that time was a constraint to their use of the service.

6.6.1.1.4 Education of consumers by medicine sellers

Whether medicine sellers educate consumers about MAS was a variable that was explored during the interview as this may have an impact on consumer use of the service. If consumers are educated about MAS, that may increase their awareness of the service and may make them to use the service. Most medicine sellers acknowledged that they do not tell their clients about the service as described below;

"People are not aware. The community pharmacy where I worked, the hand bills they gave us we threw it away, they don't like putting papers on their desk. We didn't show anybody".

Community pharmacist 2, female, line 255-256

"No, I won't lie I don't really tell anyone about MAS. Like what we are doing now I think we will start telling them now"

Community pharmacist 4, female, line 380-381

Some of the medicine sellers felt that it is not their responsibility to create awareness about MAS. Rather the company should be responsible for creating awareness about MAS as illustrated below;

"I don't have any business explaining that. I think it is the company's business to explain to people that they have scratch card on their products except if someone buys it and sees it and asks me. I will say yes it has scratch card"

Trader 3, male, line 136-138

6.6.1.1.5 Trust in source of medicines

Trust was a theme that arose throughout the interview. Contrary to popularly held beliefs that people may likely use MAS because of lack of trust they have for medicines obtained from outlets including the pharmacies in Nigeria, it was perceived as a barrier to MAS use by most of the medicine sellers and consumers that were interviewed. This is because they may see confirming the authenticity of the medicines through the MAS as unnecessary if they trust that they cannot get poor quality medicines from where they obtain their medicines from as described below. Almost all the pharmacists expressed this view.

"Usually because most of them trust what I sell to them, they tell me there is no problem, they know there won't be a problem with it. May be they may just try it but most of them just don't bother"

Community pharmacist 5, female, line 267-268

"Well nobody has ever come to my premises and used it because they trust that I will give them good medicines. I think that we should not bridge that trust that patients have with their pharmacists. They are like saying that don't trust this man any longer because there is a technology you have to scan in front of him and ensure that something he sells is genuine"

Community pharmacist 2, female, line 210-214

This view was also shared among the consumers as described by one of the them below;

"I don't check anything. I don't worry about quality of drugs. I know quite well that the university hospital pharmacy will not give me fake drugs because they know they will be compounding my problems"

Patient 1, male, line 32-34

6.6.1.1.6 Complacency to MAS use

In addition to trust in where people obtain their medicines being a barrier to the use of MAS, some participants felt that trust in the tag itself rather that the use of MAS may make consumers not to go on to verify the authenticity of their medicines. This is a significant factor that may considerably affect continued use of MAS. This is because Sproxil may in the long run limit its success despite reducing the incidence of counterfeit medicines because consumers may at some point become complacent to the use of MAS. This will mean that most consumers may make their judgements on the authenticity of their medicines based on previous feedbacks they have received from Sproxil as they will think there is no need to send the authentication message every time. About 2 participants in the patient category interviewed were not aware they needed to check the authenticity of their medicines at each purchase. They felt that if they have ever checked it, then that was enough as noted below;

"I check with them to know if it is original, I have checked it once and that is ok. I don't send it every time I purchase Glucophage®. I did it the first time and I am ok or am I supposed to keep scratching and sending every time?"

Patient 3, female, line 41-43

"I use Glucophage® and I see those things on it, anyone that is good they can write such a thing, you know it is real. I remove it and just laugh. I can't be wasting my credit when the tag is already on it"

Patient 7, male, interview not tape-recorded

From the statement above, it seems that these patients may judge the authenticity of subsequent Glucophage® they buy based on the response they received the first time they authenticated Glucophage® or merely by seeing the tag on the medicines. One community pharmacist interviewed seemed to echo the same view as described below;

"More than 50% or 60% don't even bother to open it. You get what I'm saying. Once they look and see it (the tag), they are ok"

Community pharmacist 7, male, line 424-425

This perceived attitude of consumers seeing medicines with the scratch cards as authentic without texting to confirm may be a serious setback to MAS use because counterfeiters may attach fake codes to medicines that are not original and consumers will buy them simply because they think it bears the mark of quality.

6.6.1.1.7 Confidentiality of product use information arising from MAS

One of the policy makers was of the view that an issue that may arise as a challenge in the implementation of MAS is how the information obtained about different medicines from different companies can be kept confidential. He described the lapses that may be obtained if the information is either domiciled with the drug regulatory authority (NAFDAC) or the service providers (Sproxil) as described below;

"The only challenge could be on confidentiality of information and because you have to limit the information you give. Who keeps the database is the question? If it is NAFDAC for example who keeps the database, then fine but if it is the person who provides the service that keeps the database that means he is availed of the database of the various companies. How do you control that information? This is from a regulatory perspective; that could be the only problem and it is a surmountable problem. The database, all the servers can be domiciled within NAFDAC but how well can NAFDAC keep that because the person who provided the domain is someone who wants to make money and he will not want to play with it. Do you understand? He will prefer to keep his servers and secure it so that nobody copies anything of his and things like that. But he is keeping somebody's information. This is something that we are now still trying to resolve"

Policy maker 4, male, line 165-175

It is important that this issue of confidentiality is given due consideration as it can lead to information about different companies being improperly handled. It is important that laws relating to data protection are strictly followed by those that are in charge of such information.

6.6.1.1.8 Dispensing practices in rural areas and hospitals

Even though the service was perceived as being easy to use because it is compatible to the use of mobile phones, the majority of community pharmacists felt that the dispensing practice in rural areas where incomplete medicine doses can be purchased in loose forms rather than in their original packaging as stated below may hinder its use. This practice may not support the use of MAS because the consumers may not be able to access the authentication tags that are usually on the original packaging as described below;

"*It will be good assuming all the people are given their medicine in original packets because if is in a rural area where they dispose the capsules one by one not as should be taken, then it will not work. This is because if someone buys one or two capsules he may not remember to ask for the pin to send"*

Community pharmacist 6, male, line 211-213

Similarly, some pharmacists interviewed pointed out that the dispensing practices in some hospitals may not support the use of MAS as described below. This is because most of the hospitals unlike the pharmacies do not give out medicines in their original container. Their usual practice is to remove the medicines from their original packaging that contain the code for MAS authentication and repackage them in hospital dispensing envelopes without the name of the drug before giving them to patients. In this case, it means that authentication is left only in the hands of the medicine sellers rather than the final consumer as intended by the MAS service providers.

"You know another thing is that if they are getting from the pharmacies it is ok, but if they are getting from the hospitals, most hospitals will not give you the sachets. They will rather remove it and put in nylons so you will not know what they are giving you. So how do they verify?

Community pharmacist 5, female, line 314-317

6.6.1.1.9 Poor phone network

Sproxil works in collaboration with GSM network providers such as MTN, Glo, Airtel and Etisalat. It is through these networks that MAS users can text and receive responses to the text message authentication. Few of the traders and consumers perceived that the poor availability of poor phone network by these providers might hinder the use of MAS as it can lead to unnecessary delays during the authentication process.

"The only disadvantage is may be delay but it's not their fault. If there is network failure you cannot be able to get the response immediately. That is the only disadvantage I can think of"

Patient 11, female, line 47-49

"Well as for now it is functioning well but it is not everybody that has phone and there may be no phone network, so in rural areas they should extend, extend telephone system because the thing works with phone. If they don't have phone system or network then it is invalid so they must do that in rural areas"

Trader 4, male, line 157-160

6.6.1.2 Facilitators to MAS use

Compatibility of MAS with the use of mobile phone, Ease of use and the quick response to authentication SMS were perceived by the participants as major facilitators to MAS use and the views of the participants are presented below.

6.6.1.2.1 Compatibility of MAS

One of the constructs of the Technology Acceptance Model (TAM), which play a significant role in the adoption of an innovation, is compatibility of the innovation with the norms of the society in which it is being introduced. This is because the more compatible an idea is to the values and norms of a society, the more

easily adoptable it becomes. Some of the participants in all the stakeholder groups were of the view that MAS is used in a similar way to the use of mobile phone text messaging, an attribute which they perceive may facilitate the adoption and use of MAS as described below;

"It helps as in quick action, just take your phone type it immediately. Everybody have phone now so take your phone, type the number and send it immediately from where you bought the medicine, you will know whether what you bought is fake or original"

Patent medicine vendor 2, male, line 415-417

"Yes, well the process is simple and a lot of users of mobile phone can do text message"

Policy maker 3, male, line 297-298

From the perceptions of participants on the use of the service, one can deduce that MAS is compatible in terms of the platform it uses which is "the mobile phone"; a device that is already being used by many for other purposes such as text messaging which can be done by the majority of the people. Hence, no new skills may be required to use the MAS service. These participants seemed to feel that this compatible attribute of MAS makes it easy to use. There is evidence to show that majority of Nigerians have mobile phones for instance the Nigerian Communications Commission (NCC), (2014) reported that Nigeria has a high teledensity of about 92.24% as at April, 2014 and Okoro et al. (2010) found that more than half (66%) of patients with diabetes who attended a diabetic clinic in Nigeria where the study was conducted had active mobile phone lines. As at the beginning of the year 2013, the number of mobile phone subscribers in Nigeria was about 110 million with a market penetration of about 70% (Buddlecomm, 2014).

This seems to show that innovations such as MAS employing the mobile phone network may be relatively easier to use since majority of the people already

have and/ use a mobile phone device. Practices and conditions in some areas such as in rural settings and hospital may indirectly discourage its use in such settings as mentioned by some of the participants above. In order to ensure the widespread use of the service, there should be policies in place to ensure that as much as it is possible that medicines are dispensed in their original packaging. Phone networks should also be extended to the rural areas.

6.6.1.2.2 Ease of use

Ease of use is one of the major constructs of the technology acceptance model. It was part of the variables in the conceptual framework, which was explored in this research. Perceived Ease of Use (PEOU) is the degree to which a person believes that a particular system or technology could be used without effort. It has a direct positive effect on perceived usefulness and on behavioural intention to use (Karaiskos et al., 2007). In other words, if people perceive an innovation to be easy to use, then they are more likely to see such innovations to be useful and will tend to use the service when compared to if they perceived it to be difficult to use. Most of the participants in the entire stakeholder groups interviewed stated that the service is easy to use in terms of the ease of understanding the instructions about using the service and the sending of the text messages as described below;

"I think the hand bill is very very clear. If you read it you will understand, there is nothing so special about the service"

Community pharmacist 2, female, line 254

"It is very easy, the moment you scratch, you key it in and then send and you will get almost an instant answer within a minute."

Patient 9, male, line 83-84

"Very easy because the number is there"

Patient 11, female, line 44

However, one participant stated that she might have perceived it as easy to use because she is enlightened and has time as described below;

"It is not that it is easy to use but it is easy to use for those of us who are enlightened"

Community pharmacist 7, male, line 418-419

This means that while most of the participants in this study may have perceived MAS as easy to use. It is possible that this reflects the views of people who may be more literate rather than that of the entire MAS users in Nigeria.

6.6.1.2.3 Time it takes to respond to text message authentication

One of the major themes that arose during the interviews was the time it takes for the users to get response to their SMS authentication. Most of the participants in all the stakeholder groups stated that responses are received almost immediately as described below. This may therefore be a facilitator to MAS use as it may encourage consumers to use MAS because they know that they will not experience any delay.

"It just takes like 5 minutes. Just working down the road, before you get to where you are going and within 5 minutes you get your reply so I don't think time is a problem"

Community pharmacist 5, female, line 271-272

" You will get almost an instant answer within a minute, the answer will come back ".

Patient 9, male, line 84

6.7 Impact of MAS

This section explored consequences of MAS use in terms of participants' perceived usefulness of the service by looking at the impact or outcome of MAS from the participants' perspectives. Perceived usefulness has been shown as one of the factors that may affect the actual use of an innovation or service based on previous research on adoption of new technologies or services. This means that if users perceive an innovation to be useful, then they are more likely to use it.

Some of the variables relating to the impact of MAS on the purchasing behaviour and health of the consumers expolored are discussed below. By exploring the variables relating to impact of MAS, the perceived usefulness of MAS was revealed.

6.7.1 Change in purchasing behaviour of consumers

In order to determine if the introduction of MAS has affected the purchasing behaviour of consumers, participants in the medicine sellers category were asked whether they have noticed any change in the demand of MAS enabled medicines since the introduction of MAS while participants in the consumer category were asked if the introduction of MAS has made them buy particular MAS enabled medicines. Although none of the consumers interviewed commented on this, some of the medicine sellers believed that the introduction of MAS may have increased demand for MAS- enabled medicines as described below;

"They will tell you they want Beecham with the tag. If we don't have it, they won't buy it"

Community pharmacist 5, male, line 111

"Yes, some people do come and say what of the other one with the card (tag). If you give them medicines that don't have that tag. They will say that these people have not started putting the pin like the other ones?"

Patent medicine vendor 2, male, line 427-429

Now some people when they come in and they don't see that paper, that small leaflet attached, that scratch something, they won't buy"

Trader1, female, line 518-519

One of the policy makers interviewed stated that increase in demand of MAS enabled medicines as a result of MAS introduction can be anticipated mainly because any medicine that is MAS enabled will be promoted as described below;

"Well it is only new, they can anticipate that it will increase demand but what that means is that it is possible because if it has that one, you know it will be promoted more by NAFDAC. Because the company has lunched it, we would talk about it. It is promotion. You know since we are promoting it, it means that one is unique. People will be looking for that unique one and because of that it will improve on the returns of the company"

Policy maker 4, male, line 191-195

This raises a question of whether the introduction of MAS may lead to unnecessary promotion of specific brands over another, thereby presenting the cheaper alternatives which may not be MAS enabled but of good quality as poor quality in the sight of the consumers. This can be detrimental as it may mean that patients will pay higher to get the MAS enabled medicines that may be costlier.

6.7.2 Detection of counterfeit medicines

One of the usefulness of MAS highlighted by participants in all the stakeholder group was that it helps in the detection of counterfeit medicines as described by some participants below.

"It is a good thing because you can easily know that what you are using is the real thing. At least it shows you that what you are using is good"

Community pharmacist 5, female, line 102-103

"This one is directly to the patient. Immediately the patient buys it (medicine), they can easily check and get informed. It is a very good way of identifying good drugs and fake drugs. It is good"

Community pharmacist 8, male, line 163-165

On the contrary, one of the policy makers was of the view that the service in itself does not tell if the product is of good quality as described below;

"It (the MAS) does not say the product is genuine. It cannot! That method of authentication cannot say. It says that look I have recognised this package as the one that somebody has placed a chip on. It doesn't say anything about the quality of the drugs that are in that pack because we demonstrated something. We said; you have your scratch here identifying your product. What if I boil this product or heat this product to a stage where nothing remains as quality in the medicine, the scratch will still remain and people will continue to recognise that product as good. So we cannot stretch that authentication too far"

Policy maker 1, male, line 200-206

The policy maker above was of the view that MAS only confirms if the product is from the genuine manufacturer but does not necessary mean that the product in question is of good quality. The first line of the response given to customers if the product is from the genuine manufacturer is "OK". However in actual terms the product may have degraded and may no longer be suitable for

consumption. This means that relying on MAS alone to determine the quality of medicines may not be full proof, rather further investigations must be conducted in order to determine the actual quality of these medicines being confirmed through MAS as being "OK". Failure of which may mean that consumers are misguided into taking medicines that may be unsuitable even if they are coming from the genuine manufacturers. MAS in essence may not directly ensure that consumers take good quality medicines at all times.

Similar to the views expressed about MAS helping to detect counterfeit medicines, most of the participants in all the stakeholder groups were of the view that MAS may help to reduce faking of medical products as the introduction of MAS may make people patronise MAS-enabled medicines, thereby reducing demand for medicines that are not MAS- enabled which may be fake as shown below*;*

" People look out for that particular thing in that product, once they don't have it they will not buy it and when they don't buy it, those counterfeiters cannot sell"

Community pharmacist 5, female, line 107-108

The introduction of MAS may have also helped reduce faking of medicines because it may instil fear into the counterfeiters as they may think that they can easily be traced from where they were purchased as illustrated below;

"To an extent now, it (MAS) has been able to scare or more or less discourage fakers. At least for Ampiclox®, you hardly see any such faking whereas 2 years ago everybody knows that there were plenty fakes of it but now we are not hearing that because now those scratch tags are on everyone of them. So if they try to fake those cards they can easily be caught"

Community pharmacist 3, male, line 413-417

All the participants who expressed this view felt that MAS can reduce

counterfeiting by discouraging the counterfeiters from manufacturing since they will not bear the tags and people will therefore not patronise them.

6.7.3 Provision of intelligence information about counterfeiting

One of the policy makers also stated that MAS might also provide intelligence for the regulatory bodies, which will also aid detection of medicines counterfeiting as described below;

"It gives you additional information about the product and for you the client you will be able to know from the GSM tracking even where that particular product is located. If there are too many questions coming from one location you will know from the signals where they are coming from. You can now have a suspicion and do extra check in that location because of too many questions that are coming for there. That is the good work with the Mobile Authentication Service, the MAS"

Policy maker 4, male, line 136-142

Although participants in the policy making group were asked how detected counterfeit medicines are handled, they responded generally and made no specific reference to any detection of counterfeit medicines through the use of MAS.

6.7.4 Increased confidence in medicines purchased

Some participants in all the stakeholder groups were of the opinion that the introduction of MAS may have helped to improve patients' confidence in their drugs. The medicine sellers as described below particularly noted this;

" So that gives the patient that confidence to use that drug because they know it is original but when you do not have something like that they keep thinking otherwise, is it real? Is it fake?"

Community pharmacist 4, female, line 116-117

"The thing is that it gives the users more confidence in using the drugs. They are now more comfortable in using the drugs than before because before they will be using it and thinking that maybe it is fake and say let me just be using it but now they know it is the original so they are now more comfortable in using it".

Patent medicine vendor 2, male, line 420-423

Similarly, most of the consumers interviewed stated that MAS has helped them have more confidence in the medicines they take as described by some of them below;

"It is very good. It makes one to feel safe like the medicine you are taking is ok."

Patient 11, female, line 8

"It will make you have a relaxed mind when you take your medicines not doubting if you have taken the bad one, the fake one or something like that"

Patient 9, male, line 76-77

6.7.5 Increased knowledge about state of health

The response given by MAS includes a list of health tips, which depends on the disease for which the medicine is being used to treat. One consumer made reference to this stating that those tips help her to analyse her health status as described below;

"It will make the person to be conscious of his or her health because all those things and tips they give will at least make you to analyse whether you are sound, whether you fit in or not"

Patient 11, female, line 40-41

6.8 How to improve MAS

This section discusses the different ways participants perceived that MAS could be improved. It includes all the suggestions given by participants on actions that could be taken to help improve MAS. Participants were asked how they thought MAS could be improved. One of the major points raised by majority of the participants in all the stakeholder groups was the need to improve the awareness of MAS using more efficient means.

6.8.1 Improved awareness creation

Participants mentioned the need to raise awareness and the best ways they perceived awareness about MAS could be more efficient. One of the ways that was thought by some of the community pharmacists as a more efficient way of creating awareness about MAS is by using different languages to advertise MAS as described below;

"Well like I said, they just need awareness. They need to carry the people along. May be they should go on air. May be teaching people how to use it, say it in their dialect. It is not only learned people that use medicine. Do it in different dialects, different languages, where people will really understand the value. It's not just by them coming to me. Do you understand?"

Community pharmacist 1, female, line 293-297

Some of the medicine sellers were of the view that different means of awareness creation aimed at reaching the masses should be used. Apart from the use of other conventional means of advertising such as through the television, radio and newspapers, one of the points raised was finding a way to reach people through gatherings such as talking or advertising to them during free community health programmes or in religious gatherings such as in the churches or mosques as described below;

"They can organise like community programme, may be free health. That is another gathering that people can actually use to get people together and talk to them about their services"

"They could go to churches, go to mosque. Apart from saying it on air, they can go to where there is like a gathering"

Community pharmacist 1, female, line 377-378, 393-394

"Take the message to churches that is where you will see a lot of people everywhere, may be convention grounds just as what is happening now in the season. Go to camp there you will see a lot of people"

Community pharmacist 6, male line 231-233

"It (awareness) is low so they should create awareness, teaching people may be in church and in mosque, telling people about it"

Trader 5, male, line 174-174

6.8.2 Assistance by government and their agencies

Apart from more effective ways of raising awareness about MAS, some participants were of the view that government has a role to play in the introduction and expansion of MAS. One of the ways some participants thought that government can aid the use of MAS is by off setting the cost of putting the tags on the medicines or the cost of the SMS sent by the consumers which is currently being paid for by the manufacturers as described below. These views were expressed by the medicine sellers and the policy makers. None of the consumers shared this view.

"If only Government can come to their aid, if government can come to the aid of the manufacturers as the cost of putting all those authentication tags is high"

Community pharmacist 1, female, line 370-372

“Government should give some incentives because they are paying 20 kobo for every customer that will make a call. Government should take that bill. I mean behind the scene. That will be a big support to the industry”

Policy maker 2, male, line 148-150

Some medicine sellers and policy makers mentioned the need for government to step in to help create awareness of MAS as described below;

"Even government too, let us not create so much burden on these companies. Government let them come in. At the federal level, at the local government level, at the state level, let the government take the initiative to make sure that people are aware of it.

Community pharmacist 3, male, line 420-435

“To put up an advert on the news is how much? Half a million for one minute, half a million that is what they charge. For 2 minutes, 1 million. That is what they charge. Who wants to spend that kind of money on a product? So those things should be taken in totality if we want to help those companies, I think government has the wherewithal. Either you give them a discount, maximum discount. You say please give them 40% or 50% discount”

Policy maker 2, male, line 186-190

6.8.3 Follow-up evaluation of MAS

One of the policy markers pointed out that there should be follow-up evaluation of MAS by NAFDAC to ensure that MAS remains beneficial to the users as described below;

“The other one is to ensure that there is what we call operation research. That means some research that will follow up the deployment of the MAS to ensure

you now follow up the deployment of the MAS and see if people are even scratching and using it. Are they benefiting from what is introduced and things like that. Go back to the companies, have their market share improved? Are people still counterfeiting their products? You need to know all these. These are things which are not in place at the moment in many of these deployments"

Policy maker 4, male, line 209-215

6.8.4 PIN improvement

Some of the community pharmacists stated the need to reduce the number of digits of the pin number to make it bolder in order to enable customers to easily identify the numbers they are sending as described below;

"If they can reduce the numbers because I think the numbers are up to 12. If they can reduce it to be a little bold so that by the time you scratch it you can still see even if you injure some of the numbers, you can make it out. But if it's too tiny, every small thing you clean it off, every small mistake you clean it off. It is making it a little bit difficult for people to really know that it is the real thing"

Community pharmacist 7, male, line 275-278

The pins are printed and provided by Sproxil but are imported into the country. The counterfeiters can intercept these pins or they can get it from the people who attach these pins to the products. Therefore, it should be ensured that there is a high level of security surrounding the scratch cards that hold the pin numbers so as to prevent them from being accessed by the counterfeiters. In this regard, some traders stated that it may be better for the pin numbers to be imprinted directly on the tablet strips or made tamper proof in order to avoid people removing them and placing on other strips as described below;

"If they can place it directly on the strip, but the way it is presently someone can be able to remove it and put it on another strip. If it is not imprinted on the strips

and they are not putting any stamp on it to say if it is tampered or not tampered, it is just a sticker"

Trader 1, female, line 536-538

"Though it is moving fine but the only thing is they are just placing it on it; if they break the system before they realise it those people would have gone far. They are just placing it there but if they can print it along with the strips it will be better"

Trader 2, male, line 203-205

6.8.5 Network service improvement

One participant stated the need for phone network system to be improved in the rural areas to ensure the use of MAS as described below;

"In rural areas they should extend, extend telephone system because the thing works with phone. If they don't have phone system, it is invalid. So they must do that in those rural areas"

Trader 4, male, line 158-160

6.8.6 Authentication by the pharmacists

One of the policy makers was of the view that it may be better for authentication to be done by the pharmacists as described below;

"I think the pharmacy should be able to authenticate the medicine itself. The regulatory agencies should work with the pharmacists to authenticate"

Policy maker 1, male, line 188-189

6.8.7 Choice of medicines that will be MAS enabled

Even though there was disagreement among the participants as to which medicines should be MAS enabled, the majority of them advocated that MAS should not be for all drugs.

With the exception of the consumers, majority of the participants in all the other stakeholder groups were of the view that MAS should be targeted on medicines that are most likely to be counterfeited rather than all medicines such as expensive and fast moving medicines as described below.

“It is not every drug that people will like to copy or counterfeit. They are looking for those drugs that are in high demand, those that are moving fast and then a little bit expensive. That’s exactly the type of something they should focus on”

Community pharmacist 7, male, line 156-158

"For economic reasons, it cannot be for everything. You know why the companies are doing it is to protect their products. If a product is not at risk of being faked then there is no need"

Policy maker 3, male, line 435-438

"Well if they can introduce it to prescription medicines before they can start putting it on other OTCs, it will be better because prescription medicines are the most important. Most of the prescriptions are expensive and why people fake is that they feel they can go China, fake it, bring it down and sell it at a very cheap price and give it to the people. So that is just that"

Trader 6, male, line 70-74

One of the policy makers advocated that MAS should be focused on medicines that are commonly used, for instance medicines for endemic diseases like malaria as he described below;

“Well, my own is as I said, let us focus on anti-malarials because 60% of those that will visit the hospital or any health facility will have malaria, so let us focus on that because if we can remove that we would have saved millions of people from dying because that means you are sure of what you are giving the children, the neonates”

Policy maker 2, male, line 140-143

Contrary to the views above, some of community pharmacists were of the view that it may be better for all products to be MAS-enabled in order to help boost patients’ confidence in the medicines they take as described below;

"I think it will be better for every tablet. Let’s be sure of what we are taking. Let’s be sure that what we are taking is authentic and not fake"

Community pharmacist 1, female, line 369-370

"Of course now I think it should be placed on every medicine because no drug is small when it comes to diseases. Yes now, ordinary Vasoprin® that is 75mg Aspirin has its function. How much is it sold? About 20 or 30 naira so if you put it on them they will feel it is ok so that is it"

Community pharmacist 8, male, line 198-200

6.9 Conclusion

This chapter presented the findings from the second phase of this research, which involved semi-structured interviews. The findings were organised according to the research objectives. Extensive samples of quotations from participants were included as it is typical with qualitative research. This was done to build confidence of the readers that the views presented accurately represent the reality of the persons and issues studied.

The primary finding of this phase was that is that all the pharmacists and majority of the consumers interviewed perceived innovator branded medicines as better in quality when compared to their generic counterparts. This was deduced from some of the comments they made which implied that generic medicines usually contain less active ingredient or that the innovator brands work better than generics. Also, most of the participants perceived the quality of locally manufactured medicines as comparable to imported medicines or better in some cases in terms of quality.

Majority of the participants perceived that existence of poor quality medicine is still a problem in Nigeria even though they may not have come across medicines they thought are of poor quality. An overwhelming majority (about 90%) of the participants felt that the problem is decreasing mainly because of interventions such as the introduction of technological solutions like MAS, increased involvement of pharmacists in medicines distribution, establishment of NAFDAC, routine inspection of the outlets by NAFDAC, effective stakeholder collaboration and awareness creation by NAFDAC. Many of them went ahead to discuss reasons why Nigeria is still faced with the problem and how they thought medicine sellers could help curb the problem. Some of the factors that were identified as being responsible for the existence of poor quality medicines were high cost of medicines, poverty, corruption, high cost of product registration, low level of local drug manufacturing, ignorance and lack of awareness on how to detect medicines counterfeiting or sourcing medicines, demand surpassing supply, lack of stringent laws, inadequate law enforcement, difficulty tracing counterfeiters, inadequate knowledge of pharmacy graduates, poor availability of pharmacists, greed, existence of open drug markets, lack of commitment by the industries, porous borders, poor government financing, lack of co-operation among stakeholders and global warming.

Furthermore, majority of the participants perceived increase in cost of medicines as a result of MAS, dispensing practices in rural areas and in the

hospitals, poor phone network, lack of time by consumers and medicine sellers, lack of consumer education about MAS, low awareness level about MAS, complacency arising from the use of MAS, trust in source of medicines and the issue of confidentiality of information about use of medicines obtained from MAS service as possible barriers to adoption and use of MAS. On the other hand compatibility of MAS use with other activities such mobile phone usage, ease of use of MAS, and the time taken to respond to the text message authentication were the key factors that were identified that can encourage the use of MAS. Increase in demand of MAS enabled medicines, easier detection of medicines counterfeiting, increased confidence in medicines purchased, increased knowledge about state of health through the tips from the response sent to consumers and increased trust in medicine sellers were the major consequences of using MAS identified from this phase.

Finally, ways identified by the participants through which MAS can be improved includes awareness creation through more effective means, financial assistance by the government and their agencies, conducting follow-up studies to evaluate MAS, improvement in pin for instance reduction in pin number and in printing the pin directly on the tablet strips, improvement in phone network especially in rural areas, allowing pharmacies to authenticate medicines instead of consumers and focusing on medicines that can be easily counterfeited or commonly used.

The next chapter of this thesis will focus on the discussion of some of the key findings of this research and their implications.

Chapter 7

General discussion and implications

7.1 Introduction to chapter

The previous two chapters (chapters 5 and 6) presented the results of the first and second phases of this research. Chapter 6 focused on presenting the findings that arose from the qualitative interviews conducted. This was done by organising data from the interviews with different stakeholder groups into categories to produce a readable narrative. The purpose of this present chapter is to provide interpretive insights into the findings of the 2 phases of this research. It presents a general discussion of the findings and how they relate to existing literature and research in the field of medicine quality as well as the implication of these findings to practice and policy. It starts by showing the extent to which the objectives of the research were met. Following this, the findings are discussed in relation to existing literature in order to see how they support or refute existing knowledge in the area of medicines' quality. The limitations of the research are then presented followed by the researcher's personal reflections about the research. Finally, the practice and policy implications of the findings for different stakeholder groups are discussed.

7.2 Extent to which research objectives were met

This research is the first to validate the use of an anti-counterfeiting technology and explore the perception of a wide range of stakeholders on the use of MAS and the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria.

This research provided data that may serve as a basis for actions, which may help to improve the MAS and quality or medicines distributed in Nigeria. Information contained in this research work can also help for comparisons to be made with future evaluation of MAS. This is the first study that tried to

quantitatively compare the quality of randomly sampled innovator brand of metformin with its generic counterpart; data arising from this is necessary to making recommendation on generic prescribing and the use of medicines in Nigeria.

The key objectives of the research were;

1) To perform a test validation of the Mobile Authentication Service (MAS) by comparing the responses obtained from the service through the SMS authentication conducted with the actual quality of medicines received by the consumers via packaging analysis and experimental/chemical analyses

2) To determine if there are differences in quality between the Glucophage® with the tags and the cheapest generic versions without the tags

3) To examine stakeholder perceptions of the current situation of medicines counterfeiting and quality of medicines distributed in Nigeria

4) To identify the successes and challenges (potential problems) which may arise in MAS implementation

5) Explore the consequences of MAS (on the health and purchasing behaviour of the users)

6) To determine the perceptions of stakeholders on how best MAS can be improved in order to ensure optimum utilization and future expansion of the service

7) Make adequate feedback/recommendation based on the findings of this research towards the successful implementation of the Mobile Authentication Service in Nigeria and reduction of poor quality medicines. This should ultimately promote access to good quality medicines and translate to improved health outcomes.

These objectives were largely met by the results of the findings presented in chapters 5 and 6. The key findings of this research were that;

1) The results of the MAS authentication agree with the packaging and chemical analyses conducted. The Glucophage® samples seem to be original as stated in response to the SMS authentication and of good quality in terms of their packaging and content of active ingredient from the results of the packaging analysis, NIR and HPLC conducted.

2) No differences in quality between the tagged Glucophage® samples and generic metformin could be established via packaging and NIR analysis. However, there seems to be significant differences between the tagged Glucophage® samples and their cheaper generic counterpart (branded and unbranded) with a p value of 0.006. Therefore, the tagged Glucophage® samples seem to be of better quality than some of their generic counterparts.

3) All the participants agreed that the issue of poor quality medicine is a problem in Nigeria. However, only few of the participants seemed to have had an experience with medicines, which they thought, were of poor quality or counterfeit. Among the few participants that have encountered poor quality medicines, the common response was to stop the medicine and/ or return the medicine to where it was purchased instead of reporting it. The factors that were identified as being responsible for the existence of poor quality medicines were high cost of medicines, poverty, corruption, high cost of product registration, low level of local drug manufacturing, ignorance and lack of awareness on how to detect medicines counterfeiting or proper sourcing of medicines, demand surpassing supply, lack of stringent laws, inadequate law enforcement, difficulty tracing counterfeiters, inadequate knowledge of pharmacy graduates, shortage of pharmacists, greed, existence of open drug markets, lack of commitment by the industries, porous borders, poor government financing, lack of co-operation among stakeholders, poor NAFDAC financing and global warming.

An overwhelming majority (90%) felt that the problem is decreasing. Some of the reasons given for this decrease were adoption of technological solutions, increased involvement of pharmacists, establishment of NAFDAC, Routine

inspection of the outlets by NAFDAC, effective stakeholder collaboration and awareness creation by NAFDAC. Most of the participants perceived the quality of locally manufactured medicines as comparable to imported medicines or better in some cases in terms of quality. Almost all the pharmacists interviewed perceived innovator branded medicines as better in quality when compared to their generic counterparts. Obtaining medicines from reliable sources, proper education and training and formation of task force against poor quality medicines were the key ways identified through which those involved in selling medicine can help tackle the existence of poor quality medicines

4) Possible increase in cost of medicines as a result of MAS, dispensing practices in rural areas and in the hospitals, low level of mobile phone ownership and poor phone network especially in rural areas, lack of time by consumers and medicine sellers, lack of consumer education about MAS, low awareness level, complacency arising from the use of MAS, trust in source of medicines and the issue of confidentiality of information about use of medicines obtained from MAS service use were identified as possible barriers to adoption and use of MAS. Compatibility of MAS use with other activities such mobile phone usage, ease of use of MAS, and the limited response time were the key factors that were identified that can encourage the use of MAS.

5) Increased demand of MAS enabled medicines, easier detection of medicines counterfeiting, increased confidence in medicines purchased, increased knowledge about state of health through the tips from the response sent to consumers, increased trust in medicine sellers were the impact or consequences of MAS use identified from the semi-structured interviews conducted.

6) Awareness creation through more effective means, financial assistance by the government and their agencies, follow-up evaluation of MAS, improvement in pin for instance reduction in pin number and in printing the pin directly on the

tablet strips, improvement in phone network, allowing pharmacists to authenticate medicines instead of consumers and focusing on medicines that can be easily counterfeited or medicines that are commonly used were the key ways identified by the participants through which MAS can be improved.

7.3 Comparison with literature

7.3.1 Validation of MAS

One of the components of the Cornford et al. (1994) framework is exploring the system performance at the information processing level. This means checking whether the information given through the service in this case is correct and valid. The result of the first phase of this study showed that the result of the SMS authentication agree with the packaging and chemical analyses conducted. This suggests that the responses received from MAS regarding the authenticity of the medicines may be accurate since none of the samples were identified as counterfeit from the packaging analysis and the NIR analysis conducted. Also none of the samples of tagged Glucophage® were identified to be of low quality in terms of the content of active ingredient from the results of the HPLC analysis. The low overall failure rate of samples reported in this study seems to confirm the perceptions of the majority of the participants who agreed that the problem is decreasing as well as recent assertions by NAFDAC that there has been significant reduction in the prevalence of fake medicines in Nigeria by over 80% from what it used to be in 2001 (NAFDAC, 2006). Even though it may not be accurate to compare the findings of this research to previous studies which employed different methodologies and involved sampling and analysis of medicines other than metformin, the small overall percentage of samples that failed quality testing here may also be indicative of an improved situation of quality of medicines in Nigeria when compared to previous studies such as Taylor et al. (2001) and Bate et al. (2008) which found that nearly half of the medicines they analysed failed quality testing. This observation is similar to the findings of Bate and Hess, (2010) which showed

that the total overall failure rate of samples from Lagos that they studied had fallen from about 32% in 2007 to 13% in 2010. It is also similar to some recently conducted large scale studies such as the study by some group of scientists at the London School of Hygiene and Tropical Medicine where just about 3% of the antimalarial medicines sampled from 2 out of 5 African countries studied and Cambodia were found to be falsified (Kaur, 2013).

The extent to which the finding of the percentage of medicines of poor quality in this study and that of large scale studies mentioned above portray the true situation of poor quality medicines is still questionable owing to limitations inherent in these studies and the fact that large amount of counterfeit medicines are still being intercepted by for instance custom officials such as in Angola where about 1.4 million counterfeit antimalaria (Coartem®) sourced from China were discovered to be counterfeit (Faucon et al., 2013). Larger scale studies involving large samples of variety of medicines may help to confirm or disprove these findings, as this study was not powered to detect the extent of poor quality medicines in Nigeria.

That no counterfeits were identified from this study may be indicative that medicines counterfeiting, even though a problem in sub-Saharan African countries like Nigeria with limited regulation and enforcement, a more crucial problem may be the existence of substandard medicines; that is medicines from genuine manufacturers which fail to meet pharmacopeial standards set for them. The findings of this study which showed that there were no counterfeits among the medicines sampled also contradicts previous studies conducted in this area included in the literature review which potray a high extent of medicines counterfeiting. This contradictory finding calls to question the methodology used in arriving at estimates of the extent of medicines counterfeiting by some organisations such as the WHO and PSI among others. It may be that some of the quoted estimates of the extent of medicines counterfeiting are biased depending on whether the researchers want to find or not to find counterfeits rather than its true extent based on adequate

methodology. While medicines counterfeiting will continually be a problem as long as medicines are used, it is important to ensure that its true extent in relation to other inefficiencies that may be hindering access to good quality affordable mediicnes is correctly determined so that that strategies can be appropriately targeted to improve quality of medicines and access to medicines in general.

7.3.2 Quality of generic metformin and innovator brand (Glucophage®)

Another important finding is that there were no differences in quality between the tagged Glucophage® samples and their generic counterparts from the packaging and NIR analysis conducted; however there seemed to be significant differences between their quality in terms of the percentage of active ingredient from the HPLC analysis conducted. The packaging analysis and NIR analysis conducted were to help identify if there were any counterfeit medicines. This indicated that none of the samples (tagged Glucophage® or the generic metformin samples) analysed were counterfeit, however a few of the generics may be of lower quality, having lower concentration of metformin contrary to the BP recommended concentration range for metformin (95-105%). This can be linked to how participants perceived generic medicines in the second phase of this research where the majority of the pharmacists seemed to see generic medicines as being of lower quality.

This perception by a majority of the participants about generics being of lower quality is similar to the findings of other studies conducted in Nigeria and other related countries in Africa. Some of these include; Velasquez et al. (1998), Kaplan et al. (2012), Auta et al. (2014), Patel et al. (2012) and Patel et al. (2009b) which noted the professional and public perception that generic medicines which are cheaper alternatives to innovator brands are of lower

quality than the branded medicines sold by large firms and may have contributed in hindering the use of generic medicines in Nigeria. This situation in Nigeria is very dissimilar to what is obtainable in the developed countries such as the UK, USA, Germany and Denmark where generic prescribing and substitution has been relatively successful. It therefore seems that for generic prescribing and substitution to be successful in Nigeria, there is need for stakeholders to have a change in perception of what generics are and also some level of persuasion led by the government may be needed aside ensuring that the price of generics are affordable. This can also be applicable to other countries that may be in a similar situation as Nigeria such as other countries in sub-Saharan Africa where there is limited acceptance of generic prescribing and substitution.

The finding in this study which show that most community pharmacists see generic medicines as inferior and as such were likely to promote the use of innovator brand Glucophage® based on perceived differences in quality seems to contradict previous surveys conducted to determine the perception of Nigerian pharmacists on generic prescribing and substitution which found that most of the pharmacists would support generic substitution (Auta et al., 2014).

While generic substitution should be viewed as a crucial pharmaceutical care intervention to improve access to good quality, affordable essential medicines, if legislation on generic prescribing and substitution is to be put in place in Nigeria, it is important to ensure that pharmacists' perception of quality of generics do not hinder its practice and that pharmacists have adequate knowledge on what generic medicines are so they can give adequate information to the patients. This is so that it does not lead to confusion and non-adherence as previous research has reported (Oyetunde et al., 2014). This is also in accordance with the recommendation by the WHO working group on access to essential medicines which states that accessibility of medicines encompasses "products that are effective and of consistently good quality, that

have no financial obstacle to a patient receiving it and that have available the knowledge and guidance needed to use them properly" (UN Millenium Project, 2005). This means that for a medicine to be accessible it must be of good quality.

Generic medicines usually become available after the patent expiry of original or innovator brands. They can be unbranded (marketed under the International Non-proprietary Name), semi-branded (marketed under the International Non-proprietary Name with the manufacturer's name) or branded (copies of medicines with their own brand names) (Oyetunde et. al, 2014). They are required to show that they are of the same quality as the innovator brands as part of their registration requirement, so should be interchangeable with the innovator brands. Therefore, the finding from the first phase of this research which showed that there were significant differences between Glucophage® and their generic counterparts is worrying and points to the fact that there is need for proper regulation of generic medicines in Nigeria to ensure that they are of good quality, bioequivalent and interchangeable with their innovator counterparts through enforcing good manufacturing practices by genuine manufacturing companies. It may also be indicative of some deeper inefficiency in medicines regulation in Nigeria due partly to the limited resources available to NAFDAC. This may be associated with the inability of NAFDAC to meet up with the volume of post market drug quality monitoring required of it which may lead to manufacturers not adhering to good manufacturing practices after their products have been approved. If this is the case, then it may be necessary to identify ways by which better quality control and post market surveillance can be ensured by NAFDAC and how assistance can be sought from the Nigerian government and international agencies in areas that it may be less competent as noted in UN Millenium Project, (2005).

The significant difference in quality between the innovator brand and the generic counterparts contradicts the finding by Patel et al. (2012) where no

differences in quality were found between innovator brands and generics (branded and unbranded). This difference in the findings between these 2 studies may be because they were conducted in different countries (Nigeria and South Africa) with different extent of drug quality problem, different medicines were sampled and analysed in the 2 studies (while metformin was analysed in this study, Patel et al. (2012) analysed paracetamol tablets, amoxicillin capsules and hydrochlorothiazide tablets). Other methodological differences such as sample size may have contributed to differences in the findings. Thirty six out of thirty eight randomised controlled trials included in a study which compared generic and branded drugs for the management of heart and artery diseases (Beta blockers, diuretics, statins and warfarin) also showed no significant differences between generic and innovator branded medicines (Bera and Mukherjee, 2012).

7.3.3 Size of the problem of poor quality medicine in Nigeria

The majority of the participants agreed that the issue of poor quality medicines is a problem in Nigeria just as other studies such as Odili et al. (2006), Erhun et al. (2001), Rithenburg (2002), Bate et al. (2009a) and Seiter (2005) found. Similar to Law and Youmans (2011), this study revealed that very few medicine sellers (pharmacists, patent medicine vendors and open drug market traders) have encountered a medicine, which they thought, was of poor quality. However among the few participants in this study that have had an encounter with poor quality medicines the most common reaction was to stop the medicine and/ or return it to where it was purchased. While it is worth researching further to understand the reasons for the low reporting of incidents of poor quality medicine the most common reasons may include fear of the reporter being harassed by enforcement officials or lack of trust in how such cases will be handled based on participants' experience in other areas for instance whether the culprits will be adequately punished or not.

This low reporting rate was also found in Bate et al. (2009a) and also noted by Newton et al. (2010) as one of the reasons why determining the true impact of

medicine counterfeiting has to date proved difficult. It is therefore very important that those who use MAS such as the consumers and medicine sellers are informed of the need to report any cases of counterfeit medicines they may encounter as this can serve as a means of tracking the counterfeiters and help reduce medicines counterfeiting.

The lack of experience with poor quality medicines observed in this study may be due to precautions taken by the participants in ensuring they purchased medicines of good quality or it may be due to difficulty in linking any experiences they have had to poor quality medicines especially when there are possibilities of other causes for in stance if consumers do not respond to treatment, they may not link it directly to poor quality medicines but to other reasons such as inappropriate diagnosis or prescribing.

The finding that the majority of the participants felt that locally manufactured medicines were of good quality is similar to the finding in Auta et al. (2014) where over half of the respondents felt that locally manufactured medicines in Nigeria is of high quality. This perception may contribute in making consumers to patronise locally manufactured medicines and may in return encourage local drug manufacturing. However it is contrary to Bate et al. (2009) where about 75% of those who indicated that they knew manufacturers of fake medicines stated that they were within the country and blamed the existence of poor quality medicines in Nigeria on local drug manufacturers. This finding is also contrary to popularly held view that people in Nigeria tend to trust the quality of imported products more than those that are locally produced. It may be because people tend to view the quality of medicines differently from those of other goods for some reasons. Some of these reasons may include their lack of trust in how imported medicines are regulated and the conditions such medicines have been subjected to before arriving in Nigeria.

The reasons identified as the causes of poor quality medicines in Nigeria is similar to that found in Akinyandenu (2013) and Erhun et al. (2001). The involvement of non-professionals in medicine distribution due to lack of commitment by the pharmaceutical industries is similar to the concerns raised by participants in Garuba et al. (2009). Community pharmacists in the Garuba et al. (2009) study expressed concern that the control of the retail pharmacy by rich business persons who use their wealth and influence to cut corners and sell poor quality medicines while hiring pharmacists for the purpose of obtaining licensure was a major cause for the continued existence of poor quality medicine in Nigeria. Similar to the findings of this research, participants in Garuba et al. (2009) noted that bribery and corruption is a common practice in Nigeria and a major cause of rampant counterfeiting due to difficult living conditions.

The majority of the participants stated that the problem of poor quality medicine in Nigeria is decreasing mainly due to public awareness by NAFDAC. This view about the positive impact of public awareness is an improvement over findings of Erhun et al. (2001), a study conducted at a time when NAFDAC was commencing its reforms. Erhun et al. (2001) found that public awareness on drug matters as at 2001 was below average contrary to this study, which seems to show a high level of awareness of medicines counterfeiting. It is important to note here that awareness created by NAFDAC applauded by most of the participants is awareness about how they can identify counterfeit medicines or differentiate medicines that are of poor quality from good quality medicines for instance showing them differences in packaging or appearance of the medicines and/ publicising list of banned or blacklisted medicines. This is in line with the conclusions from the economic model proposed by Lybecker, (2007) which stated that awareness creation aimed at teaching consumers how to distinguish between fake and genuine pharmaceuticals may be more beneficial than strategies or campaigns that raise awareness of consumers of dangers of counterfeiting. This is because the later may result in fall in the sale of

medicines and may consequently lead to lack of access to good quality medicines.

Furthermore, although this study did not aim at establishing whether there were differences in quality of medicines from the community pharmacies when compared to informal sources such as the patent medicine vendors and the open drug market, The low failure rate from the medicine outlets sampled (community pharmacies and open drug market) and that no counterfeits were obtained from the open drug market indicate a situation contrary to the general perception of most community pharmacists that the drug markets are a major source poor quality medicines especially counterfeit medicines, as they are often not well regulated. This is also contrary to the findings of previous studies such as Onwujekwe et al. (2009), Tipke et al. (2009), Lon et al. (2006) and PSN (2007) where a large proportion of samples sourced from places such as streets and open drug market were discovered to be of poor quality. However, this indication from this research is not conclusive of the nature of quality of medicines obtained from open drug markets unless large scale studies employing random sampling and powered to determine differences in quality of drugs from the open drug market compared to community pharmacies are conducted.

7.3.4 Barriers and facilitators to MAS use

One of the factors that may hinder the use of MAS observed from this research is consumer trust in source of their medicines as most of the consumers interviewed perceived there was no need to authenticate their medicines as they trust the source of their medicines. The majority of the consumers that expressed this view seemed to obtain their medicines from the pharmacies and trusted that those pharmacies will not sell counterfeit medicines to them.

This positive view about the quality of medicines sold in registered pharmaceutical outlets may be partly due to the awareness created by NAFDAC as stated by some of the participants. However, this is contrary to popularly held belief that most consumers in Nigeria would like to authenticate their medicines, as they do not trust that medicines they purchase from private outlets such as the pharmacies and patent medicine shops may be authentic. Some other previous research has obtained similar results. An example is the study by Syhakhang et al. (2004), which found that most of the consumers in Lao PDR interviewed did not worry about the quality of their medicines because they trust that the health professionals (for instance the doctors and pharmacists) will not sell poor quality medicines to them. Trust is a fundamental principle in modern institutions composed of expert systems. This is because it is not possible for members of such institutions to be an expert in every field so they tend to trust that every expert knows his/her field and delivers products and services that are of good quality (Giddens, 1990 in Syhakhang et al. 2004). However, it can be an added advantage if consumers remain alert even when they believe that they cannot get poor quality medicines from their health care providers because consumer alertness can also help reduce medicines counterfeiting.

Authentication complacency that may develop as a result of the users seeing the tags as a mark of quality may lead to such consumers relying on previous response they received to authenticate any medicine they purchase or their seeing any medicine that has the authentication tag as being of good quality even without authenticating them. This can limit the success of MAS as counterfeiters can put tags on medicines that are of poor quality and consumers will patronise them thinking they are original. This means that if the issue of complacency on the part of MAS users is not tackled, it can mean than MAS may indirectly promote counterfeiting in the long run rather than curbing the problem. Awareness creation about MAS should therefore include educating consumers of the need to authenticate their medicines at every purchase and

that the tags on their own do not indicate if the medicines are of good quality until such medicines are authenticated. The low level of awareness about MAS observed in this study is very similar to the findings of Oyetunde and Ilozumba (2013). However this may be because the MAS is relatively a new service.

This study found that most of the participants felt that MAS is easy to use mainly because of how easy they perceived the instructions on how to use MAS is and how easy they perceived the steps in authenticating their medicines. Given the cultural diversity inherent in Nigeria, a country with about 527 languages (Ethnologue, 2011), this view may be applicable to only people who are enlightened and can understand English language. This is because the instructions on how to use MAS and the text message response are both in English. The perceived ease of use (PEOU) of MAS may be a facilitator to its use as PEOU is a major variable in the Technology Acceptance Model, which can positively affect behavioural intention to use a service and consequently lead to use of the service.

7.3.5 Impact/consequences of MAS use

Comparing the findings of this research with the proof of concept result published by Sproxil, it seems that MAS may be beneficial in some ways and can be said to be a good idea based on its benefits. From the proof of concept results published by Sproxil following their pilot study of MAS in 2010, conclusions were made that MAS is a good initiative based on the advantages it confers on the users. For instance similar to the findings of this research, they noted that MAS could help users identify counterfeits and therefore may serve as a way of providing intelligence information for the regulatory agencies who can trace the source of the identified counterfeit medicines. However, it is worrying that this research showed a low reporting rate of incidents of counterfeiting experienced by consumers. This is because consumers may not report cases of counterfeiting they identify from the use of MAS if they do not see the need to do so; meaning that the main objective of MAS which is to reduce the incidence of medicines counterfeiting may not be fully achieved.

The proof of concept result also showed that the introduction of MAS helped Biofem, the distributor of Glucophage® in Nigeria regain its market share (Sproxil, 2010a). This is similar to the perceptions of participants in this study where the majority discussed the influence MAS may have on the purchasing behaviour of consumers by increasing consumer demand for MAS enabled medicines.

Another important consequence of MAS noted by the participants is that MAS increases the confidence consumers have on the medicines they take. This can indirectly promote adherence. This is because if consumers feel that they are taking the right medicines, they will be encouraged to take them as required. This increased adherence can therefore translate to better treatment outcome.

7.4 Limitations of the research

This study determined quality of medicines via packaging analysis and chemical analyses (NIR and HPLC) only. Other quality tests such as dissolution tests were not conducted. More useful result on the quality and bioequivalence of the samples would have been obtained if dissolution studies were carried out in addition to other tablet quality parameters such as uniformity of content, hardness, friability and disintegration tests. Also, inability to conduct further chemometric analysis such as the Principal Component Analysis (PCA) to help accurately identify the counterfeits may also have limited the findings of the NIR analysis. Four of the generic samples could not be analysed using packaging and NIR analysis as no original samples from their manufacturers could be obtained. It is therefore difficult to determine the extent to which not analysing these samples may have affected the conclusions of this study. However, unless they are complex counterfeits, the HPLC analysis, which showed their percentage concentration of metformin, gave an indication that they may likely be genuine samples.

The samples analysed in this study were all obtained from the private sector

(community pharmacies and the open drug market). The findings on the quality of medicines based on this research may therefore be limited as the public sector for example hospitals were excluded. Also, the exclusion of some group of stakeholders such as Sproxil, drug manufacturers, police, customs, importers, wholesalers, doctors and other health professionals from the interviews may have limited the findings of this study. This means that caution must be exercised in extrapolating any findings from this research to the entire Nigerian population, as it is possible that the stakeholders that were not sampled may have held a different perception. However given the time and resources available to complete the PhD and in order to ensure that the study is independent and free of bias, the number of stakeholder groups included in this study seemed feasible. It was also reasonable to sample from only the private rather than the public sector, in order to avoid any problems or risks that may be associated with releasing results of the quality of medicines within the public sector. Also, as samples were collected from Lagos alone, there may be some limitations in extrapolating the findings of this research to other regions of Nigeria given the social-cultural and economic differences that exist between the North and Southern Nigeria (where the samples were collected from)

The original samples to which comparisms were made via packaging and NIR analyses were obtained from the company representatives/distributors rather than directly from the manufacturers. This may limit the findings of these analyses, as it is possible that the original samples collected are not from the genuine manufacturers. Also the small number of each generic metformin product collected may have limited the findings of this research.

Fear that medicines were being sampled for quality testing may have caused some of the medicine sellers to present medicines they thought were of good quality for sale to the sample collectors. This was exhibited by one of the participants who insisted that the sample collector authenticated the medicine he purchased before leaving the shop. In line with this, some participants may not have given responses during the semi-structured interviews that reflect their

true experiences due to the sensitive nature of the topic discussed and the perceived associated risk they may be exposed to by revealing information if they thought that the researcher was linked to NAFDAC. This may be the reason why one of the participants refused to be tape-recorded. Also, some of the participants revealed more information as soon as the tape recorders were switched off and majority of the participants spoke generally about issues raised rather than narrating their individual experiences.

Although attempts were made to conduct the interviews in a quiet place with limited interruptions, most of the participants especially in the consumer and medicine seller group preferred to be interviewed on the spot when they were doing their normal duties for instance while they were in the shop for the medicine sellers and while waiting to see the doctor or to collect their medicines for the consumers. Interviewing participants at these times led to constant interruptions during some of the interviews. These constant interrupts may have limited the flow of the discussions during the semi-structured interviews.

Furthermore, only 3 consumers/patients who have used MAS were interviewed. Although qualitative studies do not aim at ensuring representation of the entire populations but to generate rich descriptions, it would have been better if more people who have used the service were interviewed. This may be an indication that the sampling strategy employed in this study may be inadequate. Therefore, it may have been better to first conduct a survey using questionnaire to help identify those who have used MAS and to help triangulate the findings. The identified users of MAS willing to participate in the semi-structured interview can then be recruited and interviewed. This way, richer descriptions can be obtained from those who have first hand experience with MAS. Also, if focus group interviews were conducted after the semi-structured interviews, it would have helped to confirm the findings from the semi-structured interviews.

7.5 Personal reflections about the research

Reflexivity is a critical concept especially in qualitative research. This is because it is a major effort aimed at addressing the preconceptions researchers unintentionally introduce in their qualitative design in order to ensure the accuracy of qualitative research outcomes (Roller 2012). Having a personal reflection about the research enables the researcher to consider ways his or her relationship with the interviewees or participants have been affected by presumptions arising from those preconceptions (Roller, 2012). This may include reflecting on assumptions the researcher may have made about the participants and their response to the interview questions and how these assumptions influenced the interview process. It also includes how the values, beliefs, life experience and socio-economic status of the researcher may have influenced the analytical process (Roller, 2014). The impact of the research location on the researcher's relationship with the interviewees and the data collection were also be reflected upon.

The researcher believes that her personal characteristics such as her nationality, tribe and professional background may have influenced some of the decisions made during the research process and the outcomes arising from this research. Therefore, she engaged in an on-going critical reflection by keeping a reflexive journal where she noted details of how she or her decisions may have influenced the interview process and data analysis in order to minimise interviewer bias. This journal helped inform the researcher of the possible preconceptions that may have affected the credibility of the outcomes of this research. This section of the thesis presents the personal reflections by the researcher.

Due to the nature of the topic being discussed, the researcher assumed that there might be some difficulty in getting the honest opinion of participants especially the medicine sellers and consumers on issues raised during the

semi-structured interviews. This is because, the nature of the topic being explored; quality of medicines in Nigeria has been an issue of concern especially for NAFDAC and has resulted in the closing down of so many outlets suspected of engaging in production of medicines of poor quality just prior to the commencement of this research. The researcher therefore, envisaged that this might make the participants unwilling to disclose any sensitive information, thereby limiting the credibility of the research. This may be worsened if the researcher sought to obtain information from the participants in groups such as through focus group interviews rather than on an individual basis as the participants may think that other members of the group may report them to NAFDAC even if the researcher does not report them. In order to overcome this difficulty, the researcher obtained data through semi-structured interviews rather than through focus groups. The researcher also prepared to take notes rather then tape recording in case the participants declined being recorded. In addition, the researcher introduced herself to all the participants as a PhD student and a pharmacist but stated explicitly that the interviews were only for research purposes aimed at improving the quality of medicines distributed in Nigeria and as such should not implicate anyone. Even though these steps were taken and a semi-structured interview method was used, some of the experiences of the researcher during the data collection stage showed that some of the participants may still not have disclosed their honest opinions about issues raised due to fear of being reported to regulatory authorities. For instance one of the consumers refused to be tape-recorded, stating that he was an ex-official of the Lagos state government and as such would not want to be implicated by the statements he may make. In this instance the researcher took notes. Also, some of the participants exhibited characteristics that showed that they did not want to take responsibility for giving information that may be incorrect by trying to confirm their views with that of the participants on issues discussed. For instance the participants below asked the researcher if his perception was right;

Doesn't it sound reasonable?

Patient 10, male, line 86

In order to avoid introducing bias, the researcher maintained a neutral stand by not answering such questions; rather the participants were reminded that they were no right or wrong answers.

The researcher also thought that it may be very difficult to recruit the open drug market traders as the open drug market has for a long time been a target for crack down of medicines counterfeiting by the drug regulatory agencies and pharmacists. It may also be difficult to recruit the open drug market traders, as they may not want to talk to the researcher if they find out that she is a pharmacist. This is because the traders often see the pharmacists as enemies who do not want them to thrive in the business of medicines distribution because they are seen as non-professionals as stated explicitly by some of the participants below;

"Even at the level of the Lagos State Pharmacists' Association. They interact with us with a long spoon. They don't want to do anything with anyone who is not a pharmacist"

Trader 3, male, line 57-59

In order to overcome this perceived difficulty of recruiting participants from the open drug market, the researcher sought the help of one of her colleagues who introduced her and the purpose of the research to the traders before they were approached by the researcher to participate in the research. This is because he has worked in the open drug market and was known by most of the traders. This step taken may have reassured the traders that participating in the research will not implicate them or lead to closure of their outlets.

While on the one hand, the researcher being a pharmacist may have posed a problem in obtaining data from groups such as the open drug market traders as discussed above, on another hand it may have aided flow of information during

the interview stage and the collection of information from some of the other participants such as community pharmacists. The researcher explored a topic in which she is not only a researcher, but could also be one of the participants because one of the groups interviewed were the community pharmacists. In addition, the topic explored is a topic of great interest to the researcher who has prior knowledge of medicines distribution and regulation in Nigeria and as such may make her more predisposed to follow discussions in this area with ease. However, this may have led to the researcher unintentionally airing her views about issues raised during the interviews or being judgemental about participants' responses to her interview questions. To overcome this, the researcher as much as possible remained open and believed that it is possible for others to have a different perception of issues. In addition, since the researcher is a pharmacist, the community pharmacists may have perceived the researcher as "one of them". This may have made the community pharmacists to feel more confortable participating in the research thereby facilitating the data collection.

Furthermore, the researcher envisaged that the medicines sellers may present medicines which they thought were of good quality if they suspect they were being sampled for quality testing. In order to overcome this, for each of the outlets, the researcher went with one of the sample collectors to collect the medicines. The sample collector collected the tagged Glucophage® while the researcher collected the cheapest generic metformin. These samples were collected at two different times to avoid any suspicion by the medicine sellers that their medicines were being sampled for testing. Also the sample collectors avoided engaging in further discussions with the medicine sellers to avoid giving any clues that they were collecting the samples for analysis.

Although it may be justifiable to sample only medicines from the private sector for quality testing since about 60-80% of health service provision comes from the private sector and the traditional medicine providers whose activities are

often unregulated and non standardised (DFID HSRC, 2000), the nature of the topic explored in the research may have influenced the decision to sample only medicines from the private sector. This is because the researcher envisaged that she might be exposed to some level of risk if she sampled from the public sector. Also it may be difficult to publish the findings arising from analysis of medicines sampled from the public sector if they are found to fail quality testing. Even though only samples from the private sector were sampled and analysed, some level of caution was exercised in reporting the findings of the analysis conducted and the information given by the participants. For instance, names of the outlets from where metformin samples were obtained were kept anonymous and codes were assigned to the samples. Also the names of the participants who took part in the semi-structured interviews were kept anonymous. Comments by some of the participants as shown below indicate that interested groups may threaten the researcher if such precautions such as maintaining anonymity of brands and companies are not taken while writing up the thesis.

'Well, this one could be an insider information that I am giving you, so you will know how to write it so that they will not come after you"

Trader 1, female, line 219-220

The researcher decided to exclude some other stakeholders such as representatives of Sproxil and the pharmaceutical industry in order to ensure that an independent view of the issues studied are presented. However, this decision may have affected the outcome of the research in that the findings may not portray the perspectives of all the relevant stakeholders in the field of drug quality in Nigeria.

Only participants who can communicate in English were selected for the interviews. This can be justified by the fact that it may be practically impossible to interview non-English speakers given the cultural diversity of Nigeria as it

may mean that the researcher will have to conduct and translate the interviews in many different languages. However this decision to interview only English speakers may have been influenced by the researcher being an English speaker and as such thought to be the most convenient.

Furthermore, there may have been increased willingness to give information to the researcher by some of the participants because of her being a fellow Nigerian. However, this may have contributed some bias to the study through the researcher introducing some preconceived ideas from her experience of being Nigerian into the study in a bid to impress the participants in return. Also, the researcher comes from the Igbo tribe; a tribe in Nigeria popularly perceived as highly involved in the manufacture and sale of poor quality medicines. This may have made the open drug market traders all of which were also Igbos to feel more comfortable speaking to the researcher as shown from the comment from one of the traders below;

"You are my sister, I will help in any way I can because I want you to come out in good colours"

Trader 4, male, line 323-324

This predisposition of the researcher may also have influenced the researcher's analysis of the qualitative data as she may have unintentionally supported the views of the traders.

As previously noted, some of the interview sessions with the patients were often interrupted by the doctors, nurses or pharmacists and noise because most of them preferred to be interviewed while they were waiting to see their doctor or while awaiting collection of their medicines from the pharmacy. This also happened with the medicine sellers who in most cases preferred that interviews be conducted at their place of work and were often interrupted if they needed to attend to patients and by noise as most of the outlets were located close to the

roads. These interruptions may have disrupted the flow of the interviews in these stakeholder categories.

The data collection took place in Lagos. The nature of roads and transportation network in Lagos may have influenced the choice of data collection methods used. For instance, it was more convenient conducting semi-structured interviews rather than focus group interviews where poor transportation network may hinder some participants from attending the focus group interviews. Also the poor transportation network coupled with the large number of pharmacies, which are located far apart from each other, may have delayed the data collection. This is because the sample collectors had to travel long distances to obtain samples from the randomly selected outlets. In order to facilitate easy location of the outlets, the second sample collector recruited for this research was a native Yoruba speaker who has lived in Lagos for a long time and therefore knew the easiest way of getting to different areas of Lagos. Yoruba language is the native language popularly spoken in Lagos.

7.6 Implications of the research findings

The findings of this research have several implications for practice and policy. Here, the discussion on how the findings of this research can lead to change in practice or policy is presented in the form of recommendations at various levels. The recommendations that follow are for;

a) Government and its agencies

b) Sproxil

c) Pharmaceutical industries

d) Pharmacy practice

7.6.1: Implications for policy- Government and its agencies

This research did not identify any counterfeits. While it is worth researching further through larger scale studies to determine the true exent of medicines counterfeiting in Nigeria, that no counterfeits were found may mean that even though medicines counterfeiting is a problem and will remain a problem for as long as people use medicines, it may be important for NAFDAC to evaluate some of the steps being taken to ensure accessibility to good quality medicines that are affordable. It may be worth determining if more efforts should be geared towards startegies that prevent substandard medicines/ improve the quality of medicines from genuine manufacturers such as ensuring good GMP and post market surveillance rather than focusing on initating expensive technological solutions such as the use of MAS and TruScan® aimed at detecting counterfeit medicines, given the very scarce resources at its disposal.

Furthermore, this research showed that majority of the participants viewed locally manufactured medicines as being of good quality and may in some cases be better than imported medicines and that most of the poor quality medicines are imported into the country. This means that some increase in patronage of locally manufactured medicines may be expected at the consumer level. It would therefore be important for government to build upon this by putting in place measures to further encourage local drug manufacturing. Even though there has been improvement in local drug manufacturing for instance there are now about 150 manufacturers in Nigeria when compared to 50 that were present in the 1990's, primary manufacturing is yet to commence in Nigeria (Ohabunwa, 2010). The ambition of the National Drug Policy to increase local production capacity to a level where about 70% of total production can cater for about 60% of local drug needs and the remaining 30% exported to generate revenue is yet to be achieved. In essence, the production capacity is still less than 30% (Erhun etal, 2001). Government should therefore encourage local drug manufacturing by providing manufacturing inducement such as giving tariff concessions to them, increasing their patronage of locally manufactured medicines as well as reducing cost of product registration by NAFDAC.

In addition, it may be beneficial for NAFDAC to intensify monitoring at the ports of entry since most of the poor quality medicines are imported as noted by most of the participants. This may include increasing staff strength and vigilance at the ports of entry of medicines into the country. Other measures such as heavy taxation may help encourage local drug manufacturing and help directly reduce influx of poor quality medicines to Nigeria. Bate and Boateng, (2007) and Raufu, (2003) stated that that the majority of counterfeits come from Asian countries like India and China. However this information may not be accurate as any evidence behind it may be biased by issues relating to the patent right of multinationals in countries such as Europe or America or by the fact that counterfeiters most often do not give accurate information on the country/ place of manufacture on the packaging of medicines thereby leading to misleading conclusions. Therefore, while discouraging importation may help to reduce counterfeiting on the one hand, it may hinder efforts of making good quality generics available on another hand. Therefore, careful consideration of these recommendations based on most pressing health care needs of Nigeria is necessary. Other ways to encourage local manufacturing is to improve local infrastructure such as ensuring electric power supply, good roads and water so as to lower production costs.

Another important finding of this study was that majority of the community pharmacists viewed generic medicines as being inferior in quality when compared to innovator brands. This finding has critical implications for the implementation of generic prescribing and substitution in Nigeria. Although the National Drug Policy of Nigeria advocates generic prescribing and substitution (Federal Ministry of Health, 2003), there is currently no legislation that empowers generic prescribing and substitution. Previous studies have revealed that generic substitution can have enormous benefits of ensuring access to medicines. However if it is not done with proper explanation to the patients, it can lead to confusion and non-adherence (Oyetunde et al., 2014). It is vital that

appropriate policy and guidelines for generic substitution in Nigeria be put in place to ensure accessibility to good quality medicines, which are affordable. However careful implementation of the policy is necessary to avoid causing confusion for the consumers and non-adherence due to ignorance and misconceptions by stakeholders. Education campaigns aimed at enlightening the consumers, pharmacists and prescribers is very necessary for a successful implementation of such policies and has been shown to be successful as noted in Portugal Pharma Profile (2008). As part of strategies to encourage generic prescribing, government should encourage research in quality of prescribing at country level using the ABC analysis method so that appropriate actions can be taken to ensure appropriate prescribing. ABC analysis is the systematic study of annual medicine consumption and cost to determine which items account for the highest amount of expenditure (UN Millenium Project, 2005). Such research will help to show the extent of generic prescribing and reveal more efficient ways to ensure or improve generic prescribing and substitution in Nigeria. Also as the first phase of this study revealed significant difference between the innovator brand; Glucophage® and cheapest generic versions in favour of the innovator brand, it would be important for government and its agencies such as NAFDAC to ensure proper monitoring of generic medicines for generic prescribing and substitution to yield optimum result. Government should therefore provide financial support to NAFDAC in the area of staffing, GMP inspection, quality control laboratories, enforcement and post market surveillance. Drug regulatory agencies like NAFDAC should also seek assistance from international organisations in drug quality assurance/monitoring in areas it may be less competent. NAFDAC should also find ways to make registration of medicines quicker, easier and cheaper. This will encourage importers of medicines and local drug manufacturers to register their products so that their quality can be ensured. It will also help to avoid situations where unregistered medicines are distributed illegally prior to registration with NAFDAC, exposing consumers to medicines that may be of poor quality.

Corruption ranked first in this research as a cause of the continued existence of poor quality medicines. Therefore, there should be increased political will by the government to tackle corruption and enforce legislation and regulation of pharmaceutical products. This means that the law enforcement agencies such as the Nigerian Drug Law Enforcement Agency (NDLEA) must become committed to its enforcement of existing laws against medicines counterfeiting rather than allowing "business to go as usual". There is need for more deterrent laws against medicines counterfeiting. Presently the maximum punishment for offenders is the sum of 70- 3000 US dollars or 3 months- 5 years jail term (Chika et al., 2011). This was perceived as an incentive by most of the participants in this study rather than a deterrent. The present bill advocated by the Director General of NAFDAC, Dr Paul Orhii for a life jail term and confiscation of assets upon conviction and compensation of victims where injury has been caused should be passed into law.

Furthermore, ignorance no doubt is a huge challenge and contributory to existence of poor quality medicines in Nigeria. This is because of low literacy rate (61% adult literacy rate) in Nigeria (US Embassy in Nigeria, 2014). This means that a large proportion of the adult population of Nigeria are unable to read and write. Government should seek cheaper and more effective means of curbing medicines counterfeiting for instance through public awareness programmes. This public awareness should not be left to NAFDAC alone but done in collaboration with other agencies and professional associations such as the Pharmaceutical Society of Nigeria and the National Medical Association. Public health media campaign against medicines counterfeiting by NAFDAC, which was applauded by majority of the participants in this study as one of the reasons for the perceived reduction of the existence of poor quality medicines in Nigeria, should continue. However it may be better if such campaigns focused on avenues to make consumers or medicine users differentiate between counterfeit and genuine medicines. As previously noted, Lybecker, (2007) noted that the most useful form of awareness campaigns are those that help

consumers to distinguish between fake and genuine pharmaceuticals rather than campaigns that raise awareness of the dangers of medicines counterfeiting which may lead to decrease in sale of medicines and reduction in access to medicines. As part of awareness creation, NAFDAC should continue to publish a list of medicines that are banned through their website and other media platforms to help reduce consumer demand for such products.

Also, increased involvement of pharmacists was one of the reasons given by participants as the reason for perceived reduction in existence of poor quality medicines in Nigeria, government should therefore provide incentives/financial support through giving low interest loans to pharmacists wishing to go into production or community pharmacy practice as a way of further increasing the involvement of professionals like pharmacists in medicines supply and distribution in Nigeria.

NAFDAC has been actively involved in promotion of MAS. MAS is part of the technological solutions which can help patients differentiate between counterfeit and genuine medicines and as such expected to be useful in helping to reduce medicines counterfeiting. The finding of this research indicates that MAS has relatively been successful in helping patients authenticate their medicines. However, it is important that it does not lead to lack of trust in health care professionals like pharmacists as stated by some of the participants in this study. It is also important to note that MAS is not immune to hacking and so there is need to continually evaluate the service to ensure that there is no infiltration by the counterfeiters and that it remains useful to its users. MAS also may be limited by computer and technological illiteracy, complexity of language in Nigeria, lack of awareness, poor phone network, dispensing practices in rural areas and in the hospitals among other issues. Therefore, policies that may help overcome some of these limitations such as policies that help promote dispensing of medicines in their original packaging and enforcing rights of consumers knowing the medicines they are being given can be promoted. In

addition, other techniques that allow only medicine sellers to authenticate medicines such as the use of RFID technology may yield additional benefit of improving trust consumers/patients have in their medicine sellers leading to better outcomes. However, this may be expensive. Hence, cheaper techniques of detection that do not need the use of additional devices such as holograms or colour shift inks may also need to be explored and promoted by the government. As previously noted, aside promotion of the use of these technological solutions, strategies aimed at promoting Good Manufacturing Practice by the pharmaceutical industries should be promoted by NAFDAC as susbstandard medicines may present a greater challenge than counterfeits as this study indicates.

Even though MAS service is free to consumers, pharmaceutical industries pay for it. It is therefore necessary for government to partner with companies in order to help offset or supplement the cost burden of MAS on these industries so as to ensure that cost of medicines are not increased as a result of MAS. This is especially useful for local manufacturers that are faced with the problem of high cost of production given the infrastructural challenge of erratic power supply, water supply and bad roads. Any increment in cost of medicines as a result of introduction of MAS will in the long run lead to lack of access to medicines if consumers are unable to afford them.

Finally, government and its agencies such as NAFDAC should be increasingly involved in the promotion of MAS in terms of creating awareness about it and not leaving it only in the hands of the manufacturers. Presently the level of awareness about MAS seems to be low as shown in this study. It may be helpful if government can offset the cost of advertising MAS on the media. However, there is need to ensure that such awareness creation do not lead to unnecessarily promotion of medicines as this may lead to increased attractiveness of such products for counterfeiting, thereby limiting the success of MAS.

7.6.2 Implications for practice- Sproxil

1) Although Sproxil has the ambition of expanding beyond the pharmaceuticals and has ventured into authenticating medicines from different therapeutic classes ranging from anti-malarials to antibiotics and antifungals, it may be better to focus on drugs that are prone to being counterfeiting such as fast moving and expensive medicines and medicines commonly used in the country for instance medicines for endemic diseases like malaria. This may yield more useful benefit than trying to make all medicines MAS enabled at the same time. This is in line with the suggestion by a group of Massachusetts Institute of Technology (MIT) students (Dedesma et al., 2011). This will also enable Sproxil determine how well MAS works before expanding into other areas. Further expansion can then be based on the disease prevalence and prevalence of poor quality medicines for those diseases so that the majority of the population can benefit from the service.

2) There is need for awareness of MAS to be created through various mass education means and medicine sellers should be encouraged to educate patients about MAS. The kind of MAS education advocated for by participants in this study includes educating consumers in their native dialects and during gatherings such as in the church, mosque or free community health programs in addition to other conventional means of creating awareness such as through devices like radio, television and newspapers. This study found that there is limited involvement of medicine sellers in consumer education about MAS. Therefore there is need for Sproxil to collaborate with NAFDAC and the medicine sellers so that the medicine sellers can be trained on the use of MAS and on the need to teach patients/ consumers about MAS. While awareness creation is crucial for the expansion of MAS, there is need to ensure that this does not lead to unnecessary product promotion. This is because product promotion will indirectly make MAS enabled medicines attractive to

counterfeiters and in turn limit its success. Also educating consumers on the need to authenticate their medicines at each purchase is necessary to avoid development of complacency, which may limit the use of MAS.

3) There is need for Sproxil to build upon some of the facilitators and positive impact of MAS use identified from this study such as quick response to authentication. This was one of the points noted by majority of the participants as a factor that will encourage the use of the service. Therefore it is important for Sproxil and the network service providers to ensure good phone network availability so as to avoid unnecessary delays in responding to MAS users.

The perceived usefulness of MAS was described by some of the participants in the form of impact of MAS on their purchasing behaviour and increased knowledge about their state of health from additional health tips contained in the authentication response message. This means that it will be good for Sproxil to continue to give those additional health tips. Increased demand of MAS enabled medicines since the roll out of MAS is an indication that companies that had their products counterfeited in the past, who have signed up for MAS may be regaining their market share back- a major objective of Sproxil. This usefulness attribute may attract other drug industries to sign up for the service.

4) There is need for Sproxil to consider imprinting the codes directly on medicine packages (primary and secondary packaging) instead of placing the cards with the codes on tablet strips. Doing this will enable those who sell medicines to authenticate them before they are sold. However, it may require adequate collaboration with the pharmaceutical industries to ensure that the codes/pin numbers can be printed directly on the packaging during product manufacturing. Sproxil can also consider making the pin numbers bolder or reducing the pin numbers in order to avoid customers mistakenly sending wrong authentication codes/ pin numbers because they were not legible enough.

7.6.3 Implications for practice: pharmaceutical industries

1) Even though majority of the participants in the medicine seller group stated they sourced their medicines from places that they consider reputable such as obtaining directly from the companies, through the medical representatives or wholesalers so believed the medicines they stock should be of good quality. This may be deceitful as some manufacturers/ wholesalers may be distributing their medicines through the open market as noted by some of the participants or through unregulated sources as noted in Spies (2003) and Law and Youmans (2011). Pharmaceutical industries should therefore ensure that their medicines are properly monitored by their surveillance departments while they are in circulation so as to ensure they are not channelled in such a way that they degrade or are exposed to counterfeiting because of their interest in making more sales rather than protecting the public from the dangers of poor quality medicines.

2) Even though the majority of the participants perceived the quality of locally manufactured medicines to be of good quality when compared to imported medicines, poor packaging of locally manufactured medicines was one of the issues raised by some of the participants which may make counterfeiting them easy. Therefore, there is need for local drug manufacturers to improve on aesthetics of their products such as product packaging. This will also ensure that they are attractive to users so as to increase their patronage both by individuals and by the government.

3) The findings of this study that there is a significant difference between the innovator brand, Glucophage® and generic metformin samples may be due to several reasons. However it indicates that there is need for genuine drug manufacturers to ensure good manufacturing practice to improve quality of medicines. There is also need for pharmaceutical industries to ensure that they

continue to manufacture good quality medicines that meet recommended specification even after their medicines have been approved.

4) Pharmaceutical industries should put measures in place to ensure that there are no situations of artificial scarcity of their products or unnecessary “out of stock”, so as not to create room for counterfeiters to go into producing such medicines to meet the demand for such products.

7.6.4 Implications for pharmacy practice

1) Pharmacists and other medicine sellers should properly counsel patients on how to detect and avoid counterfeit medicines. They should also educate consumers on how to use MAS as well as report cases of medicines counterfeiting or adverse drug reaction to NAFDAC. Advocacy materials to increase awareness of substandard and counterfeit medicines and how to report detected cases should be provided by the Pharmaceutical Society of Nigeria and made available through the retail drug outlets. This is because reporting cases of counterfeiting or poor quality medicines can help provide intelligence information to crack down counterfeiting. It can also help to provide information on how best poor quality medicines can be tackled and to avert negative consequences of poor quality medicines

2) Given the limited availability of pharmacists compared to the high demand for medicines in Nigeria, it is necessary for pharmacists to co-operate with the informal drug traders (patent medicine vendors and open drug market traders) for instance in the area of providing education and training to them on drug quality and dialoguing with them and/ their associations to see how to minimise the existence of poor quality medicines. This is one of the recommendations by some of the informal traders who seemed to dislike the attitude of the pharmacists towards them. This will ensure that good quality essential

medicines that are affordable are accessible to the public. It may also be helpful to identify ways the open drug markets can be re-structured to meet the standard regulations for good storage of medicines and engaging the Pharmacists' Council of Nigeria in monitoring and regulating how such markets should operate. In addition to this, the licencing of the patent medicine vendors can be replaced with the Accredited Drug Dispensing Outlet (ADDO) system used in Tanzania where NAFDAC can train and accredit small, privately run retail outlets by non-pharmacists to sell a list of essential medicines including some prescription drugs in the rural and poor communities.

3) Basic training in pharmacology and rational medicines use should be provided to informal medicine sellers such as PMVs and traders while continuing professional development (CPD) programmes should be implemented for pharmacists where it does not currently exist. These programs should contain talks on how to differentiate medicines of poor quality from genuine ones as well as tools and resources that they can use to educate patients on medicines counterfeiting and MAS. These trainings should be co-ordinated by the professional regulatory bodies such as the Pharmacists Council of Nigeria (PCN) and the National Medical Association (NMA) in collaboration with the drug regulatory authority, NAFDAC. All those involved in selling medicines should also be encouraged to subscribe to NAFDAC for updates on drug quality issues in the country.

4) Undergraduate pharmacy students and colleges of pharmacy should be encouraged to learn more about medicines quality and participate in activities geared towards reduction of medicines counterfeiting and poor quality medicines as a whole. As a practical step to educating undergraduate pharmacy students on drug quality, there should be a period of mandatory industrial training during the course of their training to become pharmacists. This will help give them first hand experience of what is obtainable in practice. Concepts such as generic prescribing and substitution should be included in

undergraduate pharmacy curriculum and that of other professionals like the nurses and doctors.

5) There is need for health workers involved with dispensing medicines in hospitals and rural areas such as pharmacists and pharmacy staff to ensure that medicines are dispensed in their original packaging so that patients can authenticate their medicines if they want to do so. This practice should also be advocated as a policy in the hospital settings as it will also help to ensure that patients become aware of the medicines they are taking. This will also help to promote adherence.

6) Precautionary steps taken by some of the participants in this study to avoid purchasing poor quality medicines should be promoted by professional associations such as the Pharmaceutical Society of Nigeria. These precautionary steps include sourcing medicines from reputable sources such as from the manufacturers or their distributors by the medicine sellers and for the consumers; obtaining medicines from registered pharmacies, checking the packaging and the appearance of medicines purchased for any differences which may indicate they may be counterfeit and cross checking the authenticity of medicines purchased with health care professionals such as the doctors. However it is important that the health care professionals do not unduly promote innovator brands as medicines of good quality.

7) The Pharmacists' Council of Nigeria should ensure that retail pharmacy outlets are owned by pharmacists. They should find efficient ways of monitoring to ensure that pharmacists are always present at their premises. This will help ensure that pharmacists do not give out their licences to non-professionals so as to obtain licensure while they take on other jobs.

8) As a way of increasing involvement of pharmacists in medicines distribution, the Pharmacists' Council of Nigeria in collaboration with the National

Universities Commission should consider opening more schools of pharmacy. This may help increase the number of pharmacists in Nigeria.

7.7 Conclusion

This chapter presented the discussion of the findings arising from the first (analysis of metformin samples) and the second (qualitative interviews) phases of this research. It shows that the objectives of this research were met. The findings were compared with information from existing literature. Following this, the researcher's personal reflections about the research were presented. Finally, the implications of the findings of this research for practice and policy were presented in the form of recommendations for different stakeholder groups in the field of medicines quality in Nigeria. This included Sproxil, the innovator of MAS, the pharmaceutical industries, the pharmacists and other medicine sellers as well as the government and its agencies. The next chapter is devoted to presenting future areas of research identified during the course of this study and the final conclusions of this study.

Chapter 8

Recommendations for future research and conclusions

8.1 Introduction to chapter

This chapter presents research areas that may be explored in the future and conclusions arising from the present study.

8.2 Recommendations for future research

During the course of this research, other areas in the field of medicines quality, which may need further research were identified and are discussed below.

No counterfeits were identified from this study and this calls to question the true extent of medicines counterfeiting in relation to other inefficiencies which may be hindering access to good quality medicines especially in resource limited settings such as Nigeria. Therefore, there is need for large scale studies aimed at determining the extent of medicines counterfeiting in comparison with the problem of substandard medicines in order to determine which interventions will be most useful in improving quality of medicines available in Nigeria. This is because strategies aimed at tackling substandard medicines; that is medicines from genuine manufacturers without any criminal intent is different from those aimed at tackling medicines counterfeiting where the medicines are intentionally produced with the aim of deceit. If the problem of substandard medicines is greater as this present study indicates, it may be worthwhile investing more in implementing strategies that will ensure good manufacturing practices by genuine manufacturers.

Also, this study was conducted in Lagos. It would therefore be useful to replicate this study in other settings in Nigeria for instance a state in the

Northern Nigeria given the socio-economic differences that exist between the North and South of Nigeria (where this study was conducted) and/ or sampling medicines from other therapeutic classes where there have been reports of high incidence of counterfeiting like the antimalarials and the antibiotics. Also, larger scale studies involving large sample size of innovator medicines and their generic counterparts can be conducted to help compare the quality of innovator brands and generic medicines. These would help to show the extent to which the findings of this research may apply to other settings. It will also help further inform policies on generic prescribing and substitution in Nigeria.

This study showed low failure rates for the samples from the community pharmacies and the open drug market but was not powered to detect differences in quality between them. It would therefore be useful to conduct further research to detect differences in quality of medicines obtained from informal sources such as the patent medicine vendors and the open drug market traders in comparison with the quality of medicines from the community pharmacies. This would help to determine the major sources of poor quality medicines, so that adequate strategies can be put in place. It would also help to generate evidence towards restructuring medicines distribution in Nigeria.

Furthermore, this study compared the quality of the innovator brand with that of their generic counterparts via packaging and chemical (NIR and HPLC) analyses. It is important to note that these tests/ analytical techniques conducted gave indications as to whether the samples were counterfeit or of low quality in terms of the concentration of active gradient metformin. Future studies can include other quality tests such as dissolution tests, which will yield more robust information on the bioavailability of the samples. Also mass spectroscopy can be conducted to detect impurities in the samples, which should also serve as an indicator of the quality of the medicines.

Development of complacency by users of MAS was a major factor that was identified in this study that may hinder its use and in turn limit its success of reducing medicines counterfeiting. Therefore, it may be worthwhile to conduct a research in the future aimed at detecting complacency to MAS use. This can be done by comparing data on sale volume of MAS enabled medicines from the manufacturers with the number of authentication messages received from consumers within a particular period of time. Future studies could also focus on further evaluation of MAS to detect any infiltration of the counterfeiters into the supply chain. It would also help to provide evidence for continued usefulness of MAS by showing how Sproxil continues to meet its objective of delivering in social returns such as reducing the number of casualties due to counterfeiting as a result of MAS, providing market intelligence to help intercept counterfeiters, lowering cost of health care, reducing cost of production and increasing market share of pharmaceutical industries. Also, it may necessary to conduct a before and after study aimed at determining the actual impact of MAS on the quality of Glucophage® or any other MAS enabled medicines. This can be done by determining the quality of any MAS enabled medicine and comparing it to reported incidence of counterfeiting for the particular medicine before it became MAS enabled. This will help to further show the impact of MAS on medicines quality and the trend in quality of medicines available in Nigeria. It may also be important to conduct another research in the future aimed at determining the public awareness about MAS and compare the results with the findings of this study to know if there have been improvement. This kind of research would be most beneficial if any interventions to improve awareness level about MAS are instituted before it is carried out so that it can also show the impact of such interventions.

Finally, the low reporting rate of cases of medicines counterfeiting encountered by participants in this study calls for further studies to know how encounter with poor quality medicines are handled by the consumers, medicine sellers and the drug regulatory agency; NAFDAC. This will help identify any existing

inefficiencies such as low reporting rate, reasons behind such inefficiencies and how they can best be tackled.

8.3 Conclusion

This study provided evidence to show that the information given about the authenticity of medicines via MAS may be accurate. It showed that MAS may be successful due to how easy users perceived it is, its compatibility with the use of mobile phone for text messaging and quick response to authentication. MAS may be said to be useful based on its impact on consumers identified in this study such as increased demand of MAS enabled medicines which may lead to regaining of market share by genuine pharmaceutical industries, easier detection of medicines counterfeiting, reduction in incidence of medicines counterfeiting, increased confidence in medicines purchased, increased knowledge about state of health through the tips from the response sent to consumers and increased trust in medicine sellers.

Factors such as possible increase in cost of medicines, dispensing practices in rural areas and in the hospitals, poor phone network, lack of time by consumers and medicine sellers, low awareness level, complexity of language, development of complacency by the users, consumer trust in source of medicines and the issue of confidentiality may hinder its use. Therefore for MAS to be more useful, there needs to greater public awareness through more effective means such as education about MAS in different languages and increased involvement of medicine sellers in consumer education about MAS. Other ways noted by the participants through which MAS can be improved include; focusing the service on medicines that are most likely to be counterfeited, inprinting the codes/pin numbers directly on the product packaging (primary and secondary) and reducing the pin numbers to help avoid human error of entering the wrong numbers when customers try to authenticate their medicines.

This study further showed that there was a significant difference in quality between the innovator brand; Glucophage® and generic metformin in terms of the content of active ingredient. While this finding is worrying, the low overall failure rate (3.9%) and that no counterfeits were detected; may suggest an improved situation of quality of medicines in Nigeria and that while medicines counterfeiting present some challenge, a much greater concern may be the existence of substandard medicines. Most of the participants interviewed in the consumer and medicine seller group perceived that generic medicines were of lower quality than innovator brands. To ensure accessibility to good quality medicines in Nigeria, there is need for legislature on generic prescribing and substitution policies. However, the findings of this study reveal that such policies will be more successful if they are accompanied by strategies aimed at making sure that generic medicines are of good quality, bioequivalent and interchangeable with innovator brands. Education campaigns targeting the prescribers, pharmacists and consumers and aimed at helping to effect a change in misconceptions of the quality of generic medicines is therefore necessary.

All the participants in this study agreed that poor quality medicines is a problem in Nigeria and different reasons were identified as being responsible for the continued existence of poor quality medicines. However, very few of the participants seem to have encountered medicines that they thought were of poor quality. Among those who have experienced poor quality medicine, the common response was to stop taking the medicine and/ return it to where it was purchased. An overwhelming majority (90%) felt that the problem is decreasing mainly due to awareness creation by NAFDAC. Other factors identified that may be responsible for this decrease and which need to be built upon are adoption of technological solutions such as MAS, increased pharmacists' involvement in medicines supply and distribution in Nigeria, establishment of NAFDAC, routine inspection by NAFDAC and effective stakeholder

collaboration. Therefore, while identifying counterfeit medicines through technological innovations may be useful, it must exist with other government driven initiatives, which will ensure that incidents of counterfeiting are reported and that counterfeiting business becomes unattractive.

Another interesting finding from this study is that majority of the participants felt that the quality of locally manufactured medicines were comparable and in some cases better than imported ones, with the overwhelming majority stating that imported medicines are more likely to be of poor quality than locally manufactured medicines. This perception of the participants may help encourage local drug manufacturing through increased patronage of locally manufactured medicines at the consumer level. However, there is need for the government to provide incentives for local manufacturers and adopt policies that will encourage local production. This may include reducing cost of registration of medicines and providing low interest loans for local manufacturers, increasing patronage of locally manufactured medicines for instance purchasing medicines from them for major government programmes, improving local infrastructure (such as electric power supply and good roads) to help reduce cost of local drug manufacturing and increasing taxes for imported medicines. While increasing taxes for imported medicines may help encourage local drug manufacturing, appropriate considerations may need to be made as this may lead to lack of or inaccessibility of good quality and affordable generics.

In addition, financial incentives should also be provided for local manufacturers by government for instance by assisting to offset the cost of MAS for local manufacturers so that they can be encouraged to participate in the programme and to ensure that costs of medicines are not increased because of MAS. Government also needs to provide financial support to NAFDAC especially in the areas of staffing, laboratories and drug monitoring/post market surveillance.

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Appendices

Appendix 1: Percentage of Urban Pharmacy Premises in Nigeria with Total Number of Pharmacies in Each State

State	% Urban	No. of pharmacies	State	%Urban	No. of pharmacies
Abia	80	86	Kano	77	74
Adamawa	66	38	Kastina	75	14
Akwa Ibom	60	27	Kebbi	50	7
Anambra	60	139	Kogi	80	28
Bauchi	96	22	Kwara	90	40
Bayelsa	100	5	Lagos	98	861
Benue	99	36	Nasarawa	66	22
Borno	90	51	Niger	87	54
Cross River	80	31	Ogun	77	97
Delta	70	66	Ondo	81	51
Ebonyi	100	7	Osun	80	37
Edo	93	94	Oyo	93	131
Ekiti	65	15	Plateau	87	81
Enugu	90	60	Rivers	90	125
FCT	50	159	Sokoto	100	11
Gombe	80	10	Taraba	95	11
Imo	70	63	Yobe	100	8
Jigawa	0	0	Zamfara	83	6
Kaduna	90	106			

PCN, (2000) cited in Peterson and Obileye, (2002)

Appendix 2: Nigerian pharmacy laws

Nigerian Pharmacy Laws	Aim
Drug and Related Products (Registration, etc.) Decree of 1993; Food, Drugs and Related Product (registration etc,) Act cap F33 laws of the Federation of Nigeria, 2004,	Prohibits the manufacture, sale, and circulation of unregistered drugs and ultimately protecting the consumers/patients from illicit medicines. It also stipulates the procedure for applying for registration of a drug product, conditions under which information supplied by an applicant is disclosed, and provisions for the suspension or cancellation of certificates of registration and clinical trials as well as Penalties for failing the law
Consumer Protection Council Decree No. 66 of 1992	Makes provision of the offending company or firm or individual to protect, compensate and provide relief and safeguards to injured customers in the event that defective products are sold to the consumers due to its failure to ensure drug distribution through proper channels
Trade Malpractices (Miscellaneous Offences Decree No. 67 of 1992	Creates certain offences regarding trade malpractices and established a special trade malpractices investigation panel to investigate such offences
Counterfeit and Fake Drugs Miscellaneous Provisions Act (Cap 73, Law of the Federation, 1990)	Prohibits the production, importation, manufacture, sale and distribution of any counterfeit, adulterated, banned or fake drugs. It also prohibits persons to sell any drug in an open market without permission from the proper authority
Counterfeit and fake drugs and unwholesome processed food (miscellaneous Decree 25 of 1999); Counterfeit and fake drugs and unwholesome processed food (miscellaneous provision act cap C34 Laws of the Federation of Nigeria, 2004)	Dictates locations, which are inappropriate for the sale of medicines such as the open markets, kiosks, motor parks, roadside, stalls, premises unauthorised by the PCN or in any bus, ferry or other means of transportation. It authorises the Federal and state task forces which are arms of NAFDAC to close illegal drug markets in Nigeria
Patent and Proprietary Medicines Vendors Licence (PPMVL)	PPMVL are to be issued where there is a limited availability of pharmaceutical resource. Holders of the licence are authorised to sell only OTC medicines
National Drug Law Enforcement Agency (NDLEA) Act (Cap 253 LFN 1990, as amended)	Regulates controlled drug consumption
Food and Drugs Act (Cap 150 LFN 1990, as amended); Food and Drugs Act Cap F32 Laws of the Federation of Nigeria, 2004	It provides for the regulation, manufacture, sale and advertisement of food and drugs. It prohibits the sale an advertisement of certain foods and drugs or their use for certain diseases and other misleading practices as well as manufacture under unsanitary conditions. It empowers inspectors and analysts to enter premises and take samples as well as to detain violators
Poisons and Pharmacy Act (Cap 535 LFN 1990)	Regulates the sale, distribution, dispensing, custody and supply of drugs and poison
NAFDAC Decree 15 of 1993 (as amended)	It is the decree upon which NAFDAC was created; mandating it to regulate and control the importation, exportation, manufacture, advertisement, distribution, sale and use of food and drugs. NAFDAC also conducts necessary quality control tests. An arm of NAFDAC, the Federal Task force was established under the provisions of the counterfeit and fake drugs (miscellaneous provisions) Act and is mandated to regulate unregistered drug premises
Pharmacists Council of Nigeria (PCN) Decree 91 of 1992	PCN is the only body that licenses, controls and regulates pharmacy practice and pharmaceutical manufacturing in Nigeria. It provides training in all aspects of pharmacy and is in charge of registering pharmacists. This replaced the Pharmacist Act of 1964

Appendix 3: Summary of studies on extent of poor quality medicines

(Please note that this table is presented over 18 pages)

Author, Country, Title/ Aim of study	Study design	Methods	Principal findings/conclusions	Limitations/ Comments
Newton et al. (2008). Samples from Vietnam, Cambodia, Lao PDR, Myanmar (Burma) and the Thai/Myanmar border. To determine the source of fake Artesunate in south east Asia	391 samples of genuine and counterfeit Artesunate: Vietnam (75), Cambodia (48), Lao PDR (115), Myanmar (Burma) (137) and Thai/Myanmar border (16) were collected for analysis from larger surveys that had been conducted in the region beginning in the year 2000. They subjected the samples to analysis (HPLC and/ mass spectrometry, X-ray diffraction, gas chromatographic analysis, pollen analysis and detailed packaging inspection). A subset of the samples also underwent detailed forensic and botanical examination	Samples were collected by convenience sampling and random sampling (in Laos only) and ad hoc at the request of individuals and non-governmental organisations in the region	Sixteen different fake hologram types were identified. Analysis confirmed that 49.9% contained no or small quantities of Artesunate (up to 12mg per tablet as opposed to 50mg per genuine tablet). Some of the counterfeit Artesunate were manufactured in China.	Artesunate collections were ad hoc and only a small subset of the samples could be analysed due to financial constraints
Taylor et al. (2001). Nigeria. Pharmacopeial quality of drugs supplied by Nigerian pharmacies. To investigate the quality of different drugs obtained from retail pharmacies in two urban areas of Nigeria, and in instances of poor quality, to ascertain the reason why.	581 samples of 27 different drugs (antimalarials, antibacterials, anti-TB, Anthelmintic: mebendazole and anti-fungal: Ketoconazole from randomly collected from 35 Pharmacies in Lagos and Abuja.	The collected samples were analysed by validated chromatographic methods. The results obtained were then compared to pharmacopeial requirements.	48% of the samples did not comply with set pharmacopeial limits, and this proportion was uniform for the various types of drugs tested. The issues identified ranged from the total absence of active ingredients to either over or under concentration of the active ingredient (s). Three Chloroquine (CQ) samples did not contain any active ingredient.	Although random sampling was conducted. The two urban cities selected may not be fully representative of drug quality in some rural areas of Nigeria. Since packaging was not assessed, some medicines, irrespective of their chemical content, could have still been counterfeit. There were no power calculations to arrive at the sample size used.

Shakoor et al. (1997). Nigeria. Assessment of the incidence of substandard drugs in developing countries	81 samples were collected. 34 of the samples were from Pharmacies while 47 were from drug outlets. These included chloroquine, amoxicillin, clotrimoxazole, tetracycline and Ampiclox®	The samples collected were analysed using HPLC	36% of the samples did not meet set standards. Decomposition appeared to be the cause of poor quality in a number of samples, but poor manufacturing was prevalent. The majority of the poor quality samples were from non-pharmacy outlets (43%). 2 CQ samples and one amoxicillin sample from Nigeria did not contain any active ingredient. The substandard Ampiclox® sample from Nigeria was found to be degraded.	The samples were not randomly collected, thereby contributing some level of bias in the findings and conclusions made from this study. Also, the sample size was very small. It was stated that the result presented little evidence to implicate fraudulent manufacturing. This statement was however challenged since the researchers acknowledge that the method employed cannot differentiate between counterfeit and substandard medicines. Also the selection of samples based on high cost and/ high usage is challengeable in that it resulted in selection of a limited range of drugs (CQ and 4 antibiotics, of which 3 were broad spectrum Verduin-Mutiganzi R and Verduin-Mutiganzi G, 1998)
Shakoor et al. (1997). Thailand. Assessment of the incidence of substandard drugs in developing countries	15 samples were collected. 5 of the samples were from Pharmacies while 10 were from drug outlets. These included chloroquine, amoxicillin, clotrimoxazole, tetracycline and Ampiclox®	The samples collected were analysed using HPLC	40% of the samples did not meet set standards	The samples were not randomly collected, thereby contributing some level of bias in the findings and conclusions made from this study. Also the sample size was very small
Maponga and Ondari (2003). Ghana, Kenya, Mali, Mozambique, Sudan and Zimbabwe. Study conducted as part of a pilot study to determine the quality of anti-malarials in selected African	278 Samples of anti-malarials; Chloroquine tablets (CQT) and sulphadoxine-pyrimethamine tablets (SPT) were collected and analysed.	The samples were analysed by carrying out HPLC and dissolution tests	Percentage failure of samples based on ingredient content ranged from 20% to 67% for CQT and 5% to 28% for SPT, and in dissolution failures ranging from 5% to 33% for CQT and 75% to 100% for SPT.	The evaluated products may have been susceptible to handling problems as they were removed from their original packaging. Also some of the samples could not be analysed as

countries and to determine whether the quality of the products was related to the level of distribution chain from which they were collected (district hospitals, district medical stores, households, vendors, pharmacies).				they were crystallized due to exposure to high temperature. Many of the samples lacked the required units for performing all the tests. In addition, it was not clear which sampling technique the country team leaders used for collection.
Bate et al. (2009a). Nigeria. To assess the awareness of the problem of counterfeit and substandard drugs among health personnel and how this influences their professional behaviour as well as their impact on regulatory initiatives to eliminate spurious medicines.	An informal questionnaire was administered to 211 Healthcare personnel in Lagos, Ondo and Ogun states in Nigeria about their awareness of and exposure to poor quality medicines, patient and prescribing behaviour. A simple sampling protocol was used to collect 140 treatment parks of anti-malarial drugs (SP, Amodiaquine, Mefloquine, Artesunate, Dihydroartemisinin, Arthemeter-lumefantrine, antibiotics (ciprofloxacin, erythromycin) and antimycobacterial drugs (isoniazid and rifampicin from pharmacies randomly selected from urban and peri-urban areas of Lagos.	A preliminary testing using TruScan® device was used to test ciprofloxacin. The Global Pharma Health Fund e. V. Minilab was used to run semi-quantitative TLC and disintegration tests on the samples in order to determine the presence and concentration of active ingredient (s) in the samples.	Irrational drug use was evident. High costs of medications seemed to be the most common reason for the proliferation of poor-quality medicines. Most healthcare personnel were aware of the problem but their ability to identify and respond to poor quality medicines differed widely. 18% of the drugs failed TLC and/or disintegration tests.	Unavailability of reference standards resulted in failure to use the TruScan® handheld Raman spectrometer for all the samples. The method used to analyse the data retrieved from the questionnaires were unclear. Also some of the samples could not be tested using the Minilab. The movement of drugs to different locations may have influenced the results.
Bate et al. (2009b). India. A pilot study of essential drug quality in India (Delhi and Chennai). The aim was to explore the extent of substandard and counterfeit drugs available in the market.	Random samples of 541 (antimalarial- chloroquine, antibiotic-ciprofloxacin and erythromycin, antimycobacterial- rifampicin and isoniazid) drugs were collected from 52 pharmacies in urban and peri-urban areas of Delhi and Chennai (26 pharmacies) respectively.	Semi-quantitative thin-layer chromatography and disintegration tests were used to measure the concentration of active ingredients against internationally accepted standards.	12% of all samples tested from Delhi failed either one or both testes and were substandard. 5% of all samples from Chennai were substandard. The study revealed that there is a 38% chance of obtaining a substandard medicine when purchasing a medicine from a pharmacy in Chennai while in Delhi; the chances could be as high as 80% with a range of 6% to 30% being counterfeit medicine in any single pharmacy. In a worse case scenario, there is a 27% chance that 20-30% would be substandard some of which may be counterfeit (Bate et al., 2010). There is a need for a larger study involving pharmacies from rural, urban and peri-urban areas, which is aimed at determining the extent of poor quality medicines to be carried out.	This study used the random sampling technique, reported the number of outlets from which samples were collected and the variations between these outlets. However, the small sample size in this study may have led to inconclusive findings. The authors acknowledged that no forensic analysis was conducted to determine if the drugs were counterfeit or sub standard as attempts to obtain valid samples and

				batch information from the manufacturers proved futile. The results reveal that some pharmacies are buying a large quantity of poor quality medicines some of which may be counterfeit (Bate et al., 2010). Although rural areas were not included in this study; poorer results are expected in such areas due to high levels of illiteracy and low levels of surveillance by the government in these areas.
Bate et al. (2008). Nigeria, Ghana, Kenya, Rwanda, Tanzania and Uganda. Antimalarial Drug Quality in the Most Severely Malarious Parts of Africa – A Six-Country Study.	195 treatment packs were randomly collected from private pharmacies in the major cities of six African countries within the high endemic band. The drugs sampled include SP, Amodiaquine, Mefloquine, Artemisinin and Artemisinin Combination Therapies (ACTs).	The Global Pharma Health Fund e.V. Minilab was used to run semi-quantitative thin-layer chromatography (TLC) and dissolution tests on each sample to determine the presence and relative concentration of active ingredients	35% of all samples tested failed either or both tests, and were substandard. Nigeria and Tanzania (32%), Ghana and Uganda (35%), Kenya (38%) and Rwanda (33%). Drugs originating from poorer countries such as Africa and Asia seemed to have higher failure rates when compared to those originating from Europe and USA. 31% of the drugs that were stated to originate from India were found to fail the quality.	No forensic examination was carried out to differentiate between counterfeited drugs and substandard products. The drugs which were labelled as made in India may not actually have originated from India as some of them were counterfeited so may have been bearing a fake label also (Bate et al, 2010).
Kaur et al. (2008). Tanzania. The aim of the study was to assess the quality of anti-malarials available from retail outlets across mainland Tanzania.	1080 anti-malarial formulations (SP, Amodiaquine, Quinine and artemisinin derivatives) were collected from 21 districts in mainland Tanzania in 2005.	Laboratory based analysis was carried out (HPLC was used for dissolution and content analysis).	12.2% of the samples were found to be of poor quality. 23.5% of the quinine tablets were of poor quality, 13.4% of the SP was of poor quality and 7.5% of the amodiaquine tablets were of poor quality. The artemisinin derivatives all contained the stated active ingredient when tested with HPLC alone.	The samples were randomly selected.

Gaudiano et al. (2007), Congo, Burundi and Angola. The aim was to determine the quality of medicines available in the small informal markets in Congo, Burundi and Angola.	30 commercial tablet samples of anti-malarial drugs (quinine, sulphadoxine and pyrimethamine, chloroquine and mefloquine) were purchased from illegal vendors in small informal pharmacies in Goma (Congo), Bujumbura (Burundi) and Launda (Angola)	The samples were analysed by means of a validated liquid chromatographic method, uniformity of mass determination, disintegration and dissolution tests. Also there was an evaluation of the label and packaging characteristics of the samples.	Different kinds of problem were observed from the study: Loose tablets, products without name producer and country of production and expiry date. Presence of low quantity of active ingredient was observed in one of the samples, substitution of an active substance with a different one in one of the samples and low dissolution profile in 50% of the samples.	It was not clear which sampling method was used in the collection of the tested samples.
Eichie et al. (2009). Nigeria. In-vitro evaluation of the pharmaceutical quality of some ibuprofen tablets dispensed in Nigeria.	19 different brands of Ibuprofen tablets were purchased from pharmacies and open markets in 3 states in Nigeria. One of the researchers posed as a 'normal customer' and purchased the brands without a prescription.	A preliminary examination of the organoleptic properties of the tablets was done. The tablets were assessed for uniformity of weight, disintegration time and dissolution rate according to B.P. 2003, while content uniformity was carried out according to BP 1993. Weight uniformity was carried out by determining the weight of twenty randomly selected tablets from each brand using a digital weighing balance, while the disintegration time of six tablets per brand was determined in distilled water maintained at 37 ± 0.5°C.	12 brands passed the uniformity of content, 5 brands passed the disintegration test and only 4 brands passed the dissolution test. The different brands varied remarkably in their pharmaceutical qualities, hence the need for a more stringent measure to ensure compliance and consistency.	No particular sampling procedure was employed and only one of the researchers purchased the brands tested, this could have led to some bias in the brands selected for testing as well as outlets chosen for the collection of the samples.
Nnamdi et al. (2009). Nigeria. Evaluation of the Pharmaceutical Quality of Some Quinine Preparations Sold in Nigeria	18 different brands (6 tablets, 6 oral liquid and 6 parenteral quinine brands) were purchased from pharmacies in Onitsha, Asaba, Benin city and Warri, all in the South-eastern Nigeria. One of the researchers posed as a 'normal customer' and purchased the brands without a prescription	A preliminary examination of the organoleptic properties of the tablets was done. The tablets were assessed for uniformity of weight and content uniformity. Also, disintegration time and dissolution rate were tested according to B.P. 2003. Weight uniformity was carried out by determining the weight of twenty randomly selected tablets from each brand using a digital weighing balance, while the disintegration time of six tablets per brand was determined in distilled water maintained at 37 ± 0.5°C. Both parenteral and oral preparations were assessed for clarity, pH, specific gravity and viscosity, while only the parenteral preparations were assayed for content uniformity and sterility according to BP 2003. A modification of the procedure set out in BP 2003 was used to assay for quinine dihydrochloride.	Of the 6 brands of tablets tested, 4 passed the uniformity of content test and 5 the disintegration test, but only 2 passed the dissolution test. The PH of 2 of the 6 brands of oral liquid preparations met BP standards while only one of the oral liquid preparations met BP standard for % content. 4 brands of the parenteral preparations met BP standard for quinine content and all were sterile.	No particular sampling procedure was employed and only one of the researchers purchased the brands tested, this could have led to some bias in the brands selected for testing as well as outlets chosen for the collection of the samples. Also, the samples were collected from one part of Nigeria, which might not be representative of the entire nation.

Onwujekwe et al. (2009). Nigeria. Quality of anti-malarial drugs provided by public and private healthcare providers in south-east Nigeria	225 anti-malarials (artesunate, dihydroartemisinin, sulphadoxine-pyrimethamine, quinine and chloroquine) were either purchased or collected from randomly selected providers from 6 towns in Anambra state, Nigeria (3 urban; Awka, Nnewi, Onitsha and 3 rural; Enugwu-ukwu, Ekwulobia and Okpoko). The sites were selected using two-stage sampling method	The quality of the drugs were assessed by laboratory analysis of the dissolution profile using published pharmacopeial monograms and measuring the amount of active ingredients using HPLC	60 (37%) of the anti-malarials tested did not meet the United States Pharmacopeial (USP) specifications for the amount of active ingredients; with the suspect drugs either lacking the active ingredient or containing suboptimal quantities of the active ingredient. 78% of them were from private facilities mostly patent medicine dealers. Seven of the quinine tablets contained only chloroquine; one sample out of the 4 samples of dihydroartemisinin was counterfeit. Poor quality drugs were more common in rural areas.	The findings mean that the poor with low socio-economic status received the lowest quality of treatment as they often buy their medicines from the PMV and as such urgent measures are needed to remedy these most disadvantaged people in resource poor countries who are largely affected by the menace of counterfeiting. The purpose of the research was revealed to some hospitals and pharmacy shops during the sample collection, which may have affected the samples provided by these facilities and may have contributed in lower failure rates of the samples from these facilities as they may have provided samples which they perceived as good quality for testing.
Atemnkeng MA (2007). East Congo DR. Quality evaluation of chloroquine, quinine, sulphadoxine-pyrimethamine and proguanil formulations sold on the market in East Congo DR.	Anti-malarial drugs (8 CQ tablet batches, 2 CQ injection batches, 1 CQ syrup batch, 8 quinine tablet batches, 4 quinine injection batches, 1 quinine syrup batch and 5 batches of SP) were anonymously purchased from pharmacies and commercial stores in and around Kavumu, Mudaka and Bukavu in East congo	HPLC and UV spectrophotometric assay of the samples of tablets, injections and syrup collected was carried out	43% of the products did not have the names of the manufacturers. When expressed as a salt, 2 of the CQ batches where under-dosed by about 20% and 30% respectively while as a base, only one batch complied to set standards while the others were under-dosed by about 30-50%. In the salt form, 2 of the 8 batches of quinine were under-dosed by 15% and 25% respectively while as a base, all the batches were under-dosed. Four batches of sulphadoxine samples were underdosed (91–94%). For pyrimethamine, two batches were slightly overdosed (106.4% and 107.6. One batch of Fansidar contained neither sulphadoxine nor pyrimethamine.	The findings suggest that relatively in expensive drugs like chloroquine can also be counterfeited as opposed to previously held views.
Odeniyi et al. (2003). Nigeria Comparative analysis of eight brands of sulfadoxine-pyrimethamine tablets.	8 brands of Sulphadoxine – Pyrimethamine products which includes the innovator product; fansidar (4 of which were registered	The assessment included the evaluation of uniformity of weight, friability, crushing strength, disintegration and dissolution tests as well as chemical assay of the tablets.	All the 8 brands passed BP standards for uniformity of weight, disintegration and crushing test. Three of the eight brands failed the friability test. One of the brands failed the test for content of active	Only 3 (registered by NAFDAC) of the 8 SP brands analysed passed all the BP quality tests and

	by NAFDAC) were sourced from retail pharmacies in Ibadan, Nigeria.		ingredients while one other brand did not pass the USP specifications for dissolution test. No significant differences were observed in the amounts of pyrimethamine and sulphadoxine released from the brands.	were physically and chemically equivalent. There is therefore a need for post-market surveillance in order to ensure that new products are equivalent to the innovator products. It was not clear how the samples were collected/sampled.
Amin and Snow. (2005). The Quality of Sulphadoxine-Pyrimethamine and Amodiaquine Products in Kenyan Retail Sector. Kenya	A retail audit of 880 retail outlets was conducted in 4 districts in Kenya (Greater Kusii, Kwale, Bondo and Makueni) in 2002. 116 most commonly stocked SP and Amodiaquine (AQ) products were sampled from the top 10 wholesalers in each district and then subjected to USP tests for content and dissolution.	The content was determined spectrophotometrically for AQ and via the use of HPLC for SP. Dissolution tests were carried out with Six station Erweka DT 60 dissolution apparatus.	47 (40.5%) out of the 116 SP and AQ samples analysed were found not to meet USP specifications for content and/ dissolution. About 45.3% of SP and 33.0% of AQ were substandard.	The results show that there is a need for post market surveillance in Kenya to help ensure that good quality medicines are distributed.
Sowunmi et al. (1994). Bioavailability of sulphate and dihydrochloride salts of quinine. Nigeria	Using 6 healthy male volunteers, the absolute bioavailability of three oral salts of quinine (600mg Quinine (QN) sulphate capsule, 600mg QN dihydrochloride plain tablet and 600mg QN sulphate sugarcoated tablets to that of a standard 600mg of QN hydrochloride IV infusion was determined.	The drugs were administered in a randomised crossover design.	It was found that the sugarcoated QN sulphate tablet had no QN. There were no differences in the bioavailability of the other test drugs.	This study further confirms the presence of counterfeit anti-malarials in the Nigerian market. A very small sample size was used
Babalola et al. (2004). Absolute bioavailability of quinine formulations in Nigeria.	The absolute bioavailability of QN sulphate as capsule and as tablet was compared against the IV infusion in 12 male volunteers	Six of the volunteers received intravenous infusion over 4 hours as well as the capsule formulation of the drug in a crossover design, while the other six received the tablet formulation. Blood samples were taken at predetermined time intervals and plasma analysed for quinine (QN) using reversed-phase HPLC method	Therapeutic QN plasma levels were not achieved with the tablet formulation.	The sub therapeutic levels of the tablet form in the study can result in treatment failure.

Okeke and Lamikanra (1995). To determine the pharmaceutical and biological quality of tetracycline capsules sold in Ile-ife, Nigeria and to evaluate their possible contribution to increased incidence of tetracycline resistance. Nigeria	6 batches of tetracycline capsules were bought from dispensing outlets in Ile-ife.	The samples were subjected to weight uniformity test, test for identification of degradation products and determination of anhydrotetracycline, dissolution tests as well as comparative bioavailability study. A sample obtained from a manufacturer (Pfizer products Plc., Lagos, Nigeria) was used as a reference standard.	All the batches including the reference standard passed the weight uniformity test. While the reference standard passed all tests, the other six batches failed all other tests (low content of active ingredient and high levels of degradation products).	All samples of tetracycline capsule obtained in Ile-ife were of poor quality and as such resulted in significant differences in bioavailability. This is an important cause of resistant strains and treatment failure. This resultant effect is even worse in patients who are poor absorbers
Odunfa O.O., Adegoke O.A., Onaga I.C (2009). Pharmaceutical equivalence of some commercial samples of artesunate and amodiaquine tablets sold in Southwestern Nigeria.	15 generic brands of artesunate and five brands of amodiaquine were purchased from drug retail outlets in Oyo and Osun states in Nigeria.	The drugs were subjected to identification, weight uniformity, content uniformity, content of active ingredient and uniformity of diameter tests. Hardness, disintegration time and dissolution rate tests were also conducted to determine their bioequivalence.	Two artesunate brands contained undetectable amounts of active ingredient and 8 other brands contained excessive amounts, one artesunate brand failed disintegration test. All amodiaquine brands passed USP tests. However, one of the brands had a poor dissolution profile by not releasing the required quantity of drugs within 30 minutes.	The majority of the artesunate brands were substandard while one brand of amodiaquine was poorly formulated; hence the need for continued surveillance of drugs entering the Nigerian market. The tests conducted were limited as there was no test for impurities
Esimone et al. (2008). In vitro bioequivalence study of nine brands of artesunate tablets marketed in Nigeria.	9 different brands of artesunate were selected based on how frequently they were prescribed, how often and available they were in hospitals and community pharmacies. One of the samples was the innovator brand/reference drug. The drugs were collected from 4 major towns in Nigeria, which were taught to be representative.	In vitro dissolution study was performed on 9 different brands of artesuante using the US Pharmacopeia guidelines for the basket method. Hardness and disintegration time tests were also conducted.	All brands passes BP disintegration time tests, 5 of the brands failed the hardness test. Significant differences were observed in the dissolution profiles of the brands. One of the brands had a poor dissolution profile (releasing <70% of artesunate within 30 minutes).	The tests conducted to determine medicines quality were limited, as it did not include such tests as tests for impurities. However the results show the need for drug surveillance to ensure their quality and conformity with pharmacopeial standards

Newton et al. (2001). Fake malaria medicine in South east Asia. To investigate the distribution of counterfeit artesunate tablets in South east Asia and identify distinguishing characteristics of the fakes.	104 Samples of artesunate was procured from shops, pharmacies, NGOs and hospitals in Myanmar (Burma) (51), Cambodia (26), Laos (8) and western Thailand (8) between August, 1999 to August, 2000.	Red dye technique was used to investigate the quality of medical products. An observer unaware of the results from the dye test examined some of the packages.	91% of the samples were labelled as made by Guilin Pharma (China) or repackaged by Atlantic pharmaceuticals (Bangkok, Thailand), 29% of all the samples contained no artesunate; 38% of samples from shops and pharmacies contained no active ingredient. The results of the red dye test and those of the observer from investigating the packages coincided. Fakes were observed for all the countries; fake holograms were identified on the packages of the samples from Vietnam and Cambodia. A variety of reliable surrogate markers were observed and reported by the investigators.	The spread of fake artesunates may worsen the problem of drug resistant malaria.
Bate et al. (2010). India. To compare the results of Bate et al. (2008) on the quality of medicines in Pharmacies in Delhi and Chennai with the quality of medicines from traders.	The same 5 drug types purchased from Pharmacies in Bate et al. (2008) were purchased from Delhi based traders (4 different wholesalers). Qualitative interviews were used to investigate how substandard medicines were arriving at the pharmacies.	Tests for active ingredient(s), product disintegration in warm water within 30 minutes. A subset of the samples were analysed using the Raman spectrometer.	7% of tested samples from the traders failed the test of which 3.6% contained no active ingredient. All the traders have at least some drug failures with failure rate for each trader ranging from 1% to 18%. The trader with a 1% failure rate had erythromycin, which failed the tests probably due to degradation resulting from a broken blister pack while the trader with 18% failure rate was obviously dealing on both genuine and fake pharmaceuticals. Traders at the end of the continuum possessed the worst results and accounted for the majority of the products that contained no active ingredient. 73% of the pharmacists stated that some pharmacists knowingly purchased substandard medicines to enrich themselves, over half of the pharmacists and assistants interviewed stated that re-labelling expired drugs with a new expiry label was the most common form of counterfeiting. Twenty-seven per cent said that companies readily supplied new labels. 19% claimed their competitors bought medicines from unreliable sources. 92% of the pharmacists claimed that they have at least once in the past being approached by a trader offering sub-potent medicines.	Dissolution tests, tests for impurities or contamination were not undertaken. Only field tests were performed meaning that precise results could not be obtained since proper laboratory assessments could not be carried out. The findings show that the sale of counterfeit medicines in India seems not to be accidental- while some pharmacies and traders sell only high quality medicines; others deal on a mixture of counterfeit and fake pharmaceuticals. The study may have been biased by the fact that the samples were collected from traders in one location and may be limited by the small sample size. It also shows that although some problems could be due to degradation due to poor

				storage, much of the problem is due to deliberate, illegal activity.
Wondemagegnehu (1999). Counterfeit and Substandard drugs in Myanmar and Vietnam.	A total of 503 samples of 12 products were collected from both Myanmar and Vietnam.	500 samples were sent to the WHO laboratory for testing to determine the identity and content of active ingredients. 214 of the 500 samples were further investigated to determine if they were counterfeit (by tracing the label to source).	56 (11%) failed the quality test. Information was retrieved for 169 out of the 214 samples that were further investigated. 18% of the 169 samples failed laboratory tests while 22% of the remaining 45 samples of which further information could not be obtained failed the tests. Only 6 out of the 169 samples were counterfeit; 5 were mislabelled with respect to source but passed all laboratory tests while one contained the wrong ingredient but was produced by a licensed manufacturer. All six were from Myanmar. The overall failure rate for the 214 samples was 16% which was higher than 11%; the failure rate for the 500 samples.	The prevalence of substandard medicines seems greater than counterfeit medicines in both countries studied. Some drugs which pass laboratory tests may be counterfeit; hence further investigations are necessary to determine which products are counterfeit.
Patel et al. (2009a). Drug Quality in South Africa: Perceptions of Key Players involved in Medicines Distribution.	Participants were purposefully sampled from a South African manufacturer, SA subsidiaries of international manufacturers, national distribution companies, national wholesaler, public and private sector pharmacists and a dispensing doctor. Ten interviews were conducted.	Qualitative data collection via key informant interviews using semi-structured interview guide.	Purchasing registered medicines from licensed suppliers, use of Standard Operating Procedures (SOPs) and audits between manufacturer and distributor and/ or provider were the key strategies identified that were used to protect medicines quality.	Effective communication amongst stakeholders, especially in providing feed back regarding complaints about medicine quality seems to be a potential area for further research.

Ogwal-Okeng et al. (2003). Chloroquine in the Ugandan market fails quality test.	Chloroquine tablets (50 tablets per outlet) and injection (10x5ml ampoules and 1x30ml bottles per outlet) dosage forms were purposefully, but anonymously purchased from pharmacies and drug shops in the four regions of Uganda and the Kampala city (10 outlets from each region). In total; 47 chloroquine tablet and 45 chloroquine injection batches were sampled.	The samples were assayed for content of active ingredients based on the USP standard using the HPLC method.	39% of the tablet samples failed the test for active ingredient (11% with sub optimal concentrations, 28% with supra-normal amounts). 51% of the samples of injection failed (40% with sub-normal amounts and 11% with supra-normal amounts).	The failure rates were high. The samples were purposefully sampled, creating room for bias.
Odili et al. (2006). Identification of Counterfeit Drugs by Community Pharmacists in Lagos State.	Convenient sampling was used to sample practising community pharmacists from 17 out of 20 local government Areas in Lagos State using a list of registered pharmacists from the Association of Community Pharmacists in Lagos state.	100 copies of a 23-item questionnaire was filled by the participating community pharmacists.	69 questionnaires were completed. All the respondents agreed that Nigeria has a fake and counterfeit drug problem and 74% described it as a major problem. Scrutiny, customers' complaints and Pharmaceutical company alerts were the major means of discovering a fake drug. No respondent stated they have ever received any help from regulatory authorities. 81% has never reported any counterfeit case to drug regulatory authorities rather the most likely response was to return the product from where it was purchased whenever they encountered counterfeit medicines. Only 18.8% of the respondents thought NAFDAC is very effective.	Multiple responses may have affected the results of the study. The small sample size may not be truly representative and the use of convenient sampling may have biased the findings. The study may have been limited by the reduced response rate- as only 69% responded.
Nazerali, Muchemwa and Hogerzeil (1998). The quality and stability of essential drugs in rural Zimbabwe: controlled longitudinal study.	789 samples of medicines consisting of benzylpenicillin injection, amoxicillin, ampicillin, doxycycline, phenylmethoxypenicillin and tetracycline were collected from Zimbabwe.	Level of active ingredient was determined as percentage of stated content and whether they complied with BP specifications.	2 out of 10 samples of ampicillin tested failed the test for active ingredient. The aqueous formulation of injectable procaine penicillin was moderately unstable; loosing about 1-6% after 4.3 months although values remained with BP limits.	

Kenyon et al. (1999). Detection of substandard fixed-dose combination tuberculosis drugs using thin layer chromatography.	13 Fixed Drug Combination anti-tuberculosis (TB) drugs were collected from Botswana.	The samples were tested with TLC. A confirmatory analysis with UV or liquid chromatography was carried also carried out.	All the samples contained the stated drug. However, 31% were substandard (2 of the samples had a low rifampicin content; one had excessive rifampicin while one had excessive pyrazinamide. Rifampicin in 7 of the samples were not relatively bioequivalent to the reference standard.	
Kayumba et al. (2004). The quality of essential antimicrobial and antimalarial drugs marketed in Rwanda and Tanzania: influence of tropical storage conditions on in vitro dissolution.	Essential antibiotics (amoxicillin capsules, metronidazole tablets, sulphamethoxazole/trimethoprime tablets, etc) were collected from Rwanda and Tanzania.	Dissolution tests were conducted as well tests using HPLC based on the USP 24 specifications.	At purchase the drug content of all the samples were within USP 24 specifications, while three samples of the sulphamethoxazole/trimethoprim and one sample of sulfadoxine/pyrimethamin failed the USP 24 dissolution tests, the drug content of one sulphamethoxazole/trimethoprim and one quinine sample was reduced after 6 months. With the exception of three metronidazole samples that failed dissolution test after 6 months, all other samples were within USP 24 dissolution specifications. In all, 24% of the samples failed the dissolution test.	
Basco (2004). Quality of antimalarial drugs (chloroquine, quinine and sulphadoxine-pyrimethamine) obtained from illegitimate outlets in urban and rural areas in Cameroon used for self-medication and analyse the drug impacts on the	284 samples of the drugs 133 chloroquine samples, 70 quinine samples and 81 antifolates) used for self-medication were obtained from 132 different sources between 2000-2001. Chloroquine and quinine used for self-medication were obtained from 15 malarial infected persons; only 6 were of good quality. 8 of the	The samples were tested with a simple colour reaction test and semi-quantitative TLC.	38% of the chloroquine samples, 74% of the quinine samples and 12% of the antifolates were observed to have either no active ingredients insufficient quantities of active ingredients, wrong ingredients or unknown ingredient (s). Most of the drugs without packaging were counterfeit while those in packages and blisters were most likely to be genuine.	The samples were not representative of the quality of medicines in Cameroon as only a limited class and number of antimalarials was included. Also only the illegitimate sources were sampled and this may

patient.	patients had a negative urine test due to the use of fake or substandard antimalarial drug.			have contributed to the high level of low quality medicines obtained. The vendors provided the drug/sample details such as name which may have been incorrect and could not be verified as some of the medicines purchased had no packaging/labels.
Sengaloundeth et al. (2009). A stratified random survey of the proportion of poor quality oral artesunate sold at medicine outlets in the Lao PDR-implications for therapeutic failure and drug resistance.	Mystery shoppers purchased artesunate samples from 180 outlets in 12 of 18 Lao provinces selected using stratified random sampling by investigators who were not involved in sampling.	Packaging characteristics of all samples were observed, samples were analysed using the Fast Red Dye test, HPLC, mass spectrometry, X-ray diffractometry and pollen analysis.	25 (13.9%) of the 180 outlets sampled sold oral artesunate. 22 (88%) of the 25 outlets sold counterfeit artesunate, which contained no artesunate when chemically analysed. Package characteristics revealed 7 different counterfeit types. Similar results were obtained from HPLC, Fast Red Dye test, and Mass spectrometry. Mass spectrometry showed that the tablets contained a variety of wrong ingredients with some (4) containing small amounts of artemisinin ranging from 0.26-115.7mg/tablet.	The investigators did not perform further checks to distinguish fake from genuine samples.
Tipke et al. (2009). Substandard anti-malarial drugs in Burkina Faso.	86 anti-malarial drug samples (CQ, amodiaquine, Sulphadoxine-pyrimethamine (SP), quinine, artesunate, artemether-lumefantrine) were obtained from licensed outlets for instance public and private pharmacies and community health workers and illicit places such as markets, street vendors and shops in the Nouna Health district in North western Burkina Faso in 2006. ACTs were conveniently sampled from market places and pharmacies in Ougadougou.	77 of the samples were analysed with GPHF minilab procedures (visual inspection, disintegration tests, qualitative colour tests, semi-quantitative TLC) and re-tested with European Pharmacopeia standards for disintegration and UV-visible spectroscopy.	42% of the analysed samples were found to be of low quality; 28 (23 CQ, 4 SP, 1 artesunate and 4 amodiaquine) failing visual inspection, 9 (5CQ, 3 quinine, 1SP) having substandard concentration of active ingredient, 4 (3CQ, 1SP) failing disintegration tests and 1 (1 SP) having no active ingredient. The licensed and illicit markets were responsible for 10.6% and 90.0% of the medicines that were substandard.	The small sample size and convenient sampling employed in this study may have biased the findings.

Ofori-Kwakye, Asantewaa and Gaye (2008). Quality of Artesunate Tablets Sold in Pharmacies in Kumasi, Ghana.	17 brands of artesunate were purchased from different pharmacy shops in Kumasi, Ghana.	Mechanical properties (Uniformity of weight, breaking strength, friability and disintegration time) of the samples were determined. In addition, colorimetric methods were used to determine the presence of artesunate and to assay the tablets.	No counterfeit sample could be detected. Most of the samples possessed acceptable mass uniformity, hardness, friability and disintegration time. 11 (64.7%) were outside the International Pharmacopeia content uniformity test limits while 14 failed the European Pharmacopeia test limits for content uniformity.	The study included a small sample size. The sampling method used to obtain the brands/samples is unclear.
Atemnkeng (2006). Quality control of active ingredients in artemisinin-derivative antimalarials within Kenya and DR Congo.	24 artemisinin derivative samples (tablets, capsules, dry suspensions and injections containing either artemether (AM), arteether (AE), artesunate (ARS) or dihydroartemisinin (DHA).) were randomly collected from pharmacies in Nairobi in Kenya and Bukavu in DR Congo in 2004.	All the samples were analysed for content of active ingredient and preservatives using validated HPLC-UV methods according to European pharmacopeia requirements.	All the samples contained the claimed active ingredient. 9 (37.5%) failed the Ph. Eur requirement for content of active ingredients; 7 were under dosed while 2 were overdosed. Dihydro artemisinin was the active ingredient in 57% of the underdosed samples. Arteether injection possessed the lowest drug content (77%). Two-thirds of the dry powder suspensions were either substandard or fake. Tablets varied up to 23% out of range.	
Ifudu (1989). Analysis of street market drugs in Nigeria.	555 samples of different dosage forms of drugs (tablets and liquid) were obtained from open markets and randomly selected vendors in 4 Nigerian cities; Onitsha, Kaduna, Lagos and Ibadan. Drug quality of 486 of the samples antibiotics (83), Antimalarials (19), antipsychotic (24), Benzodiazepine (13), Haematopoietic (23), Multivitamin (52), purgatives (8), others (264) could be obtained.	The drug packages were properly examined against original packs if they were available. Chemical analyses were then conducted according to WHO guidelines for conducting basic tests for pharmaceutical substances, BP 1980 and USP XXI 1985. The tests were repeated where an unusual variance from the expected result was obtained. Percentage content between 90-120% was considered normal, 25-89% substandard while samples containing <25% were considered worthless. Samples found to contain very high dose or wrong substances were considered to be dangerous.	486 (88%) of the samples could be analysed. Half of the antipsychotic studied were outside the specifications while most of the haematopoietic and benzodiazepines were within specified limits. Other drug groups such as antibiotics, antimalarials, multivitamins and purgatives had two extremes e.g 60% of the antibiotics were within range while 7% contained very high concentration of the active ingredient or wrong ingredients while 33% were either substandard or worthless. Except the chloramphenicol made by PLIVA, the other brands contained little or no active ingredient. 53% of the antimalarials were normal, 42% were worthless or substandard while 5% were considered dangerous.	It was unclear what impact inadequate storage conditions may have had on the samples included in the study. Also information retrieved from the vendors about the medicines they sold may not be reliable as the vendors may not be well informed. Irrespective of whether medicines contain little or large amount of active ingredient; all poor quality medicines stand a chance of being dangerous. Chemical analyses of liquid dosage form is not sufficient to determine their quality as there is need to carry out bacteriological tests and tests for antimicrobial

				activity in order to find out if there has been any degradation or epimerisation as in the case of tetracycline.
Bate and Hess (2010). Anti-malarial drug quality in Lagos and Accra – a comparison of various quality assessments.	339 samples were collected from Lagos, Nigeria and Accra, Ghana between mid 2007 and early 2010. The samples were randomly collected in at least 2 occasions in the cities over 30 months (3 times in Lagos; October, 2007, December, 2008 and February, 2010) and twice in Accra (October, 2007 and February, 2010). Fifteen pharmacies were sampled in Lagos and 13 in Accra.	The samples were tested with minilabs, Raman spectrometry and by visual inspection. The results from the minilabs were compared with those from the Raman spectrometry. Only 300 of the samples could be tested with Raman spectrometer (TruScans deployed by the Nigerian government).	Failure rates fell to 29% of the findings in 2007 in Lagos when minilabs were used for testing, 53% using Raman spectrometry and 46% using visual inspection while in Accra, failure rates fell to 54% of the findings in 2007 with minilabs, 72% with Raman spectrometry and 90% using visual inspection. There was an overall improvement in drug quality in both Lagos and Accra between 2007 and 2010.	39 samples could not be assayed, as methods to be used could not be determined for the brands. The sample size was relatively small; considering that only 22 samples could be obtained from Lagos in 2007. The use of two different methodologies in this study is advantageous since there are assertions that counterfeiters are adapting their products to pass simple assays for Active Pharmaceutical Ingredients (API).

USP/USAID (2009). Survey of the Quality of Selected Antimalarial Medicines Circulating in Madagascar, Senegal, and Uganda (QAMSA study).	491 samples of antimalararials; Artemisinin Combination Therapy, Sulfadoxine-Pyrimethamine (SP) were sampled from the three countries. Locations of collection included the public sector, the regulated private sector and the informal market.	GPHF minilab kit was used to test 444/491 of the samples. Full scale laboratory testing was conducted in 150 of the samples tested with GPHF minilab and 47 other samples that could not be tested with GPHF minilab.	The tests with GPHF minilab showed that 43% of samples from Senegal did not meet the requirement for visual inspection, identification, drug content or disintegration while 12% and 6% failed quality testing in Uganda and Madagascar respectively. The Full scale laboratory testing conducted on a total of 197 samples showed that 44% of samples from Senegal failed quality tests while 26% and 30% failed tests in Uganda and Madagascar respectively. More of the SPs (35%) failed dissolution tests when compared to the proportion of ACTs (20%) that failed the test. 29% of the ACTs failed the test for impurity. ACT failure rate was lowest (16%) in Madagascar while SP failure rate was lowest (16%) in Uganda. There were no significant differences in the failure rate in the private and informal sector in Senegal (44% versus 56% respectively). In Uganda, all (11) samples from the public sector passed the test. Poor quality samples were found across the different regions in the three countries. Significant differences were observed in ACT quality across brands; while some brands were consistently of good quality even across the countries some were consistently of poor quality. All the samples passed their identification test and none lacked the stated active ingredient (s).	The study employed a relatively large sample size. Lack of uniformity of testing methods may have limited the findings from this research for instance is the 47 samples which could not be tested with the GPHF minilab as a result of non availability of minilab protocols for them. The finding that all samples from the public sector of Uganda passed the quality tests may have been due to the small number (11) of samples collected from the public sector of Uganda. The study did not conduct further investigations to determine whether any of the samples collected were counterfeit. The study showed that the drug quality problems in this study seem to emanate from source rather than during medicines passage across the distribution chain. However, this generalisation may not be accurate. The inability of the minilab to identify dissolution and impurity failures accurately when compared to the full scale laboratory testing may have affected any findings from their use.

Ofonaike et al. (2007). A study of the pharmaceutical quality of chloroquine and paracetamol products sold in a major Nigerian "market".	34 brands (10 brands of chloroquine tablets, 6 brands of chloroquine syrups, 10 brands of paracetamol tablets and 6 brands of paracetamol syrups) were purchased from pharmacies and shops in Onitsha and neighbouring towns in Asaba, Nigeria.	The brand names, manufacturer, NAFDAC registration status and expiry date of the products were documented on collection. Organoleptic properties (colour, texture, smell and taste) and physicochemical properties (content of active ingredient, disintegration time, dissolution time and tablet crushing strength) were determined. The chloroquine was assayed using non-aqueous method while the paracetamol was validated using spectrometric methods. The tests were conducted in accordance to British Pharmacopoeia, 1993.	Seven (21%) of the drugs were not registered with NAFDAC; 5 chloroquine and 2 paracetamol. None of the CO and only 3 of the paracetamol products passed the BP requirement for PH. Two imported CQ tablets failed the testes for disintegration. Imported chloroquine products seemed to have higher disintegration time (Average was 15.03 minutes) when compared to locally produced choloroquine tablets (Average was 6.27 minutes). Only one CQ tablet failed dissolution tests. Except for one CQ tablet with 11.6% of the stated active ingredient, all others were within BP range of 92.5%-107.5%. All the paracetamol tablets passed disintegration time test while 4 products failed dissolution test. Two paracetamol products failed test for content of active ingredient. Three CQ products (all were locally produced) did not have the ideal crushing strength.	No particular sampling method was used. There were no attempts to verify the product label information. The sample size was small.
Hebron et al. (2005). The Chemical and Pharmaceutical equivalence of sulphadoxine/pyrimethamine tablets sold on the Tanzanian Market.	11 brands of sulphadoxine/pyrimethamine tablets sold in the Tanzanian market were randomly collected from commercial drug distributors and from the medical stores department in Dar es Salaam, Tanzania.	Tests conducted include; hardness test, friability, disintegration, dissolution, weight uniformity and assay of active ingredient and impurity.	All brands passed quality standards of USP and BP for hardness, friability, disintegration, assay and dissolution test, except for three brands that failed friability, hardness or disintegration tests. Percentage concentration of pyrimethamine ranged from 91.04% to 100.20% while sulphadoxine concentration ranged from 91.53% to 99.88%. There were no significant differences between the brands and the innovator product; Fansidar®.	None of the brands were of very poor quality. However a small sample size was used so may not be conclusive for other brands/ samples not included in this study. All the brands were physically and chemically equivalent.
Risha et al. (2002). In vitro evaluation of the quality of essential drugs on the Tanzanian market.	22 formulations (paracetamol; PCM, acetylsalicylic acid; ASA, chloroquine; CQ or sulphadoxine pyrimethamine; SP) were obtained from 10 wholesale pharmacies in Dar es Salaam and Medical Stores Department, Tanzania.	Drug content, in vitro availability (dissolution) and stability under simulated tropical conditions were determined in according to USP 24 monograph stipulations.	All the formulations passed USP standard for drug content. Seven (2PCM, 3ASA, 2SP) formulations were outside the USP limits for dissolution. Another 5 (3PCM and 2CQ) failed to meet the dissolution specifications after they were subjected to an accelerated stability test under simulated tropical conditions (75% Relative Humidity/40 degrees centigrade) for 6 months.	Some of the tablets that contained adequate drug concentration had an unsatisfactory in vitro availability, as they could not withstand the simulated tropical storage conditions. This highlights the need for post market surveillance to ensure that drugs are stored at optimum conditions.

Lon et al. (2006). Counterfeit and substandard antimalarial drugs in Cambodia.	451 samples were collected by convenient sampling in four provinces in Cambodia; covering about 34% of all 498 known facilities and drug outlets. Samples collected include; Quinine, amodiaquine, chloroquine, tetracycline.	Physical/visual inspections, TLC and disintegration tests were conducted. Confirmatory tests were conducted in accordance to International Pharmacopeia vol. 5, 3rd ed. And USP 26-NF21.	About 79% of the outlets were unlicensed and 78% of the samples were from the unlicensed outlets and about 79% of the samples were unregistered with the Cambodian Department of Drugs and Food (DDF), 122 (27.1%) failed TLC and/or disintegration tests; all were unregistered. However 22 samples were from 17 legal/licensed outlets while 100 were from 59 unlicensed/illegal outlets. Counterfeit and substandard medicines were available in 57.9% of 38 licensed outlets and 75.2% of 133 unlicensed outlets. The problems encountered include lack of active ingredients, presence of wrong active ingredients or the presence of substandard mounts of active ingredient (s).	Although there were no significant differences between licensed and unlicensed drug outlets large proportion of samples that failed the quality tests seemed to be from the illegal/unlicensed outlets. The imbalance in sample size between the groups (38 licensed sites and 133 unlicensed sites may have led to the greater percentage of samples from unlicensed tests that failed the test when compared to the number from licensed outlets that failed the test. The sample used in this study is not representative and therefore should not be generalised to the entire Cambodia. The use of convenience sampling may have also further limited the findings of this study. The researchers also acknowledge that the data analysis method they used may have impacted negatively on the study findings.
Getu and Awot (2010). Assessment of the commonly prescribed antimicrobial drug, ciprofloxacin tablets, marketed in Tigray, Ethiopia.	Six brands of ciprofloxacin tablets were collected from retail outlets and drug stores in Mekelle, Tigray, Ethiopia.	Identity tests, weight uniformity, disintegration and dissolution tests as well as assay of the content of active ingredient were conducted in accordance to BP.	All the samples passed the identity, disintegration and dissolution tests, but one brand; Ciflox® failed to release 80% of the drug content in 30 minutes as required by BP. All the brands contained adequate amounts of stated active ingredient. There were significant differences in the drug release among the six brands in vitro ($p<0.05$).	

Minzi OM, Moshi MJ, Hipolite D et al. (2003). Evaluation of the quality of amodiaquine and sulphadoxine tablet sold by private wholesale in Dar Es Salaam Tanzania.	Samples of all AQ and SP brands available; 15 AQ and 18 SP were obtained from 8 licensed wholesale pharmacies in Dar es Salaam.	Identity, Assay for content of active ingredient and dissolution rate tests were conducted as described in the USP.	All samples passed the identity test, 2 (13%) of AQ samples failed the dissolution rate test. All AQ passed the assay for content of active ingredient. 2 (11%) and 8 (44%) of SP samples failed content of active ingredient test and dissolution rate tests respectively.	
Osadebe and Akabogu (2003). Assessment of quality control parameters and interchangeability of multisourced metformin HCl tablets marketed in Nigeria.	Five brands of metformin 500mg marketed in Nigeria (Glucophage® (Merk, Quetta), Glucophage® BDC, metformin (Medopharm), Glucophage ® (Ilsan), Glucophage® (Lipha) were randomly selected from the open drug markets and pharmacies in South Eastern Nigeria	The samples were tested quantitatively to know if they meet acceptable standards and are interchangeable based on calculations from a variation of the concept of dissolution efficiency known as Predicted Availability Equivalents (PAE). Disintegration time, dissolution rates, absolute drug content and weight uniformity was conducted for all the brands. All tests were conducted within the shelf life of the samples.	The study showed that there were variations in the hardness, disintegration and dissolution characteristics of all the five brands. Three of the brands (BDC, Lipha and Ilsan) are interchangeable with Merck brand, which is the innovator drug. These three brands in addition to Merck brand released 100% of their labelled claim within 30 minutes in Simulated Intestinal Fluid (SIF).	The total sample size for each brand is unclear; the random sampling technique seems unclear. The study was conducted in only South Eastern, Nigeria.
WHO (2011). Survey of the quality of selected anti-malarial medicines circulating in six countries of sub-saharan Africa (Cameroon, Ethiopia, Ghana, Kenya, Nigeria and United Republic of Tanzania).	Trained survey teams in each country were responsible for collecting samples according to national sampling plans from different levels of distribution (including informal markets in at least 3 geographical regions of high malaria prevalence).	935 samples were collected between April-June 2008 and were screened using GPHF-minilab® kits. Based on predefined criteria, 306 samples were selected for full quality control testing in the WHO pre-qualified laboratory in South Africa and in the USP laboratory in USA based on the International pharmacopeia and USP.	28.5% of the 267samples tested out of the 306 samples that were tested in the laboratory did not comply with pre-specified internationally acceptable quality criteria. Nigeria had the highest number of failed samples (63.9%).	Small sample sizes from the individual countries and manufacturers may have limited the result of the studies. However, attempts were made to collect samples, which will give a representative picture of the quality of antimalarials in the supply chain.
Abdi et al. (1995). Quality of chloroquine preparations marketed in Dar es Salaam, Tanzania.	Following the discovery of a negative Haskins test in a patient 2 days after ingesting chloroquine, a survey was conducted which involved sampling different CQ brands from pharmacy shops in Dar es Salaam. 9 different brands available were sampled.	The tablets were tested for content of active ingredient and dissolution tests in accordance to USP XXII edition.	All the brands passed the USP content of active ingredient test (contained >97% of CQ). 8 of the brands passed dissolution rate test; all the 8 brand were ordinary CQ tablets while one brand which was sugar coated failed the test; only 39% dissolved in 45 minutes (required minimum is 75%).	

HPLC: High Performance Liquid Chromatography, TLC: Thin Layer Chromatography, CQ: Chloroquine, CQT: Chloroquine tablet, SP: Sulphadoxine-Pyrimethamine, SPT: Sulphadoxine-Pyrimethamine tablet, QN: Quinine, ASA: Acetyl Salicylic Acid, PCM: Paracetamol; AQ: Amodiaquine; RH: Relative Humidity

Appendix 4: Actions by government bodies, professional organisations, pharmaceutical industries and regulatory authorities based on the six key areas identified by WHO and USFDA

Actions by government bodies

Securing the medicine and packaging	Securing the distribution of the medicine	Enhancing regulation, infrastructure and enforcement	Increasing penalties	Increasing vigilance and awareness	Increasing international collaboration
France: Each product is required to have a product code, batch number and expiration date (Taylor and Davies, 2008) **Turkey**: Includes a data matrix identifier in product packages (WHO, 2008a). **EU**: The European commission launched the Pharmaceutical Package; a set of initiatives aimed at enhancing medicines identification, reducing counterfeiting, enhancing	**Spain:** Incorporated the use of RFID tags (Taylor and Davies, 2008) **Russia:** An analyser using NIR for fast detection of counterfeit medicines is been piloted. A system of coded labels for authentication of medicines is been introduced (World report, 2006) **Turkey**: Introduced a track and trace system (WHO, 2008a). **China**: Employ the use of mobile labs fitted with instruments for NIR spectroscopy, TLC, Simple colour tests and microscopes. About 400 analytical automobiles have been acquired by the Chinese National Institute for the Control of Pharmaceutical and Biological products and are in the process of developing a desktop-sized high pressure liquid chromatography (Mullard, 2010) **Nigeria**: NAFDAC launched the Mobile Anti-counterfeiting Authentication Service whereby a 12-digit numerical code is sent to a free number for verification (NAFDAC, 2010b). NAFDAC in collaboration with Verification Technology Ltd has launched the use of RFID solution technology to identify and verify products, documents and other important items (Ogbebo, 2010a). NAFDAC has engaged in raids leading to confiscation and destruction of fake and substandard products; destroying over US$35, 753,014 worth of drugs found	**India:** Stepped up surveillance and increase in number of inspectors proposed (Forzley, 2005). Plans are in place to allow drug inspectors to arrest pharmacists involved in counterfeiting, carry out validation checks on drugs for export and introduce an obligatory exporting licensing and to conduct raids in areas noted for counterfeiting (Bate et al, 2010). It operates a central drug administration and improvement system (Forzley, 2005). It has organised chains of pharmacies such as Apollo pharmacy and Fortis Health World/Religare Wellness. **Philippines**: A technical working group consisting of representatives from the government and industry was created to redraft the countries drug regulation. Its government is engaged in training of inspectors, law enforcement agents and those who test drugs. **China**: A multi agency taskforce to curb sale of fake medicines as well	**France:** Tougher penalty of about 7.5m Euro fine and life imprisonment has been proposed **India**: Death penalty was proposed in 2003 and the minimum fine increased from 10, 000 rupees (about $320) to a million rupees (about $32, 000) (Patwardhan, 2010). Minimum jail term was increased from 5 years to 10 years in 2007 (Hemalatha, 2008; Partwadhan, 2010) **Philippines**: raised penalty for counterfeiting from 6 months to life imprisonment and payment of US$25, 000 (Forzley, 2005) **UK**: Additional charges on medicines counterfeiting have been instituted through the theft and forgery acts. A Jail term of 10-12 years is being	**India**: Whistle blower policy introduced to reward reporters of counterfeiting cases. However, Killugudi, 2010 cited in Bate et al, 2010 notes that this measure is not working. GSI (a supply chain organisation) in collaboration with the Food safety and Standards Authority of India developed an internet/ mobile phone-linked system for alerts and to aid recalls of food and pharmaceuticals (Miller, 2010) **China**: Whistle blower policy was introduced; rewarding reporters of counterfeit cases with up to 5, 000 Yuan ($US6, 048). **EU:** The ad hoc group of European Medicines Agency (EMEA) developed a tool (form) for easy dissemination of information on counterfeiting (Wertheimer and Norris, 2009). **Nigeria**: NAFDAC has engaged the local	**EU**: The European regional office provides support to countries of south-east Europe and the independent state of Russia, Ukraine and Kazakhstan. It also works with the council of Europe in arriving at a convention to fight medicines counterfeiting (WHO, 2008a). The European Union parliament public health committee is in support of new measures against online sale of counterfeit medicines. The first parliamentary reading of falsified medicines was held in September 2010. **Nigeria:** The Nigerian government is collaborating with the Indian and Chinese governments in the fight against medicines counterfeiting; the Chinese government has agreed to provide advanced information on drugs exported to Nigeria (Turkur, 2009). Nigeria played an active role in IMPACT; with the DG of NAFDAC acting as one of the chairs and more recently chairs the member state mechanism on combating substandard, spurious, falsified, falsely labelled and Counterfeit

supervision of pharmaceutical trade as well as introducing a stronger auditing system to ensure quality of active ingredients used in the manufacturing of pharmaceutical products Taylor and Craig, 2009). **Begium, Italy, Greece, Spain, Germany, Ireland, Turkey and Serbia** has an existing or an on-going development of national system of mass serialisation (Lery, 2010). Belgium, Italy and Greece are introducing the use of a serial number in addition to the national product code for each medicine pack.	to be fake or substandard between 2001 and 2004 (Akunyili, 2005b cited in Milissa McGinnis, 2010). Between 2001 and 2006; drugs worth US$109 million were destroyed (Edike and Obinwanne, 2006 cited in Milissa McGinnis, 2010). The Lagos state taskforce on counterfeit, fake drugs and unwholesome processed foods has also engaged in confiscation and destruction of fake drugs, sealing of premises which are illegal and arresting of persons involved in the act of medicines counterfeiting (The Tide News, 2008, This Day, 2008, Akoni, 2009, Oladunjoye, 2010 cited in Milissa McGinnis, 2010) **Sri Lanka**: The government banned importation from four Indian companies who were discovered to be dealing on substandard medicines. **Lebanon**: Pharmacies have been banned from running home delivery of medicines by the Minister of Health (Ghosn, 2010). **US:** Wal-Mart has introduced the use of RFID (Wertheimer and Norris, 2009). **South Africa**: Purchasing registered medicines from licensed suppliers, use of SOPs and audits between manufacturer and distributor and/ or provider were the key strategies identified that were used to protect medicines quality in South Africa (Patel et al., 2009a). **Ghana**: In 2008, the mPedigree developed a mobile drug anti-counterfeiting service in Ghana whereby consumers were required to text an 8-digit numerical code to a number for free authentication; similar system has been rolled out in Nigeria, Rwanda and Kenya (Mullard, 2010). An Anti Illicit Trade Coalition at Kpone Landfill has been involved in the destruction of counterfeit products for instance counterfeit toothpaste (My Joy online, 2009 cited in Milissa McGinnis, 2010). Sentinel sites were established in Bolatanga, Kumasi,	as sales over the internet have been set up. It has carried out raids which led to arrest of suspect persons (Mooney, 2010) **UK:** The government has produced guideline on counterfeit drugs (Cuff, 1996 cited in Ham, 2003). **EU**: The European union has established the EMEA, which coordinates the evaluation and supervision of medical products in the EU. It constitutes of an expert committee, which has an ad hoc group on counterfeit medicines. **Nigeria**: The Federal government submitted a draft resolution at the 63rd WHA seeking for WHO's support in tackling its chaotic drug distribution system and enhancing the regional fight against counterfeiting (Ogudipe, 2010). The Yobe state government formed a committee on fake drugs in 2002 (Daily trust, 2002) **Australia**: Focused on sanitising drug importation into Australia (WHO, 1997). **Lebanon**: 9 pharmacies and 2 warehouses involved in selling counterfeit drugs were recently shut down (Ghosn, 2010).	implemented (Lay down the law on fakes, 2010). There are proposals for the introduction of a charge of 'corporate killing' for companies who may have contributed to death of patients and those who fail to warn the public against a counterfeit product (Anonymous (2003) cited in Mehta (2006). The "disrupt and destroy" policy have been employed (WHO, 1997). **EU**: The European commission has proposed tougher penalties and awaiting confirmations by the European parliament and Council of ministers (Lay down the law on fakes, 2010). The council of Europe recently drafted the MEDICRIME convention which constitutes an international binding tool in the criminal law on counterfeiting of medical products and other related crimes aimed at promoting public health, promoting border co-operation between authorities and criminalising medicines counterfeiting (Ermert for Intellectual Property	governments at the grassroots by organising workshops, letting them know the need to join the agency in the fight against medicines counterfeiting(Ogbebo, 2010a). It engages in advocacy campaigns against medicines counterfeiting (Ogbebo, 2010a). Nigeria in collaboration with Indian authorities adopted the concept of 'whistle blower' where a cash reward of N200,000 is proposed to be given to anyone who discloses information leading to interception of fake drugs with a promise to make individual identities confidential (This Day, 2010). **Cambodia**: Engaged in public awareness programmes particularly targeted at people living in rural area at high risk through posters, radios, television spots and mobile video shows educating patients to distinguish fake drugs from genuine products as well as on recommended medicines (Newton et al, 2002 and Lon et al, 2006). Its National Malarial Control Program (NMCP) and Department of Drugs and Food (DDF) communicates the presences of counterfeit antimalarials to the Provincial	medicines (SSFFCs) set up by the WHO. Nigeria is also collaborating with medical equipment manufacturers such as Secure pharma, sproxil and Global PCCA and international organisations (Turkur, 2009). NAFDAC has entered into partnership with the USFDA to provide training to delegates. NAFDAC also aims at signing a memorandum of understanding with India and China, which will help harmonise strategies employed in curbing medicines counterfeiting (Ogbebo, 2010a). Nigeria also shares strategies with other countries in West African Drug Regulatory Authority Network (WADRAN), which they supervise, and sponsor. WADRAN is made up of 12 countries in West Africa. . **US**: USFDA collaborates with Nigeria by providing manpower training, capacity building, providing relevant equipment and intelligence (Turkur, 2009). The USP convention, 2010 identified priority areas to support developing countries such as Nigeria. One of which includes among other things supporting the provision of adequate infrastructures, human resources and sufficient funds for quality control laboratories, supporting the establishment of a strong and operational drug distribution

Turkey is implementing the use of a 2D matrix and the use of a serial number on all packaging. **France** has passed a law on the use of a mandatory 2D matrix coding. **Spain and Serbia** are implementing a legislation on the use of a mandatory serial number (Schwarze, 2010)	Ho, Accra and Tarkwa to help identify counterfeit medicines (Kwei, 2006-2009). Ghana, Rwanda and Kenya have introduced a system of drug distribution where by drug shops are franchised to improve access to cheap but high quality medicines as well as high quality dispensing services. It has also helped to ensure uniform standards among drug sellers in these countries (Centre for Global Development, 2010) **Mali**: A new technology involving the use of capillary electrophoresis to detect substandard medicines was rolled out in Mali, late 2009. This technology has been used in Switzerland, USA and Japan (IRIN, 2010a) **EU:** The European Union in collaboration with San Raffaele University in Milan, Italy embarked on a pilot project- Drug in Virtual Enterprise (DRIVE) which are involved in development of Electronic Product Code for prescription pedigrees and resulted to significant systems savings (Kontnik, 2003). The European Commission lauched the Medi-Fake initiative aimed at increasing surveillance at the borders (Taylor and Craig, 2009 **Uganda**: 5 minilabs were bought to test medicines at the point of entry to Uganda (Kariuke, 2008 cited in Taylor and Craig, 2009) **Brazil**: Introduced the use of bar coded packs to track medicines (Taylor and Craig, 2009). Brazil started a 3-year plan of drug serialisation aimed at tackling medicines counterfeiting. Law N^{0} 11.903 was passed on the 14th of January making it mandatory for all drug manufacturers and distributors to start the track and trace medicines serialisation. It created the National System of Medicines' control which will aid the monitoring of the drug supply chain in Brazil (The Sproxil Blog, 2010) **Angola**: The Government banned the sale of	**US**: The 1988 passage of the Prescription Drug Marketing Act (PDMA) was the United states first response to exposure of the Americans to medicines of poor quality (Anisfeld, 2007) **Pakistan:** set up a task force aimed at curbing counterfeiting. Drug courts were also established (Peterson and Obileye, 2002). **Vietnam** is developing more effective ways of coordination between regulatory bodies, police, customs and provincial authorities in order to improve detection of counterfeit medicines **Kenya:** Established a Pharmacy and Poisons Board which helps to identify and destroy counterfeit medicines as well as ensuring that pharmacies are licensed (Maina, 2008 cited in Taylor and Craig, 2009) **United Arab Emirates**: Its government has opened a highly equipped laboratory to detect poor quality medicines (Underwood, 2008 cited in Taylor and Craig, 2009) **Israel**: Established a Pharmaceutical Crime Unit to tackle criminal activities such as medicines counterfeiting (Taylor and Craig, 2009).	Watch, 2010) **East Africa**: The East African Community (EAC) secretariat developed a draft policy and a bill; The anti-counterfeit bill was passed in Kenya and Uganda (Michael, 2010). Kenya has enacted a law on counterfeiting (Equinet, 2010). Tanzania has developed resolutions relating to medicines counterfeiting (Equinet, 2010). Malawi is in the process of enacting a law against counterfeiting which may include a 10-year prison sentence and K50million fine **US**: The US Counterfeit Drug Enforcement Act of 2009 proposed an increase in the penalties and fines for drug counterfeiting as well as setting a requirement for drug manufacturers to report any cases of violations of authority within 48 hours. However, this proposal has not made much progress. **The United Arab Emirates, Vietnam, Oman, Bahrain, Kuwait and Qatar** have proposed	Health through alert letters, manual (s), annual malaria conferences and conducting training sessions (Lon et al, 2006) **US**: USAID in collaboration with the Rockville, Maryland-based US Pharmacopeia (USP) began airing the program: Pharmacide; a 4-minute public service announcement on national television in Cambodia, Thailand, Vietnam and Laos to publicise the dangers of counterfeit medicines. A similar program is underway for the African continent. **Pakistan**: Engaged in enlightenment campaign directed at the stakeholders (the public, manufacturers and importers) (Peterson and Obileye, 2002). **Indonesia and Mali** have started wide communication campaign to educate the public on the risks of medicines counterfeiting (Taylor and Craig, 2009). **Singapore:** Health services authority of Singapore is engaged in the global campaign against medicines counterfeiting. An example is its involvement in operation	system based on the Drug mart strategy, supporting the establishment of pharmacy chains like CVS and Walgreen in USA to improve access to cheap good quality medicines (USP Convention, 2010). The USP DQI is aiding the improvement of drug quality systems in 4 continents; Asia, Africa, Europe and South America (USP, 2010). It has also launched a guide for drug sampling and a guideline, which will aid low income countries to ensure the quality of their medicines (USP, 2010). With the assistance of USP, Ghana is improving its laboratory facilities. It has also employed the use of minilabs for the field testing of medicines (Bate and Hess, 2010) **Brazil**: Collaborates actively with INTERPOL (Taylor and Craig, 2009) **The US and New Zealand** have collaborated in shutting down an illegal internet spamming operation that sends off e-mails containing advertisements of fake drugs (Savage, 2008 cited in Taylor and Craig, 2009) **South East Asia:** In collaboration with IMPACT and other agencies, Association of Southeast Asian Nations (ASEAN) is promoting a regional network based model that will result in more effective

	medicines and surgery and hospital tools in municipal markets as they were discovered not to be sold under proper hygienic conditions (Agencia Angola Press, 2009 cited in Milissa McGinnis, 2010). **Egypt**: Warehouse raids were conducted through which a large number of counterfeit medicines were confiscated from the supply chain (CNN, Money, 2009 cited in Milissa McGinnis, 2010) **Kenya**: Its Pharmacy and Poisons board has launched a project in seven provinces geared towards closing down illegal drug distribution outlets (Maina, 2008 cited in Milissa McGinnis, 2010) **Tanzania**: Its government seized large amount of counterfeit medicines in circulation in Tanzania (Rugonzibwa, 2008b cited in Milissa McGinnis, 2010) **Zimbabwe**: Police arrests persons involved in the dispensing of unregistered and expired medicines (The Herald, 2009 cited in Milissa McGinnis, 2010)	**Iraq:** Its ministry of health is introducing new anti-counterfeiting measures to tackle medicines counterfeiting **Senegal**: Increased monetary budget for curbing counterfeiting in 2006 (Milissa McGinnis, 2010) **Sierra Leone**: The National Drug Safety Monitoring Programme was commissioned by the Pharmacy board (Koroma, 2006 cited in Milissa McGinnis, 2010) and the Pharmacy board has been engaged in raids leading to destruction of counterfeit medicines (Massaquoi, 2007 cited in Milissa McGinnis, 2010). Its ministry of health has also increased monetary budget of the Pharmacy board so that more inspectors can be hired (Horner and Hallam, 2009 cited in Milissa McGinnis, 2010)	a death sentence as punishment for medicines counterfeiting (Mehta, 2006) **Peru:** Instituted imprisonment for up to 10 years for anyone involved in selling, storing, packaging or producing adulterated, substandard or fake medicines (Ruiz, 2008 cited in Taylor and Craig, 2009)	Pangea 11 by INTERPOL (Government of Singapore, 2009) **China**: Published a list of websites involved in unscrupulous activities (China CSR, 2008 cited in Taylor and Craig, 2009) **Peru**: Its consumer protection agency destroyed a large proportion of fake medicines and containers during a public awareness campaign on medicines counterfeiting (Taylor and Craig, 2009)	regulatory and policing strategies (Taylor and Craig, 2009) **Ghana**: With the support of the US government, the government of Ghana has established drug quality monitoring sites (Bate, 2010). Through this drug quality program, fake coartem has been detected in the Ghana market (U.S Pharmacopeia press release, 2009 cited in Milissa McGinnis, 2010) **China**: China has organised several international and provincial forums on combating medicines counterfeiting such as the international forum in December, 2009 held in Guangzhon and the provincial forum in October, 2009 held in Guangdong (Yang, 2010)

Actions by professional organisations

Securing the medicine packaging and distribution of the medicine	Enhancing regulation, infrastructure and enforcement	Increasing vigilance and awareness	Collabotation
RPSGB: Advocates for original package dispensing in order to help detection of counterfeit products. **ACPN:** Destruction of fake and expired drugs (Ogbebo, 2010b). **HDMA:** The Health Distributors Management Association (HDMA) submitted guidelines for pharma distribution system integrity derived from its members' voluntary best practices. The association is made up of 89 active distributors and operates a Product Safety Task Force whose mission is to develop an industry wide plan to implement various technological solutions such as adoption of an emerging product track-and-trace effort called the MIT AutoID Center's Electronic Product Code (EPC) system (Kontnik, 2003). **The National Association of Chain Stores (NACDS) with the help of a consulting form Accenture** develops findings and recommendations in the area of medicines counterfeiting. **PCN**: The Kano chapter sealed 5 drug	**FIP:** Adoption of FIP/IFPMA statement "Ensuring the quality and safety of medicinal products to protect the patient" at the 1998 FIP congress. FIP policy statement on counterfeit medicines was adopted in Barcelona with a replacement of it adopted in 2003 at the FIP congress in Sidney (FIP, 2003). **NABP**: In order to avoid counterfeit drugs from entering the supply chain, NABP (National Association Boards of Pharmacy) developed legislation models aimed at fighting counterfeiting; this was done with contributions from different pharmaceutical organisations in Australia, Canada, South Africa, Puerto Rico, Virgin Islands and New Zealand. Florida took the lead by enacting	**PCN:** Has organised workshops and seminars on medicines counterfeiting and drug quality in Nigeria (Ogbebo, 2010b) **PSN**: The state branches of PSN organise seminars and public enlightenment campaign during its pharmacy week (Erhun et al, 2001). PSN organises meetings which provide an avenue to sharing information on drug quality in order to guide importers (Orivri, 2009). **The National Medical Association (NMA)**: Organises a monthly Continuing education programme where doctors are taught on drugs/drug quality. It also collaborates with NAFDAC from which it obtains the list of banned pharmaceuticals that it disseminates to its members (Orivri, 2009). **FIP** has also been involved in creating specific and practical tools for pharmacists for fighting counterfeiting; examples include the Tools for visual inspection and Guide for Pharmacists. Several articles have been published by FIP as a means of raising awareness of the risks of counterfeiting among pharmacists and pharmacy leaders as well as educating them. Sessions at FIP congress meetings in 2006, 2007, 2008, 2010 and 2011 were dedicated to discussions on medicines quality, which includes counterfeiting in order to sensitize pharmacists on dangers on medicines counterfeiting (FIP, 2010). **IPSF**: IPSF organised its first Anti-counterfeit Drug Campaign (ACDC) in 2007 with the aim of increasing the awareness of the risks posed by counterfeit medicines among students in health professions as well as providing them with the necessary information needed as to the threats of such as criminal acts (IPSF, 2007). **RPSGB:** The RPSGB and MHRA developed a guide for Pharmacists on counterfeiting in 2006 and were updated in 2008. RPSGB also provides pharmacists with information on medicines counterfeiting and engages in patient awareness campaigns. **FIP**: FIP through WHPA has been leading the IMPACT working group on communication. The WHPA tool kit ('Be aware, take action) for health professionals and public health advocates was developed in 2008 to aid detection, reporting and prevention of medicines counterfeiting (Kopp, 2010). The first 'Be aware, take action workshop on medicines counterfeiting was held in	**FIP**: FIP has also been collaborating with the Council of Europe ad hoc committee since 2004 in the fight against medicines counterfeiting. In 2008, this became the Committee of Experts on Minimizing Public Health Risks Posed by Counterfeiting Medical Products and related crimes (CD-P-PH/CMED).

company depots after concerns were raised that the companies were engaged in the manufacture of substandard medicines (Muhammad, 2009 cited in Milissa McGinnis, 2010). **Medical experts in Uganda** collaborates with the Police to conduct raids in order to confiscate poor quality medicines (The New Vision, 2008 cited in Milissa McGinnis, 2010).	Senate bill 2312 which contains explicit information on wholesaler registration and requirements for pedigrees (Forzley, 2005).	October, 2010 in San Jose, Costa Rica while a second workshop took place in Nigeria in November (Kopp, 2010). **France: The French Council of Pharmacists** in collaboration with The French Drug Regulatory Authority developed a guide for Pharmacists in counterfeit medicines during a campaign aimed at emphasising the risk of medicines counterfeiting. Patient information leaflets were also produced. **Germany**: An awareness campaign on medicines counterfeiting has been organised by the Federal Union of German Pharmacists Association. A video clip on this was broadcasted over the internet and cinemas as well as free post cards disseminated in public places like the restaurants and bars. **Lebanon: The Lebanese Council of Pharmacists** in collaboration with the Lebanese minister of health, FIPO-WHO EMRO Pharm. Forum and the Conference Internationale des orders de Pharmaciens Francophones (CIOPF) launched a campaign in 2008 on counterfeit medicines with the use of posters and leaflets. A guide for pharmacists was also published. They have also issued recommendations on curbing medicines counterfeiting (Chauve, 2008). **Spain:** The Association of Pharmacists in Spain and the Spanish Ministry of Health signed an agreement for a strong collaboration in the fight against medicines counterfeiting. This included development of training materials for community and hospital pharmacists on the detection on counterfeit drugs, establishing ways of ensuring the legality of medicine suppliers and an awareness campaign directed towards patients on the risk of counterfeit medicines over the internet. **American Society of Health System Pharmacists (ASHP)** has developed a list of strategies that pharmacists can use to protect against drug counterfeiting. It also alerts its members and hospital pharmacy departments of cases of counterfeiting (ASHP manual, 2003).	

Actions by Pharmaceutical industries

Securing the medicine and packaging	Securing the distribution of the medicine	Enhancing regulation, infrastructure and enforcement	Increasing penalties	Increasing vigilance and awareness	Increasing international collaboration
Sanofi-Aventis recently opened a central anti-counterfeiting laboratory in 2008 in France to research on such techniques such as the use of chemical markers in the detection of counterfeit pharmaceuticals. (Taylor and Davies, 2008). **VS International** (manufacturer of Ciprotab® (a brand of ciprofloxacin)	**Sanofi-Aventis:** It created an anti-counterfeiting organisation in 2005 and a central operational coordination team and launched a team to be in charge of the analysis of suspect products and development of a database for counterfeit drugs (Sanofi-Aventis, 2010). **Pfizer**: Pfizer capsule making division recently acquired non-exclusive rights to the Nano codes (containing encrypted information about the drug) and punched to the surface of the medicine without altering its chemical constituent (Mullard, 2010). Pfizer has also adopted the use of RFID in Viagra® (Wertheimer and Norris, 2009) **GlaxoWellcome** launched a global anti-counterfeiting strategy and operating procedures for its products which included monitored destruction of waste, field monitoring for counterfeits, and security packaging earning it an award as the winner of the Global Anti-Counterfeiting in 1998 (Kontnik, 2003). GSK announced their adoption of RFID technology to help track, trace and authenticate some of their products. It has also played a leading role trying to help maintain a closed drug supply system in the US by providing legislatures with evidence of the impact of counterfeit drugs in developing countries. Its Packaging Design and Security Team also carries out forensic investigation of suspect products. **MIT (Massachusetts Institute of Technology)** in collaboration with various industrial sponsors such as J & J, Abbot, Pfizer, P&G and other universities are involved in development of Electronic Product Code for prescription pedigrees (Kontnick, 2003). **European Federation of Pharmaceutical Industries and Association (EFPIA):** Undertook an anti-counterfeit product verification pilot project between September, 2009 and January, 2010 which showed that a product verification system based on two dimensional (2D) data matrix at the point of dispensing was effective and	**Pfizer** and many other industries are working together with enforcement agencies to trace counterfeiters and prosecute them (Pfizer, 2004 in Lybecker, 2008). Pfizer led an investigation in China leading to dismantling of an operation involving about 11 countries which included Britain and Israel (Sommerville, 2005 cited in Lybecker, 2007). Due to the tremendous increase of sales in counterfeited drugs over the internet and via mail order, firms such as Pfizer Inc. and Microsoft Corp. declared a joint effort aimed at reducing internet sales of Viagra (Tesoriero, 2005b). Similarly, Google Inc. and Yahoo Inc. both decided to limit searches performed over the internet on pharmaceutical advertising in the US to licensed US and Canadian pharmacies' (Angwin and Bialik, 2004 in Lybecker, 2008). Interpol via the OASIS (Operation Assistance, Service and Infrastrucural support), the Operation Fiela was carried out leading to confiscation of various	**Confederation of Tanzania Industries (CTI):** Seeks more deterrent penalties for medicines counterfeiting in Tanzania; recommending that the 1963 Merchandize Act be amended (Rugonzibwa, 2008a cited in Milissa McGinnis, 2010).	**IFPMA**: Published its ten principles on counterfeit medicines in order to emphasise the scope of the problem and make relevant clarifications. It also engages in awareness campaigns on medicines counterfeiting (Schwarze, 2010) **Pfizer:** Pfizer's senior director of global security and his staff train prosecutors, judges and detectives on the dangers of counterfeit medicines (Dolgin, 2010). The UK branch of Pfizer in collaboration with MHRA aired a 1-minute advertisement on medicines counterfeiting in local movie theatres and late-night TVs. Pfizer also set up a campaign website; http://www.realdanger.co.uk/ featuring a point and click rat catcher (Torres, 2010).	**Pfizer**: collaborates with other stakeholders such as drug regulatory authorities and has set up a diversified international team to help fight the problem (Pfizer, 2010). **GSK**: GSK partners with PSI in curbing counterfeiting of medical products and is involved in training of Drug Regulatory Authority (DRA) staff from different parts of the world such as staff of State Food and Drug Administration (SFDA), China (GSK, 2010). **PSI**: corporates with Interpol and shares relevant information on critical cases (Plancon, 2010). PSI and IFPMA (International Federation of Pharmaceutical Manufacturers and

popularly marketed in Nigeria has incorporated a number of anti-counterfeit measures to their products (Bate et. al, 2010). **Astrazeneca** has introduced several technological strategies to protect their products from counterfeiting (Astrazeneca, 2010)	feasible and did not increase the workload of pharmacists (EFPIA, 2010) In 2005, **Purdue Pharma LP** in collaboration with a wholesaler (H.D Smith) piloted a project involving the use of a pedigree to document and track their products as they move in the supply chain (Tesoriero, 2005a in Lybecker, 2008). **Abbott** has a global product protection team which focuses on securing its supply chain by employing the track and trace technologies and other saftety features, collaborating with key stakeholders, engaging only authorised wholesalers and advocating deterrent laws against counterfeiting (Abbott, 2010). Both J&J as well as Abbot have employed supply restrictions in a bid to make wholesalers source their products directly from the company rather than from other sources, which are usually prone to counterfeiting (Lybercker, 2008). Abbot also tried to facilitate customer access to their approved wholesalers by publicizing the names of the wholesalers who agreed to their terms and conditions (Lybecker, 2008). Following such efforts by the industries, wholesalers have also expressed their commitment in stopping buying and selling drugs among the secondary wholesalers which is strongly viewed as an entry point for counterfeiters (Lybecker, 2008). **F Hoffmann La-Roche Ltd** in India developed a serialisation technique in 2008 to protect all its products in India from being counterfeited (Bate et. al., 2010). **Eli lilly:** Engaged in securing its supply chain (Eli lilly, 2010). **Astrazeneca**: engages in market and supply chain monitoring. It conducts analysis of all suspect counterfeits of their brand and tackles the problem via a global issues management team (Astrazenca, 2010) **Roche** issued its statement on counterfeiting in April, 2009 which reaffirmed its support to stakeholders in the fight against counterfeiting and has developed its policy to help fight medicines counterfeiting, engages in product monitoring and uses technology to identify fake drugs (Roche, 2009) **Merck:** In a bid to ensure good management of its supply chain, Merck has implemented terms and conditions for the sale of their products in the US, requiring customers to purchase Merck products from authorised distributors. The firm also publishes list of their authorised distributors and conducts a regular audit of distributors. It has also initiated pilot projects to evaluate the use of 2d data matrix	counterfeit medicines in places like Lesotho (Ilston, 2009 cited in Milissa McGinnis, 2010) **The Pharmaceutical Research and Manufacturer's of America (PhRMA)** has created a five point anti-counterfeiting strategy comprising of; voluntary reporting of cases of counterfeiting within five days of discovery, concluding of PDMA pedigree requirements, request for a summit on anti-counterfeiting, opposition to importation and formation of an anti-counterfeiting taskforce (Kontnik, 2003). **Johnson and Johnson**: is also employing security companies in countries such as China and India to investigate counterfeit cases and provide necessary evidence, which may justify raids led by police officials (Goodman, 2002 in Lybecker, 2008). Between 2001 and 2003, Johnson and Johnson established 38 criminal cases against entities involved in counterfeiting their products in China when compared to just two cases that was established in the three preceding years before 2001 (Goodman, 2002 in Lybecker, 2008). **Astrazeneca**: collaborates with other stakeholders such as PSI,		**GSK:** The firm has also been involved in series of awareness campaigns for instance through leading US magazines targeting consumers It also collects data on medicines counterfeiting in order to help establish the extent of the problem as well as coordinates and disseminates information on medicines counterfeiting (PSI, 2010). **Astrazeneca:** supports increased awareness and education of patients and health care professionals (Astrazeneca, 2010) **German Pharma Health Fund (GPH**F): Developed methods of training for analysing of about 35 frequently used finished forms of essential medicines **Roche:** educates the public and helps to provide training to officials (Roche, 2009).	Associations) are collaborating with government officials in many countries in a bid to establish an intelligence network aimed at reducing medicines counterfeiting (Chatterjee, 2001 in Lybecker, 2008). **Merck**: supports the work of IMPACT and EU proposals for a new Anti-Counterfeiting Trade Agreement (ACTA) (Merk, 2008).

	bar code technology and collaborates with other stakeholders in educating the public on the dangers of counterfeit drugs and how to avoid them (Merck, 2008). **Rx 360**: this is a non-profit pharmaceutical manufacturers and suppliers consortium launched in June, 2009 to help ensure the quality of medicines as they move across the supply chain by adapting standards and best medicines supply practice procedures, developing technology to ensure product security, monitoring the supply chain and promoting shared audit program (VanTrieste, 2009) **Jiuzhonting Logistic Company**: a major medicines distributor in China has a computer quality system which contains a database of their products (Yang, 2010) **Xiangxue Pharmaceutical Company, Guangzhou, China** has an anti-counterfeit software which labels each medicine pack with a high density encryption code (Yang, 2010) **GPHF**: Developed a minilab for field testing of medicines in developing countries (Wertheimer and Norris, 2009) **Pharmasecure Inc**: Has introduces the use of mobile phones for the detection of counterfeit medicines in India (Bennett, 2010). **Sproxil and Mpedigree** have introduced similar systems in Nigeria, Ghana and Kenya **Novartis**: Novartis is rolling out a hidden digital marker technology that allows customs officials to detect whether secondary packaging of a product is authentic by placing it under an office scanner and sending the resulting image to the firm's security division for verification. The firm intends inputing this feature on all products as well as on the primary packaging (Taylor, 2010)	DRAs, IMPACT, law enforcement bodies and trade organisations (Astrazeneca, 2010) **Eli lilly:** Partners with government and non-governmental organisation and other trade unions in order to strengthen enforcement and raise awareness (Eli lilly, 2010). **Dabur India** has also engaged in raids leading confiscation of fake products (Bate et. al, 2010).			

Actions by regulatory bodies

Securing the medicine and packaging	Securing the distribution of the medicine	Enhancing regulation, infrastructure and enforcement	Increasing vigilance and awareness	Increasing international collaboration
Tanzania Food and Drug Authority (TFDA): A key resolution in 2009 was to introduce the writing of trade names and batch numbers on all medicines purchased by or sold from wholesale pharmacy outlets (TFDA, 2009). TFDA carries out inspection of Pharmacies to help detect unapproved and low quality medicines (Shekighend, 2009 cited in Milissa McGinnis, 2010).	**Tanzania Food and Drug Authority:** Put a program in place for the accreditation of drug dispensing outlets and overseas the quality of services and products sold in these outlets (Centre for Global Development, 2010) **SFDA** established the National Drug Code Management Methods to introduce labels (a 14-digit code number which indicates the country of origin and manufacturer of the product as well as the type of medicine) in order to help monitor products in China's drug supply/distribution chain (Taylor and Davies, 2008). SFDA website recently provides link to approved online medical service providers (ChinaCSR, 2008 cited in Taylor and Craig, 2009). The State Council have purchased vehicles equipped with TLC tool kit, NIR Spectrometer and a computer with drug registration software with plans on equipping the vehicles with HPLC (Yang, 2010) **USFDA:** In December 2006, wholesalers were required by FDA to supply pedigrees unless they are authorised distributors from a manufacturer. The state of California	**EDQM**: Has formed a Committee of Experts on minimizing public health risks caused by counterfeiting medical products and related crimes through which training programmes on combating medicines counterfeiting has been organised. (EDQM, 2010). It is implementing a pan-European track and trace service for medicines involving the use of the Unique Medicine Identifier (UMI). A challenge in using the UMI is that if the codes get copied and reach the consumers first before the genuine brands are scanned and sold, then counterfeited medicines can only be detected at the point of dispensing of the original product and may therefore be difficult to recall the counterfeited ones from the patients (Lery, 2010). **USFDA**: FDA formed an anti-counterfeiting task force in July 2003 in response to the growing trend of medicines counterfeiting (FDA, 2009). **FDA's Office of Criminal Investigations' (OCI)** has the responsibility of fighting medicines counterfeiting (Kontnik, 2003). In June, 2010, the white house revealed a strategic plan to fight medicines counterfeiting through an enhanced IPR protection (Kopp, 2010**)** **WHO:** WHO introduced a voluntary, confidential system to report medicines counterfeiting (Amon, 2008). The issue of counterfeiting was again discussed at the 63rd World health assembly in May, 2010; with a resolution to create a working group on counterfeit medical products which will help to examine WHO role in the fight to curb counterfeiting and ensure availability of good quality medicines as well evaluate	**WHO:** WHO was the first to set up the world's first web based system aimed at tracking counterfeiters in 2005; the Rapid Alert System (RAS) in the Western Pacific Region which was initiated to keep relevant authorities abreast of counterfeiting cases so that they could develop measures to counter the effects such activities could have (WHO, 2006 c). **IMPACT** organises conferences on drug counterfeiting and has a rapid alert system for counterfeit drugs (Newton et al., 2008). **The National Drug Authority of India** is collaborating with Kenya and Tanzania to conduct awareness campaigns on counterfeiting (Nakkazi, 2010) **European Directorate for the Quality of Medicines (EDQM**): Developed a rapid alert notification form, risk communication model and model for network and single point of contact (SPOC) and are involved in the training of officials on ways to curb medicines counterfeiting (EDQM, 2010) **USFDA**: In 2005, the FDA created an alert network between health professionals and consumer groups in order to aid rapid communication of any information regarding counterfeited products as well as developing strategies to hinder its progression. The network is made up of	**WHO:** In 1992, first international meeting on counterfeiting was held in Geneva which recommended a collaborative effort to help curb the Problem and defining a counterfeit drug. Establishment of a network for the communication of information on counterfeit medicines was advocated (WHO, 1997). In 1994, resolution WHA 47.13 was adopted to help member states in their effort to solve the problem. In 1995, DMP-DAP project was established (assisted by Japanese govt.) in pursuance of resolution WHA 47.13. This led to the to the organisation of a workshop in 1997 with outcomes of recommendations for international and national actions against counterfeiting, setting up of a database containing information on anecdotal reports from the literature and on reports from Drug Regulatory Authorities and Industry as well as the

USFDA: The U.S Secret Service's Forensic Services Division has a memorandum of understanding with FDA to conduct laboratory analysis of drug packaging and labels. FDA has also commenced consultations on the use of chemical markers on products in the US (Taylor and Davies, 2008). In July 2009 FDA issued a guide for industry in drug anti-counterfeiting with focus on the incorporation of physical-chemical identifiers into solid oral dosage form for an easy identification of	instituted the use of pedigrees starting from the manufacturer (Taylor and Davies, 2008). In collaboration with Reconnaissance, USFDA has tried to identify area of risks and opportunities for an increased security in the US drug supply. Reconnaissance organised a conference on counterfeiting in Geneva in 2002 which brought together several stakeholders (Ham, 2003). The FDA sponsored the Product Surety Project, which identifies some areas of potential counterfeiting, and terrorist attacks which may be linked to some medicine counterfeiting cases. The FDA also has started using TruScans for an easy detection of counterfeit medicines (Schwarze, 2010). **WHO:** In 1988, WHA adopted resolution WHA41.16 requiring initiation of programmes to prevent and detect poor quality drugs (Amon, 2008). The WHO in collaboration with the Pharmaceutical Institute of the University of Bonn (Germany) and the German Pharma Health Fund (GPHF) have produced a drug testing kit as a strategy against counterfeiting in developing countries (Lybecker, 2008). **IMPACT** in collaboration with INTERPOL has been conducting raids involving different countries for instance there was an operation by IMPACT/INTERPOL, which targeted internet sites that sell counterfeit medicines in 2008 and 2009. 1200 websites involved in illicit trading were found; 153 were closed down while 12 arrests were made.	the relationship of WHO with IMPACT. The group made its recommendations during the 64th WHA in 2011 (WHO, 2010c) and presently a Member State Mechanism (MSM) is in place as WHO's strategy in combating SSFCs. The Impact working group on regulation revised the WHO Good Distribution Guidelines in order to make a particular emphasis on counterfeits, developed an assessment tool to evaluate national, regional, sub-regional situation and identify any gaps and needs. They have also developed guidelines for rapid response for drug regulatory authorities in cases of medicines counterfeiting. The working group on enforcement has its main initiatives as establishing a single point of contact, regionally and globally as well as facilitation of communication among different stakeholders. It has also produced and distributed a basic investigative tool kit manual especially for countries with little or no expertise in pharmaceutical crime, in particular counterfeiting. They have also been conducting trainings and raids in different regions in collaboration with agencies such as INTERPOL for instance are the operation 'Mamba 1' in East African countries (Uganda and Tanzania) and many other agencies in early 2008 which targeted counterfeiters of life saving medicines (INTERPOL, 2008b cited in Taylor and Craig, 2009). Operation 'Mamba 11' was conducted in 2009 and involved 3 east African countries (Tanzania, Uganda and Kenya) (Sillo, 2010). Between July and August, 2010, operation 'Mamba 111' was conducted and it involved 5 East African countries (Kenya, Tanzania, Uganda, Rwanda and Burundi) (Sillo, 2010). There was operation "Storm" in South east Asia from April to September 2008, involving different countries (Cambodia, China, Laos, Myanmar, Singapore, Thailand and Vietnam) and other agencies. These resulted in closure of drug outlets, arrests and drug seizures (INTERPOL, 2008a cited in Taylor and Craig, 2009). Another operation coded as "Pangea" was held from 16-20 November, 2009; coordinated by INTERPOL-PFIPC-IMPACT involving 25 countries such as Canada, Germany, Ireland, Israel, New Zealand, Singapore, Switzerland, the UK and the USA targeting illegal internet premises (INTERPOL, 2008c cited in Taylor and Craig, 2009). INTERPOL also coordinated operation Zambezi from 12 October, 2009 to 6th November, 2009 involving raids in four African countries; Zambia, Zimbabwe, Malawi and Swaziland (INTERPOL, 2009). It also aims to develop an advanced investigation manual. The IMPACT working group on regulatory and legislative infrastructure developed	health professionals, national organisations, consumer groups and industry representative (Kopp, 2010). It also launched the Safe Medicines Partnership website, **www.safemedicines.org** which has a variety of information on medicines counterfeiting (Writer, 2005) **WHO**: Addressed medicines counterfeiting internationally in 1985 at the conference of experts on the rational use of medicines in Nairobi with a recommendation for a clearing body be set up by WHO and other international organisations in order to collect data and inform governments on the extent of the problem (Amon, 2008). The IMPACT Communications working group has developed the IMPACT Communications Strategy. Collaborated with WHPA to develop a tool kit for health professionals and patients on counterfeiting. The group has also collaborated with Interpol to develop strategies based on the media to raise awareness of counterfeiting and has produced a variety of electronic and hard copy resource materials on counterfeiting. The WHO IMPACT held its third annual meeting in Tunisia to raise awareness of the danger of medicines counterfeiting and how best to curb it (African Union, 2010) **NAFDAC:** NAFDAC engaged in re-orientation and motivation of its staff for positive outcome (Akunyili, 2007). Public enlightenment campaign via jingles on the radio and TV, alert notices about fake drugs in the supply chain for instance is an alert issued on fake maloxine tablets in circulation in 2009 (Ogundipe and Obinna, 2009 cited in Milissa McGinnis, 2010), billboards, publication in national dailies on	publication of guidelines for development of measures the combat counterfeit drugs in 1999 (WHO, 1999a). Since then there have been additional workshops for instance in Japan and Viet Nam. Training and country studies have also been carried out by WHO e.g in VietNam and in Myannmar on medicines counterfeiting. A network of 120 responsible individuals from different ministries of health was formed to inform the WHO on counterfeiting (Ham, 2003). In a bid to crack counterfeiting, WHO held a conference in Rome in 2006, which led to the Declaration of Rome and the formation of IMPACT, which was aimed at forming a collaborative effort among a range of stakeholders in order to curb medicines counterfeiting. The major areas of focus of IMPACT are legislative and regulatory infrastructure, regulatory implementation, enforcement, technology development for detection of counterfeits and technology transfer to developing countries as well as communication of risk and innovations/strategies aimed at curbing counterfeiting (WHO, 2010a). IMPACT collaborates with other bodies such as the charity-Pharmaciens sans Frontieres, professional organisations such as the

counterfeited products (FDA, 2009). **WHO**: The IMPACT working group on technology has produced a document covering technologies aimed at protecting medicines, checklist to aid authenticatio n of suspect drugs by enforcement agencies and conducting a comparative analysis of different field testing methods based on needs of users, locations and their successes/fe asibility.	**NAFDAC**: In order to mop up the fake drugs already in circulation, the Nigerian government has in collaboration with registered manufacturers confiscated and destroyed expired counterfeit medicines thereby increasing the cost of obtaining such illicit medicines (Naik, 2004 in Lybecker, 2007, Akunyili, 2007). Introduction of thermo scientific TruScan® handheld RAMAN instrument for rapid identification of fake and substandard drugs as well as the introduction of the mobile authentication service to help validate the quality of medicines (NAFDAC, 2010a) are some of the strategies in place. NAFDAC has also established control points in China and India (Ogbebo, 2010a) **National Drug Authority of Uganda**: Conducts tests on samples of medicines in Uganda in order to determine the extent of poor quality medicines (Nafula, 2008 cited in Milissa McGinnis, 2010). The National Drug Authority in collaboration with the Police conducts raids in Uganda to seize poor quality medicines (Wandera and Bagala, 2008 cited in Milissa McGinnis, 2010) **The Zambia Bureau of Standards**: Withdraws counterfeit medicines when discovered in Zambia (Africa News, 2009 cited in Milissa McGinnis, 2010). **The National Institute for the Control of Pharmaceutical and Biological Products** in China have developed rapid tests for an easy detection of counterfeit medicines	"Principles and elements for national legislation against medical products". It also initiated a study comparing existing legislation used to combat medicines counterfeiting. The Max Planck Institute is leading this and making comparison between different countries (WHO, 2010d). The WHO introduced the Certification scheme to ensure the quality of medicines and established the pre-qualification list (Wertheimer and Norris, 2009). The WHO has published a lot of guidelines in the area of medicines counterfeiting (Kopp, 2010) **NAFDAC:** Engaged in updating of NAFDAC laboratories and inspection of laboratories abroad by NAFDAC to ensure their compliance to cGMP. Appointment of analysts in India, China and Egypt who re-certify drugs for importation, mandatory pre-shipment information before importation, mandatory NAFDAC clearance permit prior to financial document processing in Nigeria for all drug importers, discontinuation of importation of drugs marked 'For export only' into Nigeria by insisting on an authenticated certificate of free sale, regular monitoring of GMP of local manufacturers and enforcement of NAFDAC registration guidelines (Akunyili, 2007) are some of the strategies NAFDAC employs. Also, the designation of Calabar and Apapa sea ports, Murtala Muhammed and Mallam Aminu Kano International Airports as the only ports of entry for the importation of drugs and pharmaceutical raw materials. NAFDAC has also conducted secondary school essay competition contests to help publicize the harmful effects of counterfeit drugs, established consumer safety clubs in schools, attempted to raise a NAFDAC army made up primary school children who are taught on the advantage of good quality products (Naik, 2004 in Lybecker, 2007, WIPO, 2008). Nigeria in collaboration with Indian authorities adopted the concept of 'whistle blower' where a cash reward of N200,000 is proposed to be given to anyone who discloses information leading to interception of fake drugs with a promise to make individual identities confidential (This Day, 2010). NAFDAC has banned importation from some Indian Pharmaceutical companies, sealed some drugs from being imported (Chinyere, 2008 in Bate et al., 2010) and set up an office for its regulator in India (The Economic Times, 2009 in Bate et al., 2010). NAFDAC conducted a survey and audit of all drugs on sale in Nigeria in order to build a	medicines counterfeiting for example; the list of counterfeited medicines, workshops/meetings/seminars for stakeholders (Akunyili, 2007). NAFDAC in collaboration with Christables started a state-to-state drug market sensitization on 15th of July 2010, which began at the Onitsha head bridge, Anambra state (Daily Sun, 2010). A quarterly bulletin which distinguishes between counterfeit medicines, original and blacklisted companies is usually published by NAFDAC (Federal Ministry of Health and World Health Organisation, 2010) **MHRA:** The MHRA published its Anti-counterfeiting Strategy for 2007-2010, highlighting the need for an effective communication with health professionals, patients and drug regulatory bodies for more positive outcomes (Taylor and Craig, 2009). The MHRA has also conducted about 5 internet days of action in over a 2-year period. A proposal by the MHRA to the WHO IMPACT prompted the conduction of an international internet day of action in November 2008; the 'operation Pangea 1'. This was coordinated by Interpol and involved different countries such as Canada, Ireland, Israel, Singapore, Switzerland, UK, USA, Germany and New Zealand. Operation "Pangea 11" was subsequently conducted in 2009, involving 25 countries (Ahmed, 2010). Following operation "Pangea 11", four national awareness campaigns were conducted and there were press releases in the countries involved. 43 countries in 6 continents and about 109 agencies indicated interest holding similar operation. **National Drug Authority of Uganda**:	FIP, Financial institutions such as the World bank and consumer groups such as International Alliance of Patients' Association (Taylor and Craig, 2009). **NAFDAC**: Initiated WADRAN in 2008 as an avenue to share strategies and experiences by member states in the fight against medicines counterfeiting as well as promote access to good quality affordable generics (Akunyili, 2007). **The Uganda National Drug Authority** in collaboration with Interpol conducted raids which led to the discovery of counterfeit medicines (Ultimate media, 2009 cited in Milissa McGinnis, 2010) **World Customs Organisation (WCO):** WCO's 176 member customs have signed a declaration to crack down medicines counterfeiting while ensuring access to safe medicines via a global initiative (Henry J Kaiser Family Foundation International news, 2010; Kopp, 2010)

	(Yang, 2010) **The Hubei FDA, China and Hubei Provincial Istitute** compiled a book for medicines testing in 2009 to aid detection of counterfeit medicines (Yang, 2010)	pharmaceutical database (Bate and Hess, 2010).	Issues alerts on counterfeit medicines in circulation in Uganda (Nyakairu and Nakabugo, 2005; Bogere and Nafula, 2007 cited in Milissa McGinnis, 2010). **The Medicines Control Authority of Zimbabwe** issues public alerts on counterfeit medicines in circulation (UN Integrated Regional Information Networks, 2007 cited in Milissa McGinnis, 2010) **Cameroon SFDA**: Exposed 30 websites in May, 2010 which are thought to be engaged in the sale of counterfeit medicines and disseminating false drug information (Kopp, 2010)	

Appendix 5: Ethical approval documents

Ethics approval document from Lagos University Teaching Hospital and Ethics approval document from UCL School of Pharmacy, London

LAGOS UNIVERSITY TEACHING HOSPITAL

HEALTH RESEARCH AND ETHICS COMMITTEE

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REF. NO: ADM/DCST/HREC/VOL.XV/364

22nd November, 2011

Chioma Joy Onwuka
PhD student
Dept. of Practice and Policy
The School of Pharmacy, University of London
29/39 Brunswick Square
London, United Kingdom
WC1N IAX.

PROVISIONAL APPROVAL OF RESEARCH PROPOSAL

I wish to refer to your request in respect of the above stated subject.

Provisional approval has been granted to you to commence with the study titled: **"PHARMACEUTICAL QUALITY AND ACCESS IN NIGERIA; VALIDATION OF THE MOBILE AUTHENTIFICATION SERVICE (MAS) AS AN ANTI-COUNTERFEITING TECHNOLOGY AND EXPLORATION OF STAKEHOLDER PERCEPTIONS AND EXPERIENCES IN NIGERIA".**

Wishing you all the best in your study.

Thank you.

DR. N.U. OKUBADEJO
CHAIRMAN, HEALTH RESEARCH & ETHICS COMMITTEE

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University of London
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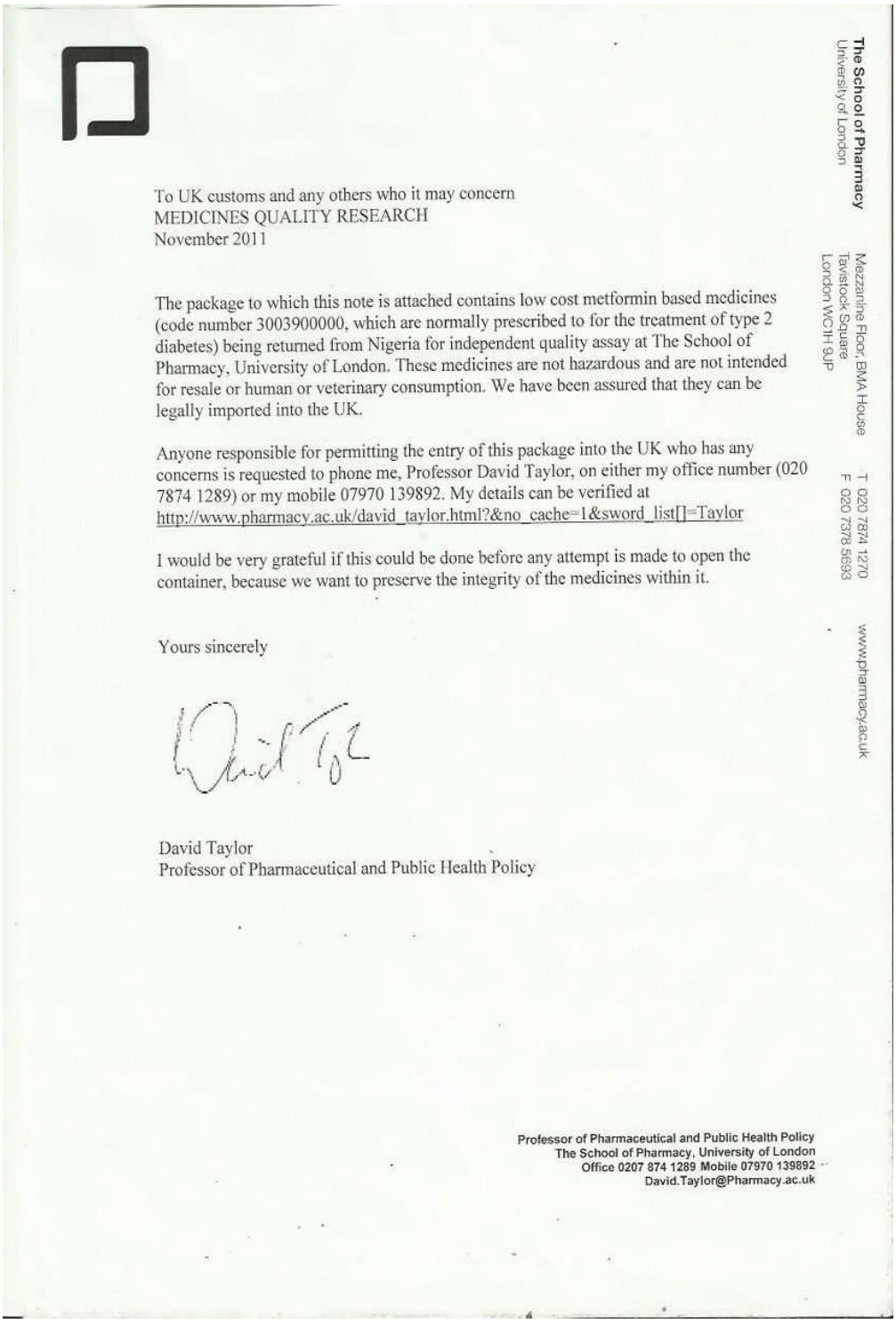
www.pharmacy.ac.uk

Research Ethics Committee

Confirmation of Outcome of Ethics Review

REC Reference	**REC/B/10/11**
Title of project: Medicines counterfeiting and pharmaceutical quality and access in Nigeria; Validation of the Mobile Authentication Service (MAS) as an anti-counterfeiting technology and exploration of stakeholder perceptions and experiences in Nigeria.	
Name of applicant(s): Chioma Joy Onwuka	
Name of supervisor (if student applicant): Professor Felicity Smith/ Professor David Taylor	
Date of submission: 20 September 2011	
Name and Department of independent reviewer: Dr Sarah Clifford, Practice & Policy	
Name and Department of second independent reviewer (if applicable): Dr Sudax Murdan, Pharmaceutics	
Date of REC review: September 2011	
Outcome of review: ☒ **Approved** ☐ Approved with minor revision (as below) ☐ Further information required (as below) ☐ Resubmission required	
Comments: The revised version of the application was approved, taking on board comments from the reviewers.	
Reviewed on behalf of the Research Ethics Committee by: Research Ethics Committee	

Appendix 6: Letter to UK Customs



The School of Pharmacy
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Mezzanine Floor, BMA House
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www.pharmacy.ac.uk

To UK customs and any others who it may concern
MEDICINES QUALITY RESEARCH
November 2011

The package to which this note is attached contains low cost metformin based medicines (code number 3003900000, which are normally prescribed to for the treatment of type 2 diabetes) being returned from Nigeria for independent quality assay at The School of Pharmacy, University of London. These medicines are not hazardous and are not intended for resale or human or veterinary consumption. We have been assured that they can be legally imported into the UK.

Anyone responsible for permitting the entry of this package into the UK who has any concerns is requested to phone me, Professor David Taylor, on either my office number (020 7874 1289) or my mobile 07970 139892. My details can be verified at http://www.pharmacy.ac.uk/david_taylor.html?&no_cache=1&sword_list[]=Taylor

I would be very grateful if this could be done before any attempt is made to open the container, because we want to preserve the integrity of the medicines within it.

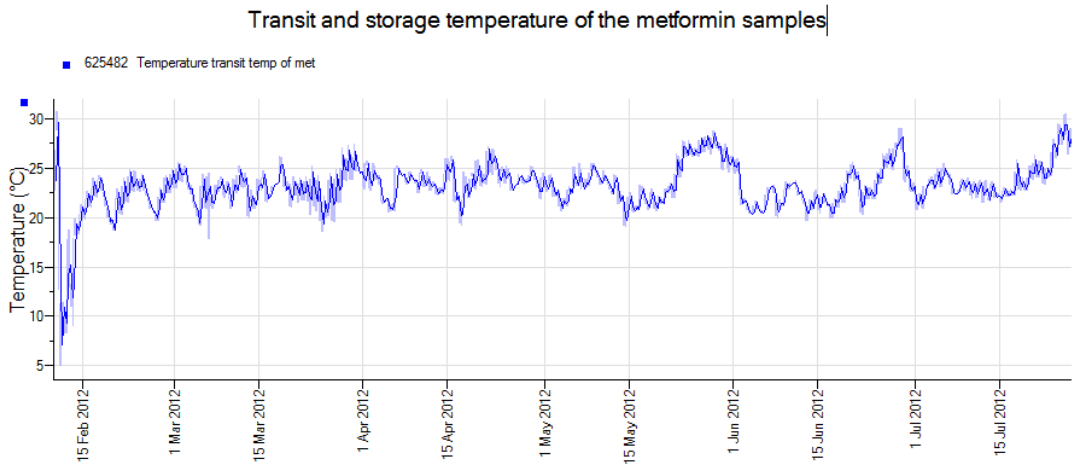
Yours sincerely

David Taylor
Professor of Pharmaceutical and Public Health Policy

Professor of Pharmaceutical and Public Health Policy
The School of Pharmacy, University of London
Office 0207 874 1289 Mobile 07970 139892
David.Taylor@Pharmacy.ac.uk

Appendix 7: Temperature log for samples during transport and storage

Temperature log for samples during transport and storage (19th October 2011- 31st July, 2012)



Appendix 8: Visual Inspection tool

1. Packaging

Any drug should be packaged in a container, which can be anything from a glass bottle to a blister pack, to a tube of glass, plastic or metal. A folding carton bearing the label very often protects the container. Check the type of packaging and compare it to known containers for the same drug from the same manufacturer. The packaging and the labeling of pharmaceutical products is a very complex and expensive business. Thus, the process and the quality of packaging material are very difficult to counterfeit. This is why a thorough visual inspection could be an important screening step for drug quality control. However, producers of counterfeit drugs are quick to copy special labeling and holograms.

	Yes	No	Other Observations
1.1 Container and Closure			
Do the container and closure protect the drug from the outside environment e.g. properly sealed?			
Do they assure that the drug will meet the proper specifications throughout its shelf life?			
Are the container and the closure appropriate for the drug inside?			
Is the container safely sealed?			

1.2 Label

The information written on the label is very important. The information can be printed on a label adhered to the container, or printed directly onto the container itself, but all information must be legible and indelible.

If there is a carton protecting the container, does the label on the carton match the label on the container?			
Is all information on the label legible and indelible?			
1.2.1 The trade name:			
Is the trade name spelled correctly?			
Is the drug (trade name) registered in the country by the DRA (drug regulatory authority)?			
Is the drug legally sold in the country?			
Does the symbol ® follow the trade name?			
1.2.2 The active ingredient name (scientific name):			
Is the active ingredient name spelled correctly?			
Do the trade name and the active ingredient name correspond to the registered drug?			
1.2.3 The manufacturer's name and logo:			
Are the manufacturer's name and logo legible and correct?			
Does the logo or hologram (if applicable) look authentic?			
Does it change colour when viewed from different angles?			

1.2.4 The manufacturer's full address:

All manufacturers are required by international law to print their complete address on the label. Many companies making substandard or counterfeit drugs do not have a traceable address on the label.

Is the manufacturer's full address legible and correct?			
Has the company or its agent registered the drug in the country?			
1.2.5 The drug strength (mg/unit):			
Is the strength - the amount of active ingredient per unit - clearly stated on the label?			
1.2.6 The dosage form (e.g., tablet/capsule):			
Is the dosage clearly indicated?			
Is the indicated drug under this dosage form registered and authorized for sale in the country?			
1.2.7 The number of units per container:			
Does the number of tablets listed on the label match the number of tablets stated on the container?			

	Yes	No	Other Observations

1.2.8 The batch (or lot) number:

Drugs under the same batch/lot number are expected to be equivalent. In a continuous process, a batch corresponds to a defined portion of the production, based on time or quantity. Drugs from the same batch number should have the same history of manufacturing, processing, packing, and coding. All drug quality control testing should be based on batch/lot numbers.

Does the numbering system on the package correspond to that of the producing company?			

1.2.9 The date of manufacture and the expiry date:

An expired drug should not be sold under any circumstances.			
Are the manufacture and expiry dates clearly indicated on the label?			

1.2.10 Storage information:

Are the storage conditions indicated on the label?			
Has the drug been properly stored?			

1.3 Leaflet or package insert:

All drug packages should contain a leaflet explaining dosage, the drug content, the adverse affects, the drug actions, and how the drug should be taken. The only exceptions are where the packaging includes all the information that would otherwise be in the leaflet.

Is the package insert printed on the same coloured or same quality paper as the original?			
Is the ink on the package insert or packaging smudge-proof?			

2. Physical Characteristics of Tablets/Capsules. All types of medicines can be and have been counterfeited from cough syrups to injections. As mentioned above, it is important to check the packaging of these drugs. Additionally, medicines in the form of tablets or capsules can be checked for signs of moisture, dirty marks, abrasion erosion, cracks, or any other adulteration.

	Yes	No	Other Observations

2.1 Uniformity of Shape:

Are the tablets/capsules uniform in shape?			

2.2 Uniformity of Size:

Are the tablets/capsules uniform in size?			

2.3 Uniformity of Colour:

Are the tablets/capsules uniform in colour?			

2.4 Uniformity of Texture:

Tablets can be film-coated, sugar-coated or enteric-coated.

Do the tablets have a uniform coating?			
Is the base of the tablets fully covered?			
Are the tablets uniformly polished, free of powder, and non-sticking?			

2.5 Markings (scoring, letters, etc):

Are markings uniform and identical?			

2.6 Breaks, Cracks and Splits:

Are the tablets/capsules free of breaks, cracks, splits or pinholes?			

2.7 Embedded surface spots or contamination:

Are the tablets/capsules free of embedded surface spots and foreign particle contamination?			

2.8 Presence of empty capsules in the case of a sample of capsules:

Is the sample examined free of empty capsules?			

2.9 Smell

Does the medicine smell the same as the original?			

Adapted from WHO (2014)

Appendix 9: Interview topic guide for the stakeholders

Interview topic guide for consumers

Major questions in bold, mini questions in normal font, *prompts in italics* and small blue font for concluding remarks

<u>What consumers think of accessibility to good quality medicines in Nigeria</u>

1) How will you describe a medicine that is a good quality?

2) Have you heard about any of these? Counterfeit medicine/substandard medicine/adulterated medicine/degraded medicine

3) Do you think that this is a problem in Nigeria?

4) Do you think that the problem is worse of/better than in the past?

….Why has the situation changed?

…..What has helped/hindered?

5) How can you know that a medicine is of good quality?

…….Before taking it

……after taking it

…are you concerned about the quality of medicines that you take?

…..Do you take any measures/ make any conscious effort to know if your medicines are fake or original? (if so, what do you do?)

……Have you/ anyone you know ever bought a medicine which you suspect not to be of good quality (can you describe what happened-where did you buy the medicine, How did you know (physical detection/ineffective/complication, what did you do about it and what was done?) if no go to question 6

6) What determines the brand/type of medicine that you purchase?

…on prescription

…Recommendation (who)

…Cost

…Brand/generic

..Country of manufacture (any preference of where your medicines should come from?)

…other

7) What determines where you buy your medicines?

..Public/private

..Pharmacy/PMV/drug market

..Cost

..what do you think of the quality of cheap generic? ?); are you comfortable asking for them?

..Outlet quality mark

…other

8) Are you aware of any initiative by the government (NAFDAC) against fake medicines?

9) What do you think about these initiatives?

10) What do you think are the major challenges to fighting fake medicines in Nigeria?

11) How do you think this can be tackled (your suggestions)

Among all these initiatives, I am particularly interested in MAS.

...MAS costs money, would you be prepared to pay more for your medicines if their cost increase as a result of MAS

…what do your family and friends think about MAS

…Overall, how satisfied are you with the service? (for only those who have used it)

<u>Perceptions and experiences of consumers about MAS</u>

12) Have you heard of this before?

13) Have you used it? (If yes proceed for consumers who have used it if no and have heard of it find why? And still proceed)

14) How does the service work?

15) What do you think of the service?

…..perception of quality as a result of the tag

….trust in the service

…usefulness

…ease of use

16) What potential or actual benefits/impacts do you think MAS has?

….quality authentication

….add on messages

…..your purchasing behaviour

…increased therapeutic response to treatment

….intercepting counterfeiters (have you experienced this as a result of MAS?)/reduction in counterfeiting

….increased confidence

…..adherence to medication

17) What potential problems/challenges do you think MAS has/will have?

18) Do you have any suggestions on how MAS can work better?

19) Would you like to learn more about medicines counterfeiting and MAS?

……Through which means?

*Do you have any more things to say on any issue that we discussed today?

*Do you have any questions which you wish to ask?

*I would like to fill in your details in the data sheet so that I can contact you to clarify any answers that you provided below. It should take about 1 minute to complete.

Thank you so much for your time (participant to fill the demographic sheet immediately afterwards)

Interview topic guide for medicine sellers

Major questions in bold, mini questions in normal font, *prompts in italics* and small blue font for concluding remarks

What medicine sellers think of accessibility to good quality medicines in Nigeria

1) How will you describe a good quality medicine?

……Have you heard about any of these?

Counterfeit medicine/substandard medicine/adulterated medicine/degraded medicine/generic medicine

…..Can you define them from your point of view?

2) Do you think that these are a problem in Nigeria?

3) Do you think that the problem is worse of/better than in the past?

….Why has the situation changed?

…..What has helped/hindered?

4) How can you know that a medicine is of good quality?

…….Before taking it

……after taking it

…are you concerned about the quality of medicines that you purchase to sell/ in general?

…..Do you take any measures/ make any conscious effort to know if your medicines are fake or original? (if so, what do you do?)

..Do you only sell medicines with NAFDAC number (if so why and if not why?)

……Have you/ anyone you know ever bought or taken a medicine which you suspect was not of good quality? (can you tell me more about what happened- where did you buy the medicine, How did you know (physical detection/Ineffective/complication, what did you do about it and what was done? Where there any difficulties?)

…..what is the most popular form of counterfeiting/fake you have experienced?

….Are there any particular group/class of medicines mostly counterfeited (if yes, what are these or their characteristics)

4) What determines the brand/type of medicine that you purchase?

…demand

…Recommendation (who)

…Cost (branded/generic)

..Country of manufacture (any preference of where your medicines should come from?)

5) What determines where you procure your medicines?

….cost

….what do you think of the quality of cheap medicines (what of generics?)

..Outlet quality mark

…Do you think that some outlets/places stock counterfeit/substandard medicines while some stock genuine? (Do you know of any such outlets?)

6) Are there factors that you consider before selling or recommending medicines to your clients?

…Quality

…Socioeconomic class

….Other

7) What do you think are the major challenges to fighting fake medicines in Nigeria?

8) How do you think this can be best tackled (your suggestions)

9) What roles do you think pharmacists/traders/PMVs can play to avoid counterfeiting?

…Educating patients

….Checking thoroughly

….Other

10) Are you aware of any initiative by the government (NAFDAC) against fake medicines?

…what are these initiatives?

11) What do you think about these initiatives?

Among all these initiatives, I am particularly interested in MAS.

<u>Perceptions and experiences of medicine sellers about MAS</u>

12) Have you heard of this before?

13) Have you used the service? (To authenticate what you purchased/ for your patients or clients?)

14) How does the service work?

15) What do you think of the service?

…..perception of quality as a result of the tag

….trust in the service

…usefulness

….ease of use

…..increased demand and sale

...MAS costs money, would you be prepared to pay more for your medicines if their cost increase as a result of MAS

…what do your clients think about MAS

…Overall, how satisfied are you with the service? (for only those who have used it)

16) What potential or actual benefits/impacts do you think MAS has?

….quality authentication

….add on messages

…..your purchasing behaviour

…increased therapeutic response to treatment

….intercepting counterfeiters (have you experienced this as a result of MAS?)

….increased confidence

…..adherence to medication

….Other

17) What potential problems/challenges do you think MAS has/will have?

18) Do you have any suggestions on how MAS can work better?

..if yes, what are these

19) Would you like to learn more about medicines counterfeiting and MAS?

…..Through which means?

* Do you have any more things to say on any issue that we discussed today?

* Do you have any questions which you wish to ask?

* I would like to fill in your details in the data sheet so that I can contact you to clarify any answers that you provided below. It should take about 1 minute to complete.

Thank you so much for your time (participant to fill the demographic sheet immediately afterwards)

Interview guide for policy makers

Major questions in bold, mini questions in normal font, *prompts in italics* and small blue font for concluding remarks

<u>What policy makers think of accessibility to good quality medicines in Nigeria?</u>

1) How can you describe a good quality medicine?

2) Have you heard about any of these?

Counterfeit medicine/substandard medicine/adulterated medicine/degraded medicine

….Can you define them from your point of view?

3) Do you think that these are a problem in Nigeria?

4) Do you think that the problem is worse of/better than in the past?

….Why has the situation changed?

…..What has helped/hindered?

5) Have you encountered a medicine which you think is of bad quality?

…..How did you discover this?

……How were the cases handled? (Prevention from going back into the distribution chain, contacting companies whose products are involved before destruction of the medicines)

…..what is the most popular form of counterfeiting/fake you have experienced?

….which group of medicines do you think are counterfeited most

6) What do you think are the major challenges to fighting fake medicines in Nigeria?

7) How do you think these can be best tackled (your suggestions)

Talking about initiatives against medicines counterfeiting, I am particularly interested in MAS.

8) What do you think about this service?

…..Quality authentication

…usefulness

….ease of use

…cost

…..increased demand and sale

10) What potential or actual benefits/impacts do you think MAS has?

….quality authentication

….add on messages

…..consumer purchasing behaviour

…increased therapeutic response to treatment

….intercepting counterfeiters (have you experienced this as a result of MAS?)

….increased confidence

…..adherence to medication

11) What potential problems/challenges do you think MAS has/will have?

12) Do you have any suggestions on how MAS can work better?

Do you have any more things to say on any issue that we discussed today?

I would like to fill in your details in the data sheet so that I can contact you to clarify any answers that you provided below. It should take about one minute to complete.

Do you have any questions that you wish to ask?

Thank you so much for your time (participant to fill the demographic sheet immediately afterwards)

Appendix 10: Information leaflet for stakeholders

Information leaflet version 1 (Community pharmacists and policy makers in pharmacy)

Information leaflet December 2011

Nigeria has been faced with the problem of fake and substandard medicines. Due to this, a lot of initiatives are in place to curb the menace. However there is a lack of systematic research on the real extent of the availability of poor quality medicines especially for chronic diseases. Also, there are very limited studies involving exploration of issues relating to accessibility of good quality medicines and the perceptions of Nigerian stakeholders on initiatives in place to improve the quality of medicines. Initiatives against medicines counterfeiting may attract more support based on evidence of their impact on the users and will perform better and prevent wastage of scarce resources if users' experiences of the advantages and disadvantages of such interventions in practice are incorporated in their future development as this will increase their likelihood of being responsive to the users' needs. It is based on this that researchers at the School of Pharmacy, University of London and Faculty of Pharmacy, University of Lagos are working together to explore the perceptions of stakeholders on issues relating to accessibility of good quality medicines in Nigeria and the recently introduced Mobile Authentication Service (MAS) in order to develop recommendations on ensuring accessibility of good quality medicines to the public and make recommendations for the future deployment of such National Agency for Food and Drug Administration and Control (NAFDAC) and allied initiatives which will in turn lead to availability of good quality medicines and improvement in health outcomes. Data arising from this research will be included in my PhD thesis and may be published in peer-reviewed journals.

Participation is voluntary and you can withdraw at anytime. If you choose to participate in the study, you will be asked to take part in the interview with the researcher at a place and time that is most convenient for you. The estimated time for each interview is between 20-30 minutes. However, you are free to talk as long as you wish. You may be contacted sometime after the interview to confirm if our findings truly represent what you meant to convey in your interview. The researcher will also ask for your permission to tape record your responses so that nothing you say will be missed out. Your tape-recorded responses will be wiped out as soon as the information is transcribed.

To ensure that your confidentiality is maintained, your name will not be included in any reports or publications arising from this research. Names of all participants in this study will be coded and extra caution will be taken to ensure that no one will be identified.

The study has been approved by The School of Pharmacy, University of London Research Ethics Committee and the Lagos University Teaching Hospital Health Research and Ethics Committee.

Thank you so much for taking out time to read this information leaflet.

If you have any question about the research, please contact;

Chioma Onwuka or Prof Felicity Smith on +44(0)2078741288 or felicity.smith@pharmacu.ac.uk
Mobile number: +2348034539090
E-mail: talk2pharmchomy@yahoo.com

Dr Chukwuemeka .P. Azubuike
Mobile no.: 08033618556
E-mail: chupcazubuike@yahoo.com or Prof. David Taylor on +44 (0) 2073875693 or david.taylor@pharmacy.ac.uk

Information leaflet version 2 (consumers, patent medicine vendors and traders)

Your medicines- Fake or Original

Most of us take medicines in our daily lives but most times we cannot guarantee the quality of these medicines we take. Some steps have been taken by NAFDAC to help certify the quality of medicines we take. Now, we want to know if these steps have worked or not and what can be done for us to get good medicines which we all deserve.
Thank you for taking out the time to read this information leaflet.

If you have any questions about this research, please contact;

Chioma Onwuka

Mobile number: +2348034539090

E-mail: talk2pharmchomy@yahoo.com

Prof Felicity Smith on +44(0)2078741288 or felicity.smith@pharmacu.ac.uk or

Dr Chukwuemeka .P. Azubuike

Mobile no.: 08033618556

E-mail: chupcazubuike@yahoo.com

Prof. David Taylor on +44 (0) 2073875693 or david.taylor@pharmacy.ac.uk

Appendix 11: The Consent Form version 1 (for Community pharmacists and policy makers)

Title of Study: Pharmaceutical quality and access in Nigeria; Validation of the Mobile Authentication Service (MAS) as an anti-counterfeiting technology and exploration of stakeholder perceptions and experiences in Nigeria.

Name of Researcher: Chioma Joy Onwuka, the School of Pharmacy, University of London

Institutional Researcher: Dr C.P Azubuike. Faculty of Pharmacy, Univeristy of Lagos

Co-researchers: Professor Felicity Smith (The School of Pharmacy, University of London); Professor David Taylor (The School of Pharmacy, University of London)

Statement of person giving informed consent:

I understand what the study involves. I understand that my participation is voluntary and will not be disadvantaged in any way if I do not take part. I know enough about the purpose, methods, risks and benefits of the research study and I agree to take part in it.

Name of the participant: .

Signature:

Date: .

This research has been approved by the School of Pharmacy, University of London Ethics Committee and Lagos University Teaching Hospital (LUTH) ethics committee. If you have any question about your participation in this research, you can contact the principal investigator Chioma Joy Onwuka at her office Department of Practice and Policy, The School of Pharmacy, University of London, Mezzanine Floor, BMA House, Tavistock Square, London, WC1H 9JP. Her phone number is 08034539090. You can also contact her supervisors, Professor Felicity Smith Prof on +44(0)2078741288 or felicity.smith@pharmacy.ac.uk and Professor David Taylor on +44(0)2073875693 or david.taylor@pharmacy.ac.uk. Alternatively you can reach the institutional researcher on 08033618556 or chupcazubuike@yahoo.com

PLEASE KEEP A COPY OF THE SIGNED INFORMED CONSENT

Appendix 12: The Consent form version 2 (For consumers, Patent Medicine Vendors and traders)

Title of study: Fake medicines; the Nigerian situation

Name of Researcher: Chioma Joy Onwuka, the School of Pharmacy, University of London

I understand what the study involves and I would wish to take part.

Name of the participant: ..

Signature: .. ..

Date: .

If you have any question about your participation in this research, you can contact the principal investigator Chioma Onwuka. Her phone number is 08034539090 or her contact person in Nigeria, Chukwuemeka Azubuike on 08033618556

PLEASE KEEP A COPY OF THE SIGNED INFORMED CONSENT

Appendix 13: Demographic data sheets for stakeholders

Demographic data sheet for Community pharmacists/Patent Medicine Vendors/traders

Completing this demographic data sheet is voluntary and the data you provide will be kept in such a manner as to guarantee your privacy.

Please mark X in the boxes or circle the answers applicable to you or fill in your answers in the spaces provided as the case may be, you may tick more than one answer if that applies to you.

I am Chioma Joy Onwuka, a doctoral researcher at The School of Pharmacy, University of London. My PhD is on the Validation of the Mobile Authentication Service (MAS) and exploring stakeholder perceptions and experiences of its use linked to the quality of medicines in Nigeria

Participant characteristics

Gender: ☐ Male ☐ Female

What is your age category: ☐ 20-30 yrs ☐ 30-40yrs ☐ 40-60yrs ☐ >60yrs

Location of outlet .. Rural/Urban

Number of years of practice .. ..

Private data – This will also be held confidential and is just used by the researcher to contact you in case clarification is required on any of the answers that you provide for the questions that we ask you. All responses will be stored and analysed anonymously and independent of any private data you provide.

Your name

.....

Your e-mail address

.....

Phone number

Demographic data sheet for Consumers

I am Chioma Joy Onwuka, a doctoral researcher at The School of Pharmacy, University of London. I am currently conducting a study to know your perceptions, experiences and attitudes towards the quality of medicines in Nigeria and the recently introduced Mobile Authentication Service (MAS).

Completing this demographic data sheet is voluntary and the data you provide will be kept in such a manner as to guarantee your privacy.

Please mark X in the boxes or circle the answers applicable to you or fill in your answers in the spaces provided as the case may be, you may tick more than one answer if that applies to you.

Participant characteristics

Gender: ☐ Male ☐ Female

What is your age category: ☐ 20-30 yrs ☐ 30-40yrs ☐ 40-60yrs ☐ >60yrs

Occupation: Employed Unemployed Retired In full or part-time education Others .

Educational level: Illiterate Nursery school Primary school Secondary school Higher institution (Diploma, Bachelor, Post-graduate degree, etc)

Place of residence ..Rural/Urban

Your name

.....

Your e-mail address

.....

Phone number

Demographic data sheet for Drug regulatory staff/ Policy makers in Pharmacy

Completing this demographic data sheet is voluntary and the data you provide will be kept in such a manner as to guarantee your privacy.

Please mark X in the boxes or circle the answers applicable to you or fill in your answers in the spaces provided as the case may be, you may tick more than one answer if that applies to you.

I am Chioma Joy Onwuka, a doctoral researcher at The School of Pharmacy, University of London. My PhD is on the Validation of the Mobile Authentication Service (MAS) and exploring stakeholder perceptions and experiences of its use linked to the quality of medicines in Nigeria

Participant characteristics

Gender: ☐ Male ☐ Female

What is your age category: ☐ 20-30 yrs ☐ 30-40yrs ☐ 40-60yrs ☐ >60yrs

Occupation

Position .

Number of years of practice in the field of medicines regulation and policies ..

Private data – This will also be held confidential and is just used by the researcher to contact you in case clarification is required for any of the answers that you provide us on any of the questions that we ask you. All responses will be stored and analyzed anonymously and independent of any private data.

Your name

.....

Your e-mail address

.....

Phone number

Appendix 14: Audit trail of outlets visited to obtain samples

Community pharmacies visited NB: Names of outlets and new codes have been omitted for confidentiality

S/No.	Random number	Location	Initial code assigned (See details including full address, quantity purchased, price and physical description of primary and secondary packaging in a separate report)		Comment	Recoded
1	336	*Ikorodu	Gl336 and Ge336	Result of Text message authentication OK- Text message sent and response received almost immediately about 11seconds after at 11pm on 5/12/11	Both purchased (Glucophage® and Diabetmin®)	
2	502	*Aguda	Gl502 and Ge502	OK- Text message sent response received after 2 seconds at 8.12am on 3/12/11	Both purchased (Glucophage® and Diabetmin®)	
3	249	*Ebute Metta	Ge249		Supplied other brand. Does not stock Glucophage®	
4	87	*Apapa	Gl87 and Ge87	OK- Text was sent and response received 4.1seconds after at 7.19pm on 05/12/2011	Both purchased (Glucophage® and Diabetmin®)	
5	376	*Bariga	Gl376 and Ge376	OK- Text message sent and response received almost immediately about 2 seconds after at 6.04pm	Pharmacy at the location but have changed name. The Glucophage® lacked information leaflet (Glucophage® and Diabetmin®) purchased	
6	300	*Gbagada	Gl300 and Ge300	OK- Text message sent and response received almost immediately about 3 seconds after at 17.35pm	Both purchased (Glucophage® and Diabetmin®)	

7	561	*Gbagada	Gl561 and Ge561	OK- Text message sent and response received almost immiditaely about 4 seconds after at 5.17pm	Both purchased (Glucophage® and 5 sachets of Diabetmin®)	
8	144	*Yaba	Gl144 and Ge144	OK- Text message sent with airtel and response received almost immediately about 6 seconds after at 12.50pm	Both purchased (Glucophage® and Glumin®)	
9	401	*Ipaja	Ge401		Supplied only other brand (Inophage®). Said Glucophage® is finished but will have it in the evening	
10	346	*Surulere	Gl346 and Ge346	Text message sent response received after 6 seconds at 8.14am on 3/12/11	Both purchased (Glucophage® and Diabetmin®)	
11	269	*Festac Town	----------		Didn't have any. Both have finished	
12	47	*Ikeja	Gl47	OK- Text message sent and response received almost immediately about 4.9 second after at 9.59am on 6/12/11	Supplied only Glucophage®. Said people don't ask for other brands so have stopped stocking them as they get expired. Showed an example of her expired Diabex®. She said she will order some Diabex® if needed and will call if available. She advised against purchasing cheap metformin stating that the cheap ones have increased side effects such as head ache.	
13	12	*Ajah	Gl12 and Ge12	Text message sent and response received almost immediately about 9 seconds after at 5.40pm	Both purchased (Glucophage® and 4 sachets of Diabetmin®)	
14	105	*Ajah	Gl105 and Ge105	OK-Text message sent and response received almost immediately about 6 seconds after at 17.22pm	Both purchased (Glucophage® and 4 sachets of Diabetmin®)	
15	211	*Anthony village	Ge211		Supplied other brand. Didn't have Glucophage®-finished but had another foreign brand at a high price. He said that it is metformin from UK that his uncle did not finish taking	
16	468	*Ajegunle	Gl468 and Ge468	OK- Text was sent and response received 11.5seconds after at 7.00pm on 05/12/2011	Both purchased (Glucophage® and Diabetmin®)	
17	265	*Ikotun	Gl265 and Ge265	OK- Text message sent and response received almost immediately about 5 seconds after at 15.53pm	Both Purchased (Glucophage® and Diabetmin®)	
18	572	*Idimu	Gl572 and Ge572	OK- Text message sent and response received almost immediately about 4 seconds after at 16.21pm.	Both purchased (Glucophage® and Diabetmin®)	

19	338	*Olodi Apapa	Gl338 and Ge338	OK- Text sent with etisalat response received after 4.7 seconds at 7.27pm on 05/12/2011	Both purchased (Glucophage® and Gluformin®)	
20	66	*Festac town	Gl66 and Ge66	Response for Gl66 received within 9seconds	Both purchased (Glucophage® and Diamet®)	
21	203	*Ikorodu	Gl203 and Ge203	OK- Text message sent and response received almost immediately about 4.6seconds after at 11.06pm on 5/12/11	Both purchased (Glucophage® and Diabetmin®)	
22	476	*Egbe	Gl476 and Ge476	OK- Text message sent and response received almost immediately about 1 second after at 4.02pm	Both purchased (Glucophage® and Gluformin®); 5 satchets of Gluformin® purchased	
23	413	*Ketu	Gl413 and Ge413	OK- Text message sent and response received almost immediately about 1 second after at 04.33pm.	Both purchased (Glucophage® and Diabex®)	
24	114	*Surulere			No longer a pharmacy but a photoshop so none could be bought	
25	215	*Ikeja	Gl215 and Ge215	OK- Text message sent and response received almost immediately about 14.9 seconds after at 10.34am on 6/12/11	Both purchased (Glucophage® and Diabetmin®)	
26	446	*Victoria Island	Gl446	OK-Text message sent and response received almost immediately about 8 seconds after at 17.29pm	Glucophage® bought. They stock only Glucophage® as that is what people request	
27	180	*Ikotun	Ge180		Other brand bought (Glucophage® by Merck (Private) Pakistan. Sells other brand but didn't see it at the parking store	
28	302	Satelite town	Gl302 and Ge302	OK- Text message sent at 6.36pm and response received after 22.9 seconds on 1/1/12	Both purchased (Glucophage® and and Diabetmin®)	
29	184	*Ikorodu	Gl184 and Ge184	OK- Text message sent and response received almost immediately about 5.3 seconds after at 8.09pm on 5/12/11	Both purchased (Glucophage® and Gluformin®)	
30	586	*Ajah	Gl586 and Ge586	OK-Text message sent and response received almost immediately about 15 seconds after at 17.58pm	Both purchased (Glucophage® and Diabetmin®)	

31	431	*Agege	Gl431 and Ge431	OK- Text message sent and response received almost immediately about 3 seconds after at 17.56pm	Didn't have any brand at first visit as he said people never ask for metformin and the few times they had; it expired so they stopped buying. However, the storekeeper promised to order it and would be available in the evening. At second visit; had Glucophage® and Gluformin®. These were purchased. He said the medicines were sourced from a distributor in Mushin. He went further to say of pharmacies that sell substandard/fake in Mushin and called names. He said in such pharmacies all medicines are stocked but the quality is the major problem	
32	452	*Ikeja	Ge452		Supplied only other brand (Climax® metformin). Sells Glucophage® but said it is finished and will have it again in about 2 days	
33	160	Somolu	Gl160 and Ge160	OK-Text message sent and response received almost immediately about 5 seconds after at 13.05pm	Both purchased (Glucophage® and Diabetmin®)	
34	334	*Festac town	Gl334 and Ge334	OK. Text message for GL334 received after 5minutes 9 seconds	Pharmacy, still at the location but has changed name. Both purchased (Glucophage® and Glucophage® by Merck (Private) limited, Pakistan	
35	541	**Ajamgbadi	----------		Couldn't locate	
36	289	*Idimu	Gl289 and Ge289	OK- Text message sent and response received almost immediately about 5 seconds after at 15.11pm 2/12/2011)	Both purchased (Glucophage® and Diamet®)	
37	270	*Ikotun	Gl270 and Ge270	OK- Text message sent and response received almost immediately about 1 second after at 3.46pm	Both purchased (Glucophage® and Diabetmin® 5 sachets remaining)	
38	141	*Ikorodu	----------		Closed at the time of visit	
39	558	*Ikotun,Lasu rd	Gl558 and Ge558	OK- Text message sent and response received almost immediately about 6 second after at 15.35pm	Both purchased (Glucophage® and Diamet®)	
40	585	*Gbagada	Gl585 and Ge585	OK- Text message sent and response received almost immediately about 1 second after at 2.38pm	Both purchased (Glucophage® and Diabex®); 2 satchets of Glucophage® remaining was purchased	
41	256	Ijora	Gl256 and Ge256	OK- Text message sent and response received almost immediately about 5 seconds after at 13.00pm	Both purchased (Glucophage® and Glucophage® by Merck (Private) Limited, Pakistan	
42	91	*Ikorodu	Gl91 and Ge91	OK- Text message sent and response received almost immediately about 4.8seconds after at 10.56pm on	Both Purchased (Glucophage® and Diamet®)	

				5/12/11		
43	514	*Ojota	Gl514	OK- Text message sent and response received almost immediately about 11.6 seconds after at 8.20pm on 5/12/11	Supplied only Glucophage®. The pharmacist requested to see the data collector and advised that his mum should monitor her blood glucose. He said that he sells only Glucophage® as that is the only brand he is sure of the quality. He seriously advised against cheap metformin, which can be fake unlike Glucophage® that now has tags to help distinguish fake from original. Supplied 3 satchets (less 2 tablets) of Glucophage®. Wanted to retain some for treatment of other patients as that was his last pack	
44	271	*Ketu	Gl271	OK- Text message sent and response received almost immediately about 5.1seconds after at 8.37pm on 5/12/11	Supplied only Glucophage®. The store assistant said that since inception that is what she knows that they sell and Glucovance	
45	186	*Ojodu	Gl186 and Ge186	OK- Text message of 2nd sent and response received late at 11.03am (not properly times). Text message for 3rd sent and response received at 5minutes 8.5 seconds at 11.09am.	Both purchased (3 sachets of Glucophage® remaining and 5 sachets of Trippleace® metformin purchased)	
46	3	*Ketu	Gl3 and Ge3	OK- Text message sent and response received almost immediately about 11.3seconds after at 8.28pm on 5/12/11	Both purchased (Glucophage® and VPL® metformin. Only 3 satchets of Glucophage® remaining in shop and these were purchased	
47	237	*Ikotun	Gl237 and Ge237	OK- Text message sent and response received almost immediately about 15 seconds after at 14.52pm	Both purchased (Glucophage® and 4 sachets Gluformin®)	
48	428	*Ikoyi	Gl428 and Ge428	OK- Text was sent and response received 4.8seconds after at 6.55pm on 05/12/2011	Supplied both but didn't know initially that he had any other brand aside Glucophage®; Glucophage® bought (3 satchets) and Diabetmin® (4 satchets)	
49	295	**Sari-Iganmu	Gl295 and Ge295	OK-Text message sent at 6.51pm and response received after 1 minute 17.8 seconds seconds on 1/1/12	Both purchased (Glucophage® and Diabex®)	
50	4	*Victoria Island	Gl4 and Ge4	OK- Text was sent and response received 5.3seconds after at 7.10pm on 5/12/2011	Both purchased (Glucophage® and Diabetmin®)	
51	480	*Aguda			Pharmacy have moved from this location	

52	333	*Ojota	Gl333 and Ge333	OK- Text message sent and response received almost immediately about 3.5seconds after at 8.40pm on 5/12/11	Both purchased (Glucophage® and Diamet®)	
53	253	*Maryland	Gl253 and Ge253	OK- Text message sent and response received almost immediately about 5 seconds after at 17.20pm	Supplied Glucophage® first and later other brand (Diabetmin®) on another day. She said that she ordered Diabetmin® by Hovid as that is next after Glucophage® in terms of quality. She said she trusts Hovid because of their track record of quality with their other good products that they make. According to her Hovid is a good company. She is not sure of others so that is why she didn't order them. She went on to say that she prefers her medicines made in the UK or America. She said she does not use Indian products. As Diabetmin® by Hovid is from Maylasia-that is better after Glucophage® by Merck	
54	116	*Yaba	Gl116	Ok- Text message sent and response received almost immediately about7 seconds after at 18.54pm	Supplied only Glucophage®. Said that since inception that is what they stock. The assistant was completely unaware of the existence of the other brands. She went on to say that I am the first person ever asking for any other brand as people only ask for Glucophage®	
55	287	*Surulere	Gl287	OK- Text message sent and response received almost immediately about 16 seconds after at 14.28pm	Had only one sachet of Glucophage®. This was purchased	
56	428	*Ikoyi	----------		Repeated random number	
57	83	*Ikeja	Gl83	OK- Text message sent and response received almost immediately about 4.9 seconds after at 10.54am on 6/12/11	Supplied only Glucophage®. Said that is what people ask for so doesn't sell any other brand	
58	48	*Oshodi	Gl48 and Ge48	OK- Text message sent and response received almost immediately about 6 seconds after at 14.14pm	Both purchased (Glucophage® and Gluformin®)	
59	211	Anthony village	----------		Repeated random number	
60	333	Ojota	----------		Repeated random number	
61	562	*Akoka	Gl562 and Ge562	OK- Text message sent response received after 5 seconds at 7.01pm	Both purchased (Glucophage® and Diabex®)	
62	475	*Isolo	Gl475 and Ge475	OK- Text message sent and response received almost immediately about 6 seconds after at 14.44pm	Cover up for repeated random no. Both purchased (Glucophage® and Diabex®)	
63	204	*Surulere	Gl204 and Ge204	OK- Text message sent and response received almost immediately about 5 seconds after at 13.49pm	Cover up for repeated random no. Both purchased (Glucophage® and Gluformin®); 2 sachets of Glucophage® remaining purchased	

64	259	*Surulere	Gl259 and Ge259	OK- Text message sent and response received almost immediately about 1 second after at 2.22pm (2/12/2011)	Cover up; Both purchased (Glucophage® and Diabetmin®)	
65	69	*Lagos Island	Gl69 and Ge69	OK- Text message sent and response received almost immediately about 2 seconds after at 1.09pm	Cover up; Both purchased (Glucophage® and Gluformin®); 2 sachets of Gluformin® remaining purchased	
66	356	*Victoria Island	Gl356	OK- Text sent with etisalat response received after 5.0 seconds at 6.50pm on 5/12/2011	Cover up; Had only Glucophage®. Normally stock Diabetmin® but said that at the moment it is finished	
67	99	*Ijegun	Gl99 and Ge99	OK- Text message sent response received after 6 seconds at 17.39pm on 3/12/11	Cover up; Supplied both (Glucophage® and Diabetmin® but one satchet of Glucophage® remaining	
68	508	*Ketu	Gl508	OK- Text message sent and response received almost immediately about 4.8 seconds after at 8.15pm on 5/12/11	Cover up .Had only Glucophage®. Said they stock only Glucophage® because of quality. She went on to say that most cheap ones don't have NAFDAC numbers so they don't sell them	
69	306	*Akoka	-------		Cover up; None was purchased. The store assistant said that at the moment they do not have any brand of metformin as Glucophage® got finished. However, they will be going to purchase medicines the next day and hopefully will have it in stock then. She went on to explain that it is only Glucophage® that they stock as that is the only one they can ascertain the quality using the tags. She said that all other brands without the tags have fake so their quality cannot be guaranteed unlike tagged Glucophage®. She strongly advised against purchasing any Glucophage® that is not tagged	
70	111	*Apapa	Gl111	OK- Text message sent and response received almost immediately about 5.4 seconds after at 7.30pm on 5/12/11	Cover up; Supplied only Glucophage®. Sales lady was unaware of any other brand in the market. She know only Glucophage®	
71	73	*Agege	Gl73 and Ge73	OK- Text was sent and response after 7.7seconds at 10.50am on 6/12/11	Cover up; Both purchased (Glucophage® and Diabetmin®)	
72	415	*Ijegun satellite	Gl415	OK- Text message sent response received after 6 seconds at 17.36pm on 3/12/11	Cover up; Supplied only 2 satchets of Glucophage. Said only Glucophage® is what they sell	
73	6	*Ejigbo	Gl6 and Ge6	OK- Text message sent and response received almost immediately about 6 seconds after at 17.44pm on 3/12/11	Cover up; Both purchased (Glucophage® and Diabex®)	
74	164	*Iju	Gl164 and Ge164	OK- Text message sent and response received almost immediately about 5.4 seconds after at 10.46am	Cover up; Both purchased (Glucophage® and Diabetmin®)	
75	432	*Agege	Gl432 and Ge432	OK- Text message sent with Etisalat and response received almost	Cover up; Both purchased (Glucophage® and Glucopac®)	

				immediately about 11.8 seconds after at 9.50am on 6/12/11		
76	112	**Ijaniki	---------		Cover up; Could not locate	
77	140	*Ikorodu	GI140 and Ge140	Ok- Text message sent 18.30pm and response was not received until after 5 minutes 26 seconds at 18.34pm	Cover up; Both purchased (Glucophage® and Diabetmin®)	
78	317	*Ebute Metta	GI317 and Ge317	OK-Text message sent and response received almost immediately about 2 seconds after at 12.56pm	Cover up; Both purchased (Glucophage®® and Life back® metformin)	
79	552	*Isolo	GI552 and Ge552	OK- Text message sent and response received almost immediately about 3 seconds after at 2.07pm.	Cover up; Both purchased (Glucophage® and Diabetmin®); Only 3 satchets of Diabetmin® remaining purchased	
80	457	*Ajao estate	GI457 and Ge457	OK- Text message sent and response received almost immediately about 6 seconds after at 13.56pm	Cover up; Both purchased (Glucophage® and Diabetmin®)	
81	310	*Ifako Ijaiye	GI310 and Ge310	OK- Text message sent and response received almost immediately about 1minute 5seconds after at 11.22am on 6/12/11	Cover up; Both purchased (Glucophage® and Diabetmin®)	
82	254	*Ketu	GI254	OK- Text message sent and response received almost immediately about 6 seconds after at 18.11pm	Only 3 sachets of Glucophage® remaining purchased. Sales lady said they sell only what people ask for because if they are not bought they get expired and they loose. They stock 2 antidiabetic tablets- Glucophage® and Glanil®.	
83	577	*Ikeja	GI577 and Ge577	OK- Text message sent and response received almost immediately about 2 seconds after at 10.59am on 6/12/11	Both purchased (Glucophage® and Diamet®) 4 sachets of each	
84	186	Ojodu	----------		Repeated random number	
85	533	Festac	GI533 and Ge533- loose sachets of Diabetmin®	OK- Text message sent at 7.00pm and response received after 1 minute 5 seconds on 1/1/12	Both purchased (4 satchets of Glucophage® and 2 loose satchets of Diabetmin®)	
86	135	Ojo			Pharmacy no longer at the location	
87	446	Victoria Island	---------		Repeated random number	

88	228	*Ikotun	Gl228 and Ge228	OK- Text message sent and response received almost immediately about 6 seconds after at 17.48pm on 3/12/11	Both purchased (Glucophage® and Diabetmin®)	
89	590	*Surulere	---------		Could not locate	
90	520	*Ikeja	Gl520 and Ge520	OK- Text message sent and response received almost immediately about 4 second after at 9.55am on 6/12/11	Both purchased (Glucophage® and Diabetmin®)	

Locations at Idumota Drug market generated from the list from which to obtain samples (Names of outlets have been omitted for confidentiality)

S/N	Random number	Location	Comments	S/N	Random number	Location	Comments	S/N	Random number	Location	Comments	S/N	Random number	Location	Comments
1	51	Church street		13	19	Church street		25	167	Between Atins	Repeated random number	36	80	Main Ashogbon	
2	120	Main Ashogbon street		14	140	Iga-Idunganran street						37	4	First Ashogbon	Repeated random number
3	138	Iga-Idunganran street		15	108	Main Ashogbon		26	111	Main Ashogbon		38	58	Church street	
4	27	Church street		16	160	Main Atins		27	113	Main Ashogbon		39	138	Iga-Idunganran street	Repeated random number
5	133	Enuowa		17	147	Iga-Idunganran street		28	74	Main Ashogbon		40	143	Iga-Idunganran street	
6	165	Main Atins		18	42	Church street		29	30	Church street		41	171	Second Atins	
7	175	Second Atins		19	26	Church street		30	20	Church street		42	164	Main Atins	
8	167	Between Atins		20	56	Church street		31	169	Between Atins		43	144	Iga-Idunganran street	
9	4	First Ashogbon		21	135	Iga-Idunganran street		32	165	Main Atins	Repeated random number	44	108	Main Ashogbon	Repeated random number
10	14	Church street		22	43	Church street		33	59	Main Ashogbon		45	151	Iga-Idunganran street	
11	193	Atins end		23	136	Iga-Idunganran street		34	116	Main Ashogbon		46	17	Church street	
12	109	Main		24	123	Main		35	138	Iga-		47	168	Between	

		Ashogbon				Ashogbon				Idunganran				Atins	
48	197	End of branch Atins		54	95	Main Ashogbon		60	135	Iga-Idunganran street		66	30	Church street	Repeated random number
49	152	Main Atins		55	121	Main Ashogbon		61	155	Main Atins		67	129	Main Ashogbon	
50	175	Second Atins	Repeated random number	56	0	----------	-	62	117	Main Ashogbon		68	174	Second Atins	
51	21	Church shop		57	21	Church street		63	17	Church street	Repeated random number	69	40	Church street	
52	166	Between Atins		58	114	Main Ashogbon	Repeated random number	64	170	Second Atins					
53	114	Main Ashogbon		59	189	End of Branch Atins		65	103	Main Ashogbon					

Locations and initial code of outlets visited at the Drug market (Final codes are exculded for confidentiality)

Name/Location	Code	Result of text message authentication	Comment (See details of primary and secondary packaging including quantity and price purchased in a separate report)	Recoded
1) Iga-idunganra street	TGLAA (1st) and TGeAA (1st)	OK-6th sent 18.33 but no response from airtel until after 17 minutes-18.50, 1st sent with MTN message after 4 seconds at 6.41pm	Both purchased (Glucophage® and VPL® metformin); 84 tablets of Glucophage at N1400 and 100 tablets of Glucophage® at N500*	
2) Eko street	TGeOB		Only other brand purchased (Diamet®) 84 tablets for N550	
3) Church street	TGeS		Only other brand purchased (Askaphage®)- 84 tablets at N500	
4) Ashogbon street	TGlPC	OK-Text message sent and response received almost immediately about 5 seconds after at 23.30 pm	Only Glucophage® purchased. 84 tablets of Glucophage® purchased at N1500	
5) Ashogbon street, off Church street	TGlRS (1st) and TGeRS(1st)	OK-Text message sent and response received almost immediately about 15 seconds after at 23.24 pm	Both purchased (Glucophage® and Glucopac®); 84 tablets of Glucophage® at N1400 and 50 tablets of Glucopac® at N300	
6) Ashogbon street, Church street	TGlRS (2nd) and TGeRS (2nd)	OK- Text message sent and response received almost immediately about 2 seconds after at 11.53pm	Both purchased (Glucophage® and Glucopac®)- 50 tablets of Glucopac® purchased at N300 and 84 tablets of Glucophage® at N1,450	
7) Church street	TGlDV	OK-Text message sent and response received almost immediately about 2 seconds after at 11.35pm	Only Glucophage® purchased-84 tablets for N1400 **Insisted on verifying the authenticity in front of the data collector	
8) Iga-iduganran street	TGlAP	OK-Text message sent and response received almost immediately about 2 seconds after at 6.29pm	Only Glucophage® purchased.84 tablets purchased at N1700	
9) Iga-Idunganran street	TGlCP and TGeCP	OK- Text message sent and response received almost immediately about 8 seconds after at 23.48pm	Both purchased (Glucopahge® and Formet®); 84 tablets of Glucophage® at N1400 and 500 tablets of Formet® at N200	
10) Iga-idunganran street	TGLAA (2nd) and TGeAA (2nd)	OK- Text message sent and response received almost immediately about 5 seconds after at 23.41pm	Both purchased (Glucophage® and Miformin®)	
11) Enu-owa street	TGlBVL and TGeBVL	OK- Text message sent and response received almost immediately about 6 seconds after at 18.13pm	Both purchased (Glucophage® and Inophage®)- 84 tablets of Glucophage at N1500 and 50 tablets of Inophage® at N250	

12) Ashogbon street	TGlHG and TGeHG	OK. The 4th from the left was sent but there was no response message until after 5minutes 7 seconds (sent 14.02 pm 1/12/2011, response message states 14.07pm	Both purchased (Glucophage® and Diabetmin®)	
13) Ashogbon street	TGlUB and TGeUB	OK- Text message sent and response received almost immediately about 7 seconds after	Both purchased (Glucophage® and Diabetmin®). Purchased 84 tablets of Glucophage® at N1500 and 100 tablets of Diabetmin® at N600	
14) Ashogbon street	TGlEZ and TGeEZ	OK- Text message sent and response received almost immediately about 8 seconds (there are only 5 cards in pack)	Both purchased (Glucophage® and Metformin by Bristol)	
15) Ashogbon street	TGeCO		Only other brand (Glucopac®) purchased	
16) Atin street	TGeAV		Only other brand (Glucopac®) purchased	
17) Off Atin street	TGeIUM		Only other brand bought (Diabetmin®)	
18) Ashogbon street, Isale-Eko, Lagos	TGeFD		Only other brand purchased (Sanformin®)	
19) Atin street	TGlUJA	OK-Text message sent and response received almost immediately about 8 seconds after at 17.05pm	Only Glucophage® purchased	
20) Ashogbon street	TGeTMH		Only other brand (Lifeback® metformin purchased). Said it is the same as Glucophage®	
21) Onikoyi street, Old Porter street, Lagos	TGlSNC	OK- Text message sent at 4.48pm and response received almost immediately about 2 seconds after	Only Glucophage® purchased	
22) Ashogbon street	TGePP		Only other brand purchased (Juformin®)	
23) Atin street	TGlSS	Text message sent and response received almost immediately about 10 seconds	Only Glucophage® purchased	

24) Ashogbon street	TGlBPM and TGeBPM	Nil- The 4th from the left was sent at 14.17pm on 1/12/2011 but there was no response was received even after 25 minutes The 5th from the left was resent at 2.29pm with another network-MTN (no response was received even after 25 minutes) The 2nd was resent at 8.24am on 03/12/11 with Glo1 and response was received after 5 minutes 9 seconds at 8.29am on 3/12/11	Both purchased (Glucophage® and Diabetmin®)	
25) Atin street	TGlEUP and TGeEUP	OK- Text message sent and response received almost immiditaely about 6 seconds after	Both purchased (Glucophage® and Glucopac®)	
26) Iga- Idunganran street	TGlVLI and TGeVLI	OK. Text message sent 1.54pm (response received after 4 seconds but response says received1.54pm).	Both purchased (Glucophage® and Gluformin®)	
27) Ashogbon street	TGlNMS and TGeNMS	OK- Text message sent and response received almost immiditaely about 7 seconds after at 16.57pm	Both purchased (Glucophage® and Betaphage®)	
28) Iga-idunganran street, Isale-Eko, Lagos (3rd)	TGLAA (3rd) and TGeAA (3rd)	OK-Text message sent at and response received almost immiditaely about 2 seconds after	Both purchased (Glucophage® and Miformin®)	
29) Iga-Idunganran street	TGlEMAU and TGeEMAU	Nil- The 4th from the left was sent but there was no response message even after 25 minutes (sent 2.46pm 1/12/2011) The 2nd from the left was resent at with another network-airtel (no response was received even after 25 minutes) The 5th was resent on 03/12/11 with MTN and response was received almost immediately after 5 seconds at 8.41am on 3/12/11	Both purchased (Glucophage® and Diamin®). Said both are the same and that Diamin® may even be better in quality	

Appendix 15: Drug sampling collection form

Adapted from Wondemagegnehu, (1999) and USP/DQI, (2004)

Code no……/……City name:	
Sample information:	
Name of location where sample was take from:	
Street address (with telephone and fax no if available)	
Type of outlet (Community pharmacy/ patent medicine shop)	
Date of sampling	
Drug name (trade or brand name)	
Dosage form and strength	
Pack size	
Manufacturers Batch/ Lot no.	
Manufacturing date	
Expiry date	
NAFDAC no.	
Manufacturers name and address as written on the pack	
With authentication scratch cards (Yes/No)	
Price	
Brief physical/visual description of sample (including description of the primary and secondary packaging)	
Name of collector (s)/Date/Sign	
Labelling requirements	
Brand name of drug sample (if applicable)	
Generic name of active ingredient	
Dosage form and strength	
Name of reference standard used (as claimed on the label for instance USP/BP/IP/EP)	
Storage conditions	
Packaging material (for instance blister pack/card)	
Is there a print on the primary or secondary packaging?	
Description of dosage form	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
No physical change (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminants/dirty marks/proper seal)	
Final comments	
The sample passed the basic testing (Yes/ No) **The sample failed basic quality testing (Yes/No)** **If sample failed, please give reasons……** **The Sample is doubtful for its basic quality testing** **If doubtful, please give reason (s)…….**	

Appendix 16: Glucophage® samples authenticated, mobile network used and time taken to receive response and response received

S/no	Glucophage® samples authenticated	Mobile network	Time taken to receive response (Seconds)	Result of response received
1	GL66	GLO	9	OK, Original
2	GL334	GLO	309	OK, Original
3	TGLVLI	MTN	4	OK, Original
4	TGLHG	GLO	307	OK, Original
5	TGLBPM	GLO	DELAYED (> 1500 seconds)	OK, Original
6	TGLEMAU	MTN	DELAYED (> 1500 seconds)	OK, Original
7	TGLEZ	AIRTEL	8	OK, Original
8	TGLEUP	AIRTEL	6	OK, Original
9	TGLISS	GLO	10	OK, Original
10	TGLUB	AIRTEL	7	OK, Original
11	TGLAA3rd	MTN	2	OK, Original
12	TGLSNC	MTN	2	OK, Original

13	TGLNMS	GLO	7	OK, Original
14	TGLUJA	AIRTEL	8	OK, Original
15	GL561	MTN	4	OK, Original
16	GL105	GLO	6	OK, Original
17	GL446	AIRTEL	8	OK, Original
18	GL300	GLO	3	OK, Original
19	GL12	MTN	9	OK, Original
20	GL586	AIRTEL	15	OK, Original
21	TGLBVL	GLO	6	OK, Original
22	TGLAP	MTN	2	OK, Original
23	TGLAA1st	AIRTEL	1020	OK, Original
24	TGLRS1st	AIRTEL	15	OK, Original
25	GL265	AIRTEL	5	OK, Original
26	GL476	MTN	1	OK, Original
27	GL572	GLO	4	OK, Original
28	GL413	MTN	1	OK, Original
29	GL253	AIRTEL	5	OK, Original
30	GL431	GLO	3	OK, Original

31	GL376	MTN	2	OK, Original
32	GL254	AIRTEL	6	OK, Original
33	GL140	GLO	326	OK, Original
34	GL116	AIRTEL	7	OK, Original
35	GL562	MTN	5	OK, Original
36	GL502	GLO	2	OK, Original
37	GL346	GLO	6	OK, Original
38	GL415	ETISALAT	6	OK, Original
39	GL99	ETISALAT	6	OK, Original
40	GL6	ETISALAT	6	OK, Original
41	GL228	ETISALAT	6	OK, Original
42	GL356	ETISALAT	5	OK, Original
43	GL428	ETISALAT	5	OK, Original
44	GL468	ETISALAT	12	OK, Original
45	GL4	ETISALAT	5	OK, Original
46	GL87	ETISALAT	4	OK, Original
47	GL338	ETISALAT	5	OK, Original

48	GL11	ETISALAT	5	OK, Original
49	GL184	ETISALAT	5	OK, Original
50	GL508	ETISALAT	5	OK, Original
51	GL514	ETISALAT	12	OK, Original
52	GL3	ETISALAT	11	OK, Original
53	GL271	ETISALAT	5	OK, Original
54	GL333	ETISALAT	4	OK, Original
55	GL91	ETISALAT	5	OK, Original
56	GL336	ETISALAT	11	OK, Original
57	GL203	ETISALAT	5	OK, Original
58	GL432	ETISALAT	12	OK, Original
59	GL520	ETISALAT	4	OK, Original
60	GL47	ETISALAT	5	OK, Original
61	GL215	AIRTEL	15	OK, Original
62	GL164	AIRTEL	5	OK, Original
63	GL73	AIRTEL	8	OK, Original
64	GL83	GLO	5	OK, Original
65	GL577	GLO	2	OK, Original
66	GL186	GLO	309	OK, Original
67	GL310	MTN	65	OK, Original
68	GL302	MTN	23	OK, Original
69	GL295	MTN	78	OK, Original

70	GL533	MTN	65	OK, Original
71	TGLPC	GLO	5	OK, Original
72	TGLDV	MTN	2	OK, Original
73	TGLAA2nd	AIRTEL	5	OK, Original
74	TGLCP	GLO	8	OK, Original
75	TGLRS2nd	MTN	2	OK, Original
76	GL144	AIRTEL	6	OK, Original
77	GL317	MTN	2	OK, Original
78	GL256	AIRTEL	5	OK, Original
79	GL160	GLO	5	OK, Original
80	GL69	MTN	2	OK, Original
81	GL204	GLO	5	OK, Original
82	GL457	AIRTEL	6	OK, Original
83	GL552	MTN	3	OK, Original
84	GL48	AIRTEL	6	OK, Original
85	GL259	MTN	1	OK, Original
86	GL287	AIRTEL	16	OK, Original
87	GL585	MTN	1	OK, Original
88	GL457	GLO	6	OK, Original
89	GL237	AIRTEL	15	OK, Original
90	GL289	GLO	5	OK, Original
91	GL558	AIRTEL	6	OK, Original
92	GL270	MTN	1	OK, Original

Appendix 17: Result of packaging analysis of tagged Glucophage® samples

Sample code	Result of packaging analysis
GL1	Passed
GL2	Passed
GL3	Passed
GL4	Passed
GL5	Passed
GL6	Passed
GL7	Passed
GL8	Passed
GL9	Passed
GL10	Passed
GL11	Passed
GL12	Passed
GL13	Passed
GL14	Passed
GL15	Passed
GL16	Passed
GL17	Passed
GL18	Passed
GL19	Passed
GL20	Passed
GL21	Passed
GL22	Passed
GL23	Passed
GL24	Passed
GL25	Passed
GL26	Passed
GL27	Passed
GL28	Passed
GL29	Passed
GL30	Passed
GL31	Passed
GL32	Passed
GL33	Passed
GL34	Passed
GL35	Passed

GL36	**Passed**
GL37	**Passed**
GL38	**Passed**
GL39	**Passed**
GL41	**Passed**
GL42	**Passed**
GL43	**Passed**
GL44	**Passed**
GL45	**Passed**
GL46	**Passed**
GL47	**Passed**
GL48	**Passed**
GL49	**Passed**
GL50	**Passed**
GL51	**Passed**
GL52	**Passed**
GL53	**Passed**
GL54	**Passed**
GL55	**Passed**
GL56	**Passed**
GL57	**Passed**
GL59	**Passed**
GL60	**Passed**
GL61	**Passed**
GL62	**Passed**
GL63	**Passed**
GL64	**Passed**
GL65	**Passed**
GL66	**Passed**
GL67	**Passed**

GL68	**Passed**
GL69	**Passed**
GL70	**Passed**
GL71	**Passed**
GL72	**Passed**
GL73	**Passed**
GL74	**Passed**
GL75	**Passed**
GL76	**Passed**
GL77	**Passed**
GL78	**Passed**
GL79	**Passed**
GL80	**Passed**
GL81	**Passed**
GL82	**Passed**
GL83	**Passed**
GL84	**Passed**
GL85	**Passed**
GL86	**Passed**
GL87	**Passed**
GL88	**Passed**
GL89	**Passed**
GL90	**Passed**
GL91	**Passed**
GL92	**Passed**
GL93	**Passed**
GL94	**Passed**

Appendix 18: Correlation coefficient (r) for the tagged Glucophage® samples

Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)	Sample code	Correlation coefficient (r)
GL1	0.999319	GL16	0.998191	GL31	0.999531	GL47	0.999025	GL63	0.999126	GL78	0.999133	GL93	0.999318
GL2	0.999319	GL17	0.99932	GL32	0.998637	GL48	0.998759	GL64	0.998466	GL79	0.999098	GL94	0.999029
GL3	0.997643	GL18	0.995604	GL33	0.998462	GL49	0.999392	GL65	0.999017	GL80	0.999371		
GL4	0.999478	GL19	0.997248	GL34	0.998853	GL50	0.999387	GL66	0.999043	GL81	0.998574		
GL5	0.999518	GL20	0.999228	GL35	0.999052	GL51	0.999267	GL67	0.998877	GL82	0.997175		
GL6	0.99912	GL21	0.997444	GL36	0.997175	GL52	0.998347	GL68	0.998234	GL83	0.999023		
GL7	0.999528	GL22	0.998713	GL37	0.99951	GL53	0.998972	GL69	0.998706	GL84	0.999393		
GL8	0.997727	GL23	0.997237	GL38	0.99828	GL54	0.9995	GL70	0.998963	GL85	0.999458		

GL9	0.9989	GL24	0.999361	GL39	0.99954	GL55	0.99932	GL71	0.998055	GL86	0.998111		
GL10	0.99918	GL25	0.998402	GL41	0.998929	GL56	0.999121	GL72	0.999252	GL87	0.99928		
GL11	0.999021	GL26	0.998612	GL42	0.999362	GL57	0.998599	GL73	0.999158	GL88	0.998737		
GL12	0.99873	GL27	0.999561	GL43	0.998039	GL59	0.999417	GL74	0.999196	GL89	0.999281		
GL13	0.999171	GL28	0.996442	GL44	0.999383	GL60	0.998581	GL75	0.998844	GL90	0.999177		
GL14	0.999457	GL29	0.996989	GL45	0.999327	GL61	0.99951	GL76	0.99939	GL91	0.999273		
GL15	0.99677	GL30	0.999126	GL46	0.999364	GL62	0.998453	GL77	0.999638	GL92	0.996973		

Appendix 19: Result of the HPLC analysis of Glucophage® samples containing the %concentration of metformin calculated from the calibration curve

Sample HPLC plot showing area under curve (chromatogram)

Data File C:\CHEM32\...MA METFORMIN STAB PRECI NOV6 EVE RUN 2012-11-06 20-14-02\015-1501.D
Sample Name: MISTAKE STD MET BENCH NOV6

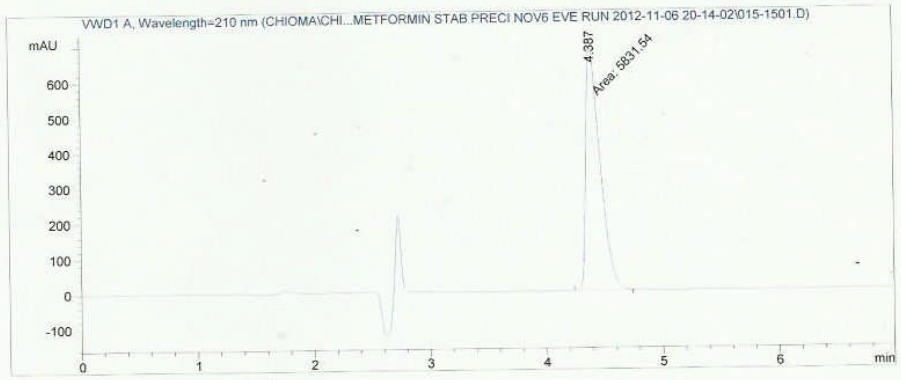
Acq. Operator : CHIOMA
Acq. Instrument : Instrument 1
Injection Date : 11/7/2012 1:20:19 AM

Seq. Line : 15
Location : Vial 15
Inj : 1
Inj Volume : 10.0 µl

Acq. Method : C:\CHEM32\1\DATA\CHIOMA\CHIOMA METFORMIN STAB PRECI NOV6 EVE RUN 2012-11-06 20-14-02\METFORMIN CHIOMA.M
Last changed : 11/6/2012 8:14:00 PM by CHIOMA
Analysis Method : C:\CHEM32\1\METHODS\ACETONE.M
Last changed : 11/6/2012 5:22:39 PM by Alberto
(modified after loading)

Sample-related custom fields:

Name	Value



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 11/6/2012 5:19:27 PM
Multiplier: : 1.0000
Dilution: : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU*s	Area %	Name
1	4.387	MM	0.1405	5831.54346	100.0000	Metformin
Totals :				5831.54346		

1 Warnings or Errors :

Warning : Invalid calibration curve, (Metformin)

Summed Peaks Report

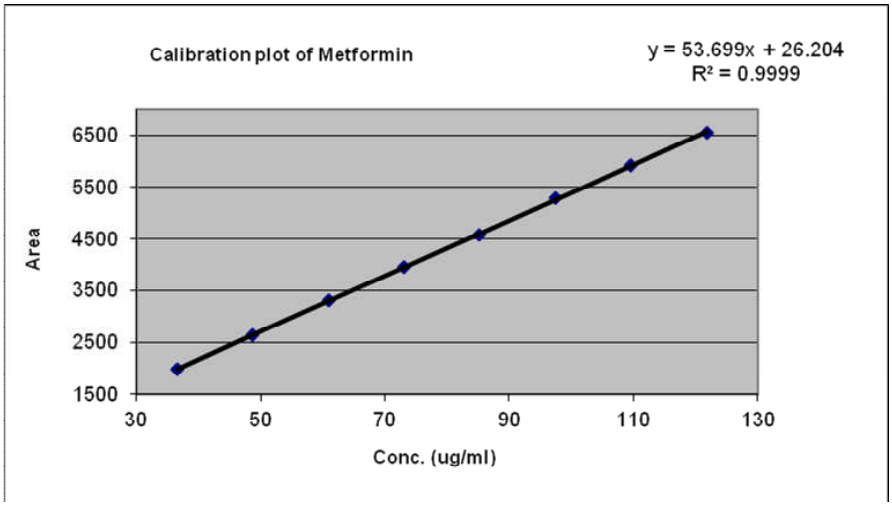
Instrument 1 11/8/2012 8:45:01 PM Alberto Page 1 of 2

Concentration of pure metformin and corresponding areas under the curve

used for plotting the calibration curve

Calibration of Metformin

Area of Metformin			Concentration	Average
inj 1	inj 2	inj 3	(μg/ml)	Area
			0	
1961.2	2002.8	1982.0	36.54	1982.000
2645.6	2621.5	2633.6	48.72	2633.550
3312.9	3298.8	3305.9	60.90	3305.850
3965.5	3952.9	3959.2	73.08	3959.200
4600.4	4574.3	4587.4	85.26	4587.350
5283.8	5295.5	5289.7	97.44	5289.650
5917.3	5920.7	5919.0	109.62	5919.000
6544.3	6543.7	6544.0	121.80	6544.000



Percentage concentration of metformin

Sample code	Percentage (%) of metformin	Result of HPLC analysis
GL1	95.78	Passed
GL2	98.53	Passed
GL3	97.34	Passed
GL4	99.81	Passed
GL5	99.84	Passed
GL6	99.22	Passed
GL7	98.86	Passed
GL8	100.19	Passed
GL9	97.66	Passed
GL10	98.79	Passed
GL11	97.60	Passed
GL12	96.12	Passed
GL13	97.52	Passed
GL14	98.16	Passed
GL15	101.11	Passed
GL16	100.85	Passed
GL17	99.98	Passed
GL18	97.89	Passed
GL19	96.84	Passed
GL20	97.71	Passed
GL21	100.18	Passed
GL22	96.15	Passed
GL23	97.15	Passed
GL24	95.08	Passed
GL25	96.41	Passed
GL26	97.85	Passed
GL27	96.61	Passed
GL28	96.67	Passed
GL29	97.48	Passed
GL30	98.08	Passed

GL31	**99.09**	**Passed**
GL32	**100.75**	**Passed**
GL33	**99.70**	**Passed**
GL34	**97.67**	**Passed**
GL35	**95.60**	**Passed**
GL36	**96.74**	**Passed**
GL37	**96.55**	**Passed**
GL38	**95.00**	**Passed**
GL39	**100.34**	**Passed**
GL41	**98.28**	**Passed**
GL42	**100.92**	**Passed**
GL43	**98.92**	**Passed**
GL44	**98.23**	**Passed**
GL45	**97.58**	**Passed**
GL46	**96.97**	**Passed**
GL47	**96.48**	**Passed**
GL48	**99.53**	**Passed**
GL49	**97.79**	**Passed**
GL50	**101.14**	**Passed**
GL51	**100.65**	**Passed**
GL52	**96.20**	**Passed**
GL53	**99.68**	**Passed**
GL54	**95.56**	**Passed**
GL55	**98.47**	**Passed**
GL56	**99.32**	**Passed**
GL57	**95.07**	**Passed**
GL59	**96.89**	**Passed**
GL60	**98.33**	**Passed**
GL61	**98.84**	**Passed**
GL62	**97.58**	**Passed**
GL63	**100.13**	**Passed**
GL64	**98.81**	**Passed**
GL65	**95.55**	**Passed**
GL66	**101.33**	**Passed**
GL67	**98.40**	**Passed**
GL68	**100.59**	**Passed**
GL69	**98.98**	**Passed**
GL70	**98.12**	**Passed**
GL71	**98.51**	**Passed**
GL72	**95.52**	**Passed**
GL73	**96.42**	**Passed**
GL74	**98.93**	**Passed**
GL75	**100.08**	**Passed**

GL76	**100.03**	**Passed**
GL77	**96.63**	**Passed**
GL78	**101.12**	**Passed**
GL79	**101.01**	**Passed**
GL80	**98.96**	**Passed**
GL81	**96.31**	**Passed**
GL82	**97.02**	**Passed**
GL83	**95.90**	**Passed**
GL84	**100.00**	**Passed**
GL85	**99.96**	**Passed**
GL86	**96.40**	**Passed**
GL87	**96.57**	**Passed**
GL88	**97.22**	**Passed**
GL89	**97.05**	**Passed**
GL90	**99.81**	**Passed**
GL91	**98.39**	**Passed**
GL92	**97.42**	**Passed**
GL93	**97.95**	**Passed**
GL94	**99.92**	**Passed**

Appendix 20: Result of packaging analysis conducted for the generic metformin samples

Sample code	Result of packaging analysis
GE1	Passed
GE2	Passed
GE3	Passed
GE4	Passed
GE5	Passed
GE6	Passed
GE7	Passed
GE8	Passed
GE9	Passed
GE10	Passed
GE11	Passed
GE12	Passed
GE13	Passed
GE14	Passed
GE15	Passed
GE16	Passed
GE17	Passed
GE18	Passed
GE19	Passed
GE20	Passed
GE21	Passed
GE22	Passed
GE23	Passed
GE24	Passed
GE25	Passed

GE26	**Passed**
GE27	**Passed**
GE28	**Passed**
GE29	**Passed**
GE30	**Passed**
GE31	**Passed**
GE32	**Passed**
GE33	**Passed**
GE34	**Passed**
GE35	**Passed**
GE36	**Passed**
GE37	**Passed**
GE38	**Not analysed**
GE39	**Passed**
GE40	**Passed**
GE41	**Passed**
GE42	**Passed**
GE43	**Passed**
GE44	**Passed**
GE45	**Passed**
GE46	**Passed**
GE47	**Passed**
GE48	**Passed**
GE49	**Passed**
GE50	**Passed**
GE51	**Passed**
GE52	**Passed**
GE53	**Passed**
GE54	**Passed**
GE55	**Passed**
GE56	**Passed**
GE57	**Passed**
GE58	**Passed**
GE59	**Passed**

GE60	**Not analysed**
GE61	**Passed**
GE62	**Passed**
GE63	**Passed**
GE64	**Passed**
GE65	**Passed**
GE66	**Passed**
GE67	**Not analysed**
GE68	**Passed**
GE69	**Passed**
GE70	**Passed**
GE71	**Passed**
GE72	**Passed**
GE73	**Passed**
GE74	**Passed**
GE75	**Passed**
GE77	**Passed**
GE78	**Passed**
GE79	**Passed**
GE80	**Passed**
GE81	**Passed**
GE82	**Passed**
GE83	**Not analysed**
GE84	**Passed**
GE85	**Passed**
GE86	**Passed**
GE87	**Passed**
GE88	**Passed**

Appendix 21: Correlation coefficient (r) for the generic metformin samples

Type	Code	r	Type	Code	r	Type	Code	r	Type	Code	r	Type	Code	r	Type	Code	r
F	GE1	0.997276	A	GE16	0.977859	F	GE31	0.996817	Q	GE46	0.999122	A	GE61	0.998831	E	GE76	0.999814
I	GE2	0.994256	E	GE17	0.999919	Q	GE32	0.99767	A	GE47	0.9977	A	GE62	0.998901	A	GE77	0.999081
G	GE3	0.99746	Q	GE18	0.998968	G	GE33	0.996527	A	GE48	0.999733	A	GE63	0.998924	A	GE78	0.998661
H	GE4	0.971704	E	GE19	0.999754	F	GE34	0.998968	A	GE49	0.999703	A	GE64	0.999232	A	GE79	0.999628
E	GE5	0.999878	J	GE20	0.997916	A	GE35	0.998844	A	GE50	0.997351	E	GE65	0.998236	A	GE80	0.998276
R	GE6	0.999477	K	GE21	0.998768	A	GE36	0.997232	A	GE51	0.999843	F	GE66	0.992498	K	GE81	0.998127
D	GE7	0.99579	A	GE22	0.998473	F	GE37	0.998816	B	GE52	0.992101		GE67		A	GE82	0.999641
E	GE8	0.999935	P	GE23	0.995126		GE38		A	GE53	0.999501	T	GE68	0.998723		GE83	
A	GE9	0.99647	Q	GE24	0.998365	A	GE39	0.999115	A	GE54	0.994219	F	GE69	0.997151	Q	GE84	0.999273
O	GE10	0.984336	Q	GE25	0.997292	Q	GE40	0.999753	A	GE55	0.999649	B	GE70	0.98964	D	GE85	0.984765
R	GE11	0.991543	A	GE26	0.99969	A	GE41	0.998933	A	GE56	0.99669	Q	GE71	0.999508	B	GE86	0.99148
E	GE12	0.999617	A	GE27	0.99892	Q	GE42	0.999399	A	GE57	0.997715	C	GE72	0.99716	A	GE87	0.999625
M	GE13	0.998337	B	GE28	0.989664	Q	GE43	0.999485	L	GE58	0.998926	B	GE73	0.985865	A	GE88	0.999658
N	GE14	0.993238	B	GE29	0.992704	F	GE44	0.996396	A	GE59	0.999617	A	GE74	0.994636			
A	GE15	0.999486	A	GE30	0.996287	A	GE45	0.99861		GE60		B	GE75	0.980374			

Appendix 22: Result of NIR analysis conducted for the generic metformin samples

Serial no.	Sample code	Result of NIR analysis
1	GE1	Passed
2	GE2	Passed
3	GE3	Passed
4	GE4	Passed
5	GE5	Passed
6	GE6	Passed
7	GE7	Passed
8	GE8	Passed
9	GE9	Passed
10	GE10	Passed
11	GE11	Passed
12	GE12	Passed
13	GE13	Passed
14	GE14	Passed
15	GE15	Passed
16	GE16	Passed
17	GE17	Passed
18	GE18	Passed
19	GE19	Passed
20	GE20	Passed
21	GE21	Passed
22	GE22	Passed
23	GE23	Passed
24	GE24	Passed
25	GE25	Passed
26	GE26	Passed
27	GE27	Passed
28	GE28	Passed
29	GE29	Passed
30	GE30	Passed
31	GE31	Passed
32	GE32	Passed
33	GE33	Passed
34	GE34	Passed
35	GE35	Passed
36	GE36	Passed
37	GE37	Passed
38	GE38	Not analysed
39	GE39	Passed
40	GE40	Passed
41	GE41	Passed
42	GE42	Passed
43	GE43	Passed

44	GE44	Passed
45	GE45	Passed
46	GE46	Passed
47	GE47	Passed
48	GE48	Passed
49	GE49	Passed
50	GE50	Passed
51	GE51	Passed
52	GE52	Passed
53	GE53	Passed
54	GE54	Passed
55	GE55	Passed
56	GE56	Passed
57	GE57	Passed
58	GE58	Passed
59	GE59	Passed
60	GE60	Not analysed
61	GE61	Passed
62	GE62	Passed
63	GE63	Passed
64	GE64	Passed
65	GE65	Passed
66	GE66	Passed
67	GE67	Not analysed
68	GE68	Passed
69	GE69	Passed
70	GE70	Passed
71	GE71	Passed
72	GE72	Passed
73	GE73	Passed
74	GE74	Passed
75	GE75	Passed
76	GE77	Passed
77	GE78	Passed
78	GE79	Passed
79	GE80	Passed
80	GE81	Passed
81	GE82	Passed
82	GE83	Not analysed
83	GE84	Passed
84	GE85	Passed
85	GE86	Passed
86	GE87	Passed
87	GE88	Passed

Appendix 23: Result of HPLC analysis of the Generic metformin samples showing percentage of metformin in each sample

Sample code	% of metformin	Result of HPLC analysis
GE1	94.06	Failed
GE2	98.37	Passed
GE3	103.36	Passed
GE4	95.03	Passed
GE5	98.57	Passed
GE6	96.06	Passed
GE7	93.80	Failed
GE8	98.29	Passed
GE9	98.16	Passed
GE10	93.03	Failed
GE11	95.34	Passed
GE12	102.90	Passed
GE13	98.28	Passed
GE14	99.75	Passed
GE15	97.49	Passed
GE16	100.63	Passed
GE17	102.28	Passed
GE18	99.26	Passed
GE19	100.84	Passed
GE20	95.55	Passed
GE21	95.0	Passed
GE22	97.25	Passed
GE23	102.03	Passed
GE24	95.76	Passed
GE25	95.85	Passed
GE26	97.39	Passed
GE27	95.83	Passed
GE28	97.39	Passed
GE29	96.35	Passed
GE30	95.27	Passed
GE31	94.02	Failed
GE32	92.85	Failed
GE33	102.69	Passed
GE34	95.09	Passed
GE35	98.01	Passed
GE36	97.79	Passed
GE37	96.36	Passed
GE38	102.13	Passed
GE39	100.97	Passed
GE40	97.23	Passed
GE41	100.37	Passed

GE42	96.96	Passed
GE43	103.24	Passed
GE44	98.29	Passed
GE45	95.69	Passed
GE46	98.73	Passed
GE47	99.36	Passed
GE48	98.93	Passed
GE49	97.78	Passed
GE50	98.26	Passed
GE51	95.27	Passed
GE52	97.10	Passed
GE53	96.43	Passed
GE54	95.84	Passed
GE55	96.47	Passed
GE56	95.0	Passed
GE57	96.56	Passed
GE58	101.17	Passed
GE59	99.36	Passed
GE60	86.68	Failed
GE61	95.14	Passed
GE62	96.15	Passed
GE63	95.88	Passed
GE64	98.49	Passed
GE65	100.13	Passed
GE66	98.98	Passed
GE67	95.72	Passed
GE68	98.52	Passed
GE69	83.11	Failed
GE70	99.19	Passed
GE71	99.70	Passed
GE72	101.72	Passed
GE73	95.86	Passed
GE74	96.51	Passed
GE75	98.73	Passed
GE77	97.49	Passed
GE78	96.54	Passed
GE79	98.20	Passed
GE80	98.09	Passed
GE81	98.93	Passed
GE82	95.43	Passed
GE83	97.50	Passed
GE84	99.55	Passed
GE85	99.62	Passed
GE86	98.94	Passed
GE87	95.14	Passed
GE88	97.80	Passed

Appendix 24: Coding frame/matrix used to categorise themes relating to perceptions of stakeholders on the current situation of quality of medicines in Nigeria

Themes/Categories
Size of the problem of poor quality medicine
Reasons for existence of poor quality medicine
Encounter with poor quality medicines
How poor quality medicines are detected
Medicines most likely to be faked
Impact of poor quality medicines
Initiatives in place
Reasons for reduction of the incidence of poor quality medicines
Awareness as an initiative against existence of poor quality medicines
How to tackle existence of poor quality medicines
Role of medicine sellers in the reduction of existence of poor quality mediicnes
Precautionary steps against poor quality medicines
Choice between generic and branded medicines
Quality of locally made medicines
Preference by country
Perception of drug quality in relation to cost of medicines
Educating consumers on generics

Appendix 25: Matrix topics relating to perceptions of the situation of quality of medicines in Nigeria and what is included in each matrix

Matrices	What is included
Trend in the size of the problem of poor quality medicine	This matrix included participant's perception of the trend of the prevalence of poor quality medicine in Nigeria
Encounter with poor quality medicines	This matrix included examples given by participants who have directly encountered poor quality medicine or who narrated an encounter with poor quality medicine they know of
Reasons for existence of poor quality medicine	This matrix included what participant's perceived were the reasons for the existence of poor quality medicines in Nigeria
How poor quality medicines are detected	This matrix included methods used by participants to detect poor quality medicines
Medicines most likely to be faked	This included medicines or groups of medicines that the participants perceived are most likely to be faked
Impact of poor quality medicines	This matrix included what participants perceived as the the impact of poor quality
Initiatives in place	This included the initiatives that are in place to help tackle the existence of poor quality medicines in Nigeria
Reasons for reduction of the incidence of poor quality medicines	This included the initiatives participants perceived have helped reduce the existence of poor quality medicines
Awareness as an initiative against existence of poor quality medicines	This included how participants perceived awareness creation as an initiative which has helped reduce the incidence of poor quality medicines
How to tackle existence of poor quality medicines	This included suggestions given by participants on how poor quality medicines can best be tackled in Nigeria
Role of medicine sellers in the reduction of existence of poor quality medicines	This matrix included suggestions on what persons that are involved in the sale of medicines can do to help reduce the incidence of poor quality medicines in Nigeria
Precautionary steps against poor quality medicines	This matrix included the precautions taken by the consumers to avoid obtaining medicines that are of poor quality
Choice between generic and branded medicines	This included the perceived quality of generic and branded innovator medicines
Quality of locally made medicines	This matrix included how the participants perceived the quality of locally manufactured medicines
Perception of drug quality in relation to cost of medicines	This included how participants perceived the quality of medicines in relation to the cost of the medicines
Educating consumers on generics	This matrix included information relating to consumer education on generic medicines by medicine sellers

Appendix 26: Themes and subthemes relating to perception of stakeholders of the situation of quality medicines in Nigeria

Themes/Categories	Subthemes
Size of the problem of poor quality medicine	*Trend in the size of the problem of poor quality medicines in Nigeria -Encounter with poor quality medicine -Precautionary steps taken -Reporting cases of poor quality medicines encountered
Reasons for existence of poor quality medicine	*High cost of some medicines *Poverty *Corruption *High cost of product registration *Low level of local drug manufacturing *Advancement in technology *Ignorance and lack of awareness *Demand surpassing supply *Lack of stringent laws and inadequate enforcement of existing laws *Difficulty tracing counterfeiters *Inadequate knowledge of pharmacy graduates *Shortage of pharmacists *Greed *Existence of open drug markets *Lack of commitment by the Pharmaceutical industries *Porous borders *Global warming *Poor government financing *Lack of co-operation among stakeholders
Reasons for the perceived reduction in the incidence of poor quality medicines in Nigeria	*Involvement of Pharmacists *Establishment of NAFDAC *Inspections by the Drug regulatory agencies *Effective stakeholder collaboration *Awareness creation
Perception of generic and innovator/branded medicines	*Choice between generic medicines and innovator brands *Perception of drug quality in relation to cost of medicines *Educating consumers on generics
Perceived quality of locally manufactured medicines	*Perceived quality of medicines made in Nigeria
What medicine sellers should do to reduce the existence of poor quality medicines	*Getting medicines from a reliable source *Education/training *Formation of taskforce
Impact of MAS	Change in purchasing behaviour of consumers Detection of counterfeit medicines Provision of intelligence information about counterfeiting Increased confidence in medicines purchased Increased knowledge about state of health
How to improve MAS	Improved awareness creation Assistance by government and their agencies Follow-up evaluation of MAS PIN improvement Network service improvement Authentication by the pharmacists Choice of medicines that will be MAS enabled

Appendix 27: Coding frame/matrix used to categorise themes relating to perceptions, attitudes and experiences of MAS

Barriers to MAS use
Change in purchasing behaviour due to MAS
Compatibility of MAS
Cost issues and MAS
Ease of use
Educating consumers about MAS by medicine sellers
How to improve MAS
Increased sale due to MAS
MAS awareness
Medicines that need MAS
Satisfaction of users
Time issues and MAS
Trust in MAS
Usefulness of MAS

Appendix 28: Matrix topics relating to perceptions, attitudes and experiences of MAS and themes included in each matrix

Matrices	What is included
Barriers to MAS use	This matrix included any information by participants relating to issues that have prevented them from using MAS or that may affect the use, introduction and expansion of MAS in Nigeria
Change in purchasing behaviour due to MAS	This matrix included any change in the purchasing behaviour of the consumers due to their awareness of MAS or since MAS was introduced
Compatibility of MAS	This matrix included information relating to the similarity between structures used by MAS and what was already available and used in the society
Cost issues and MAS	This matrix included comments relating to cost and MAS. It included comments relating to impact of MAS on cost of medicines, Impact of cost on further introduction and expansion of MAS and the impact of cost on use of MAS
Ease of use	This matrix included comments on how easy the participants perceive the use of MAS and how easy it was to use the service
Educating consumers about MAS by medicine sellers	This included comments relating to any form of education or awareness creation of MAS by the medicine sellers to the consumers
How to improve MAS	This included suggestions on how MAS can be improved. It included comments relating to different means of awareness creation suggested by the participants
Increased sale due to MAS	This matrix included the impact of the introduction of MAS on the volume of sale of medicines to which it has been introduced as reported by the medicine sellers
MAS awareness	This matrix included comments relating to how the participants perceived the awareness of MAS among the Nigerian public
Medicines that need MAS	This matrix included suggestions by participants on the type or categories of medicines which they think MAS should be introduced. It also included any reasons they gave for the suggestions made
Satisfaction of users	This matrix included comments made by participants who have used the service on how satisfied they were with the service
Time issues and MAS	This included comments on the impact of time on the use of MAS.
Trust in MAS	This included information on how the users of MAS trusted the response they received when they sent the message to authenticate their medicine
Usefulness of MAS	This matrix included how useful the participants perceived MAS is. It included comments relating to how MAS has helped the users and the potential it has.

Appendix 29: Themes and subthemes relating to MAS

Themes/Categories	Subthemes
Barriers to MAS use	Cost Compatibility of MAS MAS awareness Time Trust in source of medicine Confidentiality Dispensing practice in rural areas Dispensing practice in hospitals GSM ownership and use Availability of phone network Educating consumers about MAS by medicine sellers
Change in purchasing behaviour due to MAS	Increased demand Increased promotion
Facilitators to MAS use	Ease of use Compatibility Quick response to authentication
Cost issues and MAS	Impact of cost on purchasing behaviour of consumers Cost as an incentive for MAS use Impact of MAS introduction on the cost of medicines
Ease of use	Ease of understanding instructions given Ease of actual use of the service
How to improve MAS	Methods to raise awareness Assistance by government and their agencies Pin /unique code improvement Network service improvement Medicines that need MAS
Increased sale due to MAS	Increased sale due to increased confidence Increased sale due to reduced or no counterfeiting Increased sale due to increased promotion
MAS awareness	Perceived awareness level Ways to raise awareness
Satisfaction of users	Satisfaction of users
Time issues and MAS	Time needed to use the service Time needed to educate consumers on MAS by medicine sellers
Trust in MAS	Trust in MAS
Impact/ Usefulness of MAS	Detection of counterfeit/fake medicines Reduction of counterfeiting/faking Increased demand/sale Increased confidence Increased knowledge about state of health Knowledge about quality of medicines MAS coverage Product tracking Product promotion Trust in medicine sellers