Journal of Population Therapeutics and Clinical Pharmacology
INCORPORATING FETAL ALCOHOL RESEARCH
Journal de la thérapeutique des populations et de la pharmacologie clinique

Original Research
DOI: 10.22374/1710-6222.24.3.7

ANTICOUNTERFEITING STRATEGIES OF LOCAL DRUG MANUFACTURERS IN LAGOS, NIGERIA: DRUG SAFETY AND IMPLICATIONS FOR PUBLIC HEALTH

By Samson Fatoki[1] and Olufunsho Awodele[2]

[1]National Agency for Food and Drug Administration and Control (NAFDAC), Isolo Lagos, Nigeria.

[2]Department of Pharmacology, Therapeutics & Toxicology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria.

Corresponding Author: awodeleo@gmail.com.

Submitted: June 26, 2017. Accepted: November 13, 2017. Published: December 4, 2017.

Abstract

Background
Nigeria and many countries in the world have been plagued by counterfeit and poor-quality medicines with several studies indicating varying degree of prevalence.

Objectives
The study is aimed at determining the anticounterfeiting strategies employed by local drug manufacturers in Lagos, Nigeria.

Method
The first phase was a descriptive study which involves the use of a self-administered closed ended structured questionnaire to assess the anticounterfeiting strategies employed by local manufacturers in Nigeria. The second phase was an experimental study which selected 2 classes of most frequently faked drugs identified by the respondents in the first phase (antimalarials and antibiotics) and subjected to spot checks using the Truscan analysis deployed by NAFDAC to identify counterfeit medicines. Anticounterfeiting features on the samples were also examined. The data obtained from phase one was analyzed using SPSS while the data obtained from phase 2 was entered into the Truscan data sheet and analyzed using Chi-squared. Results were considered to be significant at $P<0.05$.

Results
The anticounterfeiting technologies indicated by the respondents as the highest in the first phase were Sequential Batch Numbering 61.1 % (overt) and Bar Codes 29.0 % (covert). While the second phase revealed

that 83% and 78% of antimalarials drawn from the manufacturing sources and open market respectively passed the Truscan spot checks. Similarly, 50% of antibiotics drawn from the 2 sampling sites passed the Truscan checks. There was no significant difference (P>0.05) between the sampled antimalarials and antibiotics from the manufacturing sources and open market.

Conclusion

Strategies to encourage the use of combination of anticounterfeiting technologies by the manufacturers should be established.

BACKGROUND

Counterfeit medicines are a global public health problem causing death, disability, and injury. It is an important cause of unnecessary morbidity, mortality, and loss of public confidence in the health care system.[1] It also wastes precious human and financial resources[2] and constitute an enormous problem facing global pharmaceutical industry.[3,4] Counterfeit medicines are available in the market worldwide, not only in the poor or resource limited countries but also in the developed world; however the problem is much more severe in the developing countries than developed countries.[4]

For many years, Nigeria has been plagued by counterfeit and poor-quality medicines. In 2002, the WHO reported that 70% of drugs in Nigeria were either fake or substandard.[5] Throughout the late 1990s to early 2000s, several peer-reviewed studies estimated the prevalence of counterfeit drugs to be between 36-48%.[6] The National Agency for Food and Drug Administration and Control (NAFDAC) survey carried out in 2006 estimated that 41% of drugs were counterfeit.[7] Furthermore, a WHO Quality of Antimalarials in Sub-Saharan Africa (QAMSA) study carried out in 2008 indicated that 64% of Nigeria's imported antimalarials were fake.[8,9] A very recent QAMSA survey; however, showed significant decline in the incidence of the counterfeiting of antimalaria drugs in Nigeria to 20% in 2012.[10] This outcome had a strong correlation with NAFDAC's regulatory efforts and 2012 survey on quality of medicine using the Truscan device (19.6%).[11]

THE NIGERIAN ANTICOUNTERFEITING STRATEGY

In Nigerian context, the use of anticounterfeiting technology has not really been on the front burner partly because most of the local drug manufacturers place more emphasis on profiteering and high returns on investment while leaving the anticounterfeiting war for the local Drug Regulatory Agency (NAFDAC) to combat. However, there appears to be a paradigm shift with the recent introduction of cutting-edge technologies in the detection of counterfeit medicines by NAFDAC and the necessity of brand protection by local drug producers. A few of these technologies are briefly explained below.

THE TRUSCAN

This is a hand-held device used for on-the-spot detection of counterfeit medicines.[12] The Truscan provides rapid, easy to use raw material identity inspection to screen out counterfeit substances and reduce supply chain risk. The device, manufactured by ThermoScientific was based on Raman spectroscopy with an in-built library of chemical compounds delivering reliable results right at the point of use.

NAFDAC is the first regulatory agency to domesticate and deploy the use of the Truscan to detect fake medicines based on the product-specific formulation.[13] The overall performance enhancement of this device provides faster pass/fail results and enables quicker method development and data synchronization.

THE GLOBAL PHARMA HEALTH FUN (GPFH) MINILAB

The Global Pharma Health Fund (GPHF) minilab is a device designed for the detection of counterfeit medicines. It boosts the testing capacity for counterfeit medicine detection and post-marketing drug quality surveillance especially in developing countries.[14] The device was invented by the GPHF, a charitable organization formerly established by research-based companies in Germany.

The minilab, as the name implies, consists of basic laboratory equipment, reference standards, analytical reagents, a kit for thin layer chromatography (TLC) assay and a kit for colour reactions. Range of test methods utilized by the minilab include physical/visual inspection, TLC analysis (to verify label claims on drug identity/content), disintegration test (to verify health risk associated with improper drug release due to poor tablet and capsule formulation) and colour reaction (e.g., dye test). Although the results generated from the minilab are accurate and reliable, they are not intended to replace compedial testing but to complement it for the purpose of making initial pronouncement on drug quality.

MOBILE PRODUCT AUTHENTICATION (MPA)

In 2010, NAFDAC launched an SMS based anticounterfeiting platform using technology from Sproxil, an American company based in Cambridge, Massachusetts that provides a consumer SMS verification through its Mobile Product Authentication (MPA) service.[15,16] The MPA solution empowers consumers to join in the war against product counterfeiting by using their mobile phones to ensure that they only purchase genuine product from the original manufacturer. Three simple steps are involved, upon purchasing a product; the consumer will find a label on the package that they can scratch off to reveal a one-time use item-specific code. The code is then sent via SMS to a secure toll-free number using a mobile phone. The consumer will then receive an immediate response confirming that the product is genuine or warning that it may be counterfeit.

Several other anticounterfeiting technologies have been used or suggested for the protection of medicine.[17] These include overt (visible) features, covert (hidden) features, forensic markers, track and trace technologies. Other anticounterfeiting measures available from literature include; marketing controls,[17] internal control mechanisms,[18] and information sharing and collaboration.[19] All the anticounterfeiting measures deployed by NAFDAC are fairly well known; however, there has been no known empirical study carried out to ascertain the strategies employed by indigenous manufacturers to fight this civic threat.

THE NIGERIAN DRUG DISTRIBUTION SYSTEM

The drug distribution in Nigeria has been aptly described by Peterson[20] and Onyebuchi[21] as chaotic and consists of open drug markets which harbour unregistered importers, distributors, wholesalers, patent and proprietary medicine vendors (PPMV, otherwise referred to as patent medicine stores) who compete with registered community pharmacies, private and public hospitals, and pharmaceutical manufacturers. The operators of the open drug markets possess little or no formal education and have no basic understanding of drug storage requirements. They constitute a financially powerful bloc and are widespread within the country. Four major open drug markets are presently in operation in Nigeria. They are located in Idumota (Lagos State, South West), Onitsha (Anambra State, South East,), Ariaria (Abia State, South East), and Kano (Kano State, North West). On the other hand, the PPMV license holders prescribe, dispense and treat all manner of disease conditions with little or no training. Consequently, they rely on hands-on experience gained over the years through apprenticeship. They sell and dispense all kinds of drugs as determined by their financial capabilities including ethical preparations in contradiction of their practicing license that allows them to sell only over-the-counter medicines. Such services that are sensitive and bother on human lives are statutorily reserved for trained community pharmacists licensed by the Pharmacists Council of Nigeria.

The Federal Government of Nigeria has however declared a state of emergency in drug distribution system[22] to address this chaotic situation announcing that with effect from June 30, 2014 drugs would no longer be sold in the open markets but distribution will be channelled through State Drug Distribution Centers and Mega Drug Distribution Centers which will be public sector and private sector driven respectively. However, it appears there has been no political will to enforce this ban as drugs are still sold in the open markets to date.

This study intends to determine the anticounterfeiting strategies adopted by drug manufacturers in

Lagos, Nigeria and also determine which class of drug is highly susceptible to counterfeiting.

METHODS

Study Settings

Lagos is popularly referred to as the commercial nerve centre of Nigeria and it has an estimated population of about 17.5 million. It is the most populous city in Nigeria, the fastest growing city in Africa and the seventh fastest growing city in the world.[23] At the time of the study, there were two-hundred and five (205) registered pharmaceutical manufacturers located all over the 6 geopolitical zones of Nigeria.[24] Lagos has sixty-six (66) which makes up about 32% of total drug manufacturers in Nigeria making it the city with the highest number of indigenous manufacturers.

Study Populations

The population includes all the superintendent pharmacists, production managers, quality assurance/control managers, regulatory affairs managers and marketing managers of the local drug manufacturers based in Lagos that are members of the Pharmaceutical Manufacturing Group of the Manufacturers Association of Nigeria (PMG-MAN).

Study Design

The study was carried out in 2 phases. The first phase was a descriptive cross-sectional study which involves the use of a self-administered closed ended structured questionnaire to determine the anticounterfeiting strategies adopted by drug manufacturers in Lagos, Nigeria and identify the classes of drugs most frequently faked. The second phase was a random sampling from the 2 classes identified as most frequently faked by the respondents in the first phase. The samples were drawn at 2 levels: within the indigenous manufacturers' plant and at the open drug market. The drugs were then subjected to spot checks using the Truscan deployed by NAFDAC to identify counterfeit medicines.

INCLUSION CRITERIA

Thirty-five (35) manufacturing companies that were actively involved in the production of pharmaceuticals for human use and that were accessible as at the time of the study were included in the survey.

EXCLUSION CRITERIA

These include:

- Companies that were no longer active in pharmaceutical manufacturing such as those that have temporarily or permanently suspended operations or relocated away from Lagos but are still maintained in the register of local drug manufacturers.
- Companies that were classified as drug manufacturers but are solely involved in production of external preparations, insecticides, disinfectants and antiseptics.
- Companies that are engaged in production of veterinary pharmaceuticals.
- Companies whose contact persons could not be reached at the time of the study.

SAMPLING TECHNIQUE

The Pharmaceutical Manufacturing Group of the Manufacturers Association of Nigeria (PMGMAN), Lagos State Chapter is the recognized umbrella body of local drug manufacturers in Lagos State. The support of the group was sought through its executive secretary to administer the questionnaire to all her members. Five questionnaires were administered to each member of the study population (mentioned above) in each of the 35 companies within a period of 3months. A total of 175 questionnaires were thus administered.

A list of drug products manufactured by the 35 drug companies included in this study as at 2015 was obtained from the NAFDAC regulated products automated database (NARPAD). Drug samples used for the Truscan survey study were obtained directly from the companies' manufacturing plant and the same set of samples were purchased from open drug market, Idumota, Lagos. It is pertinent to state that there was no Truscan internal reference for some of the samples drawn. This is attributable to the fact that the method development for the signatures as at the time of this study for the device were for a limited range of products. Subsequently, the outcome of the Truscan analysis for products without internal signatures cannot be a substitute for pharmacopoeia evaluation.

DATA COLLECTION

Properly designed and well structured closed ended questionnaires were self-administered to the target population as indicated above (175 respondents). The instrument was used to obtain information on socio-demographic data of the respondents, their general knowledge on counterfeit drugs, anticounterfeiting technologies, and barriers to anticounterfeiting. The questionnaire was validated by pre-testing the instrument among 14 chief executive officers of the local manufacturing companies in Lagos State to ensure the questions were clear, easy to understand and not subject to misinterpretation. Outcome of the pretest indicated some ambiguities which were rephrased and implemented in the final draft. A Truscan survey data sheet was designed and used for the purpose of recording outcomes of spot checks carried out during this study.

DATA ANALYSIS

The data obtained from phase one were analyzed using SPSS and the data obtained from phase 2 were entered into the Truscan data sheet and analyzed using Chi-squared. Results were considered to be significant at P-value < 0.05.

ETHICAL CONSIDERATIONS

Ethical clearance was obtained from the executive secretary of PMGMAN to carry out the study among the members of the association in Lagos. The informed consent of the respondents was sought and participation in the study was voluntary. The questionnaires were made anonymous to ensure confidentiality and elicit honest responses. Permission to conduct the study and use the Truscan was obtained from the Director General, NAFDAC.

RESULTS

A total of 162 (93.0%) questionnaires were filled, returned and analyzed.

Socio-Demographic Information

As shown in Table 1, 23.5% (38) of respondents were MD/Superintendent Pharmacists, 8.6% (14) were Regulatory Affairs Manager, and 17.9% (29) were Production Managers. QA/QC Managers constitute 33.3% (54) of respondents while marketing managers were 12.3% (20) of the respondents. Other respondents made up 4.3% (7) of the total respondents. The mean age of respondents was 39.1 ± 10.2. Furthermore, 63.6% (103) of respondents were males and 36.4%

TABLE 1 Socio-Demographic Data of Respondents

Variable	Frequency	Percentage (%)
Designation		
MD/Supt. Pharm.	38	23.5
Regulatory Affairs Manager	14	8.6
Production Manager	29	17.9
QA/QC Manager	54	33.3
Marketing Manager	20	12.3
Others	7	4.3
Total	**162**	**100.0**
Age group (years)		
20 – 30	39	24.1
31 – 40	51	31.5
41 – 50	49	30.2
51 – 60	21	13.0
>= 60	2	1.2
Total	162	100.0
Gender		
Male	103	63.6
Female	59	36.4
Total	**162**	**100.0**
Years of working experience		
1–5	41	25.3
6–10	30	18.5
11–15	35	21.6
16–20	22	13.6
> 20	32	19.8
Non response	2	1.2
Total	**162**	**100.0**
Highest qualification		
B. Pharm	85	52.5
MSc/Msc Pharm	42	25.9
FWAPCP	2	1.2
PhD	4	2.5
Others	29	17.9
Total	**162**	**100.0**

(59) of respondents were female. The mean years of working experience is 12.2 ± 7.3. More than half of respondents [52.5% (n = 85)] were Pharmacists while non-Pharmacists accounted for 17.9% (n = 29) of the respondents.

The majority of respondents, 64.8% (n = 105) had a good knowledge on definition of counterfeit drugs while 28.4% (n = 46) and 6.8% of respondents had a fair and poor knowledge score respectively.

As shown in Table 2, 95% of respondents stated that they have seen a counterfeit of their product. Open drug market (56.2%) and patent medicine store (53.1%) were places mentioned as areas with potential for sighting and purchase of counterfeit medicines.

Table 3 revealed that antimalarial (23.5%) and antibiotics (20.4%) were identified as drugs with the highest potential for faking.

Data in Table 4 showed that 61.1% of respondents indicated Sequential Batch Numbering as the most widely used overt anticounterfeiting technology. Other overt features used by respondents include hologram (28.4%), security graphics (22.8%), mobile product authentication (MPA) (29.0%) and tamper proof device (33.0%).

As shown in Table 5, the use of covert technologies was stated as invisible printing (8%), embedded image (17.9%), digital watermarks (9.3%), hidden marks and printing (4.9%), anticopy/antiscan design (4.3%) and laser coding (9.3%). Other covert technologies used by respondents include bar codes (29%), serialization (18.5%) and unique surface markings (11.7%).

In Table 6, most of the respondents (87%) claimed that there products are supplied to major distributors, registered wholesalers (69.8%) and retail (51.9%) outlets while only 16% claimed they make direct supplies to the open markets.

As shown in Table 7, weak regulations (50%), weak/inadequate penalties for counterfeiters (56.8%), chaotic drug distribution channels (56.2%) and widespread informal drug markets (63.6%) were identified as major barriers to respondents' anticounterfeiting effort.

Results in Table 8A showed that 10 (10) out of 12 antimalarials samples (i.e., 83.3%) drawn from 10 local drug manufacturers passed the Truscan spot check analysis while 2 (16.7) had no Truscan internal reference. In addition, 7 (7) out of 9 (77.8%) of the open market samples passed the Truscan spot checks while 2 out of 9 (22.2%) that were drawn from the open market had no Truscan internal references. Three (3) of the antimalarials sampled in the open market were not available. There were no significant difference

TABLE 3 Distribution of Classes of Products Being Faked

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Antimalaria	38 (23.5)	111 (68.5)	13 (8.1)
Antibiotics	33 (20.4)	119 (73.5)	10 (6.2)
Antifungals	19 (11.7)	131 (80.9)	12 (7.5)
Antitusives	14 (8.6)	134 (82.7)	14 (8.7)
Antihistamine/ Antiallergen	14 (8.6)	132 (81.5)	16 (9.9)

TABLE 2 Likely Places for Sighting Counterfeit Drugs

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Have you ever seen a counterfeit of your products If yes, where	155(95.7)	7 (4.3)	–
Patent Medicine Store	86 (53.1)	69 (42.6)	7 (4.4)
Retail Pharmacy Outlet	30 (18.5)	125 (77.2)	7 (4.4)
Wholesale Outlet	26 (16.0)	128 (79.0)	8 (5.0)
Primary Health Care	10 (6.2)	142 (87.7)	10 (6.2)
Private Hospital	10 (6.2)	144 (88.9)	8 (5.0)
General Hospital	9 (5.6)	147 (90.7)	6 (3.8)
Open Drug Market	91 (56.2)	65 (40.1)	6 (3.8)

($p > 0.05$) between antimalarial drug samples drawn at the drug manufacturers and open market.

As shown in Table 8B, 4 (4) out of 8 (50%) antibiotics samples drawn in the local manufacturing plants passed the Truscan spot check analysis while there were no Truscan internal references for the remaining 50%. Half of the open market samples of antibiotics were unavailable while the available 4 (100 %) passed the Truscan spot check analysis. There were no significant differences ($p > 0.05$) between antibiotic drug samples drawn from the 2 sampling sites.

Data in Table 9 revealed no significant association ($p > 0.5$) between drug samples and Truscan internal reference for companies' samples.

TABLE 4 Overt Technologies Used by Local Drug Manufacturers in Lagos

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Hologram	46 (28.4)	106 (65.4)	10 (1.9)
Optically Variable Devices	10 (6.2)	140 (86.4)	12 (7.4)
Colour Shifting Security Ink	15 (9.3)	134 (82.7)	13 (8.1)
Security Graphics	37 (22.8)	113 (69.8)	12 (7.5)
Sequential Batch Numbering	99 (61.1)	56 (34.6)	7 (4.4)
On-Product Markings	38 (23.5)	111(68.5)	13 (8.0)
Mobile Product Authentication	47 (29.0)	106 (65.4)	9 (5.6)
Tamper Proof Device	54 (33.0)	98 (60.5)	10 (6.2)

TABLE 5 Covert Anticounterfeiting Technologies Used by local Drug Manufacturers in Lagos State

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Invisible Printing	13 (8.0)	137 (84.6)	12 (7.4)
Embedded Image	29 (17.9)	123 (75.9)	10 (6.2)
Digital Watermarks	15 (9.3)	133 (82.1)	14 (8.7)
Hidden Marks & Printing	8 (4.9)	141 (87.0)	14 (8.7)
Anticopy & Antiscan	7 (4.3)	141 (87.0)	14 (8.7)
Laser Coding	15 (9.3)	135 (83.3)	12 (7.4)
Serialization	30 (18.5)	115 (71.0)	17 (10.5)
Bar Codes	47 (29.0)	103 (63.6)	12 (7.4)
Radio Frequency Identity (RFID)	1 (0.6)	144 (88.9)	17 (10.5)
Unique Surface Markings	19 (11.7)	127 (78.4)	16 (9.9)

TABLE 6. Respondents Drug Supply Chain

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Major Distributors	141 (87.0)	4 (2.5)	17 (10.5)
Registered Wholesalers	113 (69.5)	12 (7.4)	4 (2.5)
Open Markets	26 (16.0)	57 (35.2	79 (48.7)
Registered Retail Outlets	84 (51.9)	19 (11.7)	59 (32.7)
General Hospital	104 (64.2)	17 (10.5)	41 (25.4)
Private Hospital	87 (53.7)	22 (13.6)	53 (32.7)
State and Federal Medical Stores	85 (52.5)	18 (11.1)	59 (36.4)

TABLE 7 Barriers to Anticounterfeiting Strategies

Variables	Yes *N* (%)	No *N* (%)	Not Sure/No Response *N* (%)
Which of the following do you consider as barriers to your anticounterfeiting effort			
Inadequate Management Support	37 (22.8)	62 (38.3)	63 (38.9)
Weak Regulations	81 (50.0)	32 (19.8)	49 (30.2)
Limited Human Resources in Your Company	41 (25.3)	66 (40.7)	55 (34.0)
Weak/Inadequate Penalties for Counterfeiters	92 (56.8)	20 (12.3)	50 (30.9)
Financial Constraints	51 (31.5)	49 (30.2)	62 (38.2)
Inadequate Training	53 (32.7)	45 (27.8)	64 (39.5)
Chaotic Drug Distribution Channels	91 (56.2)	20 (12.3)	51 (31.5)
Widespread Informal Drug Markets	103 (63.6)	10 (6.2)	49 (30.3)

TABLE 8A Truscan Analysis for Locally Manufactured Antimalarials

S/N	Source of Sample	Company Sample Code	Truscan Result (In Triplicate)	Open Market Sample Code	Truscan Result (In Triplicate)
1	A108	A108C	Pass	A108M	Pass
2	A109	A109C	NTIF	A109M	NTIF*
3	A110	A110C	Pass	A110M	NA
4	A112	A112C	Pass	A112M	NA
5	A113	A113C	Pass	A113M	Pass
6	A114	A114C	NTIF	A114M	NTIF*
7	A116	A116C	Pass	A116M	NA
8	A117	A117C	Pass	A117M	Pass
9	A121	$A121C_1$	Pass	$A121M_1$	Pass
10	A121	$A121C_2$	Pass	$A121M_2$	Pass
11	A129	$A129C_1$	Pass	$A129M_1$	Pass
12	A129	$A129C_2$	Pass	$A129M_2$	Pass

NTIF = No Truscan Internal Reference; NA = Not Available.*

TABLE 8B Truscan Analysis for Locally Manufactured Antibiotics

S/N	Source of Sample	Company Sample Code	Truscan Result (In triplicate)	Open Market Sample Code	Truscan Result (In Triplicate)
1	A105	A105C	Pass	A105M	Pass
2	A108	A108C	Pass	A108M	Pass
3	A121	A121C	Pass	A121M	Pass
4	A127	A127C	Pass	A127M	Pass
5	A132	A132C1	NTIF*	NA	–
6	A132	A132C2	NTIF*	NA	–
7	A1151	A1151C1	NTIF*	NA	–
8	A1151	A1151C2	NTIF*	NA	–

NTIF = No Truscan Internal Reference; NA = Not Available.*

As shown in Table 10, 4 overt features were widely found on antimalaria drug samples drawn from the 2 sites (manufacturing facility and the open market). Security graphics (91.7%), Sequential Batch Numbering (100%), on-product markings (OPM) (100%) and tamper resistant packing (blister packing, 100%). On the other hand, only 4 (33.3%) of the antimalarials drawn had a MPA scratch card. However, none of the product sampled carried any covert anticounterfeiting technology.

Results in Table 11 showed that security graphics, Sequential Batch Numbering and OPM recorded 100% utilization on all antibiotics sampled from the 2 sites. However, only one product (12.5%) had the MPA scratch card. None of the samples drawn utilized any form of covert anticounterfeiting technology.

TABLE 9 Fischer Chi-Squared Table of Association between Class of Drug Samples and Truscan Internal Reference for Companies Samples

	Truscan Internal Reference		
Class of Drugs	**Present**	**Absent**	***P*-Value**
Antimalarials	10	2	0.161
Antibiotics	4	4	

DISCUSSION

The role of the pharmaceutical industry in combating the menace of fake medicines cannot be over emphasized. The development of anticounterfeiting measures by drug producers has been identified as a strategic approach to counter this horrid public health hazard.[17] There is a large market for drugs in Nigeria with about two-hundred and five (205) existing pharmaceutical manufacturers located all over the 6 geo-political zones as of March 2014.[24] Out of these, Lagos State alone has 66 local drug producers which make up about one-third (i.e., 32%) of drug manufacturers in Nigeria, making it the state with the highest number of indigenous manufacturer. To date and to the best of the authors' knowledge, no study has been undertaken to determine the approaches, strategies and methods used by local drug manufacturers in Nigeria to tackle counterfeit medicines problem.

The outcome of this study indicated that about 65% of respondents who work in the local pharmaceutical industries understood or could define a counterfeit medicine. This level of awareness is necessary and important for health improvement and embodies the basis for combating this public health menace. Without a good understanding of the subject of counterfeit medicine, tackling the menace of fake drugs will be an uphill or almost impossible task. This was however in contrary to the study carried out by Shahverdi et al.[25] in which pharmacists were found to have inadequate knowledge about counterfeit drugs. Reasons for this variance are not farfetched. The public outcry against counterfeiters and awareness campaign by NAFDAC in recent years, increasing collaboration between NAFDAC and PMGMAN as well as the negative publicity generated by associating a counterfeit drug with a manufacturer alongside the attendant loss of goodwill and economic loss has, in no small measure, awakened the local drug producers to understand and conceptualize the definition of a counterfeit medicine. This study indicates that the QA/QC personnel are the least knowledgeable, pointing to the need for designing and implementing appropriate educational programs for this category of personnel considering their pivotal role in detection of counterfeit medicine.

Open drug markets (56.2%) and patent medicine stores (53.1%) were identified by the respondents as places with the highest potential for purchase of fake drugs. These findings corroborate the study of Harocopos and Hough[26] in which open drug markets were identified as important targets that need to be tackled effectively in order to reduce harm that fake drugs can inflict on the local community. It was equally identified as a major threat for the nation's health sector.[27] Unfortunately, Nigeria remains one of the countries in the world where drugs are sold in the open market with people engaging in pharmaceutical trading and drugs supplied without ensuring they are safe, effective and of good quality. However, a close look at the outcome of the study showed that only 16% of local drug manufacturers still supply their products to the open markets. This, albeit doubtedly, may be indicative of progressive restraint of local manufacturers reducing drug supplies to the open markets.

Although majority of the respondents disagreed that any of the 5 classes of products highlighted in this study were faked, 23.5% and 20.4% of respondents

TABLE 10 Comparative Survey of Anticounterfeiting Features of Locally Manufactured Antimalarials

	OVERT FEATURES								COVERT FEATURES									
Company Samples	***H***	***OVD***	***CSSI***	***SG***	***SBN***	***OPM***	***MPA***	***TRP***	***IP***	***EI***	***DW***	***HMP***	***AA***	***LC***	***SZ***	***BC***	***RFID***	***USM***	***Open Market Samples***
A108C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A108M
A109C	×	×	×	+	+	+	+	+	×	×	×	×	×	×	×	×	×	×	A109M
A110C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A110M(NA)
A112C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A112M(NA)
A113C	×	×	×	+	+	+	+	+	×	×	×	×	×	×	×	×	×	×	A113M
A114C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A114M
A116C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A116M(NA)
A117C	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	A117M
$A121C_1$	×	×	×	×	+	+	+	+	×	×	×	×	×	×	×	×	×	×	$A121M_1$
$A121C_2$	×	×	×	+	+	+	+	+	×	×	×	×	×	×	×	×	×	×	$A121M_2$
$A129C_1$	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	$A129M_1$
$A129C_2$	×	×	×	+	+	+	×	+	×	×	×	×	×	×	×	×	×	×	$A129M_2$

Covert Features: *IP=Invisible Printing, EI=Embedded Image, DW=Digital Watermark, HMP=Hidden Marks & Printing, AA=Anticopy & Antiscan, LS=Laser Coding,* × = ***Absent;*** + = ***Present; NA = Not Available; NTIF = No Truscan Internal Reference.***

Overt Features: *H = Hologram, OVD = Optical Variable Device, CSSI = Colour Shifting Security Ink, SG=Security Graphics; SBN = Serial Batch Numbering; OPM = On Product Markings; MPA = Mobile Product Authentication; TRP=Tamper Resistant Packaging.*

Covert Features: *IP = Invisible Printing; EI = Embedded Image; DW = Digital Watermark; HMP = Hidden Marks & Printing; AA = Anticopy & Antiscan; LS = Laser Coding; SZ = Serialization; BC = Bar Codes; RFID = Radiofrequency Identity; USM = Unique Surface Markings.*

TABLE 11 Comparative Survey of Anticounterfeiting Features of Locally Manufactured Antibiotics

	OVERT FEATURES								
Company Samples	***H***	***OVD***	***CSSI***	***SG***	***SBN***	***OPM***	***MPA***	***TRP***	***Open Market Sample***
A105C	×	×	×	+	+	+	×	+	A105M
A108C	×	×	×	+	+	+	×	+	A108M
A121C	×	×	×	+	+	+	+	+	A121M
A127C	×	×	×	+	+	+	×	+	A127M
$A132C_1$	×	×	×	+	+	+	×	+	$A132M_1$(NA)
$A132C_2$	×	×	×	+	+	+	×	+	$A132M_2$(NA)
$A1151C_1$	×	×	×	+	+	+	×	+	$A1151M_1$(NA)
$A1151C_2$	×	×	×	+	+	+	×	+	$A1151M_2$(NA)

	COVERT FEATURES										
Company Samples	***IP***	***EI***	***DW***	***HMP***	***AA***	***LC***	***SZ***	***BC***	***RFID***	***USM***	***Open Market Sample***
A105C	×	×	×	×	×	×	×	×	×	×	A105M
A108C	×	×	×	×	×	×	×	×	×	×	A108M
A121C	×	×	×	×	×	×	×	×	×	×	A121M
A127C	×	×	×	×	×	×	×	×	×	×	A127M
$A132C_1$	×	×	×	×	×	×	×	×	×	×	$A132M_1$(NA)
$A132C_2$	×	×	×	×	×	×	×	×	×	×	$A132M_2$(NA)
$A1151C_1$	×	×	×	×	×	×	×	×	×	×	$A1151M_1$(NA)
$A1151C_2$	×	×	×	×	×	×	×	×	×	×	$A1151M_2$(NA)

× = ***Absent; + = Present; NA = Not Available; NTIF = No Truscan Internal Reference.***
Overt Features: *H = Hologram, OVD = Optical Variable Device, CSSI = Colour Shifting Security Ink, SG = Security Graphics; SBN = Serial Batch Numbering; OPM = On Product Markings; MPA = Mobile Product Authentication, TRP = Tamper Resistant Packaging.*
Covert Features: *IP=Invisible Printing, EI=Embedded Image, DW=Digital Watermark, HMP=Hidden Marks & Printing, AA=Anticopy & Antiscan, LS=Laser Coding, SZ=Serialization, BC=Bar Codes, RFID=Radiofrequency Identity, USM=Unique Surface Markings.*

agreed that antimalarials and antibiotics respectively were identified with the highest potential for faking. This is understandably at variance with the WHO report of counterfeit drugs by therapeutic class between 1999 and 2002.[17] The report stated that about 28% of antibiotics and 7% of antimalarials are faked worldwide.

These 2 classes of drugs are among the most commonly prescribed and used medicines in Nigeria. Moreover, the prevalence of malaria and common infections coupled with the ease of purchase of these classes of medicine without valid prescription, irrational drug use and routine purchase of drugs from unregistered sources are factors responsible for this development. This was corroborated by a tripartite study carried out by the American Enterprise Institute (AEI), Initiative for Public Policy Analysis (IPPA), and African Fighting Malaria (AFM).[28] The study showed that there appeared to be evidence of irrational drug use especially antimalarials and antibiotics with a failure rate of 19% and 23% respectively compared to the other classes of drugs assessed for quality evaluation.

Respondents expressed contradictory views about the various types of overt technologies used by their companies. While the survey of antimalarials and antibiotics indicated that the use of hologram, Optical

Variable Device (OVD), Colour Shifting Security Ink (CSSI) was non-existent. The use of Security Graphics (SG) (91.7%) and On-Product Markings (100%), were a regular feature of the drugs sampled. Responses from the respondents had indicated varying degrees of use of hologram (28.4%), OVD (6.2%) and CSSI (9.3%).

This inconsistency can only mean that respondents to a large extent are not familiar with these groups of overt technologies (i.e., hologram, OVD, CSSI). Defeating the counterfeiters demands a multi-level approach, an element of which is secure packaging. This lack of recognition and noticeable knowledge gaps by those who should know has been identified as a threat associated with proliferation of counterfeit drugs.[29] In addition, cost of implementing the use of the observed non-existent overt technologies on products sampled will be high and inevitably result in high prices thereby making the drugs unaffordable.

On the other hand, use of security graphics, Serial Batch Numbering (SBN), and On-Product Markings (OPM) as mentioned above were a regular feature of all the drugs sampled within the companies' manufacturing plant. This observation indicated that Nigerian local pharmaceutical industries though faced with the challenge of unfriendly economic environment are taking commendable steps in securing their products from the invasion of counterfeiters. Overt features enable instant authentication of packaging through visual inspection by the user without requiring expert knowledge. These features, if widely employed will empower consumers to rely on the evidence of their own eyes, protect public health and reduce counterfeiting. This view was also supported by USFDA,[30] in which it was stated that authentication technologies used by manufacturers and repackagers will serve as a critical components of any strategy to protect products against counterfeiting and on the long run improve health indices associated with the consumption of drugs. The ability to identify the source and provenance of products through the use of hologram is becoming a mandatory requirement spelled out by the USFDA. While the U.S. Congress considers mandating the use of security marking on some pharmaceutical products by using "overt optically variable counterfeit-resistant technologies" to protect consumers from fakes, the hologram already acts as the authentication feature on the world's only mandatory scheme for the authentication marking of registered pharmaceuticals: the meditag program in Malaysia.

This initiative requires all registered medicines, to carry a uniquely numbered label built around a hologram. A central authority supervises the system, controls the issue of tags, and trains inspectors to examine holograms through the distribution chain. Since its introduction, this system has led to a significant increase in the identification and confiscation of illegal items from the market and prevented their entry into distribution channels. As a result, consumer confidence in the integrity of pharmaceuticals has increased, public health has been safeguarded, and there has been a drastic reduction in the incidence of counterfeiting in these countries.[31]

The utilization of MPA by only 29% of the respondents is in close consonance with the field survey in which 33% of antimalarials sampled carried the MPA scratch cards. This appears to be a step in the right direction. Although the quality of pharmaceuticals cannot be confirmed by use of MPA as pointed out by Amuda,[32] it nonetheless assures the originality of the source of the product at the level of the consumer. A close comparison of MPA with other widely used overt technologies has pointed to the fact that many local producers are still non-compliant to the regulatory directives of NAFDAC that stated that all antimalarials manufactured locally should carry the MPA scratch cards for consumer use by July 2014 for all antimalarials and June 2015 for all antibiotics.[33] This low-level compliance cannot be dissociated from a number of factors one of which is financial constraints and pecuniary considerations as mentioned by 31.5% of respondents. This is corroborated by the ex-chair of PMGMAN, in a paper published by Sotunde.[34]

A rather encouraging trend is the fact that the entire product sampled had tamper evident or tamper resistant packing which provides visible evidence to consumers that tampering has not occurred. The persistence of this trend will to a large extent provide assurance that products available for sale are still in their original product packaging. This is in agreement with WHO guidelines on packaging of pharmaceutical product[35] and study of Mayberry.[36] Although tamper resistant-evident packaging is not a new invention

and provides some level of security, extra steps must be taken to ensure that the packaging reaches its full potential. This will involve the use of multiple anticounterfeiting technologies or a combination of overt and covert measures that will provide optimal security because they help prevent counterfeiting and reassure end users. A multi-level approach such as this may result in additional costs to the manufacturer as the technologies become more sophisticated and patient affordability is called to question. Bantal et al.[37] however, suggested that a multi-level approach should be implemented based on the risk analysis of the drug to be counterfeited.

The outcome of the Truscan analysis showed that 83.3% of locally manufactured antimalarials drawn from the companies' manufacturing plant passed the Truscan spot check analysis. The remaining 16.7% of samples had no signatures in the hand-held device. This outcome was supported by 77.8% of open market samples passing the spot checks. The remaining 22.2% of antimalarials in the open market had no Truscan internal reference. Similarly, 50% of antibiotics drawn from the 2 sampling areas passed the Truscan checks. The remaining 50% of companies sampled had no Truscan internal reference while that of the open market were not available for sampling. However, there was no significant difference between the antimalarials and antibiotics sampled.

The implication of this is that local manufacturing of pharmaceuticals under a functional and efficient regulatory oversight is one of the ways to curb counterfeiting activities. This ensures that drug products are not only manufactured under good manufacturing practice but distributed to an approved supply chain. A comparison of this data with previous study showed that counterfeiting of antimalarials and antibiotics is largely associated with imported drugs.[9] Consequently, building the capacity of local manufacturers for commonly used medicines through appropriate provision of incentives, infrastructures and legislation will minimize the prevalence of fakes in the Nigerian market. This finding agrees with the studies carried out by several authors in which local manufacturers of medicines with appropriate regulatory control have been found to enhance self sufficiency in drug supply, improve access to quality medicine while reducing the incidence of counterfeiting.[38–40]

None of the samples drawn from the manufacturing sources or open market had any form of covert (hidden) anticounterfeiting technology. The reason for this observation could range from cost implication for manufacturers, unavailability of local service providers of these technologies, outright ignorance of the existence and use of covert technologies. This assertion is buttressed by studies from OECD[41] which stated that the feasibility of use of a particular technology across different jurisdiction will vary in light of existing conditions, resources and economic development. It was also generally observed that the use of covert technologies in Africa or South East Asia where significant counterfeiting activity is occurring may not be feasible for cost and technological reasons.[42] In these jurisdictions, industries are considering which type of technology would be most effective. This study highlighted that most indigenous manufacturers limit the use of anticounterfeiting technologies to overt features which is by no means a fullproof approach to effectively fight counterfeits. The reliance on one anticounterfeiting technology will not adequately redress the problem of counterfeit pharmaceuticals. Therefore, the use of more than one anticounterfeiting technology has been suggested.[37] Similarly, Halling[43] indicated that anticounterfeiting technology approaches are interdependent for their effectiveness and integrating them yields a more robust system. In this respect, a combination of overt and covert measures may provide optimal security because they help prevent counterfeiting and reassure end users.[44]

Brand protection[45] has been defined as the collection of capabilities and activities conducted by a company and its stakeholders to help prevent unauthorized use of intellectual property and/or commerce associated with that company's brands or trademarks. It is a vital component of the pharmaceutical and health care markets. This is important so that companies can protect their investments, identities and market share. The Nigerian indigenous manufacturers who participated in this study appear not to place emphasis on protecting their brand as only 42% of them claimed to have a brand protection policy (which can be defined as

a statement of claim made by a company to various audiences (internal and external) that it is committed to protecting its brands and to seek enforcement against those who seek to attack them). A brand protection policy lays down the standard operating procedure the company will use in pursuing the monitoring of markets and the enforcement of its right in full accordance with relevant laws and regulations. However, the policy was not documented in any official document as only a paltry 17.9% claimed this was done. This finding was substantiated by Guido,[45] who also observed that pharmaceutical manufacturers needs to move away from a "see and treat mentality" to a more strategic and proactive role to elevate anticounterfeiting activities. Brand protection must include a well laid out procedure and strategic position against brand attacks and supply chain integrity.

A majority of the respondents about 68.5% were not sure or do not even have a priority watch list of areas where possible counterfeits of their product could be found. This is in addition to the revelation that post-marketing surveillance for the purpose of detecting fake product was limited to less than half (43.8%) of the respondents and indication that brand protection, if practiced in the real sense was not aligned with supply chain management.

The respondents identified widespread informal markets (63.6%), weak/inadequate penalties for counterfeiters (56.8%), chaotic drug supply channels (56.2%) and weak regulations (50%) as top 4 barriers to their anticounterfeiting strategies. Other barriers in order of decreasing importance are inadequate training (32.7%), financial constraints (31.5%), limited human resources (25.3%) and inadequate management support (22.8%). These outcomes align with findings by Onwuka[46] in a study carried out to elucidate the situation of medicine counterfeiting in Africa. The study indicated that conflict of interest, inadequate legislation, slow litigation process, corruption and definitional confusions among others are some of the hurdles that must be overcome if the fight against drug counterfeiting must be won.

CONCLUSIONS AND RECOMMENDATION

Medicine counterfeiting with its associated risks remains a global challenge of enormous proportion. An overview of the outcome of this study showed that given the appropriate incentives and support, local pharmaceutical industries have the capacity to enhance their product anticounterfeiting features. The fact that 83.3% of locally manufactured antimalarials drawn from the manufacturing sources passed the Truscan spot check analysis while a corresponding 77.8% of open market samples of same set of drugs passed the Truscan analysis are basically indicative of progressive attempt at combating the menace of fakes. The same finding was made for locally manufactured antibiotics in which 50% of drugs drawn at both sample sites passed Truscan analysis. However, these efforts are still highly susceptible to invasion by counterfeiters especially because the solitary use of overt features employed by the local manufacturers will not adequately tackle the problem of counterfeit pharmaceuticals in the long run. Subsequently, a combination of overt and covert features to provide optimal security for these brands is desirable although not at the expense of accessibility and affordability of these essential medicines to the consuming populace. Finally, it is worthy to underscore that the high sensitivity of Truscan used in this study compensated for the small sample size.

Based on the outcome of this study, it is recommended that:

1. Information sharing and collaboration among the stakeholders should be encouraged to curb the activities of counterfeiters while NAFDAC as the National Drug Regulatory Authority should consider a review of the relevant regulations with appropriate legal framework so as to strengthen anticounterfeiting features of locally produced Pharmaceuticals
2. A synergy of effort to encourage the use of multi-level or combination of anticounterfeiting technologies by the indigenous manufacturers should be established and the differences between approaches currently employed are proposed for further studies.
3. The Truscan internal reference data base should be broadened to enhance its usefulness in performing spot check analysis for a wider application especially for locally manufactured drugs.

COMPETING INTERESTS

There is no competing interest both financially and non-financially that is associated to this manuscript. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

FUNDING

This research was solely funded by the authors.

ACKNOWLEDGEMENTS

The authors thank all the local drug manufacturers who are members of PMGMAN that participated in the study.

REFRENCES

1. Cockburn R, Newton PN, Agyarko EK, Akunyili D, White NJ. The global threat of counterfeit drugs: why industry and governments must communicate the dangers. PLoS Med. 2005;14;2(4):e100.
2. World Health Organization. WHO IMPACT Publication. "Counterfeit Drugs Kill." Geneva: Author; 2006. Available at: www.who.int/impact.
3. Charatan F. Fake prescription drugs are flooding the United States. Br Med J 2001;16;322(7300):1446.
4. Khan AY, Ghilzai NM. Counterfeit and substandard quality of drugs: the need for an effective and stringent regulatory control in India and other developing countries. Ind J Pharmacol 2007;1;39(4):206.
5. SCRIP World Pharmaceutical News. Nigeria Fights Corruption; 2001. Available at: www.scripnews.com/home/news/Nigeria.fights corruption-77125.
6. Taylor RB, Shakoor O, Behrens RH, et al. Pharmacopoeial quality of drugs supplied by nigerian pharmacies. The Lancet 2001;16;357(9272):1933–6.
7. Yankus W. Counterfeit drugs: coming to a pharmacy near you. American Council on Science and Health; 2006. Available at: www.acsh.org/publications/pubID.1379/pub_detail asp.
8. The Economist. Bad Medicine. Available at: www.economist.com/mode/21564546; 2012.
9. World Health Organization. Survey of selected antimalarial medicine circulating in 6 countries of sub-sahara Africa. Geneva: Author; 2011. Available at: www.who.int.
10. WHO/QAMSA Report. Survey of the quality of selected antimalarial medicines circulating in 6 countries of sub-saharan Africa. Geneva: Author; 2011. Available at: WHO/EMP/QSM/2011.1
11. Iwokwagh NS. Assessment of new media use in the fight against counterfeit medicine in Nigeria. Available at: https://scholar.google.com/scholar?q=Iwokwagh+NS
12. Thermo Scientific Truscan^{RM} Next generation handheld raman for raw material identification; 2011. Available at: www.thermoscientific.com/Truscan 2011.
13. Orhii PB. An Overview of NAFDAC. Presentation at the First Regulatory Forum, Lagos; 2013.
14. GPHF. Showcasing the innovators: a practical presentation at NAFDAC in-house training for regulatory officers. Lagos, Nigeria; 2014.
15. Sproxil Fight Against Counterfeit Drugs. Available at" www.sproxil.com/Nigeria.html.
16. Obinna C, Olawole G. Nigeria: NAFDAC introduces new anticounterfeiting technologies; 2010. Available at: all Africa.com/stories/201006141446.html?mstac=0.
17. World Health Organization/IMPACT. Anticounterfeiting technologies for the protection of medicines. Geneva: Author; 2010. Available at: www.who.int/impact.
18. Berman B. Strategies to detect and reduce anticounterfeiting activity. business horizons. (May-June 2008, Vol 51(3) 191–99. Available at: http://www.sciencedirect.com/science/article/pii/S0007681308000037. 2008.
19. International Federation of Pharmaceutical Manufacturers Association. The IFPMA 10 principles on counterfeit medicine; 2010. Available at: www.ifpma.org.
20. Peterson K. How fake and substandard drugs get to Nigeria; 2015. Available at: premiumtimesng.com/features-and-interviews/189328-interview. 2015.
21. Onyebuchi OB. National drug distribution in Nigeria; implications for the goals of national drug policy. Eur J Pharm Med Res 2016;3(1):1–4.
22. Obinna C, Udemba K, Amusat M. fg bans sale of drugs in open markets. Vanguard Newpaper; 2013. Available at: vanguard.com/2013/08/fg-bans-sale-of-drugs-in-open-market.
23. City Mayors. World's fastest growing cities and urban areas from 2006 to 2020; 2006. Available at: http://www.citymayors.com/statistics/urban_growth1.html. 2006.
24. DER. List of registered pharmaceutical companies in Nigeria as at March 2014. Available at: Drug Evaluation and Research Directorate (DER), NAFDAC. 2014.
25. Shahverdi S, Hajimiri M, Pourmalek F, et al. Iranian pharmacists' knowledge, attitude and practice regarding counterfeit drugs. Ir J Pharm Res 2012;11(3);963–68.

26. Harocopos A, Hough M. Drug dealing in open-air markets. Problem-oriented guides for police. Problem Specific Guides Series No. 31; 2005. Available at: http://www.popcenter.org/problems/drugdealing_openair/
27. Business Day. "Open drug markets, major threat to Nigeria's health sector. Business Day Dec. 20, 2013; Available at: http://businessdayonline.com/2013/12/open-drug-market-major-threaten-to-nigerias-health-sector/#.VZ-2hVFkb1U.
28. American Enterprise Institute (AEI), Initiative for Public Policy Analysis (IPPA) and African Fighting Malaria (AFM). Drug use in Nigeria. An informal survey of doctors, pharmacists, healthcare workers in Lagos, Ondo, and Ogun, and a pilot quality assessment of essential drugs from Lagos pharmacies. Available at: www.ippanigeria.org/nigeria_drug_project_august2009.pdf 2009.
29. JDSU. JDSU white paper: pharmaceutical counterfeiting, tampering, and diversion: solutions for addressing a growing threat. Available at: www.jdsu.com/productliterature/pharmaceutical_white_paper.pdf.
30. USFDA. Counterfeit drug task report. February 2004 Update TECHNOLOGY. Available at: www.fda.gov/Drugs/DrugSafety/ucm173297.html.
31. Dietrich E. Hologram innovation take on counterfeiting. J Pharm Med Packaging News 2008;16(1).
32. Amuda KI. Knowledge, attitude and perception of community pharmacists in Lagos State on Mobile Authentication Service (MAS) anticounterfeiting technology. West Africa Postgraduate College of Pharmacists' (WAPCP) Dissertation; 2014.
33. NAFDAC Internal Memo. Compliance directives on mas coding of antibiotics and antimalarial medicines. August 4, 2014.
34. Olubusayo S. Over $44m invested in Nigeria pharmaceutical industry – PMG-MAN Chairman. 2013. Available at: http://venturesafrica.com/44m-investments-made-nigeria-pharmaceutical-industry-pmg-man-chairman/.
35. WHO Technical Report Series 902. WHO Expert Committee on specifications for pharmaceutical preparations. 2002. Thirty Sixth Report. Available at: www.who.int/publications.
36. Mayberry J. The proof is in the packaging. Available at: pharmpro.com/articles/2012/03/proof-packaging
37. Bansal D, Malla S, Gudala K, et al. Anti-counterfeit technologies: A pharmaceutical industry perspective. Sci Pharm 2013;81(1):1–3.
38. Kaplan W, Lain R. local production of pharmaceuticals: industrial policy and access to medicine - an overview of key concepts, issues and opportunities for future research. World Bank, HNP Discussion Paper, Human Development Network. Available at: www.medeor.de/images/themen/kaplanlocalproductionfinal5b15d.pdf.
39. Bate R. Local production in developing countries. Campaign for Fighting Disease Discussion Paper No 1; 2008. Available at: http://thefacts2014.ipa.org.au/document_root/library/Local%20Pharmaceutical%20Production%20web.pdf.
40. Mackintosh M, et al. Global Health. 2014 Mar 10;10:12 doi 10:1186/1744-8603-10-12. Available at: www.ncbi.nlm.nih.gov/pubmed/24612518.
41. Organisation for Economic Co-operation and Development. The economic impact of counterfeiting and piracy. www.oecd.org/sti/ind/2090589.pdf. 2008; Available at: and https://books.google.com.ng/books?id=Se7V.....
42. Brand News. Pharmaceutical company trials DNA labels. Vol.3, (26 January, 2006). Available at: www.oecd.org/sti/ind/2090589.pdf. 2006.
43. Halling C. Improving packaging security. Pharmaceut Tech Eur 2011;23(5). Available at: http://www.pharmtech.com/ptedigital0511.
44. Pharmaceutical Technology Europe. Improving Packaging security. 2011. Available at: http://pharmtech.findpharma.com/pharmtech/articledetail.jsp?id=718108.
45. Guido R. Designing a brand protection organization in life sciences. 2013. Available at: https://www.google.com.ng/search?q=DESIGNING+A+BRAND+PROTECTION+ORGANIZATION+IN+LIFE+SCIENCES+-+.
46. Onwuka J. "The situation of medicine counterfeiting in Africa. 2010. Available at: www.whpa.org/background_medicine_counterfeiting_in_africa.html.

Appendix 1

QUESTIONNAIRE

Anticounterfeiting Strategies of Local Drug Manufacturers in Lagos State, Nigeria: Drug Safety and Implications for Public Health

PART 1

SOCIO-DEMOGRAPHIC DATA

1. Age

a = 20-30 ( ) b = 30-40 ( ) c = 40-50 ( ) d = 50-60 ( ) e= > 60 ( )

2. Gender

a=Male ( ) b= Female ( )

3. Years of Working Experience in the local Pharmaceutical manufacturing Industry

a= 1-5years ( ) b= 6 -10years ( ) c = 11-15years ( ) d=16-20years ( ) e= ≥ 20years ( )

4. Highest Qualification

a=B.Pharm/B.SC ( ) b= M.SC/M.Sc Pharm ( ) c=FWAPCP ( )
d= PhD ( )f= Others (Please Specify)

5. Designation

a= MD/Superintendent Pharmacist ( ) b= Production Pharmacist/Manager ( )
c= QA/QC Manager ( ) d=Marketing Manager () e = Regulatory Affairs Manager ( ) f = Others (Please Specify)

PART 2 - GENERAL

1. **A counterfeit product:**
   - **a) Is deliberately/fraudulently mislabelled with respect to identity, source or both**
     a=Yes ( ) b= No ( ) c= Not Sure ( )
   - **b) Can apply only to generic products**

     a=Yes ( ) b= No ( ) c= Not Sure ( )

   - **c). Apply only to branded products**
     a=Yes ( ) b= No ( ) c= Not Sure ( )
   - **d). Apply to both generic and branded products**
     a=Yes ( ) b= No ( ) c= Not Sure ( )

   - **e). Is the same as substandard drug**
     a=Yes ( ) b= No ( ) c= Not Sure ( )

   - **f). Include drug products with correct ingredients**
     a=Yes ( ) b= No ( ) c= Not Sure ( )

g). Include products with wrong ingredients

a=Yes ( ) b= No ( ) c= Not Sure ( )

h). Include products without active ingredients

a=Yes ( ) b= No ( ) c= Not Sure ( )

i) Include products with insufficient Ingredients

a=Yes ( ) b= No ( ) c= Not Sure ( )

j) Include products with fake packaging

a=Yes ( ) b= No ( ) c= Not Sure ( )

2. Have you ever seen a counterfeit of your product?

a=Yes ( ) b= No ( ) c= Not Sure ( )

a) If yes where

i) Patent Medicine Store a=Yes ( ) b= No ( ) c= Not Sure ( )
ii) Retail Pharmacy Outlet a=Yes ( ) b= No ( ) c= Not Sure ( )
iii) Wholesale Pharmacy Outlet a=Yes( ) b= No( ) c= Not Sure ( )
iv) Primary Health Centre a=Yes ( ) b= No ( )c= Not Sure ( )
v) Private Hospital a=Yes ( ) b= No ( ) c= Not Sure ( )
vi) General Hospital a=Yes ( ) b= No ( ) c= Not Sure ( )
vii) Open Drug Market a=Yes ( ) b= No ( ) c= Not Sure ( )

3 Do you think that your range of products is prone to faking?

a=Yes ( ) b= No ( ) c= Not Sure( )

4. If Yes state reasons

i)
ii)
iii)
iv)
v)

5. If No state reasons

i)
ii)
iii)
iv)
v)

6) From your personal experience and observation, which class of your products has been faked

i) Antimalaria a=Yes ( ) b= No ( ) c= Not Sure ( )
ii) Antibiotics a=Yes ( ) b= No ( ) c= Not Sure ( )
iii) Antifungals a=Yes ( ) b= No ( ) c= Not Sure ( )
iv) Antitusives a=Yes ( ) b= No ( ) c= Not Sure ( )
v) Antiasthmatics/Antiallergies a=Yes ( ) b= No ( ) c= Not Sure ( )
vi) Others (Please Specify)

PART 3 - ANTICOUTERFEITING TECHNOLOGIES

1. **Which of the following features is employed by your company to prevent counterfeiting**

a) Overt (Visible) Features

i) Hologram a=Yes ( ) b= No ( ) c= Not Sure ( )
ii) Optically Variable Devices a=Yes ( ) b= No ( ) c= Not Sure ( )
iii) Colour Shifting Security Ink a=Yes ( ) b= No ( ) c= Not Sure ( )
iv) Security Graphics a=Yes ( ) b= No ( ) c= Not Sure ( )
v) Sequential Batch Numbering a=Yes ( ) b= No ( ) c= Not Sure ( )
vi) On Product Markings a=Yes ( ) b= No ( ) c= Not Sure ( )
vii) Mobile Product Authentication a=Yes ( ) b= No ( ) c= Not Sure ( )
viii) Tamper Proof Device a=Yes ( ) b= No ( ) c= Not Sure ( )

b) Covert (Hidden) Features

i) Invisible Printing a=Yes ( ) b= No ( ) c= Not Sure ( )
ii) Embedded Image a=Yes ( ) b= No ( ) c= Not Sure ( )
iii) Digital Watermarks a=Yes ( ) b= No ( ) c= Not Sure ( )
iv) Hidden Marks and Printing a=Yes ( ) b= No ( ) c= Not Sure ( )
v) Anticopy or Antiscan Design a=Yes ( ) b= No ( ) c= Not Sure ( )
vi) Laser Coding a=Yes ( ) b= No ( ) c= Not Sure ( )
vii) Substrates a=Yes ( ) b= No ( ) c= Not Sure ( )

c) Forensic Markers

Chemical Taggants a=Yes ( ) b= No ( ) c= Not Sure ( )
Biological Taggants a=Yes ( ) b= No ( ) c= Not Sure ( )

d) Track and Trace Technologies

Serialisation a=Yes ( ) b= No ( ) c= Not Sure ( )
Bar Codes a=Yes ( ) b= No ( ) c= Not Sure ( )
Radio frequency Identity Tagging a=Yes ( ) b= No ( ) c= Not Sure ( )
Unique Surface Marking a=Yes ( ) b= No ( ) c= Not Sure ( )

PART 4- MARKET CONTROL

1. **Your drugs are directly supplied to**

i) Major Distributors a=Yes ( ) b= No ( ) c= Not Sure ( )
ii) Registered Wholesalers a=Yes ( ) b= No ( ) c= Not Sure ( )
iii) Open Markets a=Yes ( ) b= No ( ) c= Not Sure ( )
iv) Registered Retail outlet a=Yes ( ) b= No ( ) c= Not Sure ( )
v) General Hospitals a=Yes ( ) b= No ( ) c= Not Sure ( )
vi) Private Hospitals a=Yes ( ) b= No ( ) c= Not Sure ( )
vii) State and Federal Medical Stores a=Yes ( ) b= No ( ) c= Not Sure ( )

2. **Do you have a brand protection policy in your company**

a=Yes ( ) b= No ( ) c= Not Sure ( )

3. **Do you have a brand protection team in your company**

a=Yes ( ) b= No ( ) c= Not Sure ( )

4. **Are the duties of the brand protection team stated in any of your company's official document**
   a=Yes ( ) b= No ( ) c= Not Sure ( )
5. **Do you carry out post marketing surveillance on your product**
   a=Yes ( ) b= No ( ) c= Not Sure ( )
6. **If yes, for what purpose**

i) ADR Reporting
ii) Distribution Practices
iii) Detect Fakes
iv) Sales Profile
v) Others (Please Specify)

7. **Do you have a priority watch list of areas where fake brands of your product could be found**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

PART 5 - INTERNAL CONTROL MECHANISMS

1. **How do you handle your production wastes and rejects**
   a) **Discard them in the LAWMA operators vehicle**
      a=Yes ( ) b= No ( ) c= Not Sure ( )
   b) **Hand them over to NAFDAC for destruction**
      a=Yes ( ) b= No ( ) c= Not Sure ( )
   c) **Burn them off in an incinerator**
      a=Yes ( ) b= No ( ) c= Not Sure ( )
   d) **Keep them in a dedicated area under lock and before disposal**
      a=Yes ( ) b= No ( ) c= Not Sure ( )
2. **Do you have an inventory management system for your packaging materials**
   a=Yes ( ) b= No ( ) c= Not Sure ( )
3. **Do you have a designated officer for the inventory management of your packaging materials**
   a=Yes ( ) b= No ( ) c= Not Sure ( )
4. **Who keeps your Batch Manufacturing /Processing Record**

i) Superintendent Pharmacist
ii) Production Manager
iii) QA/QC Manager
iv) Warehouse/Store Manager
v) Company's Security Personnel
vi) Others (Please Specify)

PART 6 – INFORMATION SHARING AND COLLABORATION

1. **Do you carry out regular audit of your major distributors**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

2. **Do you carry out regular consultative meetings with your distributors**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

3. **Have you ever discovered a counterfeit brand of your product**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

   a) **If yes , did you make official report**
      a=Yes ( ) b= No ( ) c= Not Sure ( )
   b) **To Who**
      i) PMG-MAN
      ii) NAFDAC
      iii) Nigerian Police
      iv) Others (Please Specify)

4. **Was any action taken after your official report**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

   a) **If no official report was made what are the reasons**
      i) Absence of counterfeit brand of your product
         a=Yes ( ) b= No ( ) c= Not Sure ( )
      ii) Response from Regulator for previous report was discouraging
         a=Yes ( ) b= No ( ) c= Not Sure ( )

      iii) Weakness of your post marketing surveillance
         a=Yes ( ) b= No ( ) c= Not Sure ( )

      iv) Insufficient Management Support
         a=Yes ( ) b= No ( ) c= Not Sure ( )
         Others (Please Specify)

PART 7 – BARRIERS TO ANTICOUNTERFEITING STRATEGIES

Which of the following do you consider as barriers to your Anticounterfeiting Effort

a) **Inadequate Management Support**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

b) **Weak Regulations**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

c) **Limited Human Resources in your Company**
   a=Yes ( ) b= No ( ) c= Not Sure ( )

Financial Constraints

d) a=Yes ( ) b= No ( ) c= Not Sure ( )

e) Inadequate Training

a=Yes ( ) b= No ( ) c= Not Sure ( )

f) Chaotic Drug Distribution Channels

a=Yes ( ) b= No ( ) c= Not Sure ( )

g) Widespread Informal Drug Markets

a=Yes ( ) b= No ( ) c= Not Sure ( )

h) Weak/Inadequate penalties for counterfeiters

a=Yes ( ) b= No ( ) c= Not Sure ( )