MINISTRY OF PUBLIC HEALTH AND SANITATION &

MINISTRY OF MEDICAL SERVICES

DIVISION OF MALARIA CONTROL & PHARMACY AND POISONS BOARD

Monitoring the Quality of Antimalarial Medicines Circulating in Kenya

With the support of
The Global Fund to fight AIDS, Tuberculosis and Malaria
&
USAID, President's Malaria Initiative (PMI)
&
USP PQM

April 2012

ACKNOWLEDGMENTS

This report presents the findings from a collaborative study between the Division of Malaria Control Pharmacy and Poisons Board, National Quality Control Lab, and the Promoting the Quality of Medicines program. Funding for this study was provided by The Global Fund to Fight AIDS, Tuberculosis and Malaria round 4 grant number KEN-405-G06-M and U.S. President's Malaria Initiative/USAID through the United States Pharmacopoeia, Promoting Quality Medicines.

The authors of this report would also like to thank the Registrar and Deputy Registrar Pharmacy and Poisons Board, the Director NQCL and the head DOMC for facilitating this noble activity.

The following members are also recognized for their participation in data collection analysis and report writing.

- Dr Stephen Kimatu — Project coordinator
- Dr Andrew Nyandigisi — Assistant Project Coordinator/Report writer
- Dr. Eunice Gathitu
- Dr. Jayesh Pandit
- Dr. Edward Abwao
- Dr. Simiyu Sibalile
- Dr. Hadley Sultani
- Dr.Mikal Ayiro
- Dr. Nicholas Mwaura
- Dr. George Wang'anga
- Mr. Patrick Kibiego
- Mr. Nehemiah Birgen
- Ms. Beatrice Obinge
- Mr. George Muthuri

TABLE OF CONTENTS

LIST OF TABLES

TABLE OF FIGURES

LIST OF ACRONYMS

ACT	Artemisinin-Based Combination Therapy
AL	Artemether Lumefantrine
DOMC	Division of Malaria Control.
DQI	Drug Quality and Information Program implemented by USP
FDC	Fixed-dose Combination
GPHF	Global Pharma Health Fund
IPTp	Intermittent preventive treatment in pregnancy
MQM	Medicines Quality Monitoring
NQCL	National Quality Control Laboratory
PMS	Post Market Surveillance
PQM	Promoting the Quality of medicines
PPB	Pharmacy and Poisons Board
QAMSA	Quality of Antimalarials in Sub-Saharan Africa
QA	Quality Assurance
QC	Quality Control
SP	Sulfadoxine-Pyrimethamine fixed-dose combination
TLC	Thin-Layer Chromatography
USAID	United States Agency for International Development
USP	United States Pharmacopeia
USP-NF	United States Pharmacopeia-National Formulary
WHO	World Health Organization

EXECUTIVE SUMMARY

One of the policy objectives in the Kenya National Pharmaceutical Policy is to ensure the quality, safety and efficacy of human and veterinary drugs in Kenya. Good quality medicines are also a pre requisite to prompt and effective treatment, the main objective of case management according to the current national malaria strategy. This report presents the findings of the second round of monitoring of the quality of antimalarials that was carried out in November 2011 in five sentinel sites representing areas with the highest malaria burden.

In total, 499 antimalarial samples were collected from the five sentinel sites according to the endemicity of Malaria. The samples included artemisinin-based combination therapy (ACT) and sulfadoxine-Pyrimethamine (SPs) among other antimalarials. The samples were collected from the public sector, the private sector and the informal sector.

Basic testing, using the Global Pharma Health Fund (GPHF) Minilab kit, was performed on most collected samples at the sentinel sites. This was followed by confirmatory analysis of 10percent of the samples that passed minilab analysis, all doubtful samples and all failed samples at the National Quality Control Laboratory (NQCL) using the Minilab. A similar sampling strategy was used to select samples that were subject to full compendial analysis at NQCL.

Of the 499 samples collected, all were assessed for registration status with PPB, 496 were analyzed using minilabs at level 1, 65 at level 2 and 25 using compendial methods in NQCL. The study findings indicate that 97percent of the samples collected were registered up from 93percent in round one. 97percent conformed at level one, 100percent conformed at level two and 76percent conformed to compendial methods (level 3).

CHAPTER ONE: INTRODUCTION

Malaria in Kenya

Malaria continues to be one of the major public health problems in Africa, Asia and Latin America. *Plasmodium falciparum* malaria is estimated to be the direct cause of 500 million cases and over 1 million deaths per year, mostly in women and children under the age of 5 years (Guerra, Gikandi, & Tatem, 2008). In Kenya, malaria is responsible for 30 per cent of outpatient consultations, 19 per cent of hospital admissions and 3–5 per cent of inpatient deaths. Seventy per cent of Kenya's population lives in malarious areas. (Ministry of Public Health and Sanitation, 2009). It is for this reason that the government has prioritised the prevention and treatment of malaria in Kenya.

In collaboration with partners, the Division of Malaria Control (DOMC) developed an 8-year Kenya National Malaria Strategy (KNMS) 2009-2017 which was launched in 4th November 2009 (Ministry of Public Health and Sanitation, 2009). The goal of the National Malaria Strategy is to reduce morbidity and mortality associated with malaria by 30percent by 2009 and to maintain it to 2017.

Prior to 2009, the country was stratified into 4 main malaria eco-epidemiological zones: endemic, seasonal transmission, epidemic-prone and low risk zones. A malaria indicator survey by DOMC in 2007 showed that there are variations in malaria parasite prevalence across the eco-epidemiological zones of the country among children under 5 years of age: 17 per cent in endemic areas, 1.4 per cent in areas of seasonal malaria transmission (arid and semiarid lowlands), 1 per cent in epidemic prone areas, and 0.4 per cent in low risk transmission areas. Increasing evidence shows that the epidemiology and risk of malaria in Kenya are declining. A comparison of previous malaria maps and recently updated maps on malaria prevalence shows the shrinking of malaria endemic areas and expansion of low transmission zones. It is estimated that 60-70 per cent of the Kenyan land mass has a parasite prevalence of less than 5 per cent where 78 per cent of the population of Kenya lives. On the other hand, there is also a decline in the level of malaria prevalence

in endemic areas characterised by a reversal in the age group with the highest prevalence among children less than five years old and those between 5-15 years of age.

In 2009, a model-based map of the intensity of *P. falciparum* transmission in Kenya as defined by the proportion of infected children aged 2-9 years in the community was produced (Noor, 2009). Based on the malaria risk map and the eco-epidemiology of malaria in Kenya, districts have been stratified into 4: Lake stable endemic & Coast seasonal stable endemic (risk class equal to or above 20 per cent); Highland epidemic-prone districts (risk class 5- <20 per cent); Seasonal low transmission including arid and Semi arid districts (risk class less than 5 per cent); low risk districts (risk class less than 0.1 per cent).

The Quality of Antimalarials

Various studies have been undertaken on the quality of medicines in Kenya. These continue to inform current and future initiatives towards a comprehensive post – marketing surveillance (PMS) system. Some of the studies are highlighted below:

a) A nationwide study of antimalarials by the Pharmacy and Poisons Board in collaboration with DOMC in May 2006, found that a wide range of antimalarials existed in the market, and the majority were not in the national malaria treatment guidelines; that a large proportion (42.6percent) of antimalarial medicines were not registered, and that some antimalarial medicines found in the market did not meet quality standards -. The survey enabled an innovative approach to the regulation of medicines for priority conditions, with the regulator and disease control programme working collaboratively to address an issue of public health importance (Ministry of Health, 2007).

b) During 2009, NASCOP and DLTLD undertook similar studies on quality of ARVs and TB medicines respectively. The studies were modeled along the 2007 AM survey, with modifications and adaptations to suit the context of ARVs and TB medicines. The results of both studies are being finalized, and are expected to inform further strategies for post-market surveillance of HIV and TB medicines.

c) PPB and DOMC also participated collaboratively in a multi-country study on quality of antimalarials in Africa (QAMSA) in 2008. Results from the study

showed that 96percent of the 44 samples collected from Kenya fully conformed to quality specifications. Only two of 24 ACT samples tested failed (both on limit tests for presence of impurities), and all SP samples were found compliant (WHO, 2010).

d) Concerning ARVs, a WHO multi-country study undertaken in 2005 did not demonstrate any failures of ARVs sampled from Kenya, which comprised both imported and locally produced ARVs. A recent follow up study is yet to be published.

CHAPTER TWO: MAIN OBJECTIVE OF THE PROGRAM

The primary objective of the program in general is to monitor the safety of medicines and conformity with established specifications for quality as declared in the registration dossier or recognized pharmacopeia specifications. It will provide regular information on the quality of medicines circulating in the country.

Specific Objectives

The specific objectives of the program include the following:

- To determine the proportion of unregistered products in the selected sites
- To determine the proportion of medicines in the selected sites that conform to quality standards
- To develop a medicine information database on the quality of medicines in circulation for trend analysis
- Disseminate information on the quality of medicines to stakeholders involved in medicines procurement, use, and regulation
- Promote communication and cooperation between stakeholders involved in medicines procurement, use, and regulation
- Provide evidence-based data for enforcement actions
- Propose possible strategies and implementation plans to address the problems identified in the study

CHAPTER THREE: METHODOLOGY

3.1 Sampling Strategy and Training

The sampling strategy involved convenience sampling from the various levels in the distribution chain including public (KEMSA, public health facilities, health centers), non-governmental organizations (NGOs), faith-based organizations (such as Mission of Essential Medicines Services (MEDS), private for-profits (pharmacies), hospitals (private and public), and illicit (informal) markets. Samples were collected using "mystery shoppers" in the private sector to simulate the real life situation in how patients access medicines to avoid alerting traders who might have hid products. For the purpose of the malaria control program, samples were collected from five sentinel sites defined in the sample site selection section. This strategy ensured that samples were obtained from all sectors where patients are likely to be exposed to medicines.

The training for round 1 was facilitated by PQM with support from DOMC, PPB and NQCL.

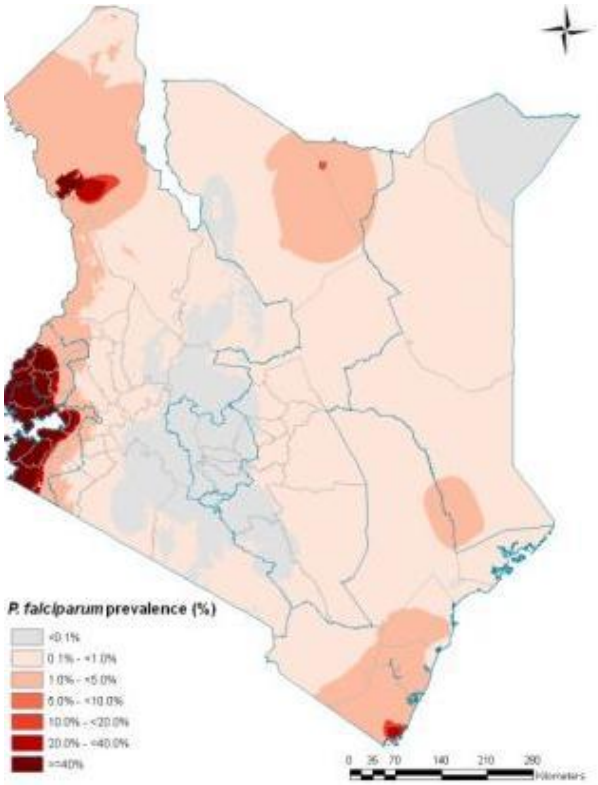
3.2 Site Selection

For the purpose of the Division of Malarial Control, five sites were identified in collaboration with PPB, NQCL, and PQM for sample collection based on epidemiological data demonstrating prevalence of the disease, medicines availability and accessibility, medicines circulating freely originating from border towns, ports of entry, and availability of human resources. The sites where sampling was done were as follows

Figure 1 Sentinel sites for post market surveillance

Sentinel Sites
Kisumu (Nyanza)
Kakamega (Western)
Eldoret (Rift valley)
Mombasa (Coastal)
Nairobi (capital city)

Figure 2 Malaria endemicity map



Samples were collected from importers, wholesalers, Non-Governmental Organizations (NGOs), central stores, regulated retailers, hospitals, private sources, and informal markets.

3.3 Medicines Selected for Sampling

The antimalarial medicines selected for sampling were based on the DOMC's national treatment guidelines and the availability of monographs for analysis. They include first-line treatment, second-line treatment, intermittent preventive treatment (IPT) for malaria in pregnant women, chemoprophylaxis, and treatment for severe malaria.

- **First-line treatment**
  - Artemether Lumefantrine (AL)
- **Second-ling treatment**
  - Dihydroartemesinin & Piperaquine (DHAP)
- **Severe malaria**
  - Parenteral quinine
  - Oral quinine
  - Artemether/Artesunate injection
  - Rectal Artesunate
- **Intermittent Preventive Treatment (IPT)**
  - Sulphadoxine & Pyrimethamine (SP)
- **Chemoprophylaxis**
  - Doxycycline
  - Atovaquone l Proguanil
- **Other ACTs**
  - Artesunate Amodiaquine
- **Monotherapies**
  - Monotherapies were only collected but not tested for purposes of monitoring the shift from monotherapies to ACTs and to evaluate their availability in the market.

3.4 Sample Definition

For the purpose of this study, a sample was defined as a medicine with a given API, dosage form, strength, and lot number from a given level in the distribution chain. Samples with the

same attributes above and including the same lot number were only collected if they were from a different level in the distribution chain, such as wholesaler versus retailer, etc. The same lots were not collected from similar or same level institutions (for example, two pharmacies or retailers).

3.5 Number of Units to Collect per Sample

The number of units collected per sample was determined by the types of conclusions which can be drawn regarding product quality. Refer to table below.

The following example of sample collection applied to solid dosage forms (tablets and capsules) only. Sampling of oral suspension, injectables, or other dosage forms was discussed in consultation with PQM.

Table 1 Field sampling strategy for tablets

Initial Sampling		
Minimum Units	Maximum Units	Comments
20	40	• If the "minimum" of **20** units is not feasible, collect what is available but no less than **5** units

Table 2 Re-sampling strategy for compendial testing

Re-sampling for Compendial Testing (if necessary)		
Minimum Units	Maximum Units	Comments
50	100	• If the "minimum" of **50** units is not feasible, refer to the Number of Units Needed in Table 1: Guidelines for Compendial Testing

3.6 Criteria for Prioritization of Sampling

Priority was given to the following APIs and dosage forms:

- First-line treatment in the DOMC treatment guidelines
- Most-sold medicines
- Most commonly-used medicines to reflect the reality of consumed medicines from all available sectors

- Medicines known or suspected to be counterfeit or sub-standard

3.7 Criteria for Diversification of Sampling

Attempts were made to try and diversify the samples collected from each site to reflect the availability in the market.
The following characteristics to diversify the sampling were considered:

- Different brands of the same API;
- Different batch/lot numbers;
- Multiple dosage forms (tablets, capsules, oral suspensions, injectables, suppositories, etc.);
- Different sectors (private/public/informal);
- Different sources or outlets of the same product with same lot number
- Suspicious medicines;
- Improperly stored medicines at the sampling site (exposed to sunlight, humid/wet conditions, etc.); and,
- Different packaging of same product (i.e., blister vs. bulk).

3.8 Sample Collection

A Sampling Checklist (Annex 1) was provided to the sampling team prior to their departure to collection sites and the need for its consistent use was emphasized. Each site planned to collect approximately 100 samples although some sites collected more than this number.

Each collected sample was secured in a plastic container or sealable plastic bag and attached to its corresponding *Sample Collection Form* (Annex 2). The *Sample Collection Form* contained all traceable data that accompanied the sample from the site of the collection to the site of Minilab testing and then to the quality control laboratory for confirmatory testing. This was done in order to maintain a traceable record of the identity of the sample should it fail or be doubtful.

Samples were then packed, transported, and stored in such a way as to prevent any deterioration, contamination, or adulteration. Samples were stored and transported in their original sealed containers, according to the storage instructions for the respective product.

3.9 Sample Analysis

Once samples were collected, they were tested at three levels (Figure 1). Level 1 is the sentinel site using Minilab tests, level 2 is the verification test carried out in the lab using Minilab basic tests to verify sentinel site data and level 3 is the confirmatory testing done using full compendial testing.

Safety & Environmental Considerations

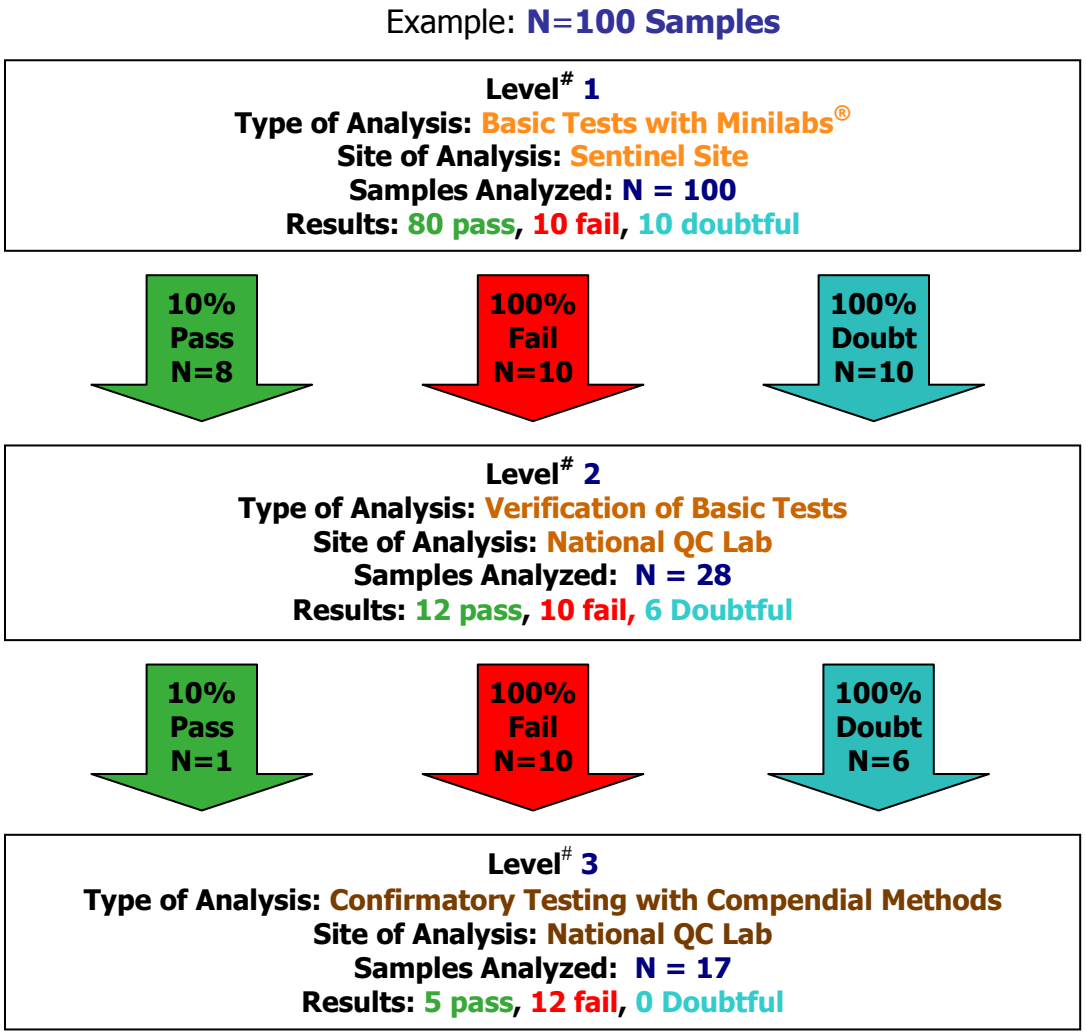
Sample analysis should be performed taking into consideration any possible safety and environmental consequences. Safety guidelines were followed as per Part Four of the WHO Technical Report Series, No. 902, Annex 3. Waste disposal was followed as per the country's national legislation.

3.9.1 Level 1 Basic Tests Minilabs at Sentinel Site

Basic tests included Physical/Visual (P/V) Inspection, Disintegration, and Thin Layer Chromatography (TLC) and this was carried out at the sentinel sites. Test results were clearly recorded for each sample on the *Basic Tests Analysis Form for Sentinel Site Staff* (Annex 3). A subset of samples was sent to the NQCL for verification testing, as follows: (Refer to Figure 1—MQM Analysis Flow Chart.)

- 10% of samples that passed*
- 100% of samples that failed**
- 100% of samples that are doubtful***

This subset of samples was sent with their respective forms attached (*Sample Collection Form* and *Basic Tests Analysis Form for Sentinel Site Staff*) to the NQCL for verification and confirmatory testing.



Protocols may define "stages" or "levels" differently; individual protocols should clearly indicate the terminology to be utilized and its specific meaning.

3.9.2 Level 2: Verification of Basic Tests at NQCL

NQCL performed verification testing by repeating basic tests on the subset of samples (as described above). Results of each sample were recorded clearly on the *Basic Tests Analysis Form for National Quality Control Laboratory Staff* (Annex 4).

For any samples that failed or were doubtful, they continued to the third stage of analysis for complete compendial testing.

Compendial testing was performed on the following samples: (Refer to Figure 1—MQM Analysis Flow Chart.)

- 10% of samples that pass verification testing*
- 100% of samples that fail verification testing**
- 100% of samples that are doubtful for verification testing***
- 50-100% of sulfadoxine-pyrimethamine (S/P) tablets/capsules and other medicines with known dissolution failures.

* Pass: Conforms to all three (3) tests

** Fail: Does NOT conform to at least one (1) of the three (3) tests

*** Doubtful: Conflicting or inconclusive results for at least one (1) of the three (3) tests

3.9.3 Stage/Level 3: Confirmatory Testing with Compendial Methods at NQCL

If compendial testing was to be conducted and there were insufficient units, more units of the same sample were collected to ensure full compendial testing took place as per Table 4.

CHAPTER FOUR: RESULTS AND DISCUSSION

4.1 Sample Description

A total of 499 samples were collected from 150 facilities across the three sectors (public, private and informal).

4.1.1 Sampling by Sector

Sampling was highest at the private sector followed by the public sector and least at the informal sector. This was because the range of antimalarials was highest in the private and public sectors and least in the informal sector. This is demonstrated in Table 3

Table 3 Sampling by Sector

Sector of Facility	Number of Samples	Percentage
Private	373	75%
Public	118	24%
Informal	8	2%
Grand Total	499	100%

4.1.2 Sampling by API

The most sampled medicines were AL, SPs and quinine according to the availability across the sectors

Table 4 Distribution of samples by API

Active Pharmaceutical Ingredient(s) (API)	Total	Percentage
Artemether/Lumefantrine	258	52%
Sulfadoxine/Pyrimethamine	105	21%
Quinine Sulphate	85	17%
Artesunate/Amodiaquine	40	8%
Sulfamethopyrazine/Pyrimethamine	11	2%
Grand Total	499	100%

4.1.3 Sampling by Sentinel Site

The sampling across the sentinel sites was even with slightly lower sampling in Coast province as shown in table 5 below.

Table 5 Sampling by Sentinel Site

Province or Region (within country)	Total	Percentage
Coast	99	20%
Eldoret	100	20%
Nairobi	100	20%
Nyanza	100	20%
Western	100	20%
Grand total	499	20%

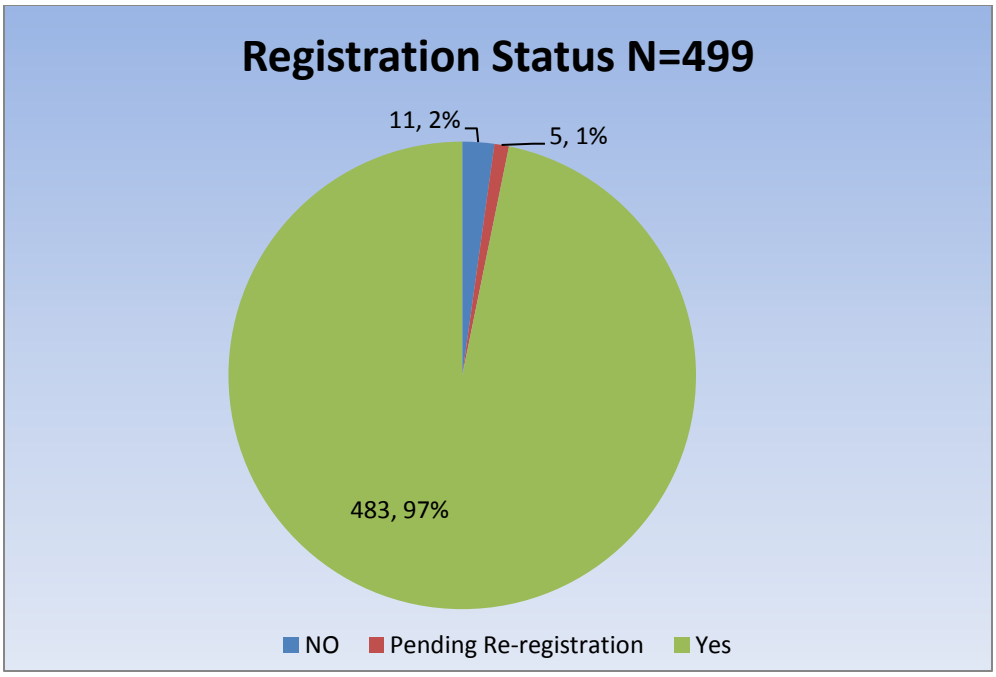
4.2 Registration with PPB

All the 499 samples collected were evaluated for registration status.

4.2.1 Registration Status of Samples

Of 499 samples collected, 483 were registered with PPB, 11 were not registered and 5 were pending re-registration. This is shown in figure 3 below

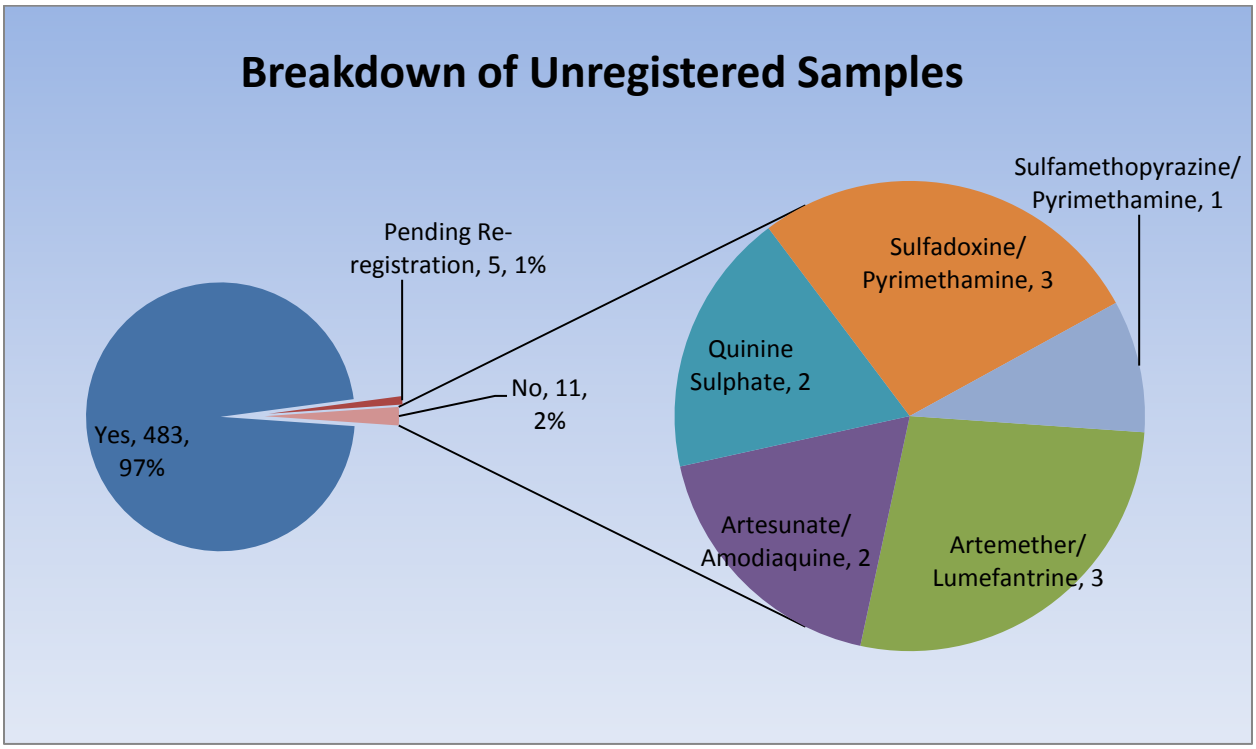
Figure 3 Registration status



4.2.2 Composition of Unregistered Samples

The unregistered samples were varied between AL, SPs, quinine and artesunate amodiaquine. This is as represented in figure 4 below;

Figure 4 Breakdown of unregistered samples



Action on companies with unregistered products is being taken by PPB in accordance with cap 244.

4.3 Basic Test Analysis

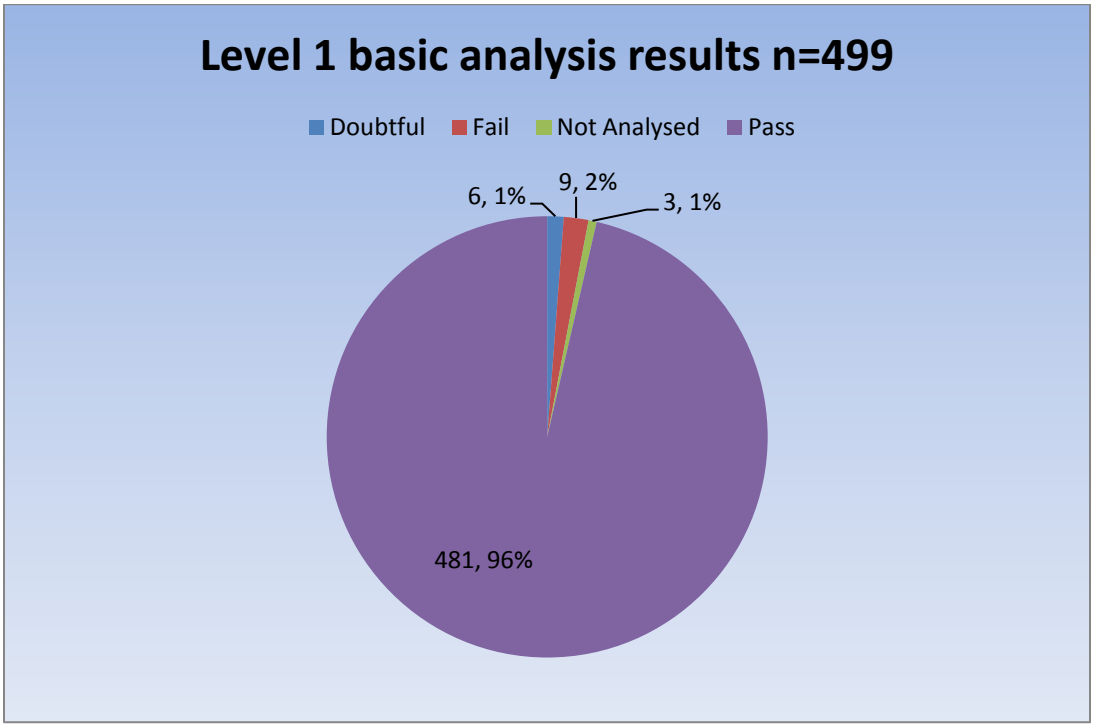
A total of 499 samples were collected from all the sentinel sites and samples were analyzed at different levels according to the protocol as follows;

Total Number of Samples Collected	Number of samples analyzed in the field using Minilab (Level 1)	Number of Samples analyzed using Minilab at NQCL (Level 2)	Number of Samples analyzed using compendial methods (Level 3)
499	496	65	25

4.3.1 Level One Basic Analysis Results

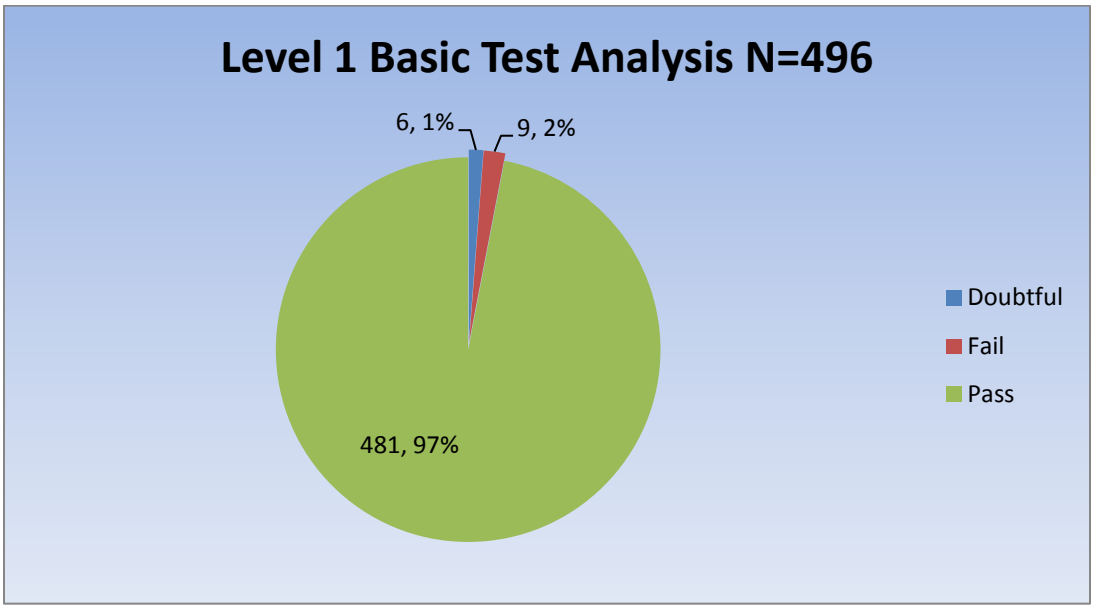
Of the 499 samples that were collected, 481 conformed to the tests, 9 failed, 6 were doubtful and 3 were not analyzed due to unavailability of monographs. This is shown in figure 5 below.

Figure 5 Level one basic analysis results (i)



The conformity rate at level one was 97percent after excluding the samples that were not analyzed due to lack of monographs as represented in figure 6 below

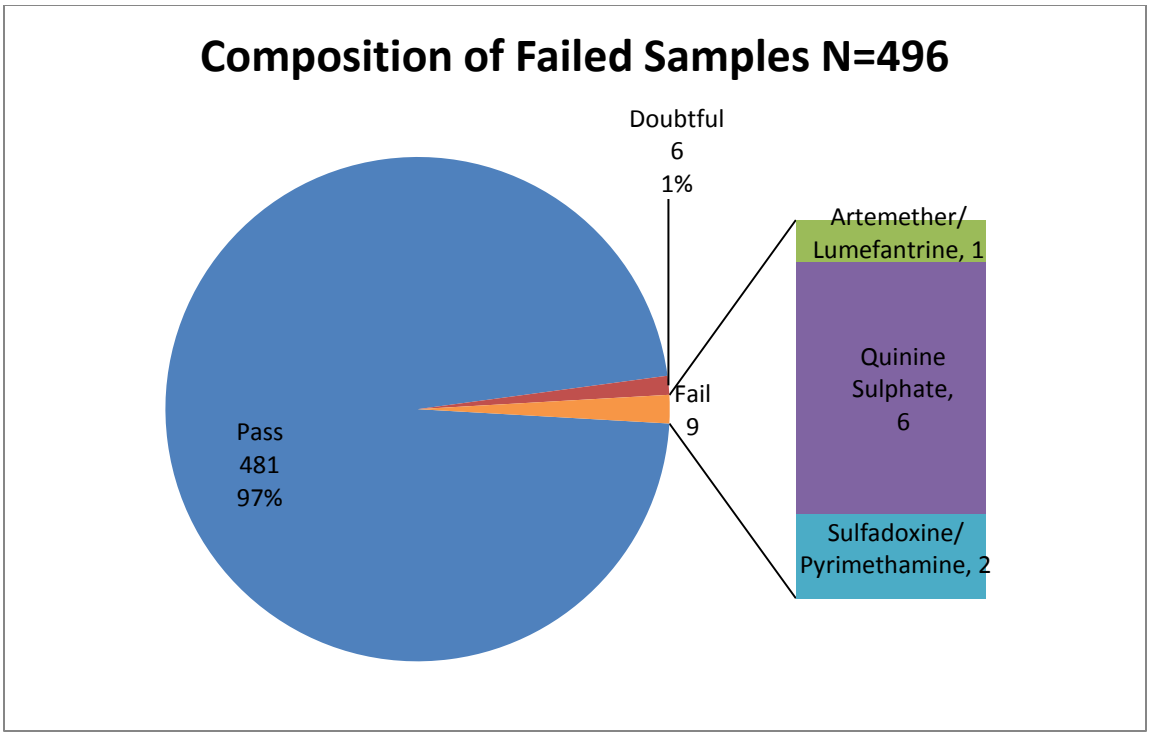
Figure 6 Level one basic analysis results (ii)



4.3.1.1 Composition of Failed Samples at Level One

The samples that failed level one testing composed mainly of quinine (6) followed by SP (2) and one sample of AL as shown in figure 7 below;

Figure 7 Composition of failed Samples at Level One



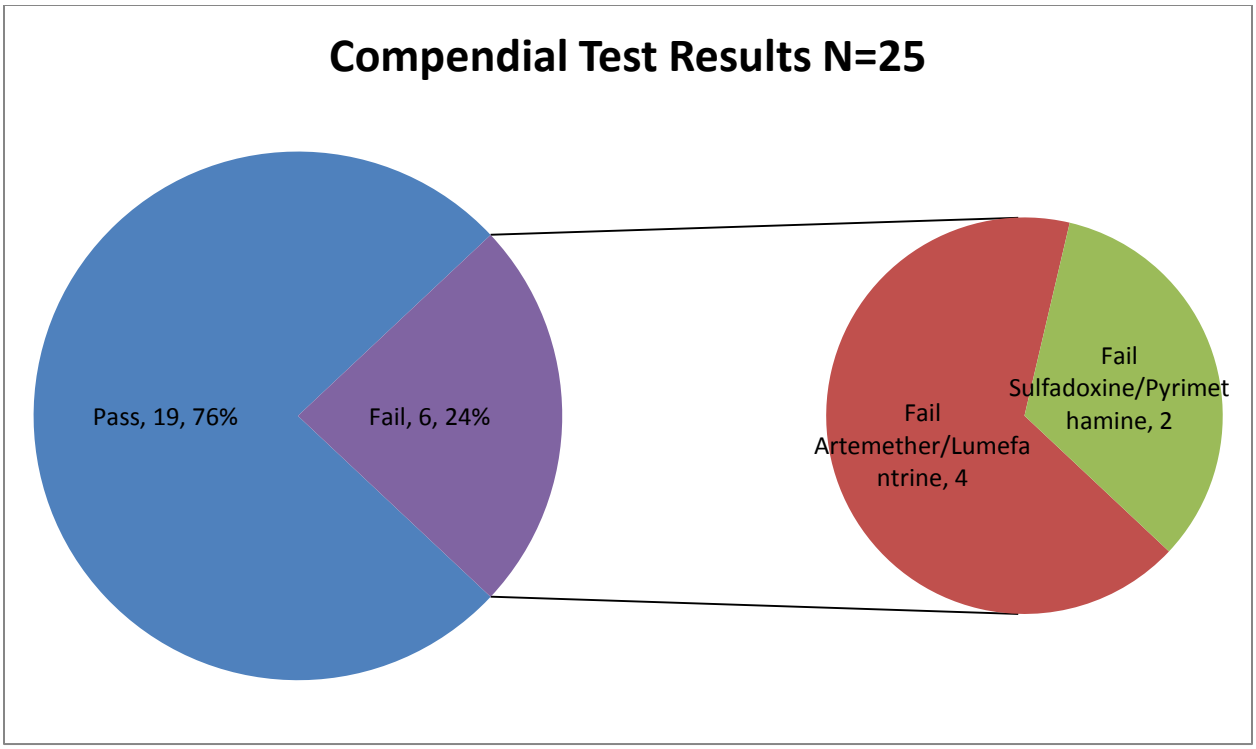
4.3.2 Level Two Basic Analysis Results

All the 65 samples sampled at level two passed the basic tests.

4.4 Compendial Testing Results

A total of 25 samples were sent to NQCL for confirmatory testing using compendial methods. Of these, 19 conformed and 6 failed. Those that failed consisted of 4 samples of Artemether Lumefantrine and 2 samples of sulfadoxine pyrimethamine as shown in figure 8 below

Figure 6 Compendial Testing Results (level 3)



Further analysis of the failed samples was done to determine the reasons for failure and is represented in table 6 below.

Table 6 Reasons for Failure

API	Reason for Failure	Total
Artemether Lumefantrine	Does not comply: assay artemether & borderline results for lumefantrine	1
	Does not comply: assay both artemether & lumefantrine	2
	Does not comply: assay both artemether & lumefantrine & artemether - dissolution	1
Sulfadoxine Pyrimethamine	Friability fails	1
	Uniformity of weight fails	1

Dissolution and assay remained the most common causes of failure which poses a significant risk in the risk to patients and therapeutic useful life of the medicines.

Table 7 Conformity and Sector

Active Pharmaceutical Ingredient (API)	Sector of Facility	Total Failed
Artemether/Lumefantrine	Public	1
	Private	3
Sulfadoxine/Pyrimethamine	Private	2

Less samples collected from the public sector failed compendial tests as compared to those from the private sector. However the differences were insignificant.

A summary of the compendial test results by API, medicine brand and manufacturer are presented in table 8 below.

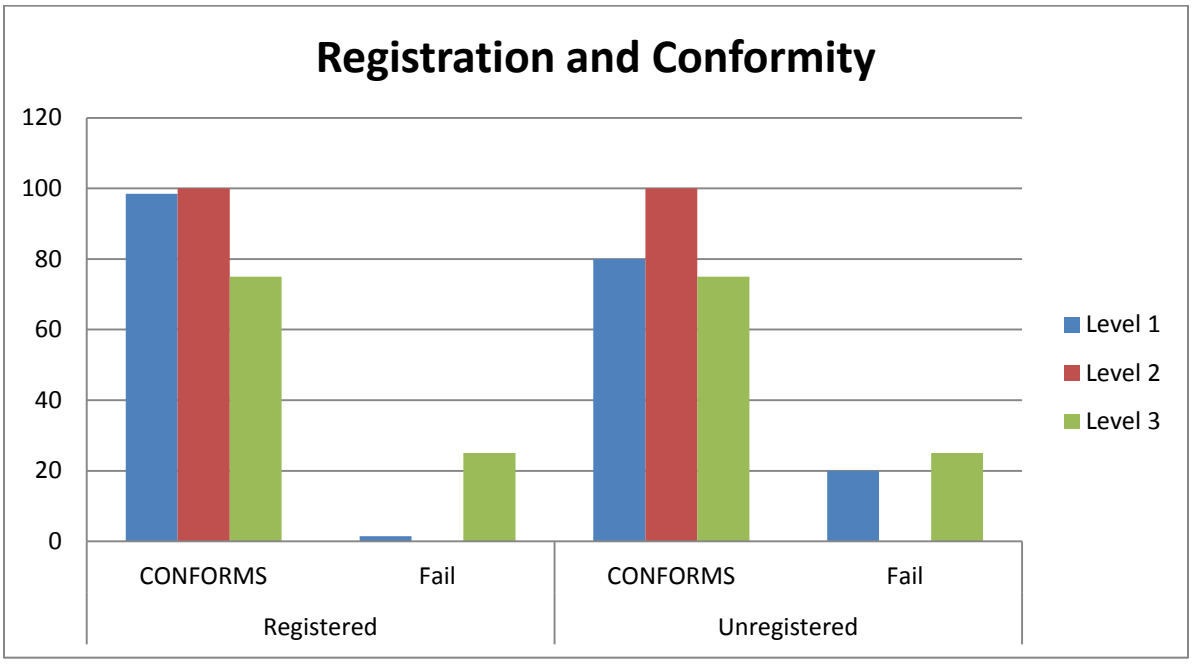
Table 8 Summary of Compendial Results

Result	Active Pharmaceutical Ingredient(s) (API)	Medicine Brand Name	Name of Manufacturer	Total
Pass	Artemether/Lumefantrine	Artefan	Ajanta Pharma Ltd	1
		Coartem Dispersible	Novartis Pharmaceuticals Corporation	1
		Co-Falcinum	Cipla Ltd	1
		Lum-Artem	Dawa Limited	1
		Lumerax	Ipca Laboratories Ltd	1
	Quinine Sulphate	Eloquine	Elys Chemical Industries Limited	1
		Flaci - Quin	Flamingo Pharmaceuticals	1
		Flaci-Quin 300	Flamingo Pharmaceuticals Ltd	1
		Quinidil	Biodeal Laboratories Limited	1
		Quinine	Universal Corporation Limited	1
		Quinine Sulphate	Elys Chemical Industries Limited	1
			Universal Corp. Ltd	1
		Quinine Tablets	Universal Cooperation Limited	1
		Quinitab	Cosmos Limited	1
	Sulfadoxine/Pyrimethamine	Falcidin	Cosmos Limited	1
		Laridox	Ipca Laboratories Ltd	2
		Pharmasidar	Sishui Xierkeng Pharmaceuticals Co Ltd	1
	Sulfamethopyrazine/ Pyrimethamine	Laefin	Laboratory& Allied.	1
Pass Total				**19**
Fail	Artemether/Lumefantrine	Artemether/Lumefantrine	Ipca Laboratories Ltd	1
		Artrin	Medreich Limited	1
		Co-Falcinum Al	Cipla Ltd	1
		Co-Fantrin Forte	Comet Healthcare	1
	Sulfadoxine/Pyrimethamine	Fansidar	Roche Products	1
		Malodar	Lab.& Allied Ltd.	1
Fail Total				**6**
Grand Total				**25**

4.5 Registration Status and Conformity

Registration status and conformity was evaluated for all the samples analyzed and expressed as a percentage as shown on figure 9 below. Although insignificant, registered products were more likely to conform to quality standards.

Figure 7 Registration status and conformity



4.6 Comparison between Round I and II

4.6.1 Sampling

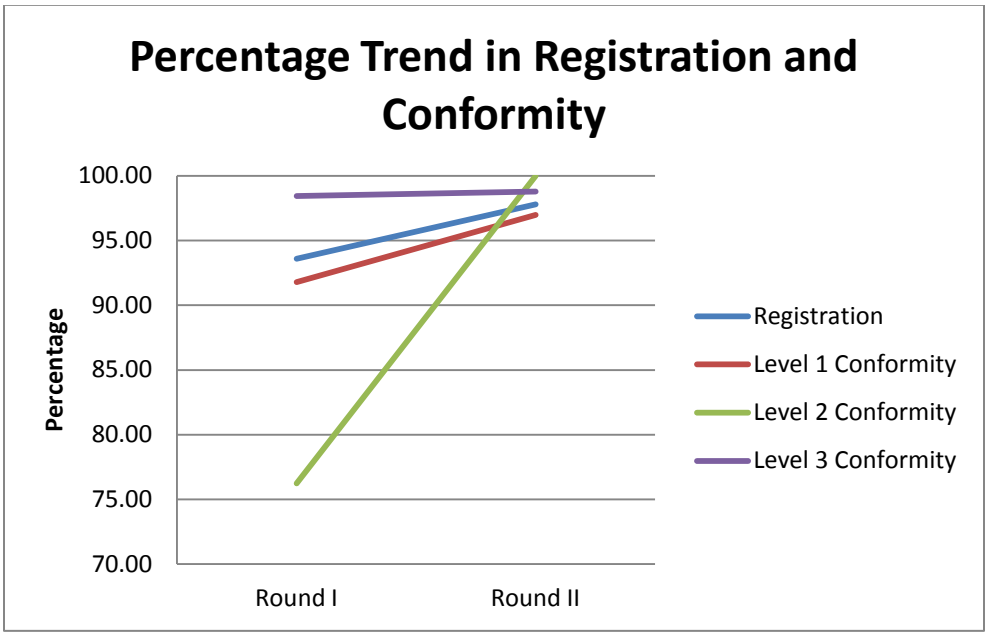
The overall sampling in round I and II was comparable. However, round I had most of the samples subjected to basic test analysis at level I. Fewer samples were tested using compendial methods in round II.

Table 9 Summary of Sampling per Round

Round	Total Number of Samples Collected	Number of samples analyzed in the field using Minilab (Level 1)	Number of Samples analyzed using Minilab at NQCL (Level 2)	Number of Samples analyzed using compendial methods (Level 3)
Round 1	536	451	80	44
Round 2	499	496	65	25

4.6.2 Registration Status and Conformity

Figure 8 Trend of Registration Status and Conformity



CHAPTER FIVE: SUMMARY AND CONCLUSION

The registration status improved from 93.6percent in round I to 97.8percent in round II. This could be an indication of the improved regulatory environment of antimalarials following the regular surveillance activities by PPB and initiatives by DOMC such as AMFm. AMFm is an initiative designed to crowd out monotherapies and other non recommended antimalarials through subsidizing the cost of the recommended treatment in the public and private sectors. Registration status however should always be maintained at 100percent for all medicines in the market in order to ensure that all products in the market have been subjected to some level of quality control before being released to the market.

The conformity marginally improved from 98.4percent to 98.8percent. Even though somewhat insignificant, it is encouraging that majority of antimalarials in the market are of good quality and therefore safe and effective. One of the major drivers of antimalarial resistance is substandard medicines which contain too little or too much of the active pharmaceutical ingredient. When the medicines contain too little of the API, the result is that the parasite is exposed to sub-therapeutic concentrations of the medicine thereby allowing the parasite to mutate and develop resistance mechanisms towards the medicine. The result is the development of tolerance and eventually full resistance. WHO recommends that once the efficacy of the first line treatment for uncomplicated malaria drops by 10percent, the country should consider changing to an alternative antimalarial whose efficacy should be above 95percent. The cost of changing policy however remains prohibitive to most countries especially in the wake of the declining funding for public health programs attributable to the global economic crisis. Moreover, there are few or no effective alternatives to ACTs currently for the treatment of *Plasmodium falciparum* malaria. The need therefore to safeguard the quality of antimalarials circulating in the market cannot be over emphasized.

The discrepancy in conformity across the various levels is still considerable. Whilst the sampling strategy provides for a robust approach in screening samples, the consistency in the results needs to be fairly comparable across the various levels. In this round of screening, all samples that were doubtful and failed minilab screening at level one were tested at level two using similar methods.

The results however at level two indicated that all samples complied with the basic analysis tests. Although the samples that failed and were doubtfully were only 9 and 6 respectively out of 451 samples analyzed at level one, none of these were confirmed at two. This points towards the need for refresher training of the analysts in the field which should include concordance testing across level one and two. This will improve the quality of the sampling for compendial testing and the eventual interpretation of the results made.

The results indicate that four out of the six samples that failed compendial testing were AL, the first line treatment for uncomplicated malaria. The failure rate for AL was higher than that of the other antimalarials therefore raising concerns about the quality of AL in the market. Out of nine AL samples that were subjected to compendial analysis, four of them failed tests for assay and one failed both assay and dissolution. This is a worrying finding for the first line treatment which is still very effective for the treatment of malaria going by recent therapeutic efficacy tests. Even of more concern is that two of the four products that failed are prequalified by WHO. Prequalification is a stringent process of ensuring that products are manufactured in accordance with good manufacturing practices. The AMFm program ensures that only products that are prequalified by WHO are subsidized and therefore availed to patients in participating countries. Regular post market surveillance studies are therefore important in ensuring the spirit of AMFm is maintained.

Part of the objectives of the regular post market surveillance studies it to develop a trend analysis of the quality of antimalarials circulating in the Kenyan market. The aim of this objective is to guide the routine procurement of antimalarials so as to ensure only quality assured products are procured. Products that consistently fail conformity testing will be forwarded to KEMSA for possible blacklisting.

CHAPTER SIX: WAY FORWARD

- More emphasis on the basic test analysis is required in subsequent PMS trainings and briefings ahead of data collection. This is with the aim of improving concordance between level one and two basic test analysis
- The sampling strategy at every level needs to be adhered to in order to avoid instances of oversampling or under-sampling across the levels.
- A concordance testing methodology needs to be devised as a means of assessing the concordance between analysts at level one and two. This will build the confidence in the use of minilabs as an effective and cost effective tool in conducting PMS.
- Regulatory action on the manufacturers whose products were not registered and failed compendial testing needs to be taken in accordance with cap 244 of the Kenyan laws.
- Products that are WHO prequalified and yet failed compendial testing need to be closely monitored in subsequent PMS studies to ensure that they maintain the same level of quality. In the event that any is found to consistently perform below expectation, the results should be shared with WHO for corrective action.
- The dissemination of PMS results need to be widely shared to all stakeholders do as to appropriately guide regulatory and policy decision making.

REFERENCES

Noor, A. (2009). Malaria endemicity map. Kenya.

Division of Malaria Control. (2010). *Malaria Standard Treatment Guidelines.* Ministry of Public Health and Sanitation.

Guerra, C. A., Gikandi, P., & Tatem, A. (2008). The limits and intensity of Plasmodium falciparum transmission: Implications for malaria control and elimination worldwide. *5, E38*.

Ministry of Health. (2007). *Antimalrials Medicines in Kenya.* Ministry of Health.

Ministry of Public Health and Sanitation. (2007). *Kenya Malaria Indicator Survey.* Kenya: Ministry of Public Health and Sanitation.

Ministry of Public Health and Sanitation. (2009). *Kenya National Malaria Strategy 2009-2017.* Kenya: Ministry of Public Health and Sanitation.

WHO. (2010). *THE SURVEY OF THE QUALITY OF ANTIMALARIALS IN SUBSAHARAN (QAMSA).* WHO.

ANNEXES

List of Teams